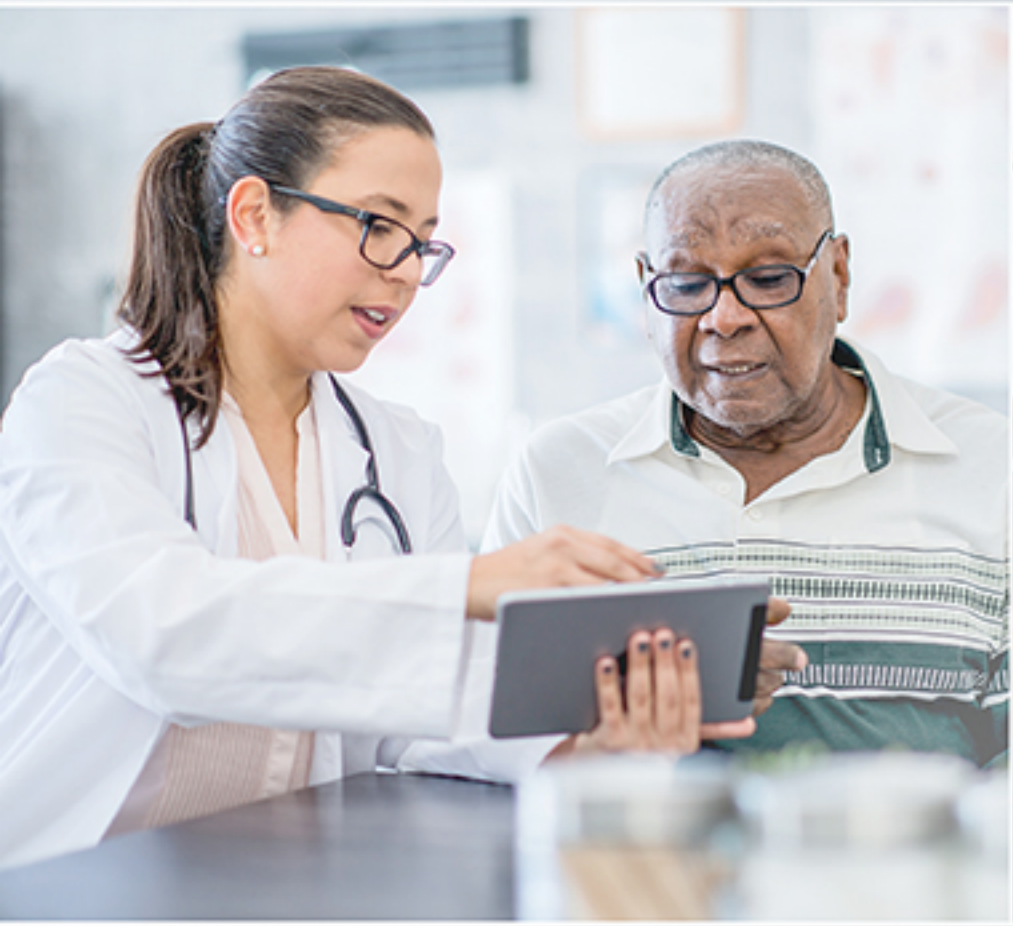
ADVANCED PRACTICE

NURSING in the Care of Older Adults

Kennedy-Malone • Groenke-Duffy

THIRD EDITION



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NURSING in the Care of Older Adults

THIRD EDITION

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I dedicate this book to my husband Chris, my son Brendan, and Clover for their unwavering support during the writing of this book. To my parents, Nancy and Edward Kennedy, you continue to be models of successful aging that motivate me to continue to be passionate about advanced practice gerontological nursing. To graduates that I have worked with over the years, your continued dedication and expertise in working with older adults is appreciated and admired; thanks especially to those who also served as contributors to this edition.

—L.K.-M.

To my husband Mark who supported me as I worked on this book during the COVID-19 pandemic. To my children, Patrick, Colin, and Caitlin, you bless me every day. To my in-laws, Shirley and Art Duffy, who continue to live vital lives in their 90s. To my aunt, Karleen Groenke Sime who inspired me to become a nurse. Finally, to all my patients who challenge me to be the best provider I can be and my students who motivate me to constantly be better.

—E. G. D.

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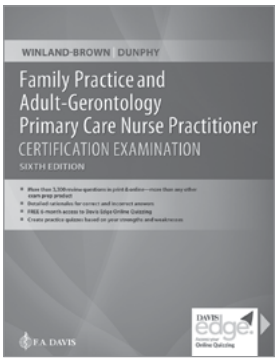

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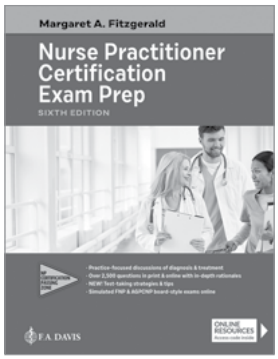

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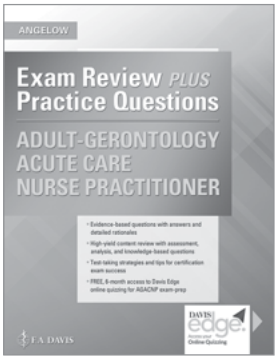

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Preface

With the continued rapid growth of the older adult population, there remains an increased demand for health-care providers to deliver age-specific care and direct disease management. *Advanced Practice Nursing in the Care of Older Adults* will serve as a guide for advanced practice nurses who are privileged to provide care to older adults. Designed as a text for students, as well as a reliable source of evidence-based practice for advanced practice nurses, this book contains information on healthy aging, comprehensive geriatric assessment, and common symptoms and illnesses that present in older adults. Given the complexity of prescribing for older adults taking multiple medications, a chapter on polypharmacy is included. The book concludes with a chapter on care delivery for patients with chronic illnesses who face end-of-life care.

Throughout the book, case studies are included to provide further practice and review. An important feature of this book is the use of the Strength of Recommendation Taxonomy (SORT) (Ebell et al., 2004). which provides a direct reference to evidence-based practice recommendations for clinicians to consider in the care of older adults.

In Unit I, "The Healthy Older Adult," the first chapter, "Changes With Aging," addresses the normal changes of aging, expected laboratory values in older adults, presentation of illness, atypical disease presentation, bimodal conditions, and the impact of chronic illness on functional capacity. In the second chapter, "Health Promotion," updated information pertaining to health promotion and disease prevention strategies for older adults from *Healthy People 2030* and the U.S. Preventive Services Task Force (USPSTF) is provided, including information on immunizations and the Welcome to Medicare and Medicare Annual Wellness Visits. Also covered is an overview of physical activity, sexual behavior, dental health, and substance use, as well as a section pertaining to the older traveler. Recommendations for exercise, safe physical activity, and nutrition are provided in this unit. New to the book in this edition is Chapter 5, "Settings of Care," which addresses the special needs older adults require if the setting is acute or primary, in the community or in an institutional setting.

Unit II, "Assessment," opens with a detailed chapter on comprehensive geriatric assessment. Information on physical, functional, and psychological health is delineated, and information on social determinants of health is included. The chapter on assessment also includes an introduction to the Age-Friendly Healthcare Systems and the 4Ms Framework. Chapter 7, "Symptoms and Syndromes," provides the clinician with a concise description of more than 20 symptoms prevalent in older adults. New topics in this edition include muscle cramps and weakness, two very frequent chief concerns. A rapid reference detailing common contributing factors and associated symptoms and clinical signs that should be worked up for each presenting condition is included. Recommendations for diagnostic tests with accompanying results are used to form a differential diagnosis.

Unit III, "Treating Disorders," provides 13 chapters of concise, updated information pertaining to disease management of illnesses common in older adults, presented by body systems. New chapters in this edition include a comprehensive chapter on gynecological conditions, often underaddressed in geriatric texts. Each chapter opens with an assessment section that provides the reader with a focused review of systems and the physical examinations needed to obtain pertinent information for diagnosis and treatment of the older adult. Signal symptoms indicating atypical presentation of illness are highlighted at the beginning of each condition. The discussion of each problem and disorder follows a consistent monograph format:

- Signal symptoms
- Description
- Etiology
- Occurrence
- Age
- Ethnicity
- Contributing factors
- Signs and symptoms
- Diagnostic tests
- Differential diagnosis
- Treatment
- Follow-up
- Sequelae
- Prevention/prophylaxis
- Referral
- Education

Unit IV, "Complex Illness," addresses complex management of patients requiring chronic illness management, palliative care, and supportive care at end of life, and includes a chapter on polypharmacy. The text concludes with two appendices—"Physiological Influences of the Aging Process" and "Laboratory Values in the Older Adult"—both of which are ready references for the busy practitioner.

In addition to the content of the book, a Bonus Chapter, "Infectious Disease," is available on fadavis.com. This chapter includes COVID-19; HIV, a growing concern in older adults; Antibiotic Resistant Organisms; and MRSA. Also available online are selected references and additional case studies, which are provided to support critical thinking and are available for users to complete on their own or for educators to incorporate into their course requirements.

For the faculty, there are PowerPoint presentations and a well-developed test bank located on fadavis.com. The Active

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Classroom Instructors' Guide is an online faculty resource that maps the resources available with the text and includes lecture notes and suggested answers for case studies.

This book is written by and for advanced practice nurses involved in the care of older adults across multiple settings of care. While this book is intended as a guide for the management of care for older adults, clinicians are encouraged to deliver individualized, patient-centered care considering the latest clinical practice guidelines on prevention and management of conditions common in older adults.

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unit I

The Healthy Older Adult

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CHAPTER 1

Changes With Aging

Laurie Kennedy-Malone

FUNDAMENTAL CONSIDERATIONS

The aged population continues to be incredibly diverse; it includes some individuals who are nearly twice as old as others and is reflective of growing cultural diversity as well. Knowing what is expected in aging, what diseases are prevalent in aging, and what constitutes successful aging is an immense challenge even for the most skillful advanced clinician. When assessing the aged individual, the advanced practice nurse should be familiar with the range of common and expected changes associated with aging so that older persons falling outside this range may be identified and interventions taken appropriately and expeditiously.

In the past, wellness was considered the mere absence of disease, but with more information from longitudinal studies of aging, we are learning a great deal about the characteristics of successful agers (Beard et al., 2016). What constitutes successful aging is beginning to emerge, and the illness–health continuum continues to expand to include adults living into old age. This chapter focuses on familiarizing the advanced practice nurse with fundamental underpinnings that serve to guide the approach to assessment and management of the older adult. In addition to appreciating the physiological changes that come with aging, the advanced practice nurse needs to understand how the changes that accompany aging influence reference laboratory values. Recognizing that presenting features of disease/illness may be different and having a greater awareness of the impact of chronic illness on functional capacity and quality of life provide the advanced practice nurse with a perspective in approaching the older adult that is different from that of younger adults.

PHYSIOLOGICAL CHANGES WITH AGING

The physiological changes associated with the usual aging process detailed by system and the impact of these changes are delineated in Appendix A. The clinician must be aware, however, that all the systems interact and, in doing so, can increase the older person's vulnerability to illness/disease. For example, the risk of respiratory infection in the older adult population is considerable, and the physiological influences may include limited chest wall expansion, cilia atrophy, and alterations in the immune system. During the clinical decision-making process, the clinician knowledgeable about physiological changes with aging will be less likely to undertreat a treatable condition. For example, the astute clinician will use the diagnostic process to differentiate the more benign seborrheic keratosis from the more serious melanoma in the aged individual. While educating the older patient, the informed professional will be less likely to attribute a finding to the aging process alone. Without knowledge of the physiological changes with aging, an age bias can lead to undertreatment, impacting the individuals' health and contributing to a growing cost of health care for older adults (Levy et al., 2020).

The major impact of these physiological changes can be highlighted with four primary points. First, there is a reduced physiological reserve of most body systems, particularly the cardiac, respiratory, and renal systems. Second, there are reduced homeostatic mechanisms that fail to adjust regulatory systems such as temperature control and fluid and electrolyte balance. Third, there are the changes in the sympathetic response, which contribute to orthostasis and falls, as well as lack of hypoglycemic response. Fourth, there is impaired immunological function: infection risk is greater and autoimmune diseases are more prevalent. The clinician is advised not to be complacent in that some processes previously considered normal, age-related changes are now being refuted. Historically, normal aging studies were conducted using a cross-sectional study method. Today, results are becoming increasingly available from longitudinal studies of aged populations, some of which began in the 1930s (Besdine, 2019).

This more-reliable methodology provides some challenges to previously held conclusions. The clinician is encouraged to stay informed regarding the research in expected and successful aging so that this information may be carefully considered, interpreted, and translated quickly into the clinical setting.

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LABORATORY VALUES IN OLDER ADULTS

Healthy individuals of all ages often have asymmetrical distribution of test results. Normality in a statistical sense may be extrapolated incorrectly to normality in terms of health. In addition, the standards with which to compare normal laboratory values that were previously available to the health-care worker have been based on randomly collected samples of younger healthy adults. Many factors can influence laboratory value interpretation in the older adult, including the physiological changes with aging, the prevalence of chronic disease, changes in nutritional and fluid intake, lifestyle (including activity), and the medications taken (Vásárhelyi & Debreczeni, 2017).

Clinicians may find reference ranges, therefore, to be preferable. Reference ranges or intervals, such as age or sex, can be defined demographically. For example, the reference range for older adults might be the intervals within which 95% of persons older than age 70 fall. These may be further defined physiologically (e.g., fasting or activity status) or pharmacologically (e.g., medication, tobacco, or alcohol use). Even this more precise method does not ensure a healthy sampled population as the standard and using the reference range method may not differentiate normal aging from disease. The reference values presented for older adults are presented in the Appendix B. Longitudinal chemical studies support the concept of biochemical individuality—that is, each individual's variation is often much smaller than that of the larger group. Biochemical individuality is of particular importance in detecting asymptomatic abnormalities in older adults. Significant homeostatic disturbances in the same individual may be detected through serial laboratory tests, even though all individual test results may lie within normal limits of the reference interval for the entire group.

The clinician must determine whether a value obtained reflects a common aging change, a disease, or the potential for disease. Although abnormal laboratory findings are often attributed to old age, rarely are they true aging changes. Misinterpretation of an abnormal laboratory value as an aging change can lead to underdiagnosis and undertreatment in some situations (e.g., anemia or urinary tract infection) and overdiagnosis and overtreatment in others (e.g., hyperglycemia or asymptomatic bacteriuria). At times, the result of a laboratory value may be within the appropriate reference range yet indicate pathology for the older adult (Vásárhelyi & Debreczeni, 2017).

The serum creatinine level may be within the normal range yet indicate renal impairment in a patient with inadequate protein stores, and different measures might need to be considered. One value of significance to the practitioner with prescriptive privileges is the calculation of creatinine clearance in the estimation of renal function—for instance, when dosing enoxaparin (Shaikh & Regal, 2017). Reduced renal function, particularly the glomerular filtration rate (GFR), affects the clearance of many drugs, and creatinine clearance provides an index of renal function for use in choosing doses of renally eliminated or nephrotoxic drugs (such as digoxin, H_2 blockers, lithium, and water-soluble antibiotics).

Finally, when considering which laboratory tests to order, it is worth remembering the doctrine *primum non nocere*, "first, do no harm." Excessive blood sampling may lower the hematocrit; repeated fasting tests may provoke nutritional compromise; and extensive use of tests often requires drugs that may cause adverse reactions. Any risks involved in laboratory testing must be considered with respect to the patient's clinical condition and weighed against the test's expected benefits. The clinician should plan in advance the use for each test result value obtained, especially for less specific or less sensitive tests such as sedimentation rate and serum alkaline phosphatase levels. "Ordering a test requires assessing the likelihood that a patient has specific conditions prior to the order, along with an understanding of the accuracy of test and as to how it will change management" (Dharmarajan & Pitchumoni, 2012, p. 267). Once laboratory tests are available for review, test results should be discussed with the patients, with abnormal test results interpreted for the aging individual and addressed with the patient and/or caregivers. In addition to understanding the fundamental changes that accompany aging and their influence on interpreting laboratory values and medication management, the advanced practice nurse needs to understand the presenting features of illness/disease in older adults (Jaul & Barron, 2017).

PRESENTING FEATURES OF ILLNESS/DISEASE IN THE OLDER ADULT

The manifestations of illness and disease in the older adult can be very different, even if the underlying pathological process is the same as in younger individuals. The advanced practice nurse should be aware of what can influence the presentation. It has long been understood that underreporting of symptoms by older adults may occur if they attribute the new sign or symptom to age itself (Fried et al., 1991; Levkoff et al., 1988). By erroneously associating aging with disease, disuse, and disability, older adults perceive this change as inevitable and either fail to present to the health-care provider or, if they do, fail to challenge the assumption that this represents normal aging. At times an acute symptom such as pain or dyspnea is superimposed on a chronic symptom, and the older adult may not recognize that it represents a new or exacerbated pathology (Bell et al., 2016). The advanced practice nurse is well advised to never attribute something to common aging without doing a careful and methodical search for a treatable condition.

Certain diseases are more common in the older adult and an understanding of the epidemiology is critical in the interpretation. Certain neoplasms and malignancies such as basal cell carcinoma, chronic lymphocytic leukemia, and prostate cancer have a high prevalence beginning in older adulthood. Neurological conditions such as Parkinson's disease, dementias, stroke, normal pressure hydrocephalus, and complex partial seizures are more common to have initial onset in older age. Polymyalgia rheumatica along with giant cell arteritis almost exclusively begins in patients older than age 50 (Narayan et al., 2017).

Complicating the care of older adults are those patients who develop geriatric syndromes that often involve multiple body systems and have more than one underlying cause (Fried et al., 1991). For patients presenting with one or more

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of the new geriatric giants—frailty, anorexia of aging, sarcopenia, and cognitive impairment—the risk escalates for falls, delirium, injuries, and depression, subsequently placing these patients at risk for iatrogenic events that could lead to hospitalization, institutionalization, and subsequently, death (Morley, 2017).

Altered Presentation of Illness

Advanced practice nurses managing the care of older adults are challenged to recognize altered, atypical, vague, or even nonspecific signs and symptoms of common conditions in older adults (Auerhahn & Kennedy-Malone, 2010). It is well documented that disease presentation may be different for the older adult, especially the frail older adult (Hofman et al., 2017). The failure to develop an elevated temperature or fever with an underlying infectious process differs greatly from presentation of illness in a younger patient. The patient with depression may not present with a dysphoric mood but rather agitation and psychotic features (Vonnes & El-Rady, 2021). The older adult may present with cardiac manifestations (atrial fibrillation, heart failure) of undiagnosed thyroid disease (Barbesino, 2019). Additional illustrative examples include jaundice, which is suggestive of viral hepatitis in younger individuals but may represent gallbladder disease or a malignancy in the older adult, and delusions or hallucinations, which are suggestive of bipolar disorder in younger individuals but may represent dementia or medication side effects in the older adult (Williams, 2009).

Because the symptoms or signs of illness or disease may be vague and nonspecific, possibly the opposite presentation than what is typically expected (Hofman et al., 2017), even a modest change in functional level or behavior should alert the clinician to carefully explore the potential for a treatable condition. Family members or caregivers may report that a patient may no longer be cooperating or participating in individual care. Unusual changes such as these become red flags to the beginning of an atypical presentation of illness. In many cases the progression of the condition is insidious, often presenting as a change in cognition or an alteration in functional status (Vonnes & El-Rady, 2021). Other significant changes in patients with altered presentation of illness often include new onset of falls, weakness, fatigue, anorexia, urinary incontinence, lack of pain, and unexplained tachypnea (Auerhahn & Kennedy-Malone, 2010; Hofman et al., 2017). Table 1-1 depicts common conditions that often have altered presentation of illness in older adults.

Bimodality of Age of Onset of Clinical Conditions

Understanding of the epidemiology of clinical conditions includes having the knowledge of etiology of the disease, prevalence and incidence rates, risk factors, age of onset, and distribution between the sexes. There are a number of conditions that are known or suggested to have a bimodal age of onset. In some conditions, the difference is not only the decade(s) in life that the disease more likely presents but the dominance of the sex in which the condition presents. Myasthenia gravis is one condition that tends to present initially in younger females, with a preponderance in older males (Dresser et al., 2021).

Often the presentation of the same illness is different for older adults as compared to their younger counterparts. The onset of the condition may be acute versus progressive, with different symptomatology and clinical signs. For instance, in patients with late onset rheumatoid arthritis, the joint involvement is more often in the larger joints such as the shoulder and they experience constitutional symptoms such as fever, malaise, weight loss, and depression (Kobak & Bes, 2018; Targońska-Stępniak et al., 2021). Knowledge of the bimodality of age onset of certain disease conditions will aid the advanced practice nurse in avoiding misdiagnosis or delay in diagnosis due to lack of recognition. Table 1-2 describes medical conditions that present differently in younger versus older adults.

TABLE 1-1 Atypical Presentation of Illness in Older Adults

ILLNESS	ATYPICAL PRESENTATIONS
Acute abdomen	Absence of symptoms or vague symptoms Acute confusion Alternation in function Change in appetite or anorexia Change in bowel habits Mild discomfort and constipation Some tachypnea and possibly vague respiratory symptoms Appendicitis pain may begin in right lower quadrant and become diffuse. Urinary urgency may also occur in appendicitis
Depression	Anorexia, vague abdominal complaints, new onset of constipation, insomnia, hyperactivity, lack of sadness, agitation, somatic complaints, change in bowel habits
Heart failure	Anorexia, change in function, confusion, nocturia, orthopnea, sacral edema in bedrest patients
Hyperthyroidism	Hyperthyroidism presenting as "apathetic thyrotoxicosis," i.e., lethargy, fatigue, and weakness; patients report palpitations, tachycardia, and new onset of atrial fibrillation; heart failure may occur with undiagnosed hyperthyroidism; resolution of chronic constipation; weight loss
Hypothyroidism	Hypothyroidism often presents with confusion and agitation; new onset of anorexia, ataxia, depression, and arthralgias may occur. In addition to elevated thyroid-stimulating hormone level in tandem with a low free or total T4 level, additional laboratory findings may be indicative of hyponatremia and hypercholesterolemia.

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TABLE 1-1 Atypical Presentation of Illness in Older Adults—cont'd

ILLNESS	ATYPICAL PRESENTATIONS
Malignancy	New or worsening back pain secondary to metastases from slow growing breast masses Silent masses of the bowel
Myocardial infarction (MI)	Absence of chest pain Vague symptoms of fatigue, nausea, and a decrease in functional and cognitive status. Anxiety, dyspnea, palpitations, discomfort, weakness, syncope, and vomiting are often experienced. A new onset of abdominal or upper extremity pain may be reported. Heart failure exacerbation or stroke Higher prevalence in females versus males Non-Q-wave MI
Infectious diseases process	Absence of fever or low-grade fever Malaise Sepsis without usual leukocytosis and fever Falls, anorexia, new onset of confusion and/or alteration in change in mental status, decrease in usual functional status
Peptic ulcer disease	Absence of abdominal pain, dyspepsia, early satiety Weight loss, anorexia, confusion, emesis, and melena New onset of confusion, unexplained tachycardia, and/or hypotension
Pneumonia	Absence of fever; mild coughing without copious sputum, especially in dehydrated patients; tachycardia and tachypnea; anorexia, decreased oral intake, myalgias, hemoptysis, lethargy, malaise, generalized weakness, and alteration in cognition Chest x-rays often unremarkable, especially in dehydrated patients, without the typical lobar consolidation
Pulmonary edema	Lack of paroxysmal nocturnal dyspnea or coughing; insidious onset with changes in function, food, or fluid intake, or confusion
Tuberculosis	Weakness, chronic fatigue, dyspnea, anorexia, impaired cognition, hepatosplenomegaly, abnormalities in liver function tests, and anemia.
Unstable angina	Fainting, weakness, dyspnea, pain in shoulder and neck, palpitation, nausea/vomiting, mid-back pain, numbness/tingling in the chest, loss of consciousness and nausea
Urinary tract infection	Absence of fever, worsening mental or functional status to include instrumental activities of daily living (ADLs), dizziness, anorexia, fatigue, weakness

Sources: Barbesino, 2019; Bhatia & Naik, 2013; Breining et al., 2018; Das et al., 2007; Dumic et al., 2019; Gajendran et al., 2019; Grosmaitre et al., 2013; Hofman et al., 2017; Jiménez et al., 1997; Jung et al., 2017; Kim, 2018; Laborde et al., 2021; Pour et al., 2015; Spangler & Manning, 2021; Vonnes & El-Rady, 2021.

TABLE 1-2 Select Bimodal Presentations of Illness in Younger Adults Versus Older Adults

TYPE OF CONDITION	YOUNGER ADULTS	OLDER ADULTS
Dermatological		
Psoriasis	• Late teens to 20s • Irregular course, which tends to generalize • Hereditary factors	• 50s—males • 60s—females • Sporadic onset
Gastrointestinal		
Inflammatory bowel disease Ulcerative colitis (UC) Crohn's disease (CD)	• 20–40 years old • Right lower UC • Insidious onset • Generally absence of perineal lesions	• >60–75 years old a second peak occurs • More often older women • Proctitis • Left-sided UC • Higher rates of anemia • May present as chronic diarrhea • Fistula development • Increased cases of associated malnutrition • Extraintestinal manifestations including arthritis spondylitis, uveitis, and erythema nodosum • More comorbid conditions • May be confused with other forms of colitis
Malignancies		
Hodgkin's lymphoma	• 20–30 years old • Possible infectious etiology	• >50 years old • Increased mortality

Continued

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TABLE 1-2 Select Bimodal Presentations of Illness in Younger Adults Versus Older Adults—cont'd

TYPE OF CONDITION	YOUNGER ADULTS	OLDER ADULTS
Musculoskeletal Conditions		
Rheumatoid arthritis	• Peak onset 30–50 years old • More common in females • Rheumatoid factor (RF) positive	• 65 years of age • Equal distribution among the sexes • Acute onset • More involvement of larger joints (shoulder) at the same time as smaller joints • Weight loss, myalgias • Polymyalgia rheumatica–like form • Comorbidities • Can present as RF negative • Lower platelet to lymphocyte ratio • Radiographic erosive changes
Neurological Conditions		
Myasthenia gravis (MG)	• 20–40 years old; predominately in females • Thymic hyperplasia frequently develops; thymoma uncommon thymoma	• 55–75 with late onset beginning ≥75, predominately in men • Dysphonia; dysphagia • More frequent ocular form MG • Increased rate of acetylcholine receptor antibody seropositivity • Increased secondary autoimmune comorbidities such as thyroiditis, systemic lupus erythematosus, rheumatoid arthritis, diabetes mellitus
Seizures	• Can begin at a very young age, different types of seizures can begin in young childhood. Contributing factors include high fever, head injury, infections such as malaria • Auras that include fear, epigastric distress and déjà-vu phenomena	• Thymoma more common presentation; thymic hyperplasia is less common • 60 years focal seizures with impaired awareness, with or without secondary evolution to tonic-clonic seizures, shorter in time duration. • Aura may present as dizziness; contributing factors include stroke, dementia, and brain tumors
Psychological Conditions		
Bipolar disorder	• 30 years old • Often presents with elation • Unlikely to present with cognitive impairment • Family history of bipolar disorder	• >50 years old • Irritability more common than elation • Common for cognitive impairment to be present • Rare that there is a family history

Sources: Dresser et al., 2021; Hernandez Fustes et al., 2020; Kobak & Bes, 2018; Lee, 2019; Mustafa et al., 2018; Singh et al., 2015; Smith et al., 1993; Smith, 2013; Targońska-Stępniak et al., 2021.

CHRONIC ILLNESS AND FUNCTIONAL CAPACITY

Approximately 80% of those 65 or older have one chronic disease, and 50% have two or more. The most common of these are related to heart disease, arthritis, respiratory problems, cancer, diabetes, and stroke (National Council on Aging, 2021). Treating patients with multimorbidities can be very complex and can result in polypharmacy. Patients with multimorbidities are known to have a treatment burden in terms of understanding and self-care management of their conditions. This burden entails patients not only managing the conditions but also attending multiple appointments and comprehending and affording complex drug regimens (van Merode et al., 2018).

These conditions often impair functional capacity and limit the person's ability to perform activities of daily living (ADLs) such as bathing and dressing, and instrumental activities of daily living (IADLs) such as managing medications and traveling. In 2018, it was found that 22% of the population aged 65 and older reported having a disability defined as having a lot of difficulty or having limited functional capacity with their vision, hearing, mobility, ability to communicate, impairment with cognition, or limitations with their self-care abilities (Federal Interagency Forum on Aging Related Statistic, 2020).

SUMMARY

Assessment and management of older adults is different from that of younger adults, and it is of critical importance that the advanced practice nurse working with the older adult have the knowledge, skill, and ability to recognize these differences and take them into consideration. This chapter highlighted how the approach of the clinician might be different based on an understanding of the physiological changes of aging and the impact

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of these changes on medication management and laboratory interpretation; how the presenting features of disease and illness may be different in the older adult; and how the older adult is disproportionately affected with chronic disease and functional impairments.

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CHAPTER 2

Health Promotion

Lori Martin-Plank

Health promotion in older adults occurs on a global population level through the World Health Organization (WHO) and the United Nations, in conjunction with other international partners who have declared 2021–2030 as the Decade of Healthy Aging. Within this platform, they are dedicated to building infrastructures for health promotion and health equity for older adults, as well as advocating for the elimination of ageism worldwide. In the United States, government agencies such as the Centers for Disease Control and Prevention (CDC), Administration on Aging (AoA), and Centers for Medicare and Medicaid (CMS), among others, champion the charge of health promotion in older adults. As providers, we work with patients and families, but it is important to be aware of these resources and to utilize them when appropriate.

Health promotion for older adults consists of proactive commitment to health and wellness, taking control of one's health and initiating lifestyle changes, following preventive screening and counseling recommendations, and maintaining healthy social contacts. Health-care providers are in a unique position to influence their older adult patients to embrace health promotion and preventive health maintenance at every visit but particularly at the Welcome to Medicare and Annual Wellness Visits (AWVs). Strategies for health promotion in older adults include prevention and focus on maintaining and building functional capacity, expanding social networks, and preserving and enhancing self-care.

PRIMARY, SECONDARY, AND TERTIARY PREVENTION

Prevention is divided into primary, secondary, and tertiary areas.

- **Primary prevention:** Intervene before there is injury or a health problem. For example, Mr. P is a 62-year-old man presenting to your office for care. When reviewing his health history, you establish that he had chickenpox as a child. You know that the varicella virus lies dormant in the body but can reactivate in the form of varicella zoster or "shingles." You order Shingrix vaccine, a 2-dose series to prevent painful varicella zoster in nerve endings.
- **Secondary prevention:** Detection of a preclinical or an asymptomatic health condition. For example, Ms. J is a healthy 68-year-old woman seen in your office for a physical examination. You recommend a mammogram to screen for signs of breast cancer.
- **Tertiary prevention:** Intervention in known disease or health condition to slow progression and prevent condition from worsening. Mr. G is a 76-year-old man with type 2 diabetes mellitus. His current A1c is 6.5, but he is reporting two episodes of feeling sweaty, clammy, shaky, and dizzy after exercising in the morning. He checked his blood sugar, and it was 70 both times. He is currently on glipizide 5 mg once daily and metformin 500 mg, 2 tablets twice daily. You recognize that glipizide could be causing hypoglycemia and you tell him to stop the glipizide at this time, continue the current metformin regime, and recheck his blood glucose daily in the morning for 5 days. You instruct him to call your office immediately if he experiences symptoms again.

HEALTHY LIFESTYLE COUNSELING

Healthy lifestyle counseling is part of every clinician encounter with an older adult, although it is often superseded by the focus on chronic disease management or an acute, limited health problem. A quick question, "I know that you are not feeling well today, and we are addressing that now. I'm just wondering if you have been able to follow up on my suggestions about changing your diet since we last met. How is that going?" can change the focus to healthy lifestyle counseling and open the conversation for further dialogue (O'Connor et al., 2020; Troutman-Jordan, 2017). During a chronic disease management visit for hypertension and diabetes, "Your blood pressure is improved today, and I see that you have lost 2 pounds since your last visit. Are you following up on the diet and exercise recommendations we agreed on in [month]? How is that going for you?" shifts the conversation to healthy lifestyle counseling. Training a staff member at the office in motivational interviewing and lifestyle counseling can save

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clinician time and give the patient individual attention, or you can do the counseling yourself and use the added time feature for billing the visit. Placing handouts in the office with links to resources such as the CDC Healthy Aging, National Council on Aging (NCOA), National Institute on Aging (NIA), WebMD Healthy Aging, and links to phone apps for exercise or nutrition in older adults, can assist with health promotion. Most Medicare Advantage plans employ health coaches who will work one-on-one with older adults; have your office manager investigate these and share with patients or even contact the plan and request a health coach for an older patient that needs individual guidance. Office staff can also connect with the local hospital or community health center and post information in the office about upcoming events related to healthy aging, such as Senior Games or a mobile mammography unit. When seeing older adults who require a family caregiver, include them in part of the visit and lifestyle counseling. Contact the Area Agency on Aging or local health department for sources of assistance in the home and low literacy materials for older adults or handouts in other languages than English if this fits your patient population. In general, keep it simple, engage the patient/family—what are their priorities for healthy lifestyle—and individualize (Cheung et al., 2019; Evans et al., 2020; Whitehead, 2017).

Aging in Place

The concept of aging in place refers to the desire and ability of older adults to continue living in their home or in a supportive home-like community environment, regardless of physical or cognitive barriers (NIA, 2017). This was the primary model for aging in past decades when multigenerational families lived together, and women stayed at home and cared for family members. Societal changes, including industrialization, women in the workplace, globalization, relocation of families, decline in numbers of children in families, and extended life years for older adults, have resulted in challenges for older adults desiring to age in place. Simultaneously, health care acquired a corporate model, and the nursing home industry grew rapidly, providing an alternative living arrangement for older adults who were unable to remain at home due to disability, frailty, lack of support, or absence of family. The costs associated with long-term care are borne by the patient/family, with Medicaid assuming responsibility when patients have exhausted their financial resources. Many older adults are dissatisfied with the nursing home environment, desiring a more home-like place. Legislation (Credit for Caring, 2021; Supporting Our Direct Care Workers and Family Caregivers Act, 2021) has been introduced to pay family caregivers and to give tax credits to family caregivers. This may promote the return of care in the home.

One of the major factors facilitating aging in place comes from the technology sector, which has introduced "smart" home technology for safety and monitoring of older adults in their homes (Choi et al., 2021; Combs et al., 2021). From passive safety features such as motion sensors illuminating the path to the bathroom at night and use of video doorbells that display the faces of visitors to more sophisticated artificial intelligence that monitors the movement patterns of older adult inhabitants through wearables and sensors, smart technology has revolutionized aging in place (Agbadjé et al., 2020). Voice-activated smartphone or smart speaker assistants can keep a calendar with appointments and remind the older adult, set up alarms for medication management, and order groceries and other essentials to support aging in place. Social robots can keep older adults with dementia engaged and service robots help with bathing and activities of daily living (ADLs) (Jensen et al., 2019). Granny cams afford family caregivers access to the older adult remotely, and a phone app can turn lights, heat, and air conditioning on and off at a distance as well as lock doors for safety at night (Choi et al., 2019). Although all of this innovation comes with trade-offs, including loss of privacy and (in some cases) loss of freedom, studies show that older adults are willing to accept this for the ability to age in place (Carroll et al., 2021; Choi et al., 2021; Chung et al., 2016; *Dermody et al., 2021; Tural et al., 2021). Cost is a factor, although vendors work with the American Association of Retired People (AARP) and offer discounts. Medicaid is the first third-party payor to reimburse for passive remote monitoring in the home (Berridge, 2018); however, costs can be prohibitive and result in excluding older adults of lower socioeconomic status.

In addition to the traditional aging in place model, there are some aging in community models initiated by older adults for support and social interaction and by public entities for older adults with lower income; there are also university-based retirement communities for those with an interest in teaching and learning (Hou & Cao, 2021). Some of these are intergenerational whereas others are limited to older adults. Challenges of aging in community are sustainability, inclusion of lower socioeconomic groups, and balance of independent members who can assist those who need help (Hou & Cao, 2021).

Nutrition

The importance of good nutrition in older adults cannot be overemphasized, yet it is often overlooked by clinicians. The Welcome to Medicare visit, subsequent AWVs, or chronic health maintenance visits are all opportunities to address nutrition. Height and weight should be measured at each encounter and tracked to assess for evidence of involuntary weight loss or excessive weight gain, and clinicians should ask about appetite and food intake patterns. Visual inspection may provide clues through ill-fitting clothing, although this may not be accurate in low-income communities where donated clothing is the norm. Asking about food insecurity can uncover financial problems that require referral to the Area Agency on Aging or a local food bank. Questions about difficulty chewing or swallowing, feeling of fullness or lack of appetite, stomach pain associated with eating, nausea or vomiting, choking, constipation, or diarrhea are helpful in uncovering problems with eating. Assessing dentition during physical examination may reveal ill-fitting dentures or an edentulous patient (Clegg & Williams, 2018). Inquiring about changes in ADLs and physical activity is also relevant because a sedentary lifestyle can dampen the appetite, or conversely, lead to excessive snacking on salty or sugary finger foods. Inability to go grocery shopping will also limit food options. Meal patterns and types of food eaten should be obtained from the patient. Medications and over-the-counter (OTC) supplement usage is also important. Does the patient live alone? Is the patient able to prepare meals and do they

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have access to cooking facilities? These questions are helpful in assessing both anorexia of aging and obesity (Landi et al., 2017; Mangels, 2018; Reber et al., 2019; van der Meij et al., 2017). Use of a mnemonic such as DETERMINE

Diseases
Eating poorly
Tooth loss/mouth pain
Economic hardship
Reduced social contact
Multiple medications
Involuntary weight loss/gain
Needs assistance in self-care
Elder years/above age 80

is recommended for screening community-dwelling older adults by the *Proceedings of the Nutrition Society* (Corish & Bardon, 2019) in the European Union, whereas most authorities in the United States use the Mini-Nutrition Assessment-Short Form (MNA-SF), a six-question document that can be completed in advance (available at https://mna-elderly.com/forms/mini/mna_mini_english.pdf).

In long-term care settings, nutrition assessment is performed by a dietitian in conjunction with nursing and direct care staff; the screening tool used frequently is the MNA. Weight is typically monitored on a regular basis, and the dietary department is tasked with individualizing interventions. In residents who require assistance with feeding, it is important to monitor the efforts of direct care staff to ensure that the resident is not rushed or just set up and abandoned when unable to feed themselves.

Obesity presents another problem with nutrition. Although there is a decline in the prevalence of overweight and obesity after age 60 years, it remains a problem for many older adults. It is a major risk factor for decreased mobility and functional impairment as well as a cardiovascular risk. Overweight and obesity are associated with heart disease, certain types of cancer, type 2 diabetes, breathing difficulties, stroke, arthritis, and psychological problems.

Counseling on nutrition should be individualized to the need of each older adult. When appropriate, consider referring to a dietitian or recommend contacting the health coach at the insurance company. Home-delivered meals may also provide needed nutrition for those who are unable to cook their own meals. General guidelines for dietary counseling include the following:

- Limit fat and cholesterol.
- Maintain a balanced caloric intake.
- Emphasize the inclusion of grains, fruits, and vegetables daily.
- Ensure an adequate calcium intake, especially for women.
- Limit alcohol, if used, to one drink daily for women and two drinks daily for men: one drink = 12 oz beer, 5 oz wine, or 1.5 oz of 80-proof distilled spirits.
- Combine dietary interventions with regular physical activity for optimal results.

Oral Health

Oral health is closely aligned with nutrition and overall physical and mental health. Older adults have more problems with oral health, including xerostomia, dental caries, periodontal disease, tooth or mouth pain, mouth infections, or missing teeth (CDC, 2021b; Coll et al., 2020c). Recent estimates show that 26% of adults aged 75 and older have lost all their teeth; 68% have periodontal disease, and one in five older adults have dental caries (CDC, 2021). Periodontal disease is associated with type 2 diabetes mellitus, cardiovascular disease, and endocarditis. There is also concern in patients who have had joint replacements or heart valve replacement that transient bacteremia occurring with periodontal treatment or caries repair can infect prosthetics (Coll et al., 2020c). Although all older adults need to be screened for oral health issues, those with diabetes and dementia are considered high risk for complications, as are long-term care residents and lower socioeconomic groups. Dental care is excluded from Medicare coverage and is expensive for most retirees. Emphasizing prevention as cost-effective to older adults may help to motivate them for self-care.

Many clinicians lack education about oral health problems. The American Dental Association (2021) has information available and the European College of Gerodontology has partnered with the European Geriatric Medical Society to create guidelines for oral care in older adults, particularly those who are frail or lack access to dental care (Kossioni et al., 2018). Older adults should have an oral inspection by a clinician at least annually, at which time the need for oral care can be addressed and options for seeing a dental health professional discussed. Interventions for a dental abscess should serve as a red flag to the clinician to identify dental care as a priority. Older adults should be seen every 6 months by a dental hygienist and a supervising dentist for routine oral health maintenance (*American Dental Association, 2021; *Coll et al., 2020c). For those with limited means, some community college dental hygiene programs offer free screening and cleaning; dental school clinics and community health agencies may also have services available. Studies have been done with those with dementia and their care partners demonstrating that older adults with mild-moderate dementia can be trained to use an electric toothbrush for 2 minutes daily (Anderson et al., 2019). Another clinical trial compared two interventions to improve oral hygiene in low-income senior housing residents—one was face-to-face, individual meetings demonstrating brushing and flossing; the other was peer-managed group meetings with a health fair theme. Both groups successfully improved their oral hygiene; the face-to-face participants scored higher on measurements of gingival and plaque indices (Schensul et al., 2021; Schensul et al., 2018). Both studies show encouraging results in hard-to-reach older adult populations.

Xerostomia is a significant problem in older adults. Aging, certain medications, uncontrolled diabetes, toxicity from cancer chemotherapy or radiotherapy for head and neck cancer, and autoimmune conditions such as Sjögren's disease, contribute to dry mouth (American Dental Association, 2021). More than 100 medications are implicated in xerostomia; those that are anticholinergic have higher risk. Examples include antihistamines, decongestants, antidepressants, antipsychotics, diuretics, NSAIDs, benzodiazepines, muscle relaxants, antimuscarinics, analgesics, and Parkinson's drugs; inhaled steroids are implicated in another oral condition—candidiasis (Coll et al., 2021c). Clinicians should review medications periodically and substitute those that are efficacious

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but do not cause dry mouth when possible. Educate patients to brush with a fluoridated toothpaste and floss regularly, avoid high-sugar foods, and seek regular dental care.

Physical Activity

Although the level of physical activity in older adults has increased slightly, they remain the least active population group in the United States, with approximately 16% of older adults between 65 and 74 years of age meeting the standard for physical activity set by *Physical Activity Guidelines for Americans* (2nd ed.) in 2018 (2018 Physical Activity Guidelines). The recommendation for older adults age 65 and older is to perform a minimum of 150 minutes weekly of moderate-intensity aerobic activity or 75 minutes weekly of vigorous-intensity aerobic physical activity, or an equivalent combination of both. Further requirements include muscle-strengthening activities using all major muscle groups, with at least moderate-intensity, two or more days weekly. If older adults cannot achieve 150 minutes of moderate-intensity aerobic exercise due to chronic health issues, they should be as active as their health conditions and abilities permit (USDHHS, 2018). Additional focal areas for older adults are balance training and safety to prevent falls. In short, any physical activity is better than none.

Since the COVID-19 pandemic, many creative ideas have emerged, including exercise classes on Zoom or YouTube, virtual exercise support groups for seniors, e-health instructions, and intergenerational programs (Callahan et al., 2021; Howell et al., 2021; King et al., 2020; Stonerock & Blumenthal, 2017; Talley et al., 2019). The NIA (2021), NCOA (2021), and AARP (2020) have fitness program resources for older adults. Many Medicare Advantage programs subscribe to Silver Sneakers programs in conjunction with a local gym or YMCA. These and similar programs offer various physical activities, such as Zumba for seniors, yoga, resistance training, and cardio. The challenge for clinicians is to learn about these resources and share them with their patients. The Welcome to Medicare visit and AWV provide a dedicated space for meeting with older adults and discussing health promotion, including physical activity, and working on a plan. A written exercise prescription is recommended by the American College of Sports Medicine in their Exercise is Medicine program for older adults. The most recent research on optimizing physical activity in older adults endorses multicomponent programs that stimulate both brain and body simultaneously (Pothier et al., 2018).

Before embarking on an exercise program, all patients should have an evaluation of health history, including medications, present physical activity and functional level, potential barriers to exercise, and a physical examination. Older adults with known or suspected cardiac risk factors should have a stress test before engaging in vigorous exercise. All participants should be reminded of the need for adequate hydration and use of caution during extreme weather conditions.

The importance of continuous physical activity in maintaining function and preventing debility in long-term care residents is often overlooked. A recent follow-up study by Rodriguez-Larrad et al. (2021) highlighted the decline in both physical function and cognitive status in the 6-month period after completion of a randomized controlled trial implementing a progressive multicomponent physical fitness program in a select group of residents.

Safety

Quality of life and function are highly dependent on safety and injury prevention in older adults. Counseling involves reinforcement of extant recommendations, including wearing lap and shoulder seat belts in a motor vehicle, avoiding drinking and driving, having working smoke detectors in the residence, and keeping hot water set below 120°F. For older adults who drive a motor vehicle, periodic assessment of their ongoing ability to drive safely is vital to the older adult and the public at large. Most motor vehicle accidents involve young drivers and older drivers. Safe storage and removal of firearms is another important area to address. Possession of a firearm combined with depression, caregiver stress, irreversible illness, or decline in functional abilities can invite self-inflicted injury, suicide pacts, or other acts of violence. Counsel patients to avoid firearms in the home and to use alternative means for self-protection such as alarm systems and pepper mace spray.

According to the World Health Organization (2021), falls are the second cause of unintentional injury deaths worldwide; adults aged 60 years and older experience the most fatal falls. Many falls are preventable with education, training, and environmental modifications for safety. Because older adults are often embarrassed by a fall, most will not volunteer information to clinicians about falls, so clinicians need to be proactive and ask about any falls in the past 6 months, any changes in mobility, ADLs, or cognition. The AWV and chronic health maintenance visits are good opportunities to address safety and falls and to reinforce this information with a basic handout. There are also fall assessments and games on the Internet that can be used (Dispennette et al., 2019). The Timed Get Up and Go can also be used for an objective measure of a patient's mobility and balance. Emphasizing the need to be physically active to maintain strength and flexibility aligns with fall education. Patients who have recently fallen or had a change in mobility should be referred to physical therapy, which is a cost-effective preventive intervention. Occupational therapy will also make a home visit (with a clinician's order) for an environmental safety assessment (Georlee et al., 2020). If a patient is deemed at risk for falling, a team-based intervention may be the optimal approach, including a caseworker evaluation from the Area Agency on Aging; physical therapy to treat and evaluate the need for assistive devices and stable footwear; occupational therapy to evaluate vision, hearing, home environment, and modifications for optimizing function and ADL ability; and nursing to assess the patient and medications as part of a fall-risk evaluation (Miranda-Duro et al., 2021). Clinicians should review medications at every visit and consider their potential to impair cognition (psychotropics, narcotic analgesics, anticholinergics) or contribute to incontinence due to slow mobility (diuretics, laxatives), adjusting when necessary (Guirguis-Blake et al., 2018). The use of smart home technology should also be considered for environmental modification.

Research has identified patient perspective as a barrier or facilitator for fall education programs (Chen et al., 2016; Tzeng et al., 2020). One program implemented a brief home hazard reduction program through the Area Agency on Aging, with a control group and intervention group in those at high risk of falling (Stark et al., 2021). Although there was a reduction in the number of falls in the intervention

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group, it did not reach significance. Programs that are multifactorial in nature and consider patient perspectives, motivation, health literacy, and available resources are most likely to be beneficial in reducing future falls (Lach & Noimontree, 2018; *Tzeng et al., 2020).

Sexuality

The topic of sexuality and sexual behavior in older adults is rarely discussed. Many clinicians lack knowledge of how to approach the topic and consequently remain silent. They may have preconceived ageist biases and view older adults as asexual. Several research studies demonstrate that most older adults are still sexually active, although health issues may limit frequency or type of sexual expression (Gewirtz-Meydan et al., 2019; Srinivasan et al., 2019). Incorporating a sexual health history into an annual wellness visit or chronic health maintenance check adds a holistic element to care and personalizes the approach, leading to a healthy, trusting relationship (Johnson et al., 2019; Kuhle et al., 2021). The PLISSIT model offers a structured way for clinicians to introduce questions about sexual health—giving the patient **P**ermission to ask about sexual concerns, then proceeding to share **L**imited **I**nformation, targeting their concerns, sharing **S**pecific **S**uggestions for treatment of symptoms if known, and referring for **I**ntensive **T**reatment to the appropriate specialist (Palisano, 2017); for an older adult this could be a urologist, urogynecologist, psychologist, or sex therapist depending on the concern. This approach preserves the clinician/patient relationship and facilitates counseling and interventions to promote healthy sexual behavior. Studies have uncovered that a variety of stereotypes exist related to older adult sexuality and particularly the role of the older woman (Ricoy-Cano et al., 2020); many of these are fueled by religious or societal norms that no longer stand. With the help of the appropriate consultant, old myths can be dispelled.

Other areas of sexual health that need to be addressed are self-protection from sexually transmitted infections (STIs) and HIV when dating, and avoiding predators. In 2018, 17% of newly diagnosed HIV patients were aged 50 and older (CDC, 2018). Many older adults mistakenly believe that barrier protection is not needed because there is no risk of pregnancy. STIs, including genital herpes, human papilloma virus, gonorrhea, syphilis, and hepatitis are omnipresent threats, as is HIV. Patients need to be educated to ask partners about their sexual history, including past STIs and HIV, and to always use barrier protection. Education about preexposure prophylaxis and postexposure prophylaxis is also necessary for those in a sexual relationship with a person with HIV or at high risk of HIV (U.S. Food and Drug Administration [FDA], 2021).

LESBIAN, GAY, BISEXUAL, TRANSGENDER, QUEER AND OTHER SEXUAL AND GENDER DIVERSE PEOPLE (LGBTQ+)

At the present time, between 3% and 6% of older adults identify as LGBTQ+ on public health surveys—around 3 million people Fredriksen-Goldsen et al., 2017). The largest group is the oldest old—those 80 years and older. Approximately one-fifth of LGBTQ+ older adults do not share their sexual orientation and/or gender identity with health-care providers out of concern related to inadequate care (Caceres, 2019; Fredriksen-Goldsen et al., 2011). Common health problems in LGBTQ+ older adults include mental health issues, cardiovascular disease, obesity, HIV, and substance use (Fredriksen-Goldsen et al., 2019).

It is worth noting that some LGBTQ+ older adults (especially among the oldest old) may be more familiar with the terminology "homosexual." In addition, because "queer" has historically been used as a pejorative term they may find the term offensive (Travis, 2017). However, the term started being "reclaimed" in the 1960s by some members of the LGBTQ+ community as an act of resilience and defiance and may be a relevant term among people in the Baby Boomer generation and younger (Tamanna, 2018).

Although knowledge of the existence of LGBTQ+ persons is not new, recent initiatives in diversity, equity, and inclusion have heightened awareness, raising issues such as implicit bias and outright discrimination in caring for this population among health professionals. Most LGBTQ+ older adults desire respect, dignity, and professionalism from health clinicians (Caceres, 2019; Fredriksen-Goldsen et al., 2019). In the case of transgender older adults, whose gender identity may not be congruent with their sex assigned at birth, clinicians and allied health personnel need to use the correct name and pronoun and realize that driver's license and health insurance documents may not match. When one's legal documentation and identity do not 'match' and facilities or rooms are segregated by sex at birth, policies should be implemented to support rooming based on gender identity (e.g., man, woman) (Lambda Legal, 2016).

Fredriksen-Goldsen and colleagues (2017, 2019) have conducted a survey of LGBTQ+ older adults with high response rates, looking at specific time stamped and longitudinal data on LGBTQ+ older adults. One theme that emerges is resilience in the face of adversity; many LGBTQ+ older adults are highly educated, with graduate degrees, but their socioeconomic status is low due to employment discrimination; many are still working into their 80s. LGBTQ+ older adults of color experience the worst living situations and health disparities (Kim et al., 2017). Clinicians providing services to LGBTQ+ older adults need to learn about their specific healthcare needs and concerns, how to best communicate with them, and identify important people who should be included in their care (Redcay et al., 2019). The National Resource Center on LGBT Aging (https://www.lgbtagingcenter.org/) is a unique source of information and training for those working with LGBTQ+ older adults as well as older adults, their families and caregivers, and the public. Guidelines for the provision of primary and gender-affirming treatment to for transgender and nonbinary individuals are available through the University of California, San Francisco's The Department of Family and Community Medicine (https://transcare.ucsf.edu/guidelines). Professional continuing education providers also offer programs in cultural aspects of LGBTQ+ communities.

The LGBTQ+ older adult population is comprised of multiple heterogeneous groups (Caceres, 2019; Kim et al., 2017; Fredriksen-Goldsen et al., 2019) with a variety of sexual, social, and health-care needs. LGBTQ+ older adults may be more likely to live alone and have fewer options for informal

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caregiving from biological family members (Choi & Meyer, 2016). "Chosen" family members (e.g., an individual's partner or other LGBTQ+ adults) may be a source of care, but may lack any legal recognition provide care to their partner or others in the community who do not have a partner or children (Stewart & Kent, 2017). LGBTQ+ older adults who are caregivers may also have fewer social supports and be at higher risk for caregiver burnout (Stewart & Kent, 2017).

The oldest old tend to be more dependent, often requiring long-term care. LGBTQ+ older adults may feel the need to conceal their sexual orientation or gender identity from other residents and staff to avoid mistreatment. Transgender adults who need a high level of personal care may find it impossible to conceal their gender history, making them among the most vulnerable to inadequate or inequitable care, including elder abuse (Movement Advancement Project and Services and Advocacy for Gay, Lesbian, Bisexual, and Transgender Elders, 2010). Feeling the need to conceal one's identity may mean disconnecting from the larger LGBTQ+ community, increasing feelings of isolation. Experiences such as direct and indirect (e.g., implicit bias and microaggressions) discrimination and rejection by other residents, direct care workers, and other professionals in this setting increase LGBTQ+ older adults' vulnerability to depression, substance use, and other chronic health conditions. As such, clinicians in these settings need to be alert to subtle discriminatory practices from staff such as ignoring call lights and not toileting on schedule, leading to the need for incontinence care, which can entail rough handling of the patient. It is also important for clinicians to recognize individuals important to the LGBTQ+ older adult and facilitate completion of Advanced Directives and other legal documents to ensure the older adult's medical decision-making wishes are known (Stewart & Kent, 2017). Social workers can support LGBTQ+ older adults and/or their caregivers by arranging for a group for socialization.

Substance Use

Substance misuse remains a silent epidemic in older adults; its prevalence is growing, and the character of the substance use is changing from primarily alcohol to alcohol and other drugs (Chhatre et al., 2017; Tucker et al., 2021; Yarnell et al., 2020). With the influx of the Baby Boomer generation (those born between 1946 and 1964) into older adulthood, there is a trend of earlier exposure to alcohol and drugs such as cocaine, crack cocaine, heroin, marijuana, and prescribed or illicit opioids. Inpatient admissions for substance abuse by older adults have doubled between 2002-2012, although outpatient treatment remains the primary model (Suntai et al., 2020). Most older adults complete treatment for substance misuse; there is a markedly lower completion rate by Black patients compared to Hispanic and White patients. This may reflect socioeconomic disparities in which insurers do not cover the entire treatment, there is lack of availability of treatment facilities, or individuals are experiencing homelessness and have no treatment options (Suntai et al., 2020). Clinicians who refer older adults for treatment need to follow up to encourage completion. Opioid abuse or opioid use disorder has more severe effects on older adults, including death. Some opioid abuse is unintentional due to forgetting about a dose already used; some results from altered cognitive status or even delirium (Dufort & Samaan, 2021).

Clinicians can use the Welcome to Medicare visit and the AWVs to ask about substance misuse. Counseling regarding alcohol or other drug use can be preventive or interventional, depending on the initial assessment. Use the Michigan Alcohol Screening Test (MAST), the CAGE questionnaire, or the Alcohol Use Disorders Identification Test (AUDIT) to assess risk. For opioid misuse, the Opioid Risk Tool (https://www.drugabuse.gov/nidamed-medical-health-professionals/screening-tools-resources/opioid-risk-tool-oud-ort-oud) can be used (Ducharme & Moore, 2019). Using a person-centered, nonconfrontational approach and active listening during a health promotion visit will yield the most disclosure. Explaining how biological changes with aging can put the older patient at higher risk of complications is helpful (Kuerbis, 2020). Understanding of some factors that lead older adults to substance misuse is also important. Chronic pain, depression, social isolation, cognitive or mental health problems, and stress are major contributors to substance misuse (Dufort & Samaan, 2021; Kuerbis, 2020). Patients should be cautioned about the risk of falls, breathing problems, auto accidents, and heart problems related to substance misuse and encouraged to seek treatment. Naloxone (Narcan) should be prescribed for emergency use by family or friends of older adults who are on scheduled opioid medication.

If older adults are using benzodiazepines, explain the additive effect with opiates or alcohol, the risks to memory and cognition as well as risks for falling and serious injury (Maree, et al., 2016). Clinicians can work with the patient to initiate deprescribing for benzodiazepines and prescribe a selective serotonin reuptake inhibitor for depression or anxiety if indicated. Also recommend cognitive behavioral therapy or other counseling.

Very little hard data exist about cannabis use in older adults; a review of medical marijuana registries in 13 states revealed that 35% to 50% of users were aged 50 or older (Kuerbis, 2020). It is the most used illicit drug by older adults due to legalization, social acceptability, and decriminalization. Even when it is dispensed as medical marijuana, there are significant effects on the cardiovascular system in older adults, including increased blood pressure, heart rate, and respiratory rate, and loss of short-term memory (Kuerbis, 2020). There are also significant drug interactions between cannabis and multiple frequently prescribed drugs for older adults, including simvastatin, warfarin, amiodarone, alprazolam, and others (Medscape Drug App, 2021). Older adults using cannabis should be counseled about the risks versus benefits of ongoing usage.

Tobacco usage (smoking) in those age 65 and older is about 8.4% (Jamal et al., 2016), with many smokers reporting concurrent medical illness such as COPD or lung cancer. Using the 5 A's, assess willingness to quit and counsel on benefits of quitting at any age.

SCREENING AND PREVENTION

The table below shows the final recommendation summaries for older adults from the U.S. Preventative Services Take Force (USPSTF).

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Topic	Recommendation	Grade	Release Date
Abdominal aortic aneurysm: Screening: men aged 65 to 75 years who have ever smoked	The USPSTF recommends 1-time screening for abdominal aortic aneurysm (AAA) with ultrasonography in men aged 65 to 75 years who have ever smoked.	B	December 2019
Aspirin Use to Prevent Cardiovascular Disease	The USPSTF recommends for adults aged 40 to 59 years who have an estimated CVD risk of 10% or greater that shared decision making is used in determining initiation of low dose (81mg/day) of aspirin. Consider potential benefits and harms to the individual when discussing ASA use for prevention.	C	April 2022
	The USPSTF recommends against initiating ASA For adults 60 years or older aspirin for primary prevention of CVD.	D	
Breast Cancer: Screening: women aged 50 to 74 years	The USPSTF recommends biennial screening mammography for women aged 50 to 74 years.†	B	January 2016
Colorectal Cancer: Screening: adults aged 50 to 75 years	The USPSTF recommends screening for colorectal cancer in all adults aged 50 to 75 years.	A	May 2021
Depression in Adults: Screening: general adult population, including pregnant and postpartum women	The USPSTF recommends screening for depression in the general adult population, including pregnant and postpartum women. Screening should be implemented with adequate systems in place to ensure accurate diagnosis, effective treatment, and appropriate follow-up.	B	January 2016
Falls Prevention in Community-Dwelling Older Adults: Interventions: adults aged 65 years or older	The USPSTF recommends exercise interventions to prevent falls in community-dwelling adults aged 65 years or older who are at increased risk for falls.	B	April 2018
Healthy Diet and Physical Activity for Cardiovascular Disease Prevention in Adults With Cardiovascular Risk Factors: Behavioral Counseling Interventions: adults with cardiovascular disease risk factors	The USPSTF recommends offering or referring adults with cardiovascular disease risk factors to behavioral counseling interventions to promote a healthy diet and physical activity.	B	November 2020
Hepatitis C Virus Infection in Adolescents and Adults: Screening: adults aged 18 to 79 years	The USPSTF recommends screening for hepatitis C virus (HCV) infection in adults aged 18 to 79 years.	B	March 2020
Hypertension in Adults: Screening: adults aged 18 years or older without known hypertension	The USPSTF recommends screening for hypertension in adults aged 18 years or older with office blood pressure measurement (OBPM). The USPSTF recommends obtaining blood pressure measurements outside of the clinical setting for diagnostic confirmation before starting treatment.	A	April 2021
Intimate Partner Violence, Elder Abuse, and Abuse of Vulnerable Adults: Screening: women of reproductive age	The USPSTF recommends that clinicians screen for intimate partner violence (IPV) in women of reproductive age and provide or refer women who screen positive to ongoing support services. See the "Clinical Considerations" section for more information on effective ongoing support services for IPV and for information on IPV in men.	B	October 2018
Latent Tuberculosis Infection: Screening: asymptomatic adults at increased risk for infection	The USPSTF recommends screening for latent tuberculosis infection (LTBI) in populations at increased risk.	B	September 2016

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Topic	Recommendation	Grade	Release Date
Lung Cancer: Screening: adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years	The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.	B	March 2021
Osteoporosis to Prevent Fractures: Screening: women 65 years and older	The USPSTF recommends screening for osteoporosis with bone measurement testing to prevent osteoporotic fractures in women 65 years and older.	B	June 2018
Prediabetes and Type 2 Diabetes: Screening: asymptomatic adults aged 35 to 70 years who have overweight or obesity	The USPSTF recommends screening for prediabetes and type 2 diabetes in adults aged 35 to 70 years who have overweight or obesity. Clinicians should offer or refer patients with prediabetes to effective preventive interventions.	B	August 2021
Prevention of HIV Infection: Preexposure Prophylaxis: persons at high risk of HIV acquisition	The USPSTF recommends that clinicians offer preexposure prophylaxis (PrEP) with effective antiretroviral therapy to persons who are at high risk of HIV acquisition. See the "Clinical Considerations" section for information about identification of persons at high risk and selection of effective antiretroviral therapy.	A	June 2019
Sexually Transmitted Infections: Behavioral Counseling: sexually active adolescents and adults at increased risk	The USPSTF recommends behavioral counseling for all sexually active adolescents and for adults who are at increased risk for sexually transmitted infections (STIs). See the "Practice Considerations" section for more information on populations at increased risk for acquiring STIs.	B	August 2020
Statin Use for the Primary Prevention of Cardiovascular Disease in Adults: Preventive Medication: adults aged 40 to 75 years with no history of CVD, 1 or more CVD risk factors, and a calculated 10-year CVD event risk of 10% or greater	The USPSTF recommends that adults without a history of cardiovascular disease (CVD) (i.e., symptomatic coronary artery disease or ischemic stroke) use a low- to moderate-dose statin for the prevention of CVD events and mortality when all of the following criteria are met: (1) they are aged 40 to 75 years; (2) they have 1 or more CVD risk factors (i.e., dyslipidemia, diabetes, hypertension, or smoking); and 3) they have a calculated 10-year risk of a cardiovascular event of 10% or greater. Identification of dyslipidemia and calculation of 10-year CVD event risk requires universal lipids screening in adults aged 40 to 75 years. See the "Clinical Considerations" section for more information on lipids screening and the assessment of cardiovascular risk.	B	November 2016
Syphilis Infection in Nonpregnant Adults and Adolescents: Screening: asymptomatic, nonpregnant adults and adolescents who are at increased risk for syphilis infection	The USPSTF recommends screening for syphilis infection in persons who are at increased risk for infection.	A	June 2016
Tobacco Smoking Cessation in Adults, Including Pregnant Persons: Interventions: nonpregnant adults	The USPSTF recommends that clinicians ask all adults about tobacco use, advise them to stop using tobacco, and provide behavioral interventions and U.S. Food and Drug Administration (FDA)-approved pharmacotherapy for cessation to nonpregnant adults who use tobacco.	A	January 2021

Continued

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Topic	Recommendation	Grade	Release Date
Unhealthy Alcohol Use in Adolescents and Adults: Screening and Behavioral Counseling Interventions: adults 18 years or older, including pregnant women	The USPSTF recommends screening for unhealthy alcohol use in primary care settings in adults 18 years or older, including pregnant women, and providing persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce unhealthy alcohol use.	B	November 2018
Unhealthy Drug Use: Screening: adults aged 18 years or older	The USPSTF recommends screening by asking questions about unhealthy drug use in adults aged 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred. (Screening refers to asking questions about unhealthy drug use, not testing biological specimens.)	B	June 2020
Weight Loss to Prevent Obesity-Related Morbidity and Mortality in Adults: Behavioral Interventions: adults	The USPSTF recommends that clinicians offer or refer adults with a body mass index (BMI) of 30 or higher (calculated as weight in kilograms divided by height in meters squared) to intensive, multicomponent behavioral interventions.	B	September 2018

†The Department of Health and Human Services, under the standards set out in revised Section 2713(a)(5) of the Public Health Service Act and Section 9(h)(v)(229) of the 2015 Consolidated Appropriations Act, utilizes the 2002 recommendation on breast cancer screening of the U.S. Preventive Services Task Force. To see the USPSTF 2016 recommendation on breast cancer screening, go to http://www.uspreventiveservicestaskforce.org/uspstf/recommendation/breast-cancer-screening1.

A = USPSTF recommends the service. High certainty that net benefit is substantial; B = USPSTF recommends. High certainty that net benefit is moderate or moderate certainty that net benefit is moderate or substantial

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Approach to Screening in Older Adults

Advances in medical science have yielded improved screening tools and preventive health interventions. For older adults with limited years to live, recent medical literature has focused on the risks, benefits, and harms of screening and treatments relative to the remaining years of life. Principles such as time to benefit (TTB) and life expectancy (LE) have been incorporated into the science of prognostication, or predicting mortality (Coll et al., 2020a, 2020b; Lee et al., 2018; Schoenborn, Jacobson, et al., 2020; Schonberg, Karamourtopoulos, et al., 2020), as part of individualizing prevention in older adults. Coll et al. (2020a, 2020b) present a comprehensive overview of cancer screening and treatment in older adults that outlines TTB, harms, and risks. If LE is deemed shorter than TTB, the test or intervention is not recommended. If TTB is shorter than LE, then the intervention or screening test should be considered. In cases where LE and TTB are closely aligned timewise, discussion between the patient and clinician is advised to arrive at a decision (Lee et al., 2018). Determination of LE can be done by using mortality indices that have been already developed. According to Lee et al. (2018), a systematic review found 16 distinctive indices; these have been compiled and translated into online calculators at a Web site ePrognosis.com (https://eprognosis.ucsf.edu/index.php). Data from trials of screening outcomes and procedure outcomes has been utilized in arriving at TTB.

Work on prognostication is ongoing, with various research groups seeking to refine the tools (Jaul et al., 2021; Schoenbornm, Massare, et al., 2020; Schonberg, Jacobson, et al., 2020) and add other variables, such as comorbidities and frailty, into the mix. Although prognostication is being advanced by researchers and population health advocates, translation to practice requires a commitment on the part of clinicians in practice. There has been some hesitancy on the part of clinicians initially, fueled in part by concerns of malpractice and interfering with the clinician-patient relationship, but this is gradually dissipating (Kotwal & Walter, 2020; Schonberg, Jacobson et al., 2020). Most recently, scripts have been created to guide the dialogue between patient and clinician for optimal communication (Kotwal & Walter, 2020; Schonberg, Karamourtopoulos, et al., 2020). Video examples of discussions are available on the ePrognosis Web site. Lee et al. (2020) acknowledge the uncertainty in using probabilistic predictions but point out that several evidence-based examples have arisen from this, including the CHADsVasc 2 for atrial fibrillation. Prognostication outcomes are indirectly related to overuse of medical testing and the Choosing Wisely initiative (discussed below).

Sensitivity and Specificity and Positive Predictive Value of Diagnostic Tests

Not every diagnostic test is useful to diagnose a disease. For older adults, selection of the right diagnostic tests should take into consideration the health status of the older adult patient and the individual's consensus for treatment. Health-care providers need to understand how effective select tests are in establishing a diagnosis in an older adult. It is important to know the strengths and weaknesses of the select tests.

Sensitivity and specificity are the usual statistical measures employed to evaluate how a test performs compared to the gold standard. Sensitivity, or true positive, is the ability of a diagnostic test to correctly identify a proportion of those patients who have the disease or condition out of all who have the disease or condition when measured against a gold standard (Monaghan et al., 2021). Specificity, or true negative, is the ability of a diagnostic test to correctly identify a

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proportion of those patients who do not have the disease or condition out of all who do not have the disease or condition (Monaghan et al., 2021). Sensitivity and specificity are inversely proportional—when sensitivity increases, specificity will decrease. How good is the test, compared to the gold standard, in identifying true positives?

$$\text{Sensitivity} = \frac{\text{Number of people correctly identified as having the disease}}{\text{Total number of people affected}}$$

OR

$$\text{Sensitivity} = \frac{\text{Number of true positives}}{\text{Number of true positives} + \text{Number of false negatives}}$$

How well does the test perform in identifying true negatives—those who do not have the disease, from true negatives and false positives?

$$\text{Specificity} = \frac{\text{Number of people correctly identified as not having the disease}}{\text{Total number of true negatives}}$$

OR

$$\text{Specificity} = \frac{\text{All not having the disease}}{\text{Number of true negatives} + \text{Number of false positives}}$$

Positive predictive value is another statistical term used when examining the value of a test to diagnose a condition. Unlike sensitivity and specificity, which are deemed stable components of a test, positive predictive value aims to predict if a person actually has the disease based upon the pre-test probability or likelihood prior to administering the diagnostic test (Loh et al., 2020). This requires knowledge of the risk factors for acquiring the disease and the prevalence of the disease in the population being tested (Aminsharifi et al., 2018; Monaghan et al., 2021). For example, a recent Cochrane Review (Dinnes et al., 2021) studied the performance of rapid antigen COVID-19 tests compared to the gold standard RT-PCR test. They sought to discover how it performed in those with symptoms and without symptoms. The positive predictive value of a test like this in a population where COVID-19 is rampant, such as the United States, would be much better than if it were used in New Zealand where COVID-19 cases are very scarce, due to a difference in risk factors and prevalence.

CHOOSING WISELY

Choosing Wisely is an initiative started by the American Board of Internal Medicine Foundation in 2012 to raise the awareness of overuse of medical tests and procedures. The American Geriatrics Society (AGS), 70 other specialty groups, and Consumer Reports are part of this national effort. The goal of Choosing Wisely is to support conversations and interactions between patients and their health-care providers about what care is necessary (Levinson et al., 2018; Wolfson et al., 2014). It began with the National Physicians Alliance and a medical ethicist calling on internal medicine, family practice, and pediatrics leaders to each identify five interventions that should not be implemented; building on this, specialty medical organizations were also asked to list five items that were evidence-based, frequently done in practice, billable, within the purview of their clinical specialty, but were unnecessary or overused. The respective medical societies utilized quality and safety committees to develop the lists, polled their membership, and sought approval from their governing board prior to publishing the list. Several organizations have written articles depicting the process underlying their recommendations, and the list has increased from five to 10 items (Levinson et al., 2018; Wolfson et al., 2014). The AGS Health in Aging patient Web site (https://www.healthinaging.org/choosing-wisely) lists 10 things that patients and health-care providers should question, along with rationale and resources (Box 2-1).

In addition to the AGS recommendations, older adults should discuss the harms and benefits of procedures and testing with their health-care provider. The Medicare AWV, chronic health maintenance visits, and the Welcome to Medicare visit offer opportunities for this dialogue.

Like prognostication, many of the Choosing Wisely recommendations incorporate age and 10-year life expectancy into their calculations, particularly screening and treatment

BOX 2-1

Choosing Wisely: 10 Things Clinicians and Patients Should Question

- Don't recommend percutaneous feeding tubes in patients with advanced dementia; instead offer oral-assisted feeding.
- Don't use antipsychotics as first choice to treat behavioral and psychological symptoms of dementia.
- Avoid using medications other than metformin to achieve hemoglobin A1c. (<7.5% in most older adults; moderate control is generally better.)
- Don't use benzodiazepines or other sedative-hypnotics in older adults as first choice for insomnia, agitation, or delirium.
- Don't use antimicrobials to treat bacteriuria in older adults unless specific urinary tract symptoms are present.
- Don't prescribe cholinesterase inhibitors for dementia without periodic assessment for perceived cognitive benefits and adverse gastrointestinal effects.
- Don't recommend screening for breast, colorectal, prostate, or lung cancer without considering life expectancy and the risks of testing, overdiagnosis, and overtreatment.
- Avoid using prescription appetite stimulants or high-calorie supplements for treatment of anorexia or cachexia in older adults; instead, optimize social supports, discontinue medications that may interfere with eating, provide appealing food and feeding assistance, and clarify patient goals and expectations.
- Don't prescribe a medication without conducting a drug regimen review.
- Don't use physical restraints to manage behavioral symptoms of hospitalized older adults with delirium.

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of cancer (Coll et al., 2020a, 2020b; Saletti et al., 2018), although the primary intent is to eliminate tests and procedures that will not benefit older adults and can cause unnecessary harm or reduced quality of life. Not all clinicians agree with using age cutoffs or life expectancy criteria for cancer screening and treatment recommendations. Schoenborn et al. (2020) found that while there was general agreement about the need to stop overscreening, clinicians questioned the use of age as the determining factor. Some felt that population health and individual patient management were misaligned and were concerned about bias and limiting access to care. Rowe et al. (2021) sought family physician rationales for not following the AGS Choosing Wisely recommendations; reasons included clinical inertia, patient preference, and underestimating harms or overestimating benefits of a test or procedure.

In addition to the AGS recommendations, other important Choosing Wisely endorsements include elimination of routine electrocardiograms and stress testing on those with no cardiovascular problems (Rehman et al., 2018), excluding lipid labs on those on statins, avoiding percutaneous coronary stents in those with stable angina, and omitting a full perioperative work-up for cataract surgery (Mafi et al., 2019). Several researchers continue to monitor health care for overuse. Morgan et al. (2019) has published an annual update on medical overuse for 5 years, noting that there is still much work to be done to eliminate the problem. Chalmers et al. (2021), using Medicare fee for service claims for 2015–2017, identified serious overuse issues in for-profit, non-teaching hospitals, primarily in the Southern United States. Zikmund-Fisher et al. (2017) identified several barriers to implementing Choosing Wisely, including malpractice, patient desire for testing or newer drugs, medication costs, insurance issues, lack of time for shared decision making, health-care providers ordering unnecessary tests, and rewards for ordering tests (payer, performance).

Welcome to Medicare Visit

Beginning in 2003 with the passage of the Medicare Modernization Act (MMA), the focus on older adults shifted to prevention and health promotion (Ng et al., 2017). In 2005, as part of the MMA, CMS introduced the Welcome to Medicare visit, also known as the Initial Preventive Physical Exam (IPPE); this includes a medical and social health history review as well as education about preventive services and their benefit. The Welcome to Medicare visit is a one-time covered service during the first 12 months of Medicare B enrollment for fee-for-service Medicare enrollees. For a variety of reasons, it has taken some time for this concept of preventive services in older adults to be adopted (Chung et al., 2018). Ng et al. (2017) reported that there was little to no change in use of preventive services by older adults since the initiation of the Welcome to Medicare visit. Chappell (2017) found that physicians were uncomfortable with the idea and did not know how to conduct this visit or the Medicare AWV. This resulted in additional tests being ordered, and the patient would then be billed for the visit, which is supposed to be a free benefit. This created some ill will between patients and clinicians over billing. There were also misunderstandings about the difference between the IPPE and a routine annual physical examination, which is not covered by Medicare. CMS has created a short video for clinicians to explain the difference (https://www.youtube.com/watch?v=r7yOUaMJyJU). The Welcome to Medicare visit and subsequent AWVs are best conducted by a clinician who is known and trusted by the older adult patient. In preparation for the visit, it is helpful to have information on local resources for health promotion, such as exercise programs, senior centers, home safety, Area Agency on Aging services, advanced directives, and substance abuse treatment sources, readily available. The goal of the visit is to develop a wellness plan using shared decision making with the patient. This can be reviewed and updated at subsequent AWVs. Components of the Welcome to Medicare visit and the AWV can be found on the CMS Medicare Learning Network Web site (https://www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/preventive-services/medicare-wellness-visits.html). Section 410.16 addresses the Welcome to Medicare Visit, which includes:

- Medical and social history with special attention to risk factors; family history, social history, medications, allergies, OTC use (including supplements)
- Functional, ADLs, home safety, hearing, and fall risk assessments
- Depression screening
- Vital signs, body mass index
- Opioid use, screening for abuse, alcohol, tobacco use
- Socialization, diet, and physical activity

Nurse practitioners, with their holistic health approach and emphasis on prevention, are the ideal clinicians to perform Medicare Welcome and AWVs.

Annual Wellness Visits

Annual wellness visits were introduced in 2011 as part of the Affordable Care Act, offering wellness and preventive health opportunities with no copay to older adults on Medicare (Fox & Shaw, 2015; Ng et al., 2017). The visit is covered once every 12 months and includes an initial health risk assessment and personalized prevention plan, jointly developed by clinician and older adult patient. After the initial visit, the health risk assessment and prevention plan are updated at subsequent visits (Coburn et al., 2018). If other elements are added (e.g., the patient comes in with an upper respiratory tract infection and asks for treatment), the patient will be billed for the visit because it is no longer an AWV (42 CFR 410.15).

Like the Welcome to Medicare visit introduced earlier, AWVs have had a slow uptake trajectory to date. Ganguli et al. (2018) reported that between 2011 and 2015 the percentage of eligible Medicare beneficiaries receiving AWVs only increased from 7.5% to 18.8%, and most of them are concentrated in higher socioeconomic areas, in practices associated with Accountable Care Organizations or with the Medicare Electronic Health Record Incentive Program (Albright et al., 2016). Using Medicare data up to 2015, Ganguli et al. (2018) found that 51.2% of practices offered no AWVs; only 23.1% offered visits to one-quarter of their eligible beneficiaries. Some practices serving lower socioeconomic groups did not offer AWVs, or those with complex care needs did not receive the visits. Tipirneni et al. (2019) proposed that AWVs be expanded to include other health-care

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team members such as social workers and community health workers and include an assessment of social determinants of health with referral to community resource agencies. This will decrease health disparities and allow those with limited access to care and complex health and social needs to benefit from preventive health planning. The Association of Community Health Centers and CMS have both developed tools to include social determinants of health in the AWVs; policy advocacy is needed to obtain funding and implement them (Tipirneni et al., 2019).

Simpson et al. (2018) and Simpson and Kovich (2019) surveyed advance practice nurses in Indiana who worked with Medicare patients related to underuse of AWVs. The survey found a deficit in their knowledge related to the content and extent of health risk appraisals and the need to develop a Personalized Prevention Plan (PPP). The main author of the survey advocates for advance practice nurses, with their focus on prevention and holistic health, to be the clinicians of choice for AWVs (Simpson, 2019). Most recently Simpson et al. (2021) reported on a research project where nurses performed monthly follow-up phone calls after AWVs to support older adults' PPP. They identified seven areas that impacted implementation of the PPP, including mental health, social support, stress, community/environment, motivation, health promotion behaviors, and healthcare access, discussing how the personalization and contact helped older adults to overcome barriers to their plan and how follow-up is needed to ensure success of the PPP. They advocate for a team-based approach to the AWV to alleviate the burden on clinicians' time and to offer patients a more holistic, comprehensive, and personalized approach to prevention, with follow-up as needed. Bluestein et al. (2017) surveyed eligible patients and providers in their practice. They found that if the provider recommended the AWV that patients would be more likely to do it; providers were also supportive but confused by the complexity of the regulations. They emphasize that staff support is essential to delivering AWVs; their model utilized a nurse care manager along with office staff for increasing awareness among eligible patients, scheduling the visit, and doing the risk assessment and personalizing the PPP under the supervision of the physician. An added benefit to the practice was that the nurse care manager learned more about the patients and was able to follow up on their specific needs while being a trusted contact with the provider.

The Welcome to Medicare visit and AWVs are important opportunities for health promotion and establishing a personalized prevention plan for older adults; clinicians are urged to devise a plan to incorporate them into their management of older adults.

Immunizations

The adult immunization schedule is updated annually and can be found on the CDC's Web site at https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html.

The information is also available on a free downloadable phone app (https://www.cdc.gov/vaccines/schedules/hcp/schedule-app.html#download)

The CDC and the Advisory Committee on Immunization Practices (ACIP) collaborate on immunization recommendations (Freedman et al., 2021).

INFLUENZA VACCINE

Everyone 6 months of age and older is recommended to get an annual influenza vaccine, including healthy adults. Vaccination is especially important for those older than 65 years because they are at higher risk of serious influenza complications and for people who live with or care for people at higher risk for serious influenza complications. Flu vaccine protects against the flu viruses that research indicates will be most common during the upcoming season. Every year vaccines are updated to better match circulating viruses. Full immunity from vaccination occurs after about 2 weeks. Influenza vaccines for older adults contain no live viruses (Schmader et al., 2021).

DIPHTHERIA, TETANUS, AND PERTUSSIS VACCINES

Adults who have never received the tetanus, diphtheria, and acellular pertussis (Tdap) vaccine should receive a single dose, even if they recently received the tetanus and diphtheria (Td) vaccine. After this dose, a booster of Tdap or Td should be administered every 10 years. Boostrix® should be used for adults 65 years or older; if this is unavailable, use either vaccine product (CDC, 2018).

RECOMBINANT ZOSTER VACCINE (SHINGRIX)

The recombinant zoster vaccine (RZV) Shingrix is currently the only zoster vaccine on the market. For those age 50 years or older, a two-dose series 2 to 6 months apart (minimum interval: 4 weeks; repeat dose if administered too soon) is recommended regardless of previous herpes zoster or history of prior zoster vaccine live (ZVL, Zostavax) vaccination (Gagliardi et al., 2019; Weinberger, 2021).

PNEUMOCOCCAL VACCINES

There are two different pneumococcal vaccines. The pneumococcal polysaccharide vaccine (PPSV23) and the pneumococcal conjugate vaccine (PCV13). Annually over 25,000 people older than age 50 die from pneumococcal disease (*Weinberger, 2021). With a weakened immune system, older adults are at greater risk for this condition, especially those with multimorbidities. Dosing recommendations are as follows (CDC, 2019):

- Routine vaccination: Age 65 years or older (immunocompetent): 1 dose PPSV23. If PPSV23 was administered prior to age 65 years, administer 1 dose PPSV23 at least 5 years after previous dose.
- Shared clinical decision making: Age 65 years or older (immunocompetent): 1 dose PCV13 based on shared clinical decision making if previously not administered. PCV13 and PPSV23 should not be administered during the same visit. If both PCV13 and PPSV23 are to be administered, PCV13 should be administered first. PCV13 and PPSV23 should be administered at least 1 year apart.

COVID-19 VACCINES

All older adults should be vaccinated against COVID-19 with one of the available vaccines licensed for emergency use in the United States. There is also an immunization global entity that collaborates with the United States and other countries on COVID-19 vaccine initiatives (Becerra, 2021; Privor-Dumm et al., 2021; Al-Tawfiq & Memish, 2019).

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As of October 22, 2021, when requested for an individual among the groups recommended for a booster consistent with the FDA emergency use authorization (EUA) and the CDC's recommendation, all CDC COVID-19 vaccination program enrolled providers must make available and administer upon request: (1) for those who received the Moderna primary series, a single Moderna COVID-19 vaccine booster dose (which is half of the dose that is administered for a primary series Moderna dose) at least 6 months after completion of the Moderna primary series, in risk groups CDC has previously recommended receive Pfizer-BioNTech booster dose, under the FDA's EUA; or (2) for those who received a primary Janssen dose, a single Janssen COVID-19 vaccine booster for all persons aged 18 years or older at least 2 months after receipt of the primary Janssen dose, under the FDA's EUA.

Among the groups recommended by CDC to receive booster vaccination after a Pfizer-BioNTech, Moderna, or Janssen COVID-19 vaccine primary series, a single booster dose of any of the currently authorized or approved COVID-19 vaccines may be provided as a heterologous booster dose, under the FDA EUAs.

With the onset of the COVID-19 pandemic, issues with vaccine hesitancy and mistrust of the health-care system by underrepresented communities came to the forefront. Bhanu et al. (2021) reported on a systematic review identifying barriers to vaccine use and suggestions to address them. Some factors included misinformation, the perception that being healthy meant that the vaccine was unnecessary, believing that the vaccine was ineffective or caused harm, mistrust of the health system, and having access to the vaccine. Reasons that facilitated acceptance of the vaccine were fear of acquiring the disease, understanding how the vaccine works, recommendation by a health-care provider trusted by the patient, vaccine setting and accessibility, realization of age as a risk factor, support from the community, and vaccine reminders (Bhanu et al., 2021). Researchers concluded that increased education efforts with the underrepresented communities combined with culturally competent discussions with trusted health-care professionals and expanded access can produce maximal vaccine action (Bhanu et al., 2021; Loskutova et al., 2020).

TRAVEL AND LEISURE

Older adults represent a significant proportion of international travelers. Reasons for travel include tourism, business, visiting friends and relatives, medical tourism, missionary work, volunteer opportunities, pilgrimage, and study abroad. Travel can be greatly rewarding but is physically demanding and poses risk to the traveler.

Travel Medicine

Travel Medicine is a worldwide interdisciplinary medical specialty and evolved from many published studies of disease risks in international travelers in the mid-70s. The first international conference on travel medicine was held in Zurich in 1988, and the International Society of Travel Medicine (ISTM) was formed during the second conference in Atlanta, 1991 (Dupont & Steffen, 2020). The ISTM has its own body of knowledge, practice guidelines, offers a Certificate in Travel Health (CTH) and continuing professional development, holds biannual conferences, and has a directory of travel clinics. Travel medicine has become increasingly complex due to constantly changing global infectious disease epidemiology, changing patterns of drug resistance, and travelers with challenging circumstances (see Box 2-2). Some of the main reasons primary care providers (PCPs) refer patients to travel medicine specialists (TMSs) include the need for yellow fever or other travel vaccines, complex itineraries, medical comorbidities, the need for malaria chemoprophylaxis, and older travelers (Gerstenlauer, 2019a). Unfortunately, many travelers do not seek pretravel health, or may obtain pretravel advice from practitioners who are not equipped to provide current and accurate information. This can result in mistakes with disastrous consequences for the traveler. To provide pretravel consultations, practitioners need to be able to impart all necessary information regarding the health risks of the destination countries and health prevention measures as well as order the appropriate vaccines and medications. Providers can access country-specific epidemiologic information from the WHO or the CDC. Travel health software programs such as Tropimed and Shoreland Travax can be used while seeing patients, but these programs do not replace travel medicine training. The *CDC Health Information for International Travel*, known as "The Yellow Book," is published biannually and is a great resource for health professionals providing care to international travelers.

The Older Traveler

More older adults (ages 60 and older) are traveling due to increased quality of life, medical technology advances, and a longer time spent in retirement. Most older travelers enjoy traveling and return home in good health. Perceived mental and physical benefits of international travel include a temporary escape from medical appointments, group camaraderie, broadening language and cultural horizons, increased physical activity, and better weather (Liew & Flaherty, 2020).

However, older travelers face higher health risks and exacerbation of their chronic disease than younger travelers because of normal age-related physiologic changes, immunosenescence, atherosclerosis, comorbid conditions, functional impairments, polypharmacy, and being in a foreign environment. Cardiovascular disease (CVD) disease is one of

BOX 2-2
International Travel During COVID-19 Pandemic

The COVID-19 pandemic declared by the World Health Organization on March 11, 2020, greatly impacted international travel. Overseas travel for U.S. citizens in 2020 decreased by 78.2% (National Travel and Tourism Office, 2021). At the time of this text's publication, The Centers for Disease Control and Prevention (2021) does not recommend traveling internationally unless a person is fully vaccinated by one of the FDA-approved COVID-19 vaccines. If an individual is not fully vaccinated and must travel, see cdc.gov/coronavirus. All travelers need to follow all airline and destination requirements related to travel, mask wearing, testing, or quarantine, before traveling.

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the most common preexisting medical conditions among international travelers, and is the leading cause of death, accounting for 70% (Liew & Flaherty, 2020). The lower atmospheric pressure during air travel may trigger decompensation of preexisting CVD and expose passengers to potentially life-threatening inflight cardiac emergencies. Malignancies and trauma are the next most common causes of death abroad, while infectious diseases account for less than 10% (Darrat & Flaherty, 2019). Older travelers are less able to adapt physiologically and less able to adjust to climatic extremes. Comorbid conditions such as hypertension, dyslipidemia, diabetes, and COPD are often coexisting, and each requires a combination of medications, leading to polypharmacy. Medication adherence during travel can be difficult because of time zone changes and travel disruption. Some travelers may withhold certain medications due to undesired effects (e.g., not taking a diuretic on a long plane ride). Selecting appropriate medication can be more difficult as older adults undergo physiologic changes that alter the pharmacokinetic and pharmacodynamic nature of medications potentially causing increased drug interactions, adverse events, and altered drug action (Lewis et al., 2019). In a large CDC study, 61% of drug-drug interactions occurred in adults 50 and older and 41% had at least three comorbid conditions (Sbaih et al., 2018). Older adults represent ~8% of ill-returned travelers but have more severe disease compared to younger travelers. Navigating airports, poorly constructed roads, walking uphill, and stair climbing can be physically demanding with risk of injury. Sensory impairments and language barriers create communication difficulties.

The Pretravel Consultation

The pretravel consultation offers a dedicated time to prepare travelers for the health risks that might arise during their trip. The objectives are to perform an individual risk assessment, communicate anticipated health and safety risks, and provide risk reduction management measures, such as immunizations, malaria chemoprophylaxis, medications as needed, and education for specific risk behaviors. During the consultation, provide copies of the individualized trip information and educational materials for later reference and recall to avoid information overload. Educational materials are available on the CDC Travelers Health Web page (www.cdc.gov/travel).

Barring any communication technology issues, telemedicine can serve as a convenient alternate to an in-person pretravel visit, reducing cost and time and improving access to care. For telemedicine pretravel consultations, providers need to follow the same professional standards as with in-person consultations (CDC, 2020). Medications and vaccinations can be prescribed during a telemedicine encounter. Travelers can then seek vaccinations in the PCP's office or local health clinics and obtain prescriptions from their pharmacy. A valuable resource on telemedicine, including requirements by state, is available at https://prognocis.com/wp-content/uploads/2017/01/Telemedicine-Whitepaper.pdf.

Air travel is contraindicated for patients with certain conditions, such as those who are less than 3 weeks post uncomplicated myocardial infarction and those who are less than 10 days post thoracic or abdominal surgery (CDC, 2020). Providers should determine whether recent outbreaks or other safety notices have been posted for the traveler's destination; information is available on the CDC and U.S. Department of State Web sites. Disease exposures related to special activities merit discussion (e.g., river rafting and schistosomiasis or leptospirosis, spelunking and histoplasmosis). Flying from lowlands to high-altitude areas and trekking or climbing in mountainous regions introduces the risk of altitude illness. Compared to tourists, individuals who are visiting friends and relatives have higher travel risks, seek pretravel health less often, and may only get required vaccines as opposed to routine and recommended vaccines (*Ferrara et al., 2019). Host factors and trip details to assess with degree of risk are listed in Table 2-1.

IMMUNIZATION STATUS

The provider needs to inform the traveler of the necessity to receive routine, required, and recommended vaccines based on their medical history, immunization status, and their travel destination. Country-specific required and recommended vaccines can be found in the travel software programs or at the CDC vaccinations page. Written confirmation of the doses taken should be noted on the WHO approved International Certificate of Vaccination or Prophylaxis (ICVP), referred to as the "yellow card." The yellow card must be kept with the traveler's passport because it serves as proof of vaccination. Preferably, all vaccinations should be taken at least 4 to 6 weeks before the planned departure to give full protection against a disease. If a traveler has an incomplete vaccine series, continue the series, regardless of how much time has passed. Providers should report all adverse events that might be caused by vaccination to the CDC/FDA Vaccine Adverse Events Reporting System (VAERS).

ROUTINE VACCINES

All travelers should be current with routine vaccines before international travel, regardless of destination. A visit for travel health is an opportunity to bring an incompletely vaccinated person current on routine vaccines. Routine vaccines for older adults include influenza, pneumococcal, Td/Tdap, zoster, COVID-19, and hepatitis B for those at risk. The CDC sets U.S. adult vaccination schedules annually, based on the recommendations of Advisory Committee on Immunization Practices (ACIP). Some travelers may be immune to the disease for which immunization is being considered. Testing for antibody titers can determine whether vaccination is needed. If a person does not have adequate written documentation of vaccinations, these persons should be considered susceptible and started on the age-appropriate vaccination schedule. Exceptions are that self-reported doses of influenza and pneumococcal 23 are acceptable (General Best Practices for Immunizations, 2021).

REQUIRED VACCINES

Country-specific required vaccines need to be prioritized because the traveler may be denied entry to the country without proof of vaccination. For example, travelers to Mecca and Medina annually for the week-long Hajj pilgrimage require COVID-19 vaccination and the quadrivalent meningococcal conjugate vaccine, which must have been received in the past 3 years and at least 10 or more days in advance of arrival because this pilgrimage is one of the largest mass gatherings and may result in the occurrence and spread of infectious diseases (Al-Tawfiq & Memish, 2019).

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TABLE 2-1 Risk Assessment During Pretravel Consultation

HOST FACTORS	LOWER RISK TRAVEL	HIGHER RISK TRAVEL
Age, gender, nationality, occupation	Younger age	Older age
Immune status, allergies	Immunocompetent	Immunocompromised
Underlying conditions	Controlled chronic disease(s)	Unstable chronic disease(s)
Mental status	Cognitively intact	Cognitive impairment
Physical status	Physically fit	Poor physical health
Functional status	High functional ability	Functional Impairments
Medications	Minimal medications	Polypharmacy (>5–6)
Special conditions, dietary restrictions, specialist care, prosthetics, medical equipment and supplies	No special conditions, routine health maintenance specialty care	Disability or handicap, psychiatric condition, seizure disorder, dietary restrictions, recent surgery, cardiopulmonary or cerebral vascular event, severe allergies, chronic diseases
Immunization status	Current with routine, prior travel vaccines	Not current with routine vaccines, refuse recommended vaccines, inadequate timing
Trip Details	**Lower Risk Travel**	**Higher Risk Travel**
Itinerary, country destination(s) including regions, order of travel	Industrialized, nontropical, one country	Developing, tropical countries, multiple countries
Duration of trip, departure and return dates	Shorter (<3 weeks)	Longer (>3 weeks)
Reason for travel	Tourism, business	Mission, medical tourism, volunteerism, visiting friends or relatives
Trip organization	Organized prepackaged	Independent
Traveling style	Group	Traveling alone
Accommodations	Tourist, luxury	Hostel, budget hotel, camp, local host family
Location of activities	Urban, large cities	Rural, smaller cities, villages, jungle, rain forests, desert, remote
Type of activities	Usual tourist	Adventure (i.e., backpacking, scuba diving, climbing, trekking, hiking, cycling, spelunking), refugee camps, disaster relief, medical missions, wading or swimming in fresh water, cruise ships
Budget	**High**	**Low**
General hygiene standards, food and water restrictions	Well-known tourist areas, adherence	Local restaurants, street vendors, tap water
Modes of travel	Commercial	Local, motor bikes, under own power
Prior international travel history	Previous travel, experience with malaria chemoprophylaxis, altitude	Novice or only traveled to Western Europe
Challenges related to prior travel	Uneventful	Eventful (illnesses, injuries, hospitalizations, evacuations)
Anticipated interaction with animals	None expected	Monkeys, bats, elephants
Risky sexual encounters	None anticipated	Anticipated
Supplemental travel insurance	Purchased	No plans to get

Yellow fever (YF) is a mosquito-borne vaccine-preventable disease that is transmitted to humans by the bites of infected mosquitoes. YF vaccination (YF-VAX) is mandatory for all travelers to certain endemic countries in tropical and subtropical regions of Africa and South America. This can include travelers who may be staying in an endemic country only briefly, such as during an airport layover, before being allowed to enter other countries on their itinerary (Tropimed, 2018). The CDC gives country-specific information on YF vaccine requirements and recommendations. Travelers need to have received their dose at least 10 or more days in advance of arrival. The ACIP published a new recommendation in 2015 that one dose of YF-VAX provides long-lasting protection and is adequate for most travelers (CDC, 2020). However,

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some countries may still require a booster after 10 years, and boosters may be recommended for certain travelers. YF-VAX is available only in certified yellow fever vaccination clinics.

RECOMMENDED VACCINATIONS FOR TRAVEL

- **Cholera** is caused by bacteria that are spread from person-to-person by drinking contaminated water or eating contaminated food. It is rare and can be prevented with practicing food and water precautions and hand washing in areas with outbreaks. A single-dose oral cholera vaccine was approved by the ACIP in 2016, but only for adults ages 18 to 64.
- **Hepatitis A** is a contagious virus found in contaminated food and water that causes liver disease. The vaccine is recommended for all international travelers regardless of travel destination (CDC, 2020).
- **Hepatitis B** is a contagious virus found in the blood and body fluids of infected people that causes liver disease. The vaccine mitigates the risk of nosocomial transmission if accessing rudimentary health services abroad, so is recommended for all international travelers (CDC, 2020).
- **Japanese encephalitis** is transmitted by mosquitoes. It occurs rarely but is a risk for travelers with rural exposure for more than 4 weeks or prolonged residence in endemic areas.
- **Meningitis** is caused by bacteria spread through close personal contact. The vaccine is recommended for Hajj pilgrims and for travelers to the meningitis belt of sub-Saharan Africa during the dry season (December through June). Only meningococcal ACWY is used for travel health.
- **Polio** is a disease caused by a virus. It is mainly spread by person-to-person contact, by eating undercooked food, or drinking fluids contaminated with the feces of an infected person. Travel to Afghanistan, Nigeria, and Pakistan may be a risk for this disease. A booster dose is recommended for previously vaccinated travelers to affected countries.
- **Rabies** kills about 60,000 people a year, 40% of whom are children (Global Alliance for Rabies Control [GARC], 2019). In the United States, rabies is mostly found in wild animals such as bats, raccoons, skunks, and foxes (CDC, 2020); however, in many other countries, especially rural areas of economically disadvantaged countries in Africa and Asia, up to 99% of human cases are acquired from infected dog bites, which are responsible for most of the rabies deaths in people (GARC, 2019). Rabies can be prevented by vaccinating pets, avoiding wildlife, and seeking medical care after exposure before symptoms start (CDC, 2020). The pre-exposure rabies vaccine will reduce the number and type of postexposure vaccines needed. When considering the rabies vaccine, consider the risk of animal exposure, access to local health care, and availability of rabies immune globulin and rabies vaccine at the traveler's destination. Providers should consult with local or state health officials for recommendations on postexposure prophylaxis recommendations (CDC, 2020).
- **Typhoid fever** is transmitted by contaminated food and water in endemic areas. Two vaccines are available: a weakened live oral with a series of 4 doses and an inactivated injectable.

Foodborne and Waterborne Illnesses

Travelers' diarrhea (TD) is the sudden onset of abnormally loose, frequent stools and affects 30% to 70% of travelers (CDC, 2020). Intestinal pathogens like bacteria cause 80% to 90% of TD, viruses 5% to 15%, and protozoa 10%. Careful selection of food and beverages and hand washing are important for prevention, but never eliminate the risk, typically due to poor local restaurant hygiene (CDC, 2020). Hepatitis A, cholera, and typhoid vaccines as appropriate, can help prevent food- or waterborne infections. Early antibiotic therapy can shorten the duration of illness, alleviate the disability associated with TD, and prevent the risk of long-term complications (CDC, 2020). Combining the antibiotic with an antimotility agent such as loperamide can shorten the course further. Using antimotility agents alone are recommended for mild TD, and antibiotics can be reserved for moderate to severe TD (CDC, 2020). To minimize the risk of antibiotic-associated side effects, colonization, and resistance, use single-dose regimens, and select an antibiotic agent that minimizes microbiome disruption and risk of colonization. The traveler will need to self-treat, so clear written guidance about TD prevention and instructions on treatment are crucial. Prophylactic antibiotics are not recommended for most travelers but may be considered for short-term travelers who are high-risk hosts (e.g., immunosuppressed, significant medical comorbidities) and where the benefits outweigh the risks (CDC, 2020; van Aalst et al., 2018). Fluoroquinolones have been the most effective antibiotics for the prophylaxis and treatment of bacterial TD, but increasing resistance to *Campylobacter* and *Shigella* species, the association with tendinitis, and increased risk of *Clostridioides difficile* infection limit their use. Alternatives include azithromycin, rifaximin, and rifamycin SV (CDC, 2020).

Mitigating Travel Risks

The pretravel consultation provides an opportunity to educate the traveler about their destination risks, as well as management of these safety risks and chronic diseases while traveling. Topics to be explored are numerous and could be organized into a checklist, placing priority on the most serious and frequently encountered issues (see Table 2-2). Provide the traveler a clinician letter on letterhead outlining allergies, existing medical conditions, prescribed medications (including generic names), and any medical equipment required. Give the traveler a list of travel clinics or sources of medical care in case they need to seek medical care; preferably with English-speaking, American-trained providers. Encourage the use of mobile applications to tract certain chronic illnesses while traveling. Medications requiring prescriptions in the United States may be available over the counter abroad; however, discourage travelers from buying these medications, especially from non-pharmacy sources, because of the risk of obtaining substandard or counterfeit medications (CDC, 2020). Advice on self-treatable conditions may minimize the need for travelers to seek medical care while abroad and possibly lead to faster return to good health.

Malaria Chemoprophylaxis

Malaria is a preventable illness but unfortunately is one of the most severe public health problems in the world. It is a leading cause of morbidity and mortality in many developing

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TABLE 2-2 Management of Safety Risks and Chronic Diseases While Traveling

CONDITION OR SITUATION	RECOMMENDATIONS
Acclimatization	• Drink at least 3 or 4 liters of bottled water or isotonic drinks daily. • Avoid intense physical activity in the first few days after arrival.
Allergies, life-threatening	• Carry EpiPen, diphenhydramine, steroid dose pack. • Avoid triggers.

Altitude	• The risk of altitude illness is dependent on the elevation at destination, rate of ascent, and exertion.
	• Inadequate acclimatization may lead to altitude sickness in any traveler going to 8,000 feet/2500 m (CDC, 2020).
	• Prior experience with altitude is a good indication of risk.
	• CDC guidelines are:
	  • Ascend gradually, if possible, not going directly from a low elevation to more than 9,000 ft/2,750 m sleeping elevation in 1 day.
	  • Once above 9,000 ft/2,750 m, move sleeping elevation no higher than 1,600 ft/500 m per day, and plan an extra day for acclimatization every 3,300 ft/1,000 m.
	  • Consider using acetazolamide to speed acclimatization if abrupt ascent is unavoidable.
	  • Avoid alcohol for the first 48 hours; continue caffeine if a regular user.
	  • Participate in only mild exercise for the first 48 hours.

Basic health practices	• Reinforce frequent hand washing, hand sanitizers, masks as required, carrying extra tissues or toilet paper, wearing safety belts, safe sexual practices, protection of passport, valuables. • Carry contact information for the primary care provider, specialists, and significant others.
Bloodborne pathogens	• Inform the patient on what to do in case of needlesticks or bloodborne pathogen exposure. • Discuss use of postexposure prophylaxis for HIV. • Avoid tattooing, body piercing, and injections with nonsterile needles.
Cardiovascular disease	• See a cardiologist pretravel. • Carry a copy of most recent electrocardiogram. • Bring identification cards for cardiac devices. • If on warfarin for atrial fibrillation, consider the use of nonvitamin K antagonist oral anticoagulants for a more favorable risk-benefit profile, easier adherence, and negation of the need for International Normalized Ratio monitoring abroad. • Carry nitrate spray.
Casual sex	• Use condoms. • Discuss use of postexposure prophylaxis for HIV. • Stress that avoidance is better.
Cognitive impairment	• If possible, have a traveling companion. • Consider treatment with acetylcholinesterase inhibitors and/or memantine. • Use pre-organized group travel. • Encourage patient to carry a hotel's business card and to photograph hotels, buses, cruise ships or tour company's names to help recall.
Diabetes	• Consider use of continuous glucose monitoring devices. • Check blood glucose every 4 to 6 hours during air travel. • Use mobile apps to tract blood glucose, activity, diet. • Accept somewhat higher blood glucose levels during travel days to avoid hypoglycemia. • Try to simplify treatment regimen to avoid multidosing. • Carry snacks to avoid hypoglycemia.
Dietary restrictions	• The patient may need to self-select from available food choices because specialty diets may not be available. • Check ahead of time to see if specialty diet can be ordered during travel. • The patient may need to bring their own food and snacks. Obtain a doctor's note allowing you to carry liquid "medical foods" through security at the airport so nothing is confiscated by Transportation Security Administration.
Environmental hazards	• Avoid contact with wild animals to reduce the potential for bites and scratches that can transmit rabies. • Avoid walking barefoot where animals can defecate to avoid certain parasitic infections. Avoid wading or swimming in freshwater where there is risk for schistosomiasis or leptospirosis. • Apply sunscreen to skin exposed to the sun. Adhere to water/food and feeding hygiene.
Fitness for travel	• Evaluation is not usually a part of pretravel consultation. • Recommend seeing the primary care provider at a separate appointment or a specialist as appropriate. • Encourage regular exercise or training in preparation.

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TABLE 2-2 Management of Safety Risks and Chronic Diseases While Traveling—cont'd

CONDITION OR SITUATION	RECOMMENDATIONS
Immunocompromised	• If a traveler cannot tolerate recommended immunizations or prophylaxis, consider counseling the traveler to change the itinerary, alter planned activities, or deferring the trip. • The traveler's specialty care provider may need to be contacted to discuss any concerns.
Jet lag	• This is a risk when traveling across more than three time zones. • It can affect mood, concentration, and coordination. • Per CDC (2020), if the destination is more than 3 hours different than your normal time zone, follow the sleep and waking routines of your destination when you arrive. • Consider scheduling travel to arrive at your destination at least 2 days before any important events.
Long-distance flights	• Use antithrombosis compression socks. • Ensure sufficient nonalcohol, non-caffeine hydration and exercise. • Take diuretics as prescribed.
Medications	• Keep medications in original bottles in carry-on luggage. • Keep a copy of medication list. • Ensure patient has enough for the entire trip plus a few days extra in case of delays. • If crossing time zones, take medication based on elapsed time and not time of day. • Check with the U.S. embassy or consulate to clarify medication restrictions in the destination country. Some countries do not allow narcotics or psychotropic medications. • Educate the patients about any drugs ordered and review for drug interactions. • Try to simplify schedules to avoid polypharmacy and help adherence. • If refrigeration is needed, consider travel ice packs, refrigerators in hotel rooms, or use of ice buckets.
Medical supplies	• Keep these in their original containers in carry-on luggage. • Check all batteries and bring extras. • Adapters may be needed. • Those on continuous positive airway pressure may need an alternative if destination has inadequate electricity.
Medical alert bracelet, necklace, or card	• Make sure those with drug allergies and certain medical conditions have one.
Motion sickness	• Try to avoid situations that tend to trigger symptoms. • Try to optimize position to reduce motion perception (e.g., drive instead of riding in a vehicle, or sit in the front seat, sit over the wing of an aircraft, choose a window seat on flights and trains) (CDC, 2020). • Maintain hydration and eat small frequent meals, limiting alcohol, caffeine. • Avoid smoking. • Use distractions such as controlled breathing, listening to music, aromatherapy, flavored lozenges.
Personal safety	• Avoid driving or riding at night in developing countries. • Avoid motor scooters, overcrowded buses and vans, walking alone, alcohol excess, which can increase the risk of personal assault, robbery, drowning. • Look for security bulletins related to the destination and consider areas to avoid (e.g., areas of civil unrest). • Have contact information for the U.S. embassy.
Foodborne or waterborne infections	• Perform regular hand washing. • Drink bottled or boiled water, carbonated drinks, beer, wine. • Avoid drinks with ice cubes, street food, unpasteurized dairy products. • Eat only fruits washed and peeled by yourself and recently cooked and hot-served food. • Avoid buffets.
Pulmonary conditions	• Notify the airline in advance if oxygen or other equipment is needed on the plane. • Prepare for chronic obstructive pulmonary disease or asthma exacerbations by having lung function tested before travel. • Have standby medications readily available.
Supplemental insurance	• Medicare and most medical insurance policies do not cover health care in other countries; consider supplemental insurance coverage for emergency medical and dental treatment, reimbursement for cost. • Consider trip cancellation insurance in the event of illness. • Provide information on medical evacuation/repatriation insurance and emergency medical assistance services.
Vectorborne diseases	• Use insect repellents with N, N-diethyl-meta-toluamide (DEET), 20%–40%. Apply over sunscreen. • Use mosquito nets. • Wear long pants, long sleeves, hats. • Avoid staying outdoors from dusk to dawn when insects are the most active. • Use air conditioning or tight window screens. • Treat clothing, gear, and bedding with permethrin up to 2 weeks before travel.

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countries (Gerstenlauer, 2019b). It occurs mostly in economically disadvantaged tropical and subtropical areas in Africa, South America, and South Asia. The most vulnerable are persons with little or no immunity against the disease, like travelers or migrants coming from areas with little or no malaria transmission. Visitors of friends and relatives have a disproportionately high prevalence of travel-related morbidity, particularly infectious diseases, including malaria (Volkman et al., 2020). They are also less successful at implementing key approaches to malaria prevention. Malaria is transmitted by the bite of an *Anopheles* mosquito that is infected by a protozoan parasite of the *Plasmodium* genus. For travelers going to malaria-endemic countries, it is important to discuss bite avoidance, insect repellents, malaria chemoprophylaxis, and symptom awareness. Malaria should always be a consideration when fever or other flu-like symptoms are present in a traveler who had risk, even after a year post travel (Gerstenlauer, 2019). Long-term travelers may face barriers in obtaining sufficient antimalarial medication to cover their entire stay because Medicaid and some private insurance plans in the United States limit antimalarial dispensing to a 34-day supply and may not permit vacation overrides (Volkman et al., 2020). Malaria chemoprophylaxis is not always covered by insurance.

Choosing a medication for chemoprophylaxis must be individualized and must consider the traveler's medical history, current medications, potential side effects, past history, cost of the medication, time till departure, as well as malaria drug resistance in the area(s) of travel. No antimalarial drug is 100% protective and must be combined with the use of personal protective measures. The drugs are generally well tolerated. Side effects may develop but do not usually require stopping the medication. All recommended chemoprophylaxis regimens involve taking a medication before, during, and after travel. Recommendations for drugs can be found in malaria information by country https://www.cdc.gov/malaria/travelers/country_table/c.html.

SUMMARY

Improved quality of life and ease of travel has increased the number of older adult international travelers. Older travelers have special considerations and unique challenges that are important to address in preventing travel-related complications. Older travelers should be specifically counseled to reduce their risks by obtaining pretravel health. PCPs are increasing called upon to provide travel health. The PCP needs to be ready to give tailored and accurate advice to a wide variety of travelers. APRNs are very suited to this role and are encouraged to seek additional professional training to become an effective travel health specialist.

CASE STUDY

J.B. is a 73-year-old widow, living alone in an urban area. It has been almost 3 years since her husband died, and J.B. has worked through her grief, settled his affairs, and is ready to move forward with her life. She has no children. Her sister lives in another state. J.B. has some close friends in the area. She currently attends Zumba classes twice weekly at the local senior center and she has joined a women's walking group. She also sings in the local community chorus group. J.B. is in good health; she takes lisinopril 10 mg PO daily for hypertension and a multivitamin. Family history includes:

- Father—deceased from a stroke
- Mother—deceased from colon cancer
- Younger sister—living with breast cancer.

Due to taking care of her late husband, J.B. has neglected some preventive health screenings. She recently began dating and is attracted to a 66-year-old divorcee, L.D., in the community chorus. He is very social; they have gone out for coffee and meals, and he is hinting that he wants to get to know her better. He has a vacation home in Florida and has invited her to come for a week.

1. You are seeing J.B. for her AWV. What are some important areas to address with her in terms of screening?
2. During the visit J.B. confides in you that she has not been sexually active in many years due to her husband's protracted illness and death. She is very attracted to L.D. but is also anxious and verbalized that L.D. seems to have had a few relationships since his divorce. How would you counsel J.B. about safe sex and dating?
3. What is the purpose of the AWV and what areas need to be addressed?
4. J.B. has a cough and a sore throat during the AWV and asks if you can examine her and prescribe something. How would you address this with her?

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CHAPTER 3

Exercise in Older Adults

Lori Martin-Plank

According to the 2020 Profile of Older Americans (Administration on Aging [AoA], 2021), people older than age 65 years represented 16% of the total U.S. population in 2019. The U.S. Census projection (2017) predicts that older adults will reach 23.4% of the population in 2034 and will outnumber children younger than 18 at that time. Most of these older adults will live in the community, either with a partner or alone, and will desire to age in place. This projection presupposes that these individuals must be physically able to function and perform most activities of daily living (ADLs) with minimal assistance or have caregiver assistance.

Data related to physical activity or exercise in older adults comes primarily from self-reported surveys, including the National Health Interview Survey (Federal Interagency Forum on Aging-Related Statistics, 2020). According to *Older Americans 2020*, in 2018 approximately 16% of older adults between 65 and 74 years of age met the standard for physical activity set by *Physical Activity Guidelines for Americans* (2nd ed.); this percentage decreased to 7% for those 85 years of age and older (Federal Interagency Forum on Aging-Related Statistics, 2020).

The Senior Report 2021 (United Health Foundation, 2021) reports that exercise in older adults in the United States (those aged 65 years and older), increased from 17.6% to 23.1% from 2017 to 2019. Although any increase in physical activity is encouraging, these figures clearly show that we are making very slow progress in this area. Recommendations from the *Physical Activity Guidelines for Americans* (2nd ed.) state that older adults aged 65 and older perform a minimum of 150 minutes weekly of moderate-intensity aerobic activity or 75 minutes weekly of vigorous-intensity aerobic physical activity, or an equivalent combination of both. Additional requirements call for muscle strengthening activities involving all major muscle groups, using at least moderate-intensity, two or more days weekly. If older adults cannot achieve 150 minutes of moderate-intensity aerobic exercise due to chronic health issues, they should be as active as their health conditions and abilities permit (U.S. Department of Health and Human Services, 2018). In addition to the above requirements, older adults should engage in balance training activities weekly and be mindful of safety in exercising related to their health conditions and abilities.

AVAILABLE RESOURCES

Guidelines and position statements for increasing physical activity in adults and older adults have been issued by several authorities, including the American College of Sports Medicine (ACSM), American Heart Association (AHA), U.S. Preventive Services Task Force (USPSTF), U.S. Department of Health and Human Services (USDHHS), and the National Strength and Conditioning Association (NSCA). Additionally, the *Healthy People 2030* initiative has several sections dedicated to health promotion in older adults. Numerous agencies, such as the Centers for Disease Control and Prevention (CDC), American Osteopathic Association (AOA), National Institute on Aging (NIA), National Council on Aging (NCOA), and Centers for Medicare and Medicaid (CMS), have programs to promote wellness and quality of life in older adults, including physical activity projects. The ACSM's Web site, Exercise Is Medicine, has extensive resources for providers and the public (http://exerciseismedicine.org), and the Preventive Cardiovascular Nurses Association (PCNA) has a Heart Healthy Toolbox (http://pcna.net/clinical-tools/tools-for-healthcare-providers/heart-healthy-toolbox) with a variety of free tools for use by clinicians. Health insurance companies, including Medicare Advantage plans, offer programs such as *SilverSneakers* at selected gyms or YMCAs, and most of these locations have individualized health coaching services available to their members. The challenge for clinicians working with older adults is learning about these free resources and discovering how to assimilate them in a meaningful way into their clinical encounters, and to engage patients in regular physical activity.

Research on Physical Activity in Older Adults

There is no shortage of research related to physical activity and older adults, including randomized clinical trials; however, the timelines in most studies are concentrated on short-term outcomes, and some studies have very specific foci, which may not easily translate into everyday life. Callow et al. (2020, 2021) and Jiménez-Pavón et al. (2020) both speak to the mental health benefits of physical exercise by older adults in the COVID-19 era, while Langhammer et al. (2018) address the overall importance of physical activity in older adults.

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Several studies focus on improving gait speed and dual-task processing to stimulate body and brain health (Merchant et al., 2021; Pothier et al., 2018; Trombini-Souza et al., 2020). Blumenthal et al. (2019) found that an aerobic exercise program in sedentary older adults with mild cognitive impairment improved their executive function abilities. Beauchamp et al. (2019) highlighted the impact of psychological mediators in promoting adherence to a group exercise program for older adults, while Cho and Kim (2020) reported on the beneficial psychological effect of exercise in older adults overall. A study by Buttelli and colleagues (2021) discovered that a Pilates program for older women with dyslipidemia successfully improved both aerobic capacity and blood glucose but had no effect on lipoprotein profile. Multiple studies addressed the positive impact of resistance training on strength and mobility (Fragala et al., 2019; Krčmárová et al., 2018; Kumbhare et al., 2019; Marcos-Pardo et al., 2019); Stojanović et al. (2021) devised a chair-based program with resistance bands that improved fitness and metabolic markers in older women. Sipilä et al. (2018) compared a program with physical and cognitive training versus physical training alone on mobility and fall prevention in older adults; Hopewell and colleagues (2020) performed a systematic review and meta-analysis of multifactorial interventions to prevent falls in community-dwelling older adults. Phu et al. (2019) found that balance training using virtual reality was effective in improving performance in older adults at high risk for falling. Muellmann et al. (2018) conducted a systematic review of the effectiveness of e-health interventions such as text messaging, phone apps, pedometers, and wearable fitness trackers in promoting physical activity in older adults; findings demonstrated that e-health interventions were effective in the short term. Results comparing the efficacy of e-health versus in-person program outcomes were inconclusive. A study by Rincé and colleagues (2021) showed the positive impact of an individualized rehabilitation program on mobility for the oldest-old.

Of the many areas of research related to older adults and physical activity, almost all demonstrate the value of interventions to promote physical activity and there has been great diversity in research approaches to this topic. Studies that focused on older adults and exercise found that short-term interventions, both individual and group and face-to-face and electronically, were effective in increasing physical activity when delivered as part of a multifaceted program of educational and cognitive-behavioral participation. Health education alone was ineffective in this population. Healthcare personnel–recommended physical activity and an exercise prescription were effective in the short term. None of the studies reviewed had a long enough duration to measure persistence of effort.

BARRIERS AND FACILITATORS TO EXERCISE FOR OLDER ADULTS

Patient Barriers

- Lack of time
- Perceived need for equipment
- Perceived barrier to beginning exercise/physical activity
- Disability or functional limitation
- Unsafe neighborhood or weather conditions
- No parks or walking trails
- Depression
- High body mass index (BMI)
- Lack of motivation
- Interpersonal loss or significant life event
- Ignorance of what to do

Patient Facilitators

- Social support
- Positive self-efficacy
- Motivation to engage in physical activity
- Good health, no functional limitations
- Frequent contact with prescriber
- Regular schedule, planned program
- Satisfaction with program
- Insurance incentive
- Improvement in mobility or health condition
- Staff (of exercise or physical therapy facility) support

Clinician Barriers

- Time to assimilate information on physical activity specific to older adults
- Time to counsel patients on the importance of physical activity and lifestyle changes
- Lack of knowledge about how to write an exercise prescription
- Lack of awareness of resources in the community to support physical activity in older adults
- Focus on medical interventions for chronic disease management in lieu of lifestyle changes
- Failure to follow up to insure implementation of recommendations for physical activity

Examples of Medical Contraindications for Exercise Therapy

- Unstable angina
- Uncompensated heart failure
- Severe anemia
- Uncontrolled blood glucose
- Unstable aortic aneurysm
- Uncontrolled hypertension or tachycardia
- Severe dehydration or heat stroke
- Low oxygen saturation

PLAN FOR INCORPORATING EXERCISE INTO PATIENT ENCOUNTERS

One of the easiest ways to address exercise or physical activity with older adults is utilizing the Welcome to Medicare visit or the Annual Wellness Visit (AWV). Both visits are focused on individual patient issues, including lifestyle, items identified during the health risk assessment (such as sedentary lifestyle), and patient goals, and both have more encounter time built into the visit.

There are several helpful professional resources that focus on the components of an exercise prescription and how to

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write one, including Medscape, the American College of Sports Medicine (ACSM), *UpToDate*, and the American Academy of Family Physicians (see Resources). Clinicians' knowledge about their older adult patients and their functional levels and interests can help in designing the exercise prescription or plan. For example, some older adults enjoy dancing; some like to play golf, bike, or swim; while others may prefer tai chi or yoga in addition to walking. The ideal exercise prescription is one that the patient will follow; any increase in physical activity is better than none. For many older adults who are sedentary, walking is an aerobic activity. The four recommended components for maximal benefit from an exercise program are aerobic activities, resistance training for muscle strengthening, flexibility exercises (stretching), and balance training to lessen the chance of falls (DiPietro et al., 2019; Fragala et al., 2019; King et al., 2019; Tricco et al., 2017). Recent studies have demonstrated that there are comparable benefits from high-intensity interval training (HIIT) and moderate-intensity continuous training (Campbell et al., 2019). Erickson et al. (2019) found that physical activity benefited those with cognitive deficits in later life. Another systematic review by Jakicic et al. (2019) reported that, contrary to prior evidence, physical activity of any bout duration was correlated with improved health outcomes, including all-cause mortality; this is encouraging for those with limited endurance or attention span.

The ACSM recommends that clinicians discuss the benefits of exercise and physical activity at every visit (2021); their *ASCM's Guidelines for Exercise Testing and Prescription* (11th ed., 2021) is a comprehensive resource and includes exercise prescriptions that are specific to several health conditions. This can serve as a quick resource for busy clinicians in addition to their Exercise is Medicine Web site.

Clinicians can now schedule visits billed with extra time to initiate or follow up on a prescribed exercise program. Busy practices can train a staff member to meet with patients to monitor progress of existing exercise programs, contract with an exercise physiologist or coach, or incorporate physical therapy training into the initial program. Older patients can also be referred to health coaching services or gym programs included in their medical insurance. Clinicians can set an example of healthy exercise by scheduling times to walk with patients in a nearby park or somewhere close to the office or sponsoring a patient walking group. Telehealth visits utilizing motivational interviewing can be used for exercise counseling and follow-up. The clinician office can display materials promoting exercise and other healthy lifestyle behaviors or have a dedicated closed-circuit TV with messages. Handouts depicting online programs dedicated to older adult fitness can be made available to patients.

Clinician judgment should be used when assessing the patient and prescribing an exercise routine. Major authorities agree that all adults who do not have symptoms and have no diagnosed chronic health condition, such as osteoarthritis, heart disease, or diabetes mellitus, do not need to consult with a health-care professional about increasing physical activity (Centers for Disease Control and Prevention [CDC], 2021). Patients with chronic conditions should consult a health-care provider for physical activity goals that are realistic and safe (U.S. Department of Health and Human Services, 2018). Healthy adult men older than 45 years and healthy women older than 55 years who are considering a *vigorous* exercise program need health-care provider screening and routine stress testing. Sedentary older adults and all adults with cardiac disease or strong risk factors should undergo screening and stress test if they are undertaking a *vigorous* exercise program (Lee et al., 2017).

In 2018, 1.2 million U.S. adults aged 65 and older resided in a long-term care (LTC) facility (AARP, 2019), many of them representing frail older adults. Izquierdo et al. (2016) raised the question of whether it is ethical not to provide physical activity for frail older adults. At the same time, a group of preeminent geriatricians, physical therapists, and gerontologists formed a taskforce under the auspices of the International Association of Geriatrics and Gerontology Global Aging Research Network (IAGG-GARN) and the European division of IAGG to make recommendations for physical activity and exercise standards in long-term care settings (de Souto Barreto et al., 2016). Acknowledging the heterogeneity of the population, the group devised two sets of recommendations—one advocating for a decrease in sedentary behavior for all residents of LTC settings, and the other utilizing evidence from metanalyses and other research to develop a guideline for a select subset of LTC residents capable of participating in a structured exercise program to maintain functional and ADL abilities for as long as possible. For the first group, utilizing short breaks in sitting two to five times daily, such as walking to the dining room instead of using a wheelchair, is recommended. For those capable of structured exercise, a multicomponent program of moderate intensity done twice weekly for 35 to 45 minutes each time is recommended (de Souto Barreto et al., 2016). The importance of promoting physical activity in older adults living in LTC facilities cannot be underestimated because this age-group increases in numbers; benefits are not only individual, but also economic in terms of preventing costly hospitalizations and delaying functional decline.

KEY GUIDELINES FOR SAFE PHYSICAL ACTIVITY

The key guidelines for adults also apply to older adults (Physical Activity Guidelines Committee, 2018). In addition, the following key guidelines are for older adults only:

- As part of their weekly physical activity, older adults should do multicomponent physical activity that includes balance training as well as aerobic and muscle strengthening activities.
- Older adults should determine their level of effort for physical activity relative to their level of fitness.
- Older adults with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely.
- When older adults cannot do 150 minutes of moderate-intensity aerobic activity a week because of chronic conditions, they should be as physically active as their abilities and conditions allow (Table 3-1).

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TABLE 3-1 Examples of Common Health Conditions in Older Adults with Exercise Recommendations

HEALTH CONDITION: CONSIDER COMORBIDITIES FOR ALL	RECOMMENDED ACTIVITIES: START LOW INTENSITY, GO SLOW	COMMENTS: CONSIDER COMORBIDITIES FOR ALL
Osteoarthritis	Walking, aquatic activities, tai chi, resistance exercises, cycling	Vary type and intensity to avoid overstressing joints; heated pool
Coronary artery disease	Walking, treadmill walking, cycle ergometry	Supervised program with blood pressure and heart rate monitoring
Heart failure	Walking, treadmill walking, cycle ergometry	Individualize to patient; supervised program
Type 2 diabetes mellitus	Resistive, aerobic, aquatic, recreational activities	Proper shoe fit; may need insulin reduction if insulin dependent
Anxiety disorders	Walking, biking, weightlifting	If able to do high-intensity exercise, this benefits anxiety
Depression	Walking, cycling, recreational activities	Group participation helpful to keep patient engaged
Fibromyalgia	Aerobic, aquatic therapy, strengthening, tai chi, Pilates	Heated pool, gentle stretches, counsel about possible increased pain initially
Chronic obstructive pulmonary disease	Cycle ergometer, treadmill walking; individualize	Supervised program—consider pulmonary rehabilitation program
Chronic venous insufficiency	Walking, standing exercises	Supervised program
Osteoporosis	Weight-bearing exercises, weight training	Assess balance and risk for falls before beginning
Parkinson's disease	Walking, treadmill walking, stationary bike, dancing, tai chi, Pilates, boxing	Assess balance and risk for falls before beginning; American Parkinson Disease Association resources
Peripheral arterial disease	Lower extremity exercises, treadmill walking, walking	Very short intervals initially, progress as tolerated
Age-related sleep disorders	Tai chi, walking, aquatherapy, biking	Assess balance and risk for falls before beginning
Dementia	Walking, recreational activities	Provide safe environment, assess fall risk and ability to participate

Source: Adapted from Goodman, C., & Helgeson, K. (2011). Exercise prescriptions for medical conditions. *F.A. Davis.*

Clinical Recommendation	Evidence Rating	References
Exercise alone and various combinations of interventions reduces the risk of injurious falls in older adults.	A	Lee & Kim, 2017 Tricco et al., 2017
Strong evidence demonstrates that participation by community-dwelling older adults in multicomponent group or home-based fall prevention physical activity and exercise programs can significantly reduce the risk of injury from falls, including severe falls that result in bone fracture, head trauma, open wound soft tissue injury, or any other injury requiring medical care or admission to hospital.	A	2018 Physical Activity Guidelines Advisory Committee (PAGAC), 2018
Strong evidence demonstrates that aerobic, muscle-strengthening, and multicomponent physical activity improves physical function in the general aging population.	A	PAGAC, 2018
Strong evidence demonstrates that physical activity improves several physical function outcomes, including walking, balance, strength, and disease-specific motor scores in individuals with Parkinson's disease.	A	PAGAC, 2018
Limited evidence suggests that for individuals with cognitive impairment, physical activity programs improve physical function, including measures of activities of daily living (ADLs).	B	PAGAC, 2018 Blumenthal et al., 2019 Erickson et al., 2019
Strong evidence demonstrates that physical activity improves measures of physical function in older people with frailty.	A	PAGAC, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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SUMMARY

There is strong evidence from a variety of sources that increasing physical activity in older adults will improve health and quality of life in both healthy adults and those with chronic health conditions, in the community and in long-term care settings (Buttelli et al., 2021; Campbell et al., 2019; de Souto Barreto, 2016; DiPietro et al., 2019; Hopewell et al., 2020; Kumbhare et al., 2019; Langhammer et al., 2018; Lee et al., 2017). Primary care providers can play an important role in promoting physical activity for all older adult patients at every visit, using an individualized approach. Resources are available to assist with this effort.

CASE STUDY

A. G., a 72-year-old man, comes in for follow-up of laboratory test results. He has coronary artery disease (CAD), hypertension (controlled), impaired fasting glucose (IFG), benign prostatic hyperplasia, and mild degenerative joint disease (DJD). Since being diagnosed with IFG he has cut back on soda consumption and is also seeing a dietitian for counseling. He is a former smoker (last use 12 years ago) and admits to being a "couch potato." Current medications: Lisinopril 20 mg orally (PO) daily, hydrochlorothiazide 12.5 mg PO daily, simvastatin 20 mg PO daily in the evening, and tamsulosin 0.4 mg PO daily. He has a prescription for nitroglycerin 0.4 mg sublingually as needed for chest pain but has never needed to use it. He occasionally takes Tylenol Arthritis Pain or Aleve if the DJD bothers him. Vital signs are blood pressure (BP) 134/72, heart rate (HR) 70 (reg), respiratory rate 18 breaths per minute (bpm) (afebrile), and BMI 34.2. Pulse oximetry is 99% on room air. Laboratory test results are unremarkable except for high-density lipoprotein (HDL) 32 and fasting blood sugar (FBS) 125. Mr. G expresses frustration at the lack of change in his fasting glucose despite cutting back on soda. He asks you, "What else can I do? I don't want to get diabetes." You encourage him to increase his physical activity level gradually, beginning with walking.

1. What strategies will you use to promote increased physical activity in this patient?
2. What additional objective data will you be assessing for?
3. What national guidelines are appropriate to consider?
4. Will you need to order any tests before he begins this program? If so, what tests?
5. Are there any screening tools that you want to use?
6. What is your plan of care?
7. Are there any *Healthy People 2030* objectives that you should consider?
8. What additional patient teaching may be needed?
9. How will you follow up on the planned increase in physical activity?

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ADDITIONAL RESOURCES FOR CLINICIANS

https://www.ncoa.org/article/exercise-programs-that-promote-senior-fitness
https://www.ncoa.org/professionals/health/center-for-healthy-aging
https://www.nia.nih.gov/health/how-older-adults-can-get-started-exercise#plan
https://www.who.int/news-room/fact-sheets/detail/physical-activity
https://www.cdc.gov/physicalactivity/basics/index.htm
https://emedicine.medscape.com/article/88648-overview
https://www.aafp.org/afp/2017/0401/p425.html
https://www.acsm.org/docs/default-source/publications-files/acsms-exercise-testing-prescription.pdf?sfvrsn=111e9306_4
https://www.exerciseismedicine.org/eim-in-action/health-care/health-care-providers/

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CHAPTER 4

Nutritional Support in the Older Adult

Evelyn Duffy

AGING EFFECTS ON NUTRITIONAL HEALTH

Nutritional issues in older adults are common. Both extrinsic and intrinsic factors contribute to the risk for developing undernutrition and overnutrition/obesity (Kalan et al., 2020). Malnutrition can be present in both conditions (Scrinis, 2020). Identifying factors that can contribute to a decline in nutritional health can allow for safeguards to be put into place before the patient experiences malnutrition (Haines et al., 2020). Extrinsic factors include access to transportation, which can limit access to both food and health service, safety of the environment in which the patient lives that can compromise the ability to get outside and exercise, and the cohort of the older adult. If more traditional male and female roles were adopted, with the loss of a spouse, a male may have no experience in food preparation and undernutrition becomes a very real possibility. Food insecurity in older adults was evaluated in a study by Fernandes et al. (2018). They note that 23% of older adults live in a food insecure household. Those 70 to 74 years old, females, those with less education, and those with low income or reporting it, was difficult to live within their current income. The group living in a food insecure household were also more likely to have a chronic disease or obesity. When the choice is between medical care, medications, or food, the latter is the priority. It is not surprising that the group reporting food insecurity also reported a lower quality of life (Fernandes et al., 2018, Steiner et al., 2018).

PHYSIOLOGICAL CHANGES WITH AGING THAT AFFECT NUTRITIONAL HEALTH

The process of aging itself affects the ability of older adults to achieve adequate nutrition. Changes in physiology from the loss of olfactory sense, decrease in the sense of taste, compromised dentition, decreased saliva, decreased gastric acidity, lactose intolerance, decreased intestinal mobility, and constipation all affect the nutritional status of older adults. The result of these challenges can be involuntary weight loss (Chapter 7, Symptoms and Syndromes) and malnutrition. Patients may not be aware of the loss of weight, or they present with that concern.

Age affects the gastrointestinal (GI) system from the mouth to the rectum. In the mouth the tooth enamel thins, increasing the risk of decay, which is increased further by the wearing down of the surface of the tooth, often exposing the pulp. There is bone loss in oral structures so that teeth may become loose. Improved dental hygiene and regular dental care have resulted in fewer older adults becoming edentulous, but dentures are not yet a thing of the past and tooth loss is still quite common. Root canals and implants are costly and not covered by Medicare, leaving many older adults unable to afford these options. Medicare managed care plans often include dental coverage and have resulted in the increase in the older adult population choosing these commercial insurance plans (Meyerhoefer et al., 2019).

In older adulthood, the oral mucosa thins and there is less saliva production. This is compounded by many medications commonly used by older adults, especially those with anticholinergic properties. The lack of saliva makes the creation of a food bolus difficult and increases the risk of dysphagia. The number of taste buds on the tongue declines with age, decreasing or changing the sense of taste. The sense of smell may decrease or be absent, and the combination of decreased taste and smell results in a decrease in the perception of the flavor of food. Flavor is what is often referred to as the "taste" of food, but flavor is a result of smell and taste, as well as the qualities of food that stimulate the pain fibers on the tongue, namely spiciness, temperature, and texture. When older adults cannot appreciate the flavor of food, they often lose their appetite and loss of appetite is a leading cause of malnutrition (Fluitman et al., 2021).

With aging there is an increase in body fat and decrease in lean muscle mass. Fat doesn't metabolize nutrients, so the result is a decrease in the metabolic rate and calories burned. This decreases the caloric need but not the nutrients required, which remain the same or increase. The diet of older adults

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needs to include foods that are nutrient dense (Baugreet et al., 2017). Both medication and disease common in older adults contribute to a decrease in hydrochloric acid production and a subsequent decline in the absorption of micronutrients. Although the liver decreases in size with aging, it maintains function, and decreased serum albumin should not be considered a normal change with aging. However, serum albumin is not a reliable marker for malnutrition because it is a negative acute phase protein and decreases in response to inflammation, which occurs with many chronic diseases that are common in older adults. There is a decline in intestinal motility which, when combined with decreased fluid intake and a decrease in body fluid, increases the possibility of constipation (An et al., 2018).

A loss of functional ability can also compromise the ability to meet nutritional requirements. When instrumental activities of daily living (IADLs) are affected, it may impair ability to get to the store and purchase food, as well as coordinate and prepare food in the kitchen. A decline in activities of daily living (ADLs) can make the process of eating challenging. Diseases such as depression, cognitive impairment, or stroke can all affect the ability to use utensils or the desire to feed oneself. To help those with physical limitations, the use of positioning or adaptive equipment, the introduction of finger foods, or feeding the patient can improve nutrition. Nurse practitioners should consider referral to occupational therapy for any patient experiencing feeding, eating, or swallowing difficulty. Occupational therapists are essential to helping patients address these needs and improve functional independence (American Occupational Therapy Association, 2017).

CALORIC NEED

A calorie is a measure of energy, and caloric needs are based on energy expenditure. As adults age and muscle mass declines, so does the metabolic rate, energy expenditure, and caloric need. The recommended daily caloric intake is dependent on activity level and sex. Recommendations for women older than 65 years include: sedentary 1,600 kcal; moderately active 1,800 kcal; or active 2,000 kcal. For men, the requirement is greater: sedentary 2,000 kcal; moderately active 2,200 kcal; active 2,600 kcal to age 75 years, and then it declines to 2,400 kcal. To calculate caloric needs for an individual, an excellent online resource is available at http://www.bmi-calculator.net. At this site, using the Harris Benedict Equation, you can calculate caloric needs as well as body mass index (BMI), body fat percentage, and basal metabolic rate (BMR). Using the calculator, you can also determine calories needed for weight loss or weight gain over a specified amount of time.

NUTRIENTS

Although the need for calories decreases as adults age, the need for nutrients does not, and in some cases may increase, as it does for calcium (Clegg & Williams, 2018). This increases the challenge of meeting nutritional needs. The current edition of *Dietary Guidelines for Americans 2015–2020* (8th ed.) was published in 2020 and is available for download at https://health.gov/sites/default/files/2019-09/2015-2020_Dietary_Guidelines.pdf. Appendix 7, *Nutritional Goals for Age-Sex Groups Based on Dietary Reference Intakes & Dietary Guidelines Recommendations*, is a comprehensive list of all nutrients for adults over the age of 50 years (see Table 4-1).

TABLE 4-1 Daily Nutritional Goals for Age–Sex Groups Based on Dietary Reference Intakes and *Dietary Guidelines* Recommendations

	FEMALE 51+	MALE 51+
Calorie level(s) Assessed	**1,600**	**2,000**
Macronutrients		
Protein, g	46	56
Protein, % kcal	10–35	10–35
Carbohydrate, g	130	130
Carbohydrate, % kcal	45–65	45–65
Dietary fiber, g	22.4	28
Added sugars, % kcal	<10%	<10%
Total fat, % kcal	20–35	20–35
Saturated fat, % kcal	<10%	<10%
Linoleic acid, g	11	14
Linolenic acid, g	1.1	1.6
Minerals		
Calcium, mg	1,200	1,000[a]
Iron, mg	8	8
Magnesium, mg	320	420
Phosphorus, mg	700	700
Potassium, mg	4,700	4,700
Sodium, mg	2,300	2,300
Zinc, mg	8	11
Copper, mcg	900	900
Manganese, mg	1.8	2.3
Selenium, mcg	55	55
Vitamins		
Vitamin A, mg RAE	700	900
Vitamin E, mg AT	15	15
Vitamin D, IU	600[b]	600[b]
Vitamin C, mg	75	90
Thiamin, mg	1.1	1.2
Riboflavin, mg	1.1	1.3
Niacin, mg	14	16
Vitamin B_6, mg	1.5	1.7
Vitamin B_{12}, mcg	2.4	2.4
Choline, mg	425	550
Vitamin K, mcg	90	120
Folate, mcg DFE	400	400

[a] *Calcium RDA for males aged 71+ years is 1,200 mg.*
[b] *Vitamin D RDA for males and females aged 71+ years is 800 IU.*
Data from: U.S. Department of Health and Human Services and U.S. Department of Agriculture. (2015). 2015–2020 Dietary Guidelines for Americans *(8th ed.). https://health.gov/dietaryguidelines/2015/guidelines/appendix-7/#table-a7-1; Institute of Medicine. (2006).* Dietary reference intakes: The essential guide to nutrient requirements. *National Academies Press; and Institute of Medicine. (2010).* Dietary reference intakes for calcium and vitamin D. *National Academies Press.*

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Calcium and Vitamin D

Aging affects the levels of both calcium and vitamin D. The role of both calcium and vitamin D in maintaining healthy bones and teeth is well understood. Calcium is also important in maintaining cell structure and has a role in almost every system in the body. It is responsible for vascular contraction and vasodilation, muscle function, nerve transmission, intracellular signaling, hormonal secretion, and in the clotting cascade. An expanded role of vitamin D in the health of the cardiovascular, respiratory, endocrine, nervous, and immune system has been noted, as well as its effect on the expression of genes that can cause cancer.

Serum calcium levels are maintained with very narrow limits of 8.5 to 10 mg/dL. Serum calcium reflects both calcium bound to protein and ionized calcium. When albumin is low for any reason, the serum calcium may be artificially low, and a corrected calcium needs to be calculated. The formula, *Corrected calcium (mg/dL) = measured total Ca (mg/dL) + 0.8 (4.0 - serum albumin [g/dL]), where 4.0 represents the average albumin level in g/dL*, is complex, but apps and online calculators are readily available. To complete the calculation, you must know both the serum calcium and albumin, so it is important that the laboratory test includes both measures. Many basic metabolic panels do not include albumin. Although ionized calcium will provide a more accurate measure, it is not used routinely due to the cost. It is appropriate to order if the patient has either hypocalcemia or hypercalcemia as calculated from serum calcium. Aging affects the absorption of calcium from the intestines and the ability of the kidney to synthesize $1,25(OH)_2D_3$, which helps to regulate calcium absorption. The increase in lactose intolerance with aging can contribute to low intake of calcium due to the avoidance of dairy products. The current daily nutritional goal for calcium for adults older than 50 years is 1,200 mg a day for women and 1,000 mg a day for men. Acquiring calcium from food sources rather than taking supplements is preferred because that approach also results in the consumption of other nutrients.

Screening for vitamin D deficiency has become routine in many practices, and a serum 25(OH)D is the correct test to order. Levels less than 30 nmol/L (less than 12 ng/ml) are associated with poor bone health. Levels between 30 and 50 nmol/L (12 to 20 ng/mL) may represent inadequate levels, but a level greater than or equal to 50 nmol/L (greater than or equal to 20 ng/mL) is considered adequate. Very high levels greater than 125 nmol/L (greater than 50 ng/mL) can result in adverse effects. Synthesis of vitamin D occurs in the skin and depends on exposure to sunlight. With aging, the skin's ability to convert vitamin D declines. Dark-skinned individuals require more sunlight to stimulate the production of vitamin D. Vitamin D is not present in many foods, but it is often fortified in dietary sources. The current daily recommendation for vitamin D is 600 IU for those adults older than 50 years and 800 IU for those older than 70 years. High doses of vitamin D supplementation are contraindicated in hyperparathyroidism, so a parathyroid level may be indicated prior to initiating therapy if there are symptoms or signs of that disorder. The current use of vitamin D supplementation is being questioned as several intervention studies have not been able to show a benefit (Amrein et al., 2020).

Vitamin B_{12} and Folate

Vitamin B_{12} is necessary for DNA synthesis and red blood cell production. It is a nutrient present in animal-based foods or from supplements. Vegetarians and those who abuse alcohol are at risk for B_{12} deficiency. Several common medications can interfere with the absorption of B_{12}, including metformin, proton pump inhibitors, and H_2 blockers (Mohn et al., 2018). A deficiency of vitamin B_{12} can result in a megaloblastic, macrocytic anemia and neurological symptoms. Peripheral neuropathies, cognitive impairment, and functional disability can all result from the deficiency.

Folate, folic acid, is also a B vitamin, B_9. Large amounts of folic acid have the potential to mask a vitamin B_{12} deficiency. Like B_{12}, it is necessary for DNA metabolism and red blood cell development. Folate is present in dark leafy green vegetables, liver, and lentils. Analysis of older adults' food and energy intake found that there was a decline in the consumption of micronutrients, including B vitamins. Their diets were high in fats and added sugars, and they were possibly consuming too much folate (vitamin B_9), which since 1996 has been mandated by the U.S. Food and Drug Administration (FDA) to be included in grain products to prevent neural tube defects in babies. If older adults don't get enough vitamin B_{12} in their diet the folic acid may exacerbate some of the symptoms of B_{12} deficiency.

Fiber

The recommended daily reference intake for fiber in adults older than 50 years is 22.4 g for women and 28 g for men. To put this into perspective, a cup of oatmeal contains 9 g of fiber whereas an apple is just over 2 g. The intake of dietary fiber is often low in older adults and if increased too quickly can result in bloating and gas. Barkoukis (2016) recommends increasing intake of fiber at 3 to 5 g increments twice weekly. The role of fiber in improving glycemic control, reducing cholesterol, increasing stool bulk, and decreasing transit time, which is increased in older adults and contributes to constipation, is critical to adequate nutritional health.

In addition to these benefits, fiber-rich foods such as fruits, vegetables, and whole grains increase the total intake of vitamins, minerals, and antioxidants. Foods low in fiber are also often those foods with a lower nutrient composition and decrease the nutrient density of the older adult's diet and increase the risk of malnutrition and obesity. When older adults are very frail, careful assessment is needed to balance their nutritional need with the possibility that a diet high in fiber may cause early satiety. A diet high in fiber requires adequate fluid intake to avoid the development of constipation or, even in the most severe case, bowel obstruction.

DEHYDRATION

Dehydration is a form of malnutrition. The risk for dehydration increases with age. The physiological changes with aging increase the risk of inadequate fluid. A decrease in fluid consumption can be a direct result of the decline in thirst sensation or result from a fear of incontinence. More fluid means more trips to the bathroom, which can be challenging to older adults with functional limitations from arthritis or other chronic disease, cognitive decline, or frailty. Concentration of urine by the kidneys is decreased, resulting in less fluid being

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reabsorbed and smaller fluid reserves (Vilmundardottir & Skuladottir, 2021). These changes may be complicated by medications, particularly anticholinergics and diuretics.

Dehydration can result in constipation, fecal impaction, cognitive impairment, further functional decline, and even death. The role of dehydration in the development of delirium, while often multifactorial, is drawing increased attention (Mudge et al., 2021). Conversely, delirium can result in dehydration. Risk factors for dehydration include frailty and cognitive and sensory impairment, all of these are also risk factors for delirium.

FEEDING

Current practice encourages the use of oral food intake to meet the nutritional needs of older adults in all settings in patients with the ability to consume food orally. If a patient is having difficulty with oral intake, a complete physical examination is warranted to determine whether there is a treatable cause. A multidisciplinary team evaluation can help determine whether there are means, such as therapy or utensil modification, that could ameliorate the problem without the use of nutritional supplementation. Discussing the patient's food preferences, modifying the environment, or providing assistance with feeding are all strategies that may be effective. Speech therapists can be particularly helpful in finding a way for patients to meet their nutritional needs by prescribing thickened liquids, special straws that control the amount of liquid delivered, or diets to address swallowing challenges. If the issue is a lack of appetite, adding an appetite stimulant to the patient's regimen temporarily may be appropriate. Several options are available, although none have clear evidence for use in older adults. Megestrol (Megace) improves appetite and increases weight in patients with cancer and cachexia, but there is limited evidence of effectiveness in older adults. It should not be used in patients who are sedentary, due to an increased risk of thromboembolism. Mirtazapine (Remeron) is an antidepressant that has a noted side effect of weight gain. Use as an appetite stimulant would be off label but could be a choice in those patients who also have a depressed mood. Risk factors include dizziness, orthostatic hypotension, and falls. Dronabinol (Marinol) is a manmade form of cannabis used as an appetite enhancer. It acts on the central nervous system (CNS) and could have significant CNS side effects. If the patient is unable to meet his or her caloric or nutritional needs despite these measures, nurse practitioners must identify the least invasive intervention to increase the patient's intake to meet his or her needs.

ORAL NUTRITIONAL SUPPLEMENTS

Oral nutritional supplements can be recommended for those patients whose diet alone is not adequate to meet their caloric or nutritional requirements. Coverage by Medicare or Medicaid in ambulatory patients is inconsistent, but if available, it requires documentation of weight loss, albuminemia, or other symptoms of malnutrition. The Centers for Medicare and Medicaid Services (CMS) defines involuntary weight loss that must be clinically investigated as 5% in 1 month, 7.5% in 3 months, or 10% in 6 months.

Most oral supplements contain from 240 to 360 calories. Depending on the patient's needs, one to three cans daily can be recommended. The best practice is to take the supplements between meals, not instead of a meal. See Table 4-2 for a comparison of commonly used nutritional supplements. There are subtle differences among products, and most are available in sugar-free versions for use in older adults with diabetes. Formulas to help with diabetic nutrition while protecting blood glucose control are sold as Boost Glucose Control (Boost, 2018) and Ensure Glucerna (Abbott Nutrition, 2018). Nutritional beverages, such as Ensure and Boost, contain a base of calories from carbohydrates, fats, and proteins, with added vitamins and minerals. Each supplement brand also offers versions with higher levels of nutrients, such as protein, to meet a patient's individual needs (see Table 4-2). For patients who cannot tolerate the shake consistency, Abbott makes a clear liquid product.

In 2018, Sauer et al. analyzed original studies on the impact of nutritional interventions in community-dwelling older adults who had or were at risk for malnutrition. Twenty articles

TABLE 4-2 Comparison of Common Nutritional Supplements

	MANUFACTURER	CALORIES	PROTEIN (G)	FAT (G)	SODIUM (MG)	CARBS (G)	SUGAR (G)
Boost Original	Nestlé	240	10	4	150	41	25
Boost Compact 125 ml	Nestlé	240	10	6	150	37	10
Boost Plus	Nestlé	360	14	14	200	45	22
Boost Max Gluten Free	Nestlé	270	27	8	230	22	13
Carnation Instant Breakfast	Nestlé	130	5	0.05	90	27	19
Ensure	Abbott	220	9	6	190	33	15
Ensure Plus	Abbott	350	13	11	220	51	22
Ensure Enlive	Abbott	350	20	11	240	45	22
Ensure Clear	Abbott	180	8	0	45	37	18
Glucerna	Abbott	180	10	9	210	16	4

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were included in the analysis. In addition to oral nutritional supplements other interventions were implemented in the studies, including advice from a dietitian, counseling, and home visits. These benefits included improved nutritional and functional status, increased weight, improved muscle (handgrip) strength. There was inadequate evidence in the 20 studies included to conclude that nutritional interventions had an impact on complications, readmissions to hospital, morbidity, or mortality.

NUTRITIONAL SUPPLEMENTS AND THE HOSPITALIZED PATIENT

Hospitalized patients have a high incidence of malnutrition. Malnourished patients are more likely to experience poor outcomes, be hospitalized longer, and incur higher health-care costs (Ruiz et al., 2019). For the surgical patient this can be complicated further by the surgical stress response that results in metabolic activation requiring an increase in nutrients, particularly protein, to support healing and recovery (Gillis & Wischmeyer, 2019). Gillis and Wischmeyer recommend that nutritional interventions need to be implemented before the surgical procedure and continued postoperatively to address increased nutritional need. The use of the Duke University Preoperative Malnutrition Score is one method for assessing the need for intervention. For critically ill hospitalized patients this often means the use of enteral nutrition (EN) or parenteral nutrition (PN). Currently there is much debate regarding the best time to initiate either EN or PN, the proper nutrients for best outcome, the tradition of measuring gastric residual, and the method of continuous feeding (Arabi et al., 2017). These are all areas that present the challenge of future exploration to determine the best practice based on evidence. Enteral feedings in the hospitalized patient can contribute to GI motility disorders. The most commonly seen problems are constipation and diarrhea.

NUTRITION AND DISEASE

Wound Healing

Nutritional intervention can help to both prevent and heal pressure injuries (Wong et al., 2019). The financial benefit is greatest for prevention of pressure ulcers. Inadequate nutrition alters several important components of wound healing, including immune function, collagen synthesis, and wound tensile strength and yet the contribution of nutrition in wound healing may be overlooked. Patients with involuntary weight loss and protein calorie malnutrition are at increased risk for delayed and impaired healing. Chronic wounds are associated with a long-term inflammatory state that can cause catabolic metabolism, protein calorie malnutrition, and dehydration. Patients given adequate nutritional supplements, orally or with the use of enteral or parenteral feedings develop fewer pressure ulcers, and their existing pressure ulcers heal faster. Providing nutritional supplements corrects deficiencies of macronutrients and micronutrients and provides nutrients for safeguarding and strengthening tissue and supporting tissue repair. The 2019 Prevention and Treatment of Pressure Ulcers/Injuries: Quick Reference Guide includes nutrition as one of its five key recommendations. In addressing nutrition, they include 15 specific evidence-based actions.

Oral nutritional supplements available over the counter can be recommended for enhancement of healing in those with calorie and protein malnutrition. When extra calories are not desirable for the enhancement of healing in the normal-weight or overweight adult, consider the use of whey protein supplements, which are low in calories in the powder form, widely available, and inexpensive. The 2019 Guidelines recommend the specific addition of arginine, zinc, and antioxidant nutrition along with protein for malnourished patients with stage 2 or greater wounds. See Table 4-3 for a comparison of oral nutritional supplements designed to optimize wound healing.

USE OF ENTERAL NUTRITION

A guideline for the Care and Management of Enteral Feeding in Adults was published by the Royal Devon and Exeter National Health Foundation Trust (2015). They emphasize that oral food intake is always preferred, and that enteral feeding should only be considered when nutritional needs cannot be met orally. The overall consideration for enteral feeding is that the patient is malnourished or at risk and has an inadequate or unsafe intake and an intact gastrointestinal (GI) tract. For EN to be effective and safe, the patient must have a GI tract with sufficient length and absorptive capacity to obtain nutritional benefit. Their recommendations include the use of multidisciplinary teams, the use of nasogastric route for a short term of less than 4 weeks with the use of a percutaneous endoscopic gastrostomy (PEG) tube when nutrition is required for more than 4 weeks. Common reasons to consider PEG tube insertion include dysphagia due to neurological disease or stroke, head and neck malignancy with accompanying dysphagia, GI dysfunction or malabsorption, upper GI obstructions, cystic fibrosis, or psychiatric disease. The American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.) clinical practice guideline recommends that patients on admission to the intensive care unit (ICU) are assessed for nutritional risk and that enteral nutrition (EN) be initiated within 24 to 48 hours in patients who are unable to maintain nutrition themselves (Taylor, et al., 2016). Early initiation of EN in those patients unable to eat maintains the integrity of the GI system, which in turn decreases physiological stress and improves the immune response with the result of decreasing disease severity and rate of infection as well as a reduction in mortality (Taylor et al., 2016). An exception to the recommendation for early initiation of EN is when prolongation of life is not in the patient's best interest.

ENTERAL FEEDING IN PALLIATIVE CARE

Malnutrition and cachexia adversely affect cancer patients' quality of life at many points during the course of their care. During noncurative phases of cancer treatment, improved nutrition via enteral feeding can improve the patient's quality of life by decreasing nausea, vomiting, and pain related to eating. It can also postpone loss of autonomy. Oral feeding problems and weight loss in patients with dementia are expected in the late course of the disease, at a point where it

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TABLE 4-3 Comparison of Common Nutritional Supplements Used to Enhance Wound Healing

	PROSTAT AWC	JUVEN (UNFLAVORED)	PRO-SOURCE POWDER	PRO-SOURCE ZAC	LPS SUGAR FREE	ARGIN-AID	ARGIN-AID EXTRA	BENE-PROTEIN
Manufacturer	Medical Nutrition USA, Inc. (a division of Nutricia, North America)	Abbott Nutrition	National Nutrition	National Nutrition	ND Labs	Nestle Nutrition	Nestle Nutrition	Nestle Nutrition
Calories/serving	108	70	30	70	100	45	250	25
Serving size	30 mL	24 g powder	1 scoop/7.5 g	30 mL	30 mL	9.2 g powder	237 mL/ brik pak	1 scoop/7 g packet
Total protein (g)	17	0	6	17	15		10.5	6
Arginine (g)	2.5	7	0	3.2	0	4.5	4.5	0
Vitamin C (mg)	175	0	0	175	0	156	250	0
Zinc (mg)	10	0	0	10	0	0	15	0
Phosphorus (mg)	5.9	0	23	55	10	0	850	15
Potassium (mg)	3.9	0	18.9	25	23	5	<22	35
Carbohydrates (g)	10.2	4	0	0	8	2	52	0
Sugar (g)	10.2	0	0	0		0	52	0
Sodium (mg)	13	0	30	40	14	30	<70	15

is not possible to determine the patient's desires. In addition, oral feeding may increase the risk of developing pneumonia due to aspiration. In view of conflicting results from recent research about whether enteral feeding improves nutrition and length of life, particular care should be taken in deciding whether patients with dementia should have a gastrostomy. A review of current evidence regarding the advantage of artificial nutrition in end-stage dementia warned that initiating tube feeding resulted in negative outcomes, including aspiration pneumonia, malnutrition, and expedited death (Newman et al., 2020)—the very outcomes initiating tube feeding was intended to prevent. Decisions regarding enteral nutrition (EN) during end-of-life care or where patients are not lucid enough to make an informed judgment are particularly challenging and must be made on a case-by-case basis, considering the patient's wishes, if known.

A multidisciplinary approach is appropriate to determine whether all the patient's needs have been assessed. Request a consultation from a speech and language therapist to evaluate for dysphagia, which is common in late dementia, as well as other neurological disorders, including Parkinson's disease and head and neck malignancies. Educate the family about the possible complications and the possibility that the patient may need to be restrained, should a feeding tube be inserted, to prevent unintentional removal. Offer the alternative of comfort feeding, in which the patient is offered safe and preferred foods in a supported and assisted environment as desired.

Clinical Recommendation	Evidence Rating	References
In older adult patients unable to meet their nutritional needs with their current oral dietary intake, high-protein oral nutritional supplements provide benefits.	A	Sauer et al., 2018
The Mini-Nutritional Assessment can be a useful for simultaneously identifying malnutrition and frailty.	A	Soysal et al., 2019
Malnutrition, inadequate protein intake, and unintended weight loss are independent risk factors for the development of pressure ulcers.	A	Wong et al., 2019 European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel and Pan Pacific Pressure Injury Alliance, 2019
Early initiation of enteral nutrition in critically ill patents unable to eat on admission to the hospital has a positive effect on patient outcomes, including reduced mortality.	B	Taylor et al., 2016

Continued

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Clinical Recommendation	Evidence Rating	References
A review of current evidence regarding the advantage of artificial nutrition in end-stage dementia warned that initiating tube feeding resulted in negative outcomes including aspiration pneumonia, malnutrition and expedited death.	A	Newman et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

MALNUTRITION

Signal Symptoms: Deficit in muscle mass, depleted visceral protein.

Description: Malnutrition is a condition resulting from inadequate intake of calories and/or protein, or an inability to absorb and/or digest adequate calories and/or protein (Corish & Bardon, 2019). Malnutrition can result in decreased quality of life, is a predictor of mortality, and results in higher health-care costs, especially during hospitalization (Mangels, 2018). The World Health Organization "Malnutrition Fact Sheet" (2021) further expands the definition to include "undernutrition (wasting, stunting, underweight), inadequate vitamins or minerals, overweight, obesity, and resulting diet-related noncommunicable diseases." Obesity and the related nutritional challenges are discussed later in this chapter. Although undernutrition and malnutrition are often used interchangeably and represent the same nutritional deficit, there are varying types of malnutrition depending on the initial insult. Malnutrition is the result of many interconnected factors both related to diet and non-dietary factors, and each of these can affect the health outcomes (Scrinis, 2020). The role of inflammation has been identified as a key component of malnutrition. Starvation-related malnutrition is a result of chronic starvation but lacks an inflammatory component (e.g., anorexia nervosa); chronic disease-related malnutrition is a result of the presence of mild to moderate chronic inflammation (e.g., organ failure or rheumatoid arthritis); and acute disease/injury-related malnutrition is attributed to acute and severe inflammation (e.g., burns, trauma, or acute systemic infection) (Scrinis, 2020). Protein-calorie malnutrition is diagnosed by a combination of clinical factors. Generally, an unexplained involuntary weight loss and a drop in the serum albumin level to less than 3.5 g/dL may be indicative of a nutritional deficit. However, because a decrease in serum albumin and prealbumin levels is also understood to reflect the inflammatory response it is important to focus on the history and physical examination of the patient rather than depending on laboratory values alone (Keller, 2019; Soeters et al., 2019). Undernutrition in older adults is multifactorial: age-related organ changes; psychosocial factors such as depression, social isolation, and poverty; and functional decline pose risks for developing this often underrecognized medical condition (Mangels, 2018; O'Keeffe et al., 2019). Despite the increased prevalence of malnutrition in older adults, it often remains underdiagnosed.

Etiology: To identify modifiable determinants of malnutrition, O'Keeffe et al. (2019) embarked on a systematic review of the literature. They included 23 studies and 30 potential factors in the final analysis. The quality of the studies and what they identified as a high risk of bias resulted in their concluding that strong evidence is lacking in identifying modifiable factors. They did note that moderate evidence supported hospitalization, eating dependency, poor self-perceived health, poor physical function, and poor appetite as determinants of malnutrition (O'Keeffe et al., 2019). Although several factors can lead to malnutrition in older adults, certain age-associated factors are precursors to malnutrition, including reduced food and micronutrient intake, decreased absorption of ingested food, and the increased bodily demands for protein, calories, or micronutrients because of physiological stressors (O'Keeffe et al., 2019). Inflammation is increasingly recognized as a risk factor for malnutrition due to the metabolic stressors on the body during an inflammatory state. Inflammation influences both nutritional requirements and intake, causing anorexia while increasing resting energy expenditure (Keller, 2019).

Occurrence: The State of Senior Hunger in America 2019 (https://www.feedingamerica.org/research/senior-hunger-research/senior) notes that nearly 5.2 million seniors, or 1 in 14, were food insecure in 2019.

Age: Malnutrition can occur at any age. Frail older adults and people more than 80 years old are at the highest risk for malnutrition. Prevalence is higher in women because of the higher number of women than men in this age bracket. In 2016, the Administration for Community Living (ACL) estimated that 50% of older Americans are malnourished (ACL, 2020).

Ethnicity: Because the reason for malnutrition varies, no specific ethnic prevalence is known.

Contributing Factors: Any of several factors may contribute to malnutrition in older adults. Some physical factors include decreased olfactory sensitivity; loss of taste buds; being edentulous; gastroesophageal reflux disease; dysphagia; poor dietary habits; certain chronic diseases with or without an inflammatory component such as intestinal ischemia, hyperthyroidism, chronic pain, chronic obstructive pulmonary disease, stroke, constipation, chronic impaction, malabsorption syndromes, obesity, and cholelithiasis (O'Keeffe et al., 2019; Scrinis, 2020). Limitations in the ability to not only prepare

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food but also to eat due to tremors and arthritic upper extremity conditions can lead to malnutrition. Using the Mini-Nutritional Assessment, an association between frailty and malnutrition was found to be bidirectional, meaning that those who are frail are more likely to be malnourished and malnourishment is a risk factor for frailty (Lorenzo-López et al., 2017). Medications have the potential to affect nutritional status in multiple ways and deserve a careful review. As the number of medications increase, the likelihood of interference increases. Medications may alter taste and smell (antibiotics, antihistamines, antifungals, chemotherapeutic agents), decrease salivary gland production contributing to dry mouth (anticholinergic agents), and cause malabsorption of nutrients (acetylcholinesterase inhibitors, proton pump inhibitors, statins, antiplatelet medications, and metformin) (Little, 2018). Psychosocial factors including dementia, depression, social isolation, low income, and lack of transportation all can contribute to the risk for malnutrition (Mangels, 2018). Hospitalization and living in a residential care setting with a restricted diet, drug-nutrient interactions related to polypharmacy, social isolation, and ultimately poverty, also may contribute to malnutrition (Mathewson et al., 2021).

Signs and Symptoms: Identification of older adults at risk for malnutrition is a complex process; however, unexplained weight loss is identified as the best factor for predicting increased risk of malnutrition. Assessment of malnutrition is complex because it involves investigation of physiological, pathological, psychological, social, functional, environmental, and financial parameters to determine the possible causes of the malnutrition. Comprehensive assessment of the following diagnostic characteristics is essential in identifying at-risk and presently malnourished patients: history and clinical diagnoses, physical examination/clinical signs, anthropometric data, laboratory data, food/nutrient intake, and functional assessment (Keller, 2019). In patients with suspected malnutrition, all risk factors for poor nutritional status should be assessed using objective measures as indicated including screens for depression, mental status examinations, functional status assessments. Several nutritional screening tools have been developed and are available for use. The Mini-Nutritional Assessment-Short Form (MNA-SF) was designed for older adults and includes six questions regarding weight loss, appetite, mobility, psychological stress, neuropsychological problems, and body mass index (BMI) (Haines et al., 2020). It may be used as an initial screening tool and followed by using the full 18-question MNA, including the measurement of albumin, prealbumin, cholesterol, and lymphocyte count. These forms are the most commonly used and have been validated as a nutritional screening device for older adults (Soysal et al., 2019). Another frequently used screening tool is the Malnutrition Universal Screening Tool (MUST), which adds the BMI and the presence of acute disease. Unlike the MNA, the MUST does not include the use of biomarkers.

A thorough review of prescribed and over-the-counter medications is indicated to determine whether the patient is taking any substance that can cause anorexia, such as acetylcholinesterase inhibitors, thiazide diuretics, angiotensin receptor blockers, angiotensin-converting enzyme inhibitors, and potassium-sparing diuretics (Little, 2018). Other medications of concern are those that inhibit the absorption of micronutrients such as proton pump inhibitors, statins, high-dose aspirin, or metformin. The patient on multiple medications, especially when they are medications that appear on the *Beers List of Potentially Inappropriate Medications*, are at increased risk.

An important purpose of the physical examination is to determine whether malnutrition is related to abnormalities in the cardiac, respiratory, intestinal, endocrine, hepatic, neurological, or renal systems. Inspect for signs of nutritional deficiencies such as nail abnormalities, brittle hair, bruising, the presence or jaundice or pallor, cheilosis, glossitis, loss of subcutaneous body fat, muscle wasting, or edema. If a patient is found to be 15% or more below ideal body weight or had a recent loss of 10% under baseline weight, consider protein-calorie malnutrition. Weight loss alone is not diagnostic; using a tool such as the MNA will provide a more reliable assessment (Mathewson et al., 2021)

Body mass index (BMI) is calculated using the formula weight in kilograms divided by height in meters squared. BMI is an effective measurement for obesity, but it is generally not as sensitive in indicating malnutrition. In the normal healthy older adult, the BMI should range from 18.5 to 24.9 kg/m^2; BMI less than 18.5 kg/m^2 generally indicates a weight deficit and is an indication that nutritional intervention is required. A higher mortality rate has been noted in older adults with a BMI less than 23 kg/m^2. Due to changes with aging, the BMI should be used with caution as an indicator of malnutrition in older adults (Padilla et al., 2021).

In older adults, skinfolds may be used as an estimate of body fat. The skinfolds that best represent adiposity include the triceps and subscapular (Padilla et al., 2021). The disadvantage of the use of skinfolds is that the ratio of fat and total body fat is not constant and decreases with age. Handgrip strength should also be assessed over time; a decrease in strength can indicate nutritional deficits related to the loss of muscle function. Low handgrip strength with malnutrition have been found to increase mortality risk (Wang et al., 2019).

Diagnostic Tests: There is no gold standard test for diagnosis of malnutrition. If physical examination raises the concern that a disease is the cause of malnutrition, appropriate studies should be completed to further assess those concerns. Diagnostic studies may also be useful to identify the severity and type of malnutrition. In screening for malnutrition, laboratory values should be considered only as an indirect measurement or as a tool to evaluate treatment. A complete blood count should be ordered to determine anemia and rule out infection and immunocompromised status. Inflammatory markers such as leukocytosis, elevated blood glucose, or C-reactive protein level may be indicators of a nutritional deficit; however, they are not yet considered diagnostically specific for malnutrition (Haines et al., 2020; Keller, 2019). Total lymphocyte counts less than 1,500 $cells/mm^3$ can be noted in malnutrition (Keller, 2019). Protein, iron, folate, and/or vitamin B_{12} deficiencies should be assessed to further identify nutritional deficiencies.

A serum albumin level less than 35 g/L—especially less than 30 g/L—predicts protein depletion and had been the most common biochemical parameter indicated when considering malnutrition (Keller, 2019). However, serum albumin levels can be skewed in patients who are acutely ill or

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have systemic inflammation. These conditions reduce albumin synthesis and can increase its degradation. A low serum albumin can be a predictor of poor surgical outcomes. Because the half-life of albumin is 21 days, serum albumin levels rise slowly following nutritional supplementation. Prealbumin has an average life span of 2 to 3 days; this shorter life span increases its usefulness as an indication of acute change in nutritional state (Keller, 2019). A level below 10 mg/dL is associated with short-term malnutrition. It can be a useful indicator of repletion, especially when refeeding an older adult (Keller, 2019).

Serum transferrin is an acute phase reactant and a transport protein for iron. Its half-life is 10 days. Iron levels, liver disease, and inflammation will impact levels of serum transferrin. In patients with coexisting iron-deficiency anemia, the results will be misleading (normal to elevated serum transferrin). Its usefulness as a measure of malnutrition has been questioned (Keller, 2019). Some of the nutritional screening tools use cholesterol as a measure of malnutrition, but the sensitivity and specificity of this is a measure is very low (Keller, 2019).

Differential Diagnosis: When determining whether a person is suffering from malnutrition, discern if any of the following conditions coexist:

- Anorexia
- Dehydration
- Dementia—alcohol related
- Dementia—Alzheimer related
- Depression—major
- Dysphagia
- Eating disorder
- Failure to thrive
- Feeding problem/older adult
- Nutritional deficiency not otherwise specified

Treatment: Identifying the contributing factors to malnutrition in each individual patient is essential to treating this condition. When possible, a 3-day diet intake should be obtained to determine the severity of the nutritional deprivation. All medications that can cause drug-induced malnutrition should be discontinued or reconsidered or an alternative should be used. Any fecal impaction should be identified and removed. Maximizing the management of chronic diseases that contribute to a decline in appetite or increase the demand for nutrients is critical. Understand that chronic disease will always challenge nutritional adequacy. Because not all factors can be treated, dietary consultation should be ordered to assist in the diagnosis of malnutrition and planning of diet supplementation. Any older adult experiencing a physiological stressor such as surgery, infection, or trauma requires an increase in protein, calories, and micronutrients. If the patient is diagnosed with protein-energy malnutrition (PEM), nutritional support will depend on the patient's medical condition and the degree of the PEM. Enteral nutritional support is considered when the patient's nutritional intake is inadequate to meet physiological requirements for more than 7 days or when the weight loss is more than 10% of the patient's pre-illness weight.

Follow-Up: Patients who are hospitalized for malnutrition or who develop malnutrition secondary to an acute-care hospitalization should be monitored daily for response to the nutritional supplementation. Prealbumin levels can be helpful in this setting. The patient's weight should also be monitored with weekly weights until the malnutrition has been corrected. If a psychosocial factor contributed to the malnutrition, periodic review of the patient's improvement is warranted.

Sequelae: An older person's initial reaction to prescribed nutrient supplements may worsen malnutrition when used as a meal replacement instead of supplementation. Patients who are malnourished can develop sarcopenia and/or cachexia. Sarcopenia, defined as a loss of muscle mass together with low strength and loss of physical performance, has been associated with inadequate intake of calories, malnutrition, and the use of certain medications (Montes et al., 2017). Cachexia is defined as a complex syndrome characterized by loss of weight, mostly due to loss of muscle mass resulting from metabolic abnormalities due to disease (Marshall & Agarwal, 2019). Long-term malnutrition increases the risk of morbidity and mortality.

Prevention/Prophylaxis: All older adults should be assessed for food insecurity and signs of malnutrition. A two-step approach for identifying malnutrition is suggested using the MNA (Haines et al., 2020). The MNA-SF has been studied and approved as an initial screening tool when undernutrition is suspected in the older adult population. The MNA-SF is highly correlated with the MNA, with a diagnostic accuracy of 98.7% for predicting undernutrition. The six-item MNA-SF can be easily used in the first step of the process because it does not require anthropometric testing. A score between 8 and 11 points indicates risk for malnutrition. For the second level of screening, the MNA is considered the most reliable and validated nutritional tool. It is appropriate for use in the outpatient and nursing home settings. It does not require invasive laboratory testing and is cost-effective. The tool consists of an anthropometric assessment, general assessment, dietary assessment, and a self-assessment that engages the older adult to assess their nutritional status. International studies have validated that an MNA score between 17 and 23.5 indicates risk of malnutrition and intervention is indicated. (Haines et al., 2020).

Referral: Referring patients who are malnourished to a specialist depends on the cause of the nutrition depletion. If food insecurity is an issue because of access to food or financial concerns, many health systems are now developing "Food Pharmacies" that allow providers to write prescriptions to meet dietary needs. A dietitian should be consulted for a nutritional support, evaluation, and patient education, including help with meal planning. Community-dwelling older adults can be referred for Meals on Wheels or provided information on the location of Agency on Aging congregate meal sites. Meal sites can serve the additional purpose of providing socialization and may combat depression and loneliness, contributors to malnutrition. If social isolation, low income, and/or functional status contributed to the development of malnutrition, the patient should be referred for social services. Patients with financial needs should be evaluated to see if they can qualify for food assistance and could be enrolled in the Supplemental Nutrition

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Assistance Program (SNAP) (Pomeranz, 2017) and/or participate in community-based food bank programs. Older adults who have difficulty with food preparation or eating can be referred to an occupational therapist for evaluation for adaptive equipment and retraining.

Patients with swallowing difficulties need to be referred to a speech therapist for evaluation and plan of care. Patients who need long-term enteral support should be referred to a gastroenterologist for consideration of a percutaneous endoscopic gastrostomy (PEG) tube or, in some cases, a feeding jejunostomy. For the patient diagnosed with a terminal illness, discuss the patient's and family's decision on nutritional support before beginning any intervention.

Education: For the alert ambulatory older adult, review the Dietary Guidelines for Americans and My Plate guidelines (www.myplate.gov). Teach family members caring for patients who are cognitively impaired or physically disabled about dietary requirements and nutritional supplementation. Caregivers and older adults can improve nutritional status by simple measures, such as preparation of an adequate diet, hand feeding, adequate-fitting dentures and oral hygiene, and adding liquid nutritional supplements between meals.

Clinical Recommendation	Evidence Rating	References
The MNA tool has been used successfully globally to assess for malnutrition risk in older adults.	B	Haines et al., 2020
Malnutrition as measured by the MNA was found to be a predictor of preterm death in older adults.	B	Haines et al., 2020
All medications that can cause drug-induced malnutrition should be discontinued or reconsidered, or an alternative should be used.	C	Little, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

OBESITY

Signal Symptoms: Elevated body mass index (BMI), central obesity, generalized obesity.

Description: Obesity rates among older adults have been increasing over the past several decades, making it important to pay particular attention to weight and associated metrics to manage risk for chronic disease and disability. Obesity can be defined as abnormal or excessive fat accumulation that presents a risk to health. There are a variety of methods to determine whether an individual is obese; simply weighing a patient, however, does not distinguish the effect of muscle versus body fat on weight. A very muscular patient may weigh the same as an individual living with obesity. Other metrics, such as BMI, have been internationally accepted as a good indicator of percentage of fat mass at the population level. A BMI ≥25 kg/m^2 is considered overweight and a BMI ≥30 kg/m^2 is obese. Standardized nomograms or online calculators can easily determine BMI, and to further stratify health risk, obesity is often subdivided into classes (Class I: BMI=30.0–34.9, Class II: BMI=35.0–39.9, Class III: BMI ≥40.0) (Centers for Disease Control and Prevention [CDC], 2021a). Unfortunately, there are limitations to BMI because it does not take into consideration differences in age, fat distribution, sex, and ethnicity. These limitations are important to understand, particularly when interpreting and translating research data into practice. For example, the decrease in bone mineral content with increasing age leads to a decrease in height, which can lead to an overestimation (inflation) of BMI. Another aging consideration is the medical hypothesis called the "obesity paradox," which suggests that fat mass becomes less harmful or even "protective" in individuals as they age with catabolic, chronic comorbidities. New research suggests, however, that age-related redistribution of subcutaneous adipose tissue from the extremities to the trunk (and especially to the visceral organs) is not protective and that survival advantage of a higher BMI in older adults may instead be explained by a higher lean (muscle) mass (Bosy-Westphal & Muller, 2021; Carbone et al., 2019). BMI does not consider sex differences, and women tend to have greater amounts of total body fat than men with an equivalent BMI. Established BMI cut points correspond to adverse disease processes (Batsis & Zagaria, 2018); however, these cut points may not be appropriate for all individuals and populations. Individuals who are physically fit will also have a higher BMI due to increased lean muscle mass compared to fat mass (Centers for Medicare and Medicaid Services [CMS], 2011). Risk for disease may be greater at lower BMI in some populations. Among those of Asian descent, for example, there is a higher risk of developing type 2 diabetes mellitus and cardiovascular disease at lower BMI cut points currently established for overweight and obesity, and clinicians may potentially miss opportunities for earlier treatment/intervention if these differences are not recognized (Misra et al., 2018; WHO, 2004).

More recently, the evolution and implementation of body composition analysis has highlighted the limitations of BMI and obesity-associated health risk (Bosy-Wesphal & Muller, 2021). As noted earlier, BMI does not reflect the percentage of lean (muscle) mass nor the distribution of fat mass (i.e., visceral adipose tissue vs. subcutaneous adipose tissue). Although body site adiposity distribution is clinically

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important, particularly among older adults who have age-associated changes (i.e., a progressive decrease in muscle mass and increase in fat mass), the availability of more sophisticated body composition analysis equipment may not be available in all clinical settings. Hence, the inclusion of waist circumference (WC) as a screening indicator for abdominal obesity in older adults presenting with both general and abdominal obesity (Afonso et al., 2021; Bosy-Wesphal & Muller, 2021). WC is measured from the uppermost lateral border of the iliac crest and should be adjusted by age and BMI; central obesity is a waist measurement of more than 88 cm (35 inches) in females and more than 102 cm (40 inches) in males (NIH National Heart, Lung, and Blood Institute [NHLBI], 2021b). WC cut points can be standardized across all adult ethnic populations except for individuals less than 5 feet tall or individuals with a BMI more than 35. Advanced practice nurses are well-positioned to encourage healthy lifestyles among older adults that include activities to help attain/maintain lean muscle mass, regardless of BMI.

Etiology: Obesity occurs when an individual consumes more calories than they expend. The etiology of obesity is genetic as well as environmental; however, it is difficult to separate the influence of genetics versus the influence of lifestyle habits that individuals and families share. Environmental, social, and cultural influences also determine the risk of obesity. Obesity tends to occur more often when individuals eat high-calorie, high-fat, processed foods or are unable to participate in enough physical activity or exercise. Some medications may cause weight gain by stimulating appetite, affecting how the body absorbs and stores glucose, slowing overall metabolism, and/or causing fatigue (i.e., making physical activity challenging). Examples include antidepressants (selective serotonin reuptake inhibitors), anxiolytics, mood stabilizers, antipsychotics, diabetes medications (insulin, thiazolidinediones, sulfonylureas), steroid hormones, anticonvulsants, antimigraine, treatment for neuropathic pain, opioids, antihypertensives (beta blockers, alpha blockers, calcium channel blockers), antihistamines, hypnotics, and antiretrovirals (Welcome, 2017). Weight gain is often seen as patients quit smoking. A lack of sleep has also been associated with the development of obesity (Norton et al., 2018)

Occurrence: Obesity rates in the United States are on an upward trajectory. Currently, more than two-thirds of Americans are overweight (defined as BMI between 25 and 30 kg/m^2) or obese (defined as BMI greater than 30 kg/m^2).

Age: In 2017–2018, the age-adjusted prevalence of obesity and severe obesity was 42.4% and 9.2%, respectively (Hales et al., 2020). There was no significant difference in the prevalence of obesity between men and women or by age-group: among older adults, aged 60 and older, obesity rates were 43.3% in women and 42.2% in men. Severe obesity in those aged 60 and older was 5.8%.

Ethnicity: Obesity affects some groups more than others. In the United States, non-Hispanic Blacks have the highest age-adjusted rates of obesity (49.6%), followed by Hispanics (44.8%), non-Hispanic Whites (42.2%), and non-Hispanic Asians (17.4%) (Hales et al., 2020).

Contributing Factors: Obesogenic behaviors are complex and influenced by a range of genetic, individual, and environmental factors. Over-consumption of high-energy foods and a lack of physical activity are the main behavioral risk factors for people to develop obesity, but other social determinants/drivers of health, lack of sleep, high stress levels, and sedentary behavior (i.e., prolonged sitting) are just a few of the factors that can play a critical role over the course of a lifetime (Lakerveld & Mackenbach, 2017).

Signs and Symptoms: Usually, obesity can be recognized by the initial physical examination. A height and weight measurement should be obtained when medically necessary at each visit to the care provider. The use of the BMI is the most convenient method to quantify overweight/obesity in the office setting. Measurement of WC can help predict the development of the metabolic syndrome. Skin calipers can be used to measure subcutaneous fat thickness by "pinching" and measuring skinfold thickness. Unfortunately, this assessment technique requires training and strict adherence to measurement protocols that may be impractical to use in a clinical setting.

Associated symptoms that older adults with obesity often present with include feelings of worthlessness, sadness, and hopelessness; individuals should be evaluated for functional limitations, joint pain, decreased mobility, and activity intolerance (Batsis & Zagaria, 2018; Qian et al., 2021). Evidence of loss of muscle strength due to sarcopenia in sedentary older adults with obesity should be assessed, and functional ability to perform ADLs should be measured so that exercise and dietary interventions can be prioritized (Bales & Porter Starr, 2018; Batsis & Zagaria, 2018). Although being underweight significantly increases the odds of pressure injuries, skin conditions are prevalent among older adults living with obesity, making it critical to assess the skin for excoriation and pressure injury (Alipoor et al., 2021).

Diagnostic Tests: Laboratory tests are ordered based on history and clinical presentation. For example, if considered at risk for metabolic syndrome, a lipid profile and fasting glucose levels should be obtained. If hypothyroidism is suspected, a thyroid-stimulating hormone (TSH) level should be ordered. If Cushing's syndrome is suspected, a 24-hour urine cortisol and dexamethasone suppression test is recommended. Laboratory results will help guide future follow-up and/or intervention.

Differential Diagnosis: Determine the ideal body weight (IBW) for height. Patients 20% above are considered obese; those 40% above are morbidly obese. BMI can be determined with easily accessible online BMI calculators.

Treatment: In June 2013, the American Medical Association adopted a policy that recognized obesity as a disease requiring a range of medical interventions to advance obesity treatment and prevention. This policy comes after decades of various weight-loss-targeted (or bariatric/metabolic) surgeries with variable outcomes and health insurance coverage (Batsis & Dolkart, 2015; Purath et al., 2014). Obesity management includes a comprehensive nutritional evaluation and a complete history and physical examination. Important considerations include social drivers/determinants of health, dietary and physical activity patterns, and medication review for medications that may promote weight gain. There are many comorbidities associated with obesity, including but not limited to diabetes, hypertension, dyslipidemia, heart

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failure, coronary artery disease, obstructive sleep apnea, osteoarthritis, and some forms of cancer (American Society of Metabolic and Bariatric Surgery [ASMBS], 2021). The basic treatment for obesity involves a reduction of caloric intake while increasing physical activity. The goal of a standard weight loss regimen should be about 1 to 2 pounds per week; however, it is also important to have a clear understanding of a patient's expectations and degree of motivation (CDC, 2021a, 2021b; Elran-Barak & Segel-Karpas, 2020).

The initial diet should aim at reducing the caloric intake for the female patient to 1,200 to 1,500 calories per day and the male patient to 1,500 to 1,800 calories per day. This goal of caloric reduction can often be obtained by decreasing portion size and limiting high-calorie but poorly nutritious foods. Keeping a daily food diary and counting calories will often help patients to see how much they really consume each day. Commercial programs typically include prepackaged meals, meal replacement entities, or recipes with predetermined calories. Very low-calorie diets that reduce the caloric intake to less than 800 to 1,200 calories per day require strict medical monitoring through a structured program. There are few data to support the use of low-carbohydrate diets over the typical balanced but calorie-restricted diet in terms of safety or efficacy (CDC, 2021a, 2021b). A combined approach of a weight-reduction diet plus a program of exercise is generally recommended. In patients with sarcopenic obesity, an increase in dietary protein and protein supplements should be encouraged, unless contraindicated by other concomitant conditions that restrict protein intake (Bales & Porter Starr, 2018). Weight loss therapy in an older patient with sarcopenic obesity should be tailored to minimize loss to bone and muscle mass (Bales & Porter Starr, 2018).

A high-protein, modest calorie restriction diet combined with exercise for older adults with sarcopenic obesity is recommended because it helps increase caloric expenditure while preserving muscle quality and function (Bales & Porter Starr, 2018; CDC, 2021c). Before beginning any exercise regimen, older adults should determine their level of effort for physical activity relative to their level of fitness; those individuals with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely. In addition, older adults should participate in physical activity that includes balance training as well as aerobic and muscle-strengthening activities to improve/maintain physical function (Bales & Porter Starr, 2018). Current physical activity recommendations call for approximately 30 minutes of moderate activity 5 to 7 days per week; for weight loss without calorie restriction, 1 hour of moderate activity is required. More than 300 minutes a week of moderate-intensity activity, or 150 minutes a week of vigorous-intensity activity, results in greater health benefits. When older adults cannot do 150 minutes of moderate-intensity aerobic activity (i.e., brisk walking) per week because of chronic conditions, they should be as physically active as their abilities and conditions allow (CDC, 2021c). In addition to aerobic activity, muscle strengthening activities that work all the major muscle groups (i.e., legs, hips, back, abdomen, chest, shoulders, arms) is recommended to prevent sarcopenia (Bales & Porter Starr, 2018; CDC, 2021c).

Currently, there are three major groups of drugs used to manage obesity. Drugs work either centrally to limit dietary intake, peripherally to impair dietary absorption, or increase energy expenditure. Although pharmacological therapy is often not used for weight loss among older adults due to lack of safety and efficacy data, there are a few medications currently approved by the U.S. Food and Drug Administration (FDA) for long-term (≥1 year) chronic weight management. These include orlistat (Alli, Xenical), phentermine and topiramate extended-release (Qsymia), naltrexone hydrochloride and bupropion hydrochloride (Contrave), liraglutide (Saxenda), and semaglutide (Wegovy) (Karam & Nathan, 2021). Loraserin hydrochloride (Belviq) was withdrawn from the market in February 2020 and is no longer available in the United States. Despite the proven efficacy of FDA-approved medications, few clinicians prescribe medications for chronic weight management. It is essential to carefully review prescribing information to avoid medication-related side effects and drug/drug interactions and to consider the benefits of weight loss that improve cardiovascular and metabolic risk profiles (Carbone & Dixon, 2018). The FDA does not regulate herbal (botanical) products, vitamins, or supplements the same way it does prescription and over-the-counter medicines; therefore, the use of appetite suppressants/anorexiants (noradrenergic/sympathomimetic agents) should be used with caution because they may be contraindicated in older adults with multimorbidities.

Follow-Up: The treatment of obesity should focus on the short-term weight loss phase and the long-term maintenance phase. Weight loss has been associated with reduced risk of developing type 2 diabetes, improvement in lipid profile, and reduced blood pressure. Patients should be followed closely after they start a diet and exercise program. As patients lose weight, there should be close monitoring of potentially harmful side effects of weight loss, including fluid and electrolyte shifts, cardiac arrhythmias, exacerbation of gout, development of gallstones (cholelithiasis), mood disorders, or disordered eating. The goal is to promote the long-term management of weight with a healthy lifestyle.

Prevention/Prophylaxis: A healthy diet and active lifestyle should be encouraged. (CDC, 2021b; NIH NHLBI, 2021a, 2021b). Those who are eligible for Medicare are now eligible to receive intensive behavioral therapy counseling services for obesity management (BMI ≥30) (CMS, 2011).

Referral: The management of obesity is challenging; commercially available programs may be helpful if more structure is needed. Medically supervised, structured diets that use meal replacements or energy restriction (i.e., low or very low energy) can be effective not only in weight loss but also in improvement in comorbid conditions, depending on the intensity and duration of the intervention (Bales & Porter Starr, 2018). Referral to an endocrinologist is appropriate when dealing with such illnesses as hypothyroidism, Cushing's syndrome, or a history of polycystic ovary syndrome. Finally, referral to a bariatric surgeon may be considered for individuals who have a BMI ≥40 or have a BMI ≥35 and at least two obesity-related comorbidities who are unable to achieve a healthy, sustained weight loss (Mechanick et al., 2020). Bariatric/metabolic surgery works by restricting food intake, causing food malabsorption, or a combination of both methods (ASMBS, 2021). The most common types of metabolic/bariatric surgeries performed include the sleeve gastrectomy and the Roux-en-Y gastric bypass (ASMBS, 2021;

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Thereaux et al., 2015). Emerging evidence suggests that metabolic/bariatric surgery may establish a new body weight set point by altering the physiological mechanisms of body weight regulation, thereby causing acceptable and sustained weight loss and improved quality of life (Nor Hanipah et al., 2018; Susmallian et al., 2018). Age alone should not be a limiting factor as a surgical candidate (ASMBS, 2021; Nor Hanipah et al., 2018).

Education: Teach patients and significant others meal preparation, calorie counts, and fat gram calculation. There are commercial weight loss programs that are available for individuals who prefer individualized, group, or online methods to assist with weight loss. They range in costs so that everyone should be able to find a weight loss program that suits their individual needs. To sustain the clinical benefits of weight loss (i.e., improved insulin sensitivity), exercise training needs to be added to the weight loss intervention. It is important to encourage patients to begin a safe exercise regimen like walking, which is the most recommended exercise program (CDC, 2021b). Older adults should also be encouraged to include resistance, flexibility, and strength training in their aerobic exercise programs. Partnering with older adults to comanage the complexities of obesity will help identify individual goals and optimize care outcomes. Providers should provide the older adult with numerous safe options for increased activity and/or exercising as well as opportunities to learn, shop, prepare, and/or receive balanced nutrition to achieve weight and health-related goals.

Clinical Recommendation	Evidence Rating	References
High-protein, low-carbohydrate diets are more effective at weight loss than low-fat diets. This helps address concerns of lean (muscle) mass and bone loss that often occurs with weight loss.	A	CDC, 2021c Bales & Porter Starr, 2018
Increased activity and exercise are important strategies to increase caloric expenditure. Before beginning any exercise regimen, individuals with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely. Older adults should participate in physical activity that includes balance training as well as aerobic and muscle-strengthening activities to improve/maintain physical function Current physical activity recommendations call for approximately 30 minutes of moderate activity 5–7 days per week; for weight loss without calorie restriction, 1 hour of moderate activity is required. More than 300 minutes a week of moderate-intensity activity, or 150 minutes a week of vigorous-intensity activity, results in greater health benefits. When older adults cannot do 150 minutes of moderate-intensity aerobic activity (i.e., brisk walking) per week because of chronic conditions, they should be as physically active as their abilities and conditions allow. In addition to aerobic activity, muscle strengthening activities that work all the major muscle groups (i.e., legs, hips, back, abdomen, chest, shoulders, arms) is recommended to prevent sarcopenia.	A	CDC, 2021c Bales & Porter Starr, 2018
To help facilitate weight loss and prevent or minimize sarcopenia, muscle strengthening activities on major muscle groups (i.e., legs, hips, back, abdomen, chest, shoulders, arms) should occur on at least 2 days per week.	A	CDC, 2021c Bales & Porter Starr, 2018
Partnering with older adults to comanage the complexities of obesity will help identify individual goals and optimize care outcomes. Motivational interviewing is an important strategy for short- and long-term success.	A	Wadden et al., 2020 Purath et al., 2014
Those receiving motivational interviewing, intensive dietary, and behavioral therapy can produce significant weight loss.	A	Batsis & Dolkart, 2015 Batsis & Zagaria, 2018 Purath et al., 2014
Pharmacological therapy is often not used for weight loss among older adults due to lack of safety and efficacy data, but there are a few medications currently approved by the U.S. Food and Drug Administration. These medications work best with other behavior modification techniques. If deemed ineffective (weight loss less than 5% at 3 months) or there are safety or tolerability issues at any time, it is recommended to discontinue the medication, consider an alternative medication, or consider an alternative treatment approach.	A	Carbone & Dixon, 2018 Karam & Nathan, 2021
Bariatric surgery is the only available therapeutic modality associated with clinically significant and sustained excess weight loss. Sleeve gastrectomy and Roux-en-Y-gastric bypass (RYGB) are the most common surgical procedures; referral to a bariatric surgeon may be beneficial. Age alone should not be a limiting factor as a surgical candidate.	A	ASMBS, 2021 Nor Hanipah et al., 2018 Susmallian et al., 2018

Continued

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Clinical Recommendation	Evidence Rating	References
Recognize that individuals who achieve weight loss of 2%–5% are more likely to have clinically meaningful improvement in health outcomes and quality of life.	A	Nor Hanipah et al., 2018 Susmallian et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

A. D., an 80-year-old widow, is brought to see you by her concerned daughter, who reports that her mother is not eating and has lost 15 pounds in the past 8 months, "Her clothes just hang on her now." A. D. lives alone in an apartment in low-income senior housing. She has been independent in ADLs, and her daughter takes her shopping or shops for her. Recently, her daughter has noticed spoiled food in the refrigerator, and A. D. seems to be tired all the time, despite her claim that she sleeps well at night. When asked about eating, A. D. responds, "I just don't have an appetite like I used to. It seems like so much trouble to cook a meal just for me."

Past medical history: Coronary artery disease, currently stable—has prescription for Nitrostat 0.4 mg SL as needed for chest pain but has never had to use the medication. Hypertension, currently stable—takes Vaseretic 10 to 25 mg once daily. Hyperlipidemia—stable—takes simvastatin 20 mg PO daily in evening. The patient also takes vitamin D_3 2,000 IU PO daily and omega-3 fish oil daily at bedtime. The patient has no known drug allergies.

A. D. is a retired homemaker and high school graduate. Her husband has been deceased for 5 years. She has three children, all alive and well; her oldest daughter lives nearby, and her other two children live far away but keep in touch by phone. A. D. likes to play bingo at senior housing. She participates in no other activities but has friends in the building. A. D. denies any change in status or any acute health problems outside of feeling more tired than usual and having a poor appetite.

Objective: Petite, slender older woman, using a cane for support, appears her stated age; well-groomed but clothing is too large.

Blood pressure (BP) 134/78 mm Hg, pulse 84 and regular, respiratory rate 16 breaths/min and afebrile. Height 58 inches, weight 88 pounds, BMI 18.4. Last visit 6 months ago, weight was 100 pounds, BMI was 22. Physical examination unremarkable.

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What national guidelines are appropriate to consider?
4. What tests will you order?
5. What are the differential diagnoses that you are considering?
6. What is your plan of care?
7. Are there any *Healthy People 2030* objectives that you should consider?
8. What additional patient education may be needed?
9. Will you be looking for a consultation?

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CHAPTER 5

Settings of Care

Marie Grosh and Evelyn Duffy

Nurse practitioners (NPs) caring for older adults must possess a solid understanding of different settings of care, what services are available to patients in each setting, and the risk versus the benefits of those settings. Additionally, NPs must understand their roles within different contexts, the methods and models of providing care, pertinent information for assisting patients during transitions in care, and advanced care planning. NPs are often the clinicians who can foresee and anticipate a need to change settings (such as sending a patient to the emergency department [ED] or recommending an assisted living placement). Patients and caregivers can easily become overwhelmed trying to navigate through this complex maze, and the NP must play an active role in facilitating successful transitions to and from different settings and providing ongoing care coordination, guidance, and support.

ROLES AND CARE DELIVERY METHODS

Primary Care Providers

Of the more than 325,000 nurse practitioners (NPs) certified in the United States, over 90% of them are primary care providers (PCPs). Primary care includes health promotion, wellness and prevention services, diagnosis and treatment of acute and chronic conditions, and ongoing management of patient health needs, including the needs of older adults (American Association of Nurse Practitioners, 2021). When care is well managed by primary providers, patients have statistically better outcomes. CMS has recognized this concept by initiating financial incentive programs for patients to seek care from their PCP first rather than report to acute care settings or go directly to a specialist, for example the "Primary Care First" program (CMS, 2021a).

NPs are particularly well prepared to serve as PCPs for older adults. Their initial preparation as nurses focuses on the patient's immediate health needs as well as wellness, psychosocial needs, and the patient's environment. Preparation for the role of NP adds differential diagnosis, medical decision making, and prescribing to their scope of practice.

When a patient develops any new symptom, experiences an injury, or has a chronic condition that becomes exacerbated, the NP who serves as a PCP should be the patient's first call. As PCPs, NPs also identify indications for referral and initiate consults to specialty clinicians when needed and are responsible for the overall coordination of patient care. They are essential to the safe transition of the patient from one care setting to another.

In addition to coordinating care with other providers, it is often necessary for NPs to include a family member or friend whom the older adult depends on in patient care. The role these advocates play in an older adult's care can range from minimal assistance (such as attending appointments or providing transportation) to more hands-on assistance in supporting instrumental or basic activities of daily living (ADLs).

Settings for NPs who provide primary care to older adults are not limited to the ambulatory clinic. NPs may evaluate patients using telehealth modalities or make house calls and provide care to patients in their family home or assisted living facility. Skilled and long-term care facilities are also including NPs to provide primary care to residents of those facilities. A study by Mileski et al. (2020) found that when NPs served as PCPs in long-term care, there was a decrease in unnecessary hospitalizations, an increase in access to health care, and improved overall health outcomes. They also found that NPs built relationships with residents and families and were essential to providing information essential for decision making. The study concluded that "utilization of NPs in a long-term care setting should be encouraged to improve access to care, decrease hospitalizations, and enhance quality of care" (p. 1 of 20).

During the COVID-19 pandemic of 2020, several restrictions on reimbursement for NPs were modified. Removing the requirements for telehealth had a huge impact in facilitating access to care, allowing providers additional opportunities to provide care remotely and virtually. Traditional evaluation and management of a patient can now be accomplished with live video encounters (often referred to as "real-time" or "virtual visits") or audio-only encounters. Primary care NPs can also be reimbursed for virtual check-ins and remote patient monitoring, which are additional ways for providers to receive data about patients and improve patient care management (Centers for Medicare and Medicaid Services [CMS], 2021b). Telehealth is not appropriate in all situations; if it is suspected that the health concern may require a procedure, or if the physical examination might change the treatment

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plan, the patient needs to be evaluated in person. Older adults also may have limited access to technology and/or require the assistance of another person to effectively engage in a telehealth encounter.

Acute Care Providers

Acute care providers are often caring for older adults because those older than age 65 have the highest rate of inpatient hospital use (Sun & Sosnoff, 2018). NPs in acute care settings whose scope of practice includes the care of adults should be prepared to address the challenge of diagnosing and treating patients who are unfamiliar to them and present with multiple chronic conditions. Chronic conditions often have different baseline symptomatology, which requires providers to spend more time on assessment. Older adults may present with common problems in uncommon ways, and acute providers should know the atypical presentations of common conditions in an older adult. Baseline mental status should be documented so that acute delirium is not dismissed as dementia and to ensure treatable causes for the decline are assessed. Timely follow-up and quality communication between acute care providers and PCPs are important to maintain continuity of care. Knowledge of gerontological principles and coordinating care with PCPs will improve outcomes.

Specialty Care

Some NPs choose to provide care to older adults in a specialty practice. With the increasing complexity of managing chronic conditions, primary providers depend on specialists to assist in the comanagement of patients with these conditions. Many specialties, including cardiology, pulmonology, nephrology, urology, endocrinology, dermatology, and oncology, are including an NP in the practice to improve patient outcomes and satisfaction. Disease-specific practices may include interdisciplinary teams in which an NP can play a vital role. Centers of geriatric comprehensive assessment are included in many large health-care systems. These clinics evaluate older adults who are experiencing ambiguous symptoms, a general decline, or a need for transition in care settings. NPs in these comprehensive centers should collaborate with PCPs, share the results of the assessment and the recommendations of the geriatric experts involved in the center, and coordinate the implementation.

SETTINGS AND SERVICES

There are many settings in which older adults can receive care (Table 5-1). These settings are designed to meet the needs of older adults across the health spectrum. It is often up to the nurse practitioner (NP) to identify the best option for the patient, considering not only their immediate needs but also what their needs will be going forward. Accepting some decreased independence initially may prevent further decline and support mental and functional health. The informed NP will be able to correct the patient's misconception that the only option is a nursing home, which they may envision as a facility only for frail individuals with dementia who are at the end of life. Recommendations that the NP provides to the patient regarding the best setting of care should involve joint decision making and consideration of the patient's preferences, need for autonomy, and safety. Financial considerations are an additional factor, including whether the setting is covered by the patient's insurance or accepts Medicaid.

Acute Care

The setting in which treatment for an acute issue is provided depends on the nature of the problem. Primary care providers can help patients in decision making regarding what is urgent and what is emergent or life threatening. When the patient is experiencing an acute change in condition that is not life threatening, contacting their primary care NP who is familiar with their chronic conditions and medications and has access to recent laboratory results may prevent an unnecessary visit to the emergency department (ED). Seeking care at the ED for minor conditions can put the older adult at risk for contracting healthcare-associated infections and communicable diseases. The urgency and time-sensitive nature of the problem may require a more immediate evaluation in an outpatient acute care setting or in the ED.

OUTPATIENT ACUTE CARE

Referring to outpatient settings, such as convenient care clinics and urgent care facilities, is appropriate for patients who need acute care for issues such as lacerations, which have a very low likelihood of complications or the need for a hospital admission. More serious conditions, such as an acute mental status change, should be assessed in an ED that has access to more sophisticated testing and the ability to admit the patient to the hospital if necessary. The NP must be skilled in assessing an acutely presenting issue, anticipate the potential needs, and possess an understanding of services available within outpatient acute care settings in their community. Not all convenient care or urgent care clinics have an x-ray machine or on-site laboratory, and very few have the ability to perform other imaging, such as computed tomography.

INPATIENT ACUTE CARE

Inpatient acute care may start with an evaluation in the ED. An ED, while not without its risks, does offer access to sophisticated diagnostics and consultation with specialists. If after careful assessment in the ED the diagnosis is unclear, the patient may be observed in the inpatient setting for a period of up to 48 hours. Even before the COVID-19 pandemic, this practice of inpatient observation was becoming more common. The observational period is not considered a hospital admission, which would be covered by traditional Medicare Part A; the patient remains an outpatient for insurance purposes. This delineation is important for financial considerations and availability of rehabilitation after discharge. Admission to a skilled nursing facility or to a rehabilitation unit requires a hospital admission for three overnights (Centers for Medicare & Medicaid Services [CMS] & Medicare Learning Network [MLN], 2021). Patients may be faced with a huge bill from both the hospital and the skilled nursing facility if the patient was never actually admitted to the hospital.

Inpatient hospitalization can put an older adult, especially one who is frail, at risk for harm. Providers in inpatient acute

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TABLE 5-1 Common Services and Settings for Older Adults With Payment Options

	COVERAGE AVAILABLE	STIPULATIONS/RULES	DURATION	ADVANTAGES	DISADVANTAGES
Short-term rehabilitation in a skilled nursing facility	Medicare	Traditional Medicare: Hospital inpatient stay for 72 hours Advantage plans: Precertification and in-network facility	24/7 for up to 100 days	24-hour skilled nursing Daily therapy	Institutional environment Care not managed by primary care provider (PCP)
Short-term rehabilitation with home health agency	Medicare	Meet homebound status criteria Encounter with ordering provider within 30 days Advantage plans: Precertification and in-network home health agency (HHA)	Approximately 1-hour visits daily or every other day	Patient is in the comfort of their home Care managed by PCP	Intermittent visits only
Long-term care in a nursing home	Medicaid	n/a	24/7 indefinitely	24-hour skilled nursing	Institutional environment Expensive
Assisted living	Some accept Medicaid	n/a	24/7 until care needs exceed care offerings	Caregivers 24/7 Homelike environment	No 24/7 skilled nursing If patient's needs surpass the services offered, patient needs to relocate Expensive
Long-term ancillary home health	Most accept Medicaid	n/a	Hourly basis (typically 3-hour minimum), indefinitely	Patient stays in their home	Expensive
Independent living facility	None	None	Until care needs exceed care offerings	A la carte nonskilled services and meals available A true home environment	If patient's needs surpass the services offered, patient must relocate Expensive

care settings must be aware that primary care providers (PCPs) may not follow their patients in the hospital setting and may be unfamiliar with the course of events during acute care. Ideally, the PCP would be contacted whenever one of their patients is admitted to the hospital. Additionally, contacting the PCP at the time of discharge can help prevent miscommunications and medication errors. These points of contact allow for a thorough handoff.

Medicare recognized that lack of adequate communication has resulted in unnecessary rehospitalizations. Medicare's Hospital Readmissions Reduction Program (HRRP) encourages hospitals to improve communication and care coordination to engage patients and caregivers in discharge plans and, in turn, reduce avoidable readmissions (CMS, 2021h). This program links payments for the hospitalization to the quality of patient care. Additionally, the National Quality Forum (2011) developed a list of serious reportable events to educate providers regarding serious, preventable, and costly medical errors. For these events, patient readmissions that occur within 30 days of discharge are not reimbursed.

In response to the errors that occur in transitions between settings, CMS in 2015 began to reimburse for transitional care management (TCM) encounters. The TCM billing codes are based on complexity of the admission as well as the time frames for follow-up. This TCM program designates that a patient should have at a minimum a telephone encounter with their PCP within 48 hours of discharge, followed by a face-to-face or telehealth evaluation within 7 to 14 days (CMS, 2021c). Contacting the patient soon after discharge allows for any miscommunication to be addressed before there is harm to the patient.

Subacute Care

When a patient is discharged from the inpatient setting, they may need rehabilitation or continued complex skilled nursing care. Subacute care can be provided in a long-term acute care hospital (LTACH), a skilled nursing facility (SNF), an outpatient rehabilitation facility, or in the patient's home with services from a skilled home health agency (HHA). Communication between the inpatient and subacute setting is critical for safe transition of care, especially to a setting

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where the patient's previous health information may not be available. Informing the PCP of the patient's admission to these facilities is recommended for continuity.

LONG-TERM ACUTE CARE HOSPITALS AND SKILLED NURSING FACILITIES

LTACHs provide care to patients who are technologically dependent and have highly complex medical needs that may take months to resolve. Those patients who must remain on a ventilator, those patients with unhealing pressure wounds, patients with severe burns, and patients requiring nonroutine or daily dialysis that require the care of a highly skilled nurse would be candidates for admission to an LTACH.

SNFs offer the opportunity for more oversight if rehabilitation after hospitalization is required. A SNF can provide more sophisticated treatments than those available in the home setting. Common services provided in a SNF include physical, occupational, and speech therapies; wound care; postoperative management; and administration of IV antibiotics and other parenteral treatments. A hospital admission for a minimum of 72 hours is required to be eligible for SNF services to be covered by Medicare. While a patient is in a SNF, care is managed by the facility's medical director or house physicians along with NPs and physician assistants.

A SNF may be located in an acute care hospital, part of a rehabilitation facility, or part of the services offered by a nursing facility. If the SNF is located in a nursing facility and the patient does not meet the rehabilitation goals to enable them to return to their home, they may become a resident in that facility and receive custodial care (discussed below) rather than skilled care. When patients are discharged to home from LTACHs or SNFs, the TCM program applies to the primary provider's follow-up care.

OUTPATIENT REHABILITATION

Outpatient rehabilitation centers are ideal for patients who are not homebound, when rehabilitation does not require much nursing intervention, and for patients who do not have significant barriers to transportation. Many outpatient rehabilitation centers specialize in different types of surgical rehabilitation and may even partner with surgeons for very specific treatment plans (e.g., a neurosurgeon specializing in deep brain stimulator implants for Parkinson's disease). Outpatient rehabilitation centers often have interdisciplinary teams including many different types of therapists who can see a patient during one visit.

HOME HEALTH AGENCIES

HHAs provide subacute care to patients whose rehabilitation and skilled nursing needs can be met in the home setting. Home health care is overseen and managed by the patient's PCP. The PCP must certify that the patient is homebound, and recertification needs to occur every 60 days unless rehabilitation goals are met and the patient is discharged. CMS guidelines define patients as homebound if "leaving the home requires a considerable and taxing effort due to chronic illnesses and/or injuries where patient needs the aid of supportive devices including crutches, canes, wheelchairs, or walker; the use of special transportation; and/or the assistance of another person to leave their place of residence" (CMS, 2021d). The decision to discharge to home with services by HHAs is most often made by inpatient providers who are unfamiliar with the supports available to the patient at home. When evaluating the patient for home health care, communication with the PCP is critical to assess the ability of the patient to be safe when alone or with the support of a caregiver to avoid unnecessary rehospitalization.

Custodial Care

The Centers for Medicare & Medicaid Services (CMS) distinguishes the type of care provided in home health and in institutions as *custodial* or *skilled.* While skilled services may be covered by Medicare or Medicaid, custodial care is not billable to Medicare but may be covered by Medicaid. It is not a perfect distinction because even when a patient is receiving primarily custodial care provided by nonlicensed caregivers in a nursing home, licensed providers still care for wounds or provide medications. This is also true in home health, where a licensed provider oversees the care provided by a nonlicensed provider on a scheduled basis. The licensed provider may also perform skills such as changing catheters.

HHAs do not require a hospital evaluation or admission for a patient to be eligible for Medicare coverage of services. Providers seeing patients in the ambulatory setting should consider referral for any problem a patient has, such a frequent falls, wounds, or medication management, that would benefit from a HHA nursing assessment. HHAs can offer chronic long-term (versus short-term, recovery-related) services to patients in their homes. These services are separated into two categories: skilled (requiring a nurse) and nonskilled (personal services and not requiring a registered nurse). Examples of skilled long-term services in the home include a patient with a permanent indwelling catheter that needs to be changed every month or a chronic implanted central line port that needs to be flushed routinely. Nonskilled home health care is provided by nursing assistants and arranged on an hourly basis on a schedule mutually agreed upon by the HHA and the patient or family. It may be further determined by what insurance providers, including Medicaid, or the patient can afford to pay personally. These services follow an individualized care plan, which can include reminding a patient to take their medications, bathing, meal preparation, cuing and guidance through ADLs, housekeeping, and transportation to appointments. Whether the services provided by the HHA are skilled or unskilled, they do require oversight by the PCP.

NURSING HOMES

Nursing homes are licensed as Nursing Facilities (NFs) by the state and Skilled Nursing Facilities (SNFs) by Medicare. A nursing home is a strictly regulated environment that provides a greater level of clinical oversight and more complex care than a residential care facility (RCF). In addition to skilled and residential care, some facilities have special units that provide memory care or dialysis. The CMS established the Five-Star Quality Rating System (https://www.cms.gov/Medicare/Provider-Enrollment-and-Certification/CertificationandComplianc/FSQRS) to help consumers, families, and caregivers compare facilities. The system provides an overall rating and a separate score for health inspections,

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staffing, and quality measures (CMS, 2021e). Nursing homes are also surveyed by the state health department at least annually to assess compliance with the state's rules and regulations.

A patient in a nursing home can reside there permanently to have their needs met 24 hours a day. They may also receive short-term, intermittent rehabilitation after a hospitalization. Although the atmosphere of a nursing home may not be as homelike as an assisted or independent living facility, there are increasing efforts being made to address that issue. The previous image of the hospital-like institution is rapidly being revised. Patients in a nursing home are referred to as residents, and although some facilities have shared rooms, the movement is to provide each resident with their own space. Provider care in a nursing home is managed by the facility's physicians, NPs, and physician assistants (PAs), but patients may leave the facility to see specialists as needed.

ASSISTED LIVING

Assisted living facilities are licensed through their states as RCFs. They provide a place for an older adult to reside in a homelike atmosphere while receiving nursing services as needed. Residences in an RCF are like apartments, and most provide a menu of options, with options for increasing services as necessary. Patients have their own unit with their own furnishings and a kitchenette. They may choose to take all meals in a dining room or cook for themselves. Housekeeping, laundry, and medication management are optional. Professional nursing services are limited and may only include one registered nurse with additional staffing by licensed practical nurses (LPNs) for daily care from 16 to 24 hours per day. Unlicensed caregivers are available to assist patients with their ADLs and housekeeping needs. Patients in RCFs are usually given the option of whether they would like their primary care provided by their community provider or the facility's physician, NP, or PA (Ohio Department of Health, 2020).

MEMORY CARE UNITS

Memory care units are becoming a common option in many custodial care settings, including nursing homes and RCFs. Memory care units offer unique programming for patients with a low level of cognitive function. Patients diagnosed with dementia do not have to reside in a memory care unit, but the facility has a dedicated area to support those patients, especially if they also have behavioral and psychiatric symptoms of dementia (BPSD). To support those special needs, memory care units include higher staffing ratios so that patients have access to one-to-one guidance, redirection, and supervision. There may also be adaptations in the physical facility, such as locking exits and entryways equipped with alarms.

RESPITE CARE

Respite care may be an option in a nursing home or RCF. Rooms in these facilities are available for short-term stays to give caregivers temporary relief. The rooms can be any level of care that the caregiver feels is appropriate for the patient. Respite care is not typically covered by insurance, and although it is very important to the mental health and well-being of family caregivers, particularly those caring for patients with dementia and BPSD, respite stays are not widely used due to the high cost.

ADULT DAY-CARE PROGRAMS

In an adult day-care program, older adults engage in activities, receive meals, and are under the supervision of personnel. Many programs even offer personal care such as bathing. This can be a more cost-effective option for caregivers, and some adult day-care centers are even authorized to be reimbursed by Medicaid.

PROGRAM FOR ALL-INCLUSIVE CARE FOR THE ELDERLY

The Program for All-Inclusive Care for the Elderly (PACE) is a national program that provides comprehensive care to frail older adults capable of living in the community with the program's support. The participants in the program need to require a nursing home–level of care. PACE services are covered by Medicare and Medicaid with the goal of keeping patients out of nursing homes and in the community as long as possible. The program improves the quality of life for the patients and their families and saves the federal government money. PACE receives capitated funding for each life enrolled and assumes all financial risk. The program negotiates with nursing homes and hospitals for beds as needed. Individual programs may partner with pharmacies to provide a formulary of medications. Currently there are 263 PACE programs in 31 states.

Independent Living Communities

Independent living communities (ILs) are unlicensed apartment- or condominium-style buildings that offer housing to those aged 55 and older. They have the least oversight and are the least institutional of care settings. They may offer services such as restaurant-style meals in a dining room, a housekeeper, and transportation. They may not provide any nursing services, but residents may choose additional services such as medication reminders, assistance with bathing, and laundry or housekeeping service. Some communities have an on-site clinic that may be staffed by an NP or PA. Medical care is commonly provided by the patient's PCP and other specialists as needed. Patients who need a higher level of support or supervision than can be provided in the IL setting can choose from different levels of residential facilities. Each state's health department licenses residential facilities, sets forth the rules and regulations for their operations, and visits the facilities at least annually to assess compliance.

Continuing Care Retirement Communities

Continuing care retirement communities (CCRCs) are groups of facilities located on a single campus that offer all levels of care described earlier: independent living, assisted living, and nursing home services. Some may even add adult day-care services. The goal of CCRCs is to provide the full spectrum of care so that residents can move through the levels of care as their needs change without leaving the CCRC (Fig. 5-1). CCRCs may require an initial investment. If the NP's patients are considering a CCRC, they must understand what is covered by the investment and whether refunds are allowed should the resident leave early.

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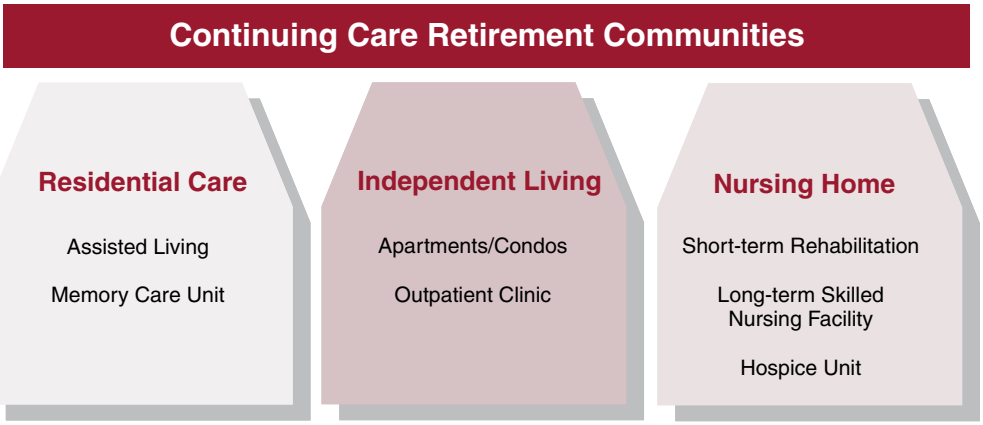

FIGURE 5-1 A theoretical setup of common continuing care retirement community (CCRC) service offerings.

Hospice and Palliative Care Services

Hospice is a Medicare reimbursement option that provides advantages in addition to classic Medicare. The service is underutilized by patients and families who envision it as an option that should be accessed only when death is eminent. Hospice is a service that is provided to a patient who has a terminal diagnosis with a life expectancy of less than 6 months, and that service can be provided in any setting where the patient resides including a private home, an assisted living facility, or a nursing home. A certificate of terminal illness needs to be signed by a physician, but a nurse practitioner can continue to be the primary care provider for their patients. Patients enrolled in a hospice program elect to forgo interventions to prolong life and sign the associated Do Not Resuscitate (DNR) order paperwork. It is not uncommon that with the support provided by hospice, patients improve and may go on what is labeled "navigator status" until their condition worsens again. Patients may also change their minds about stopping life-sustaining treatments and DNR status. Hospice agencies include registered nurses, social workers, chaplains, counselors, and nursing assistants to visit the patient wherever they are located to support the patient and provide comfort care throughout their end-of-life experience.

A referral for hospice services can be made by a patient's PCP or upon discharge from the hospital with a new terminal diagnosis (CMS, 2021f). An important but little-known service of hospice is to provide bereavement counseling to survivors for 13 months after the death of the patient.

Hospice agencies may also have inpatient units where they can admit a patient for short-term symptom management. Symptom management units can be particularly helpful for patients receiving hospice services in a private home who are struggling with pain control, BPSD, or other distressing symptoms.

Palliative care is a service offered by many hospice agencies to provide symptom management and comfort care to patients who may not have a terminal diagnosis, cannot be certified as having a life expectancy of less than 6 months, or do not want to sign a DNR or forgo other life-sustaining or curative treatments (such as a patient with cancer who wants to continue to receive chemotherapy but is having pain, nausea, or shortness of breath that is poorly controlled). Palliative care services may be provided by a physician, NP, or PA; counselor/social worker; and chaplain who may assess the patient in the inpatient setting and continue visits once a month (CMS, 2021g). Chapter 23 includes details of symptom management in hospice and palliative care.

MEDICAL RECORDS

As a patient moves from one setting to another, access to medical records is critical. Older adults may not have the ability to provide accurate history. They may never have received a clear explanation of all that occurred in a particular episode of care. When patients transition from one setting to another, continuity of care may be compromised unless there is access to important information. Miscommunication can be costly and result in duplication of services or, worse, medical errors. In 2016, the 21st Century Cures Act promoted interoperability between organizations by outlining requirements for states to begin utilizing health information exchange applications that provide authorized clinicians with secure, encrypted access to confidential patient information (Office of the National Coordinator for Health Information Technology, 2021). Although this movement has greatly improved the ability to access information, participation is not always 100%, and there are still challenges. There are many vendors that provide software for electronic medical records, and they are not all compatible, which prevents the desired accessibility to patient data.

PSYCHOSOCIAL ISSUES IN TRANSITIONS

It can be challenging to balance safety and risks while honoring patient preferences when selecting a setting of care. Older adults are reluctant to move to a setting where they must give up some of their independence or change their routines. The nurse practitioner (NP) should be aware that what matters most to the provider (medication compliance) or the patient's family (decreasing fall risks) might not be what matters most to the patient (staying in their home with their pet). Competent older adults can weigh the pros and cons of each setting and have the right to accept the risk of staying in their own home.

If a transition occurs, patients may grieve the loss of independence and changes that may require them to relinquish

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their car or to rely on strangers to help with activities of daily living (ADLs). If the change in setting was the result of the loss of a loved one who provided care and support, that compounds grief and puts patients at high risk for a new or exacerbation of existing mood disorders. The NP should be vigilant during transition periods, watching for symptoms of mood disorders and ineffective coping, even suicidal thoughts.

Caregivers need support during the process of selecting the right setting for their loved one. Feelings of guilt are a common response to the reality that they are not able to provide the care their loved one requires. Conflict may result from disagreement among family members regarding the decision to relocate the older adult. NPs should think of caregivers as an extension of the patient and support their needs by providing education on caregiver support groups or the availability of respite care.

Strategies that the NP can use to ease the psychosocial turmoil of care transitions include starting the discussion with the patient and their family early in the disease process. The NP can provide information about settings of care and what each setting offers, involving the patient and allowing them to have as much control over the decision making as possible. What matters to the patient should be the most important. Discussions about the cost of care and the possibility that Medicaid may be necessary in the future can help families in their planning. Referrals can be made to a social worker who can help provide additional information and resources.

Advanced Care Planning

Sometimes older adults, particularly those with cognitive impairments, are not able to make their own decisions about care services and settings. There are two types of advance directives that a patient can implement to ensure that their wishes are honored if they are unable to make them known themselves: (1) appointing a surrogate decision maker and (2) written directives. Advance directives do not become active unless a patient becomes incapacitated, so patients maintain their autonomy to make their own health-care decisions until they are unable to do so. Capacity is defined by the patient's ability to understand and reasonably apply information a clinician provides to them to make a choice about their care that is congruent with their values and preferences, using logic and appreciation of risks and benefits. Assessing a patient's capacity to give informed consent for any medical treatment or transfer in their setting of care is within the scope of the NP, and many tools and algorithms are available. Determination of incapacity can be transient (such as in delirium) or persistent (such as in dementia). Capacity can also vary depending on the complexity of the decisions at hand. For example, a patient with early-stage dementia may have the capacity to give consent to be sent to the emergency department (ED) after a fall but may lack the capacity to consent to a surgical procedure or to go to a skilled nursing facility (SNF) for rehabilitation (Tannou et al., 2020).

Centers for Medicare & Medicaid Services (CMS) delineates that advance care planning conversations should take place at a minimum during every annual wellness visit with an older adult and that there are reimbursements for the service, providing incentive to primary care physicians (PCPs) for specifically making time for these important discussions. Advance directive legal forms can generally be found on the Web site of each state's attorney general's office. Once signed and witnessed, the document should be kept in a safe place with the patient's will and a copy on file with the PCP's office and/or the facility where they live.

Appointing Surrogate Decision Makers

A durable health-care power of attorney (HCPOA) is both a legal document that empowers an individual chosen by the patient to make health-care decisions on their behalf if they become incapacitated and that individual. The patient must select the individual and formulate the HCPOA document during a time when they have full capacity to do so. Patients should be encouraged to give thoughtful consideration when choosing the HCPOA and be sure to select a person who they are confident would honor their wishes even if they disagree individually with them or are emotionally distraught. Older adults should have open and explicit conversations with their HCPOA about what they do and do not want in terms of care services, particularly end-of-life services.

If a patient becomes incapacitated and did not appoint an HCPOA, they become a ward of the state. A legal guardian is appointed through the patient's county probate court. The process must start with the ward being deemed legally incompetent (which differs from incapacitated, as discussed later), which requires official examination by more than one clinician and a judge's ruling. Individuals, who may be family members, can apply to be guardian, and the probate officer will typically grant them guardianship in the absence of any objections. The process of establishing guardianship can take many months to complete. If no individual applies for guardianship, the ward is appointed a volunteer guardian through adult guardianship service agencies. Guardianship is often avoidable and a main reason why advanced care planning is essential.

Written Directives

Living wills are documents that specifically outline select care services that a patient does or does not ever want. For example, a patient who feels very strongly about not wanting a feeding tube or being mechanically ventilated would put together a living will with this information. Code status, often referred to as Do Not Resuscitate (DNR) orders, is another important aspect of written advance directives. Each state creates standards for DNR orders, has specific forms to sign, and designates what type of clinician (physician, NP, etc.) is permitted to sign the forms. There are three types of code status: full code, DNR, and DNR-Comfort Care (DNRCC). A full code means that if a patient becomes noncommunicable and needs emergency care, they will receive all related treatment and/or resuscitative care available, including cardiopulmonary resuscitation. Full code status is the default status for all patients when a DNR status is not known. This is important because if a patient signs a DNR form and it is not kept visibly on file and/or the status is not communicated effectively between care providers and settings, the patient may be resuscitated in an emergency situation against their wishes.

This difference between a DNR and a DNRCC code status can be confusing, and definitions and terms vary state by

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state. When a patient signs a DNR order, they are agreeing to have all treatment-related care provided to them up until the point that they may experience a cardiac or pulmonary arrest. When arrest occurs, the patient is not resuscitated. A DNRCC order means that in addition to not wanting to be resuscitated after cardiac arrest, they also do not want all treatment-related care available; the patient only wants comfort care provided. Patients enrolling in hospice programs sign DNRCC orders as part of the admission process; however, patients who do not qualify for hospice may also sign DNRCC orders. Examples include a patient who prefers homeopathic approaches to their care or individuals who do not want to be hospitalized or participate in invasive testing/procedures. Code status documents should be kept in a safe place with the patient's will and on file with the PCP's office and/or the facility where they live. Many state health departments offer wallet cards, ID bracelets, and other identification tools to help address this issue of communicating the patient's wishes.

A common question patients ask is, "If I put my wants and wishes in writing with a living will and a DNR order, why do I need to appoint a power of attorney?" It is impossible for a living will document to outline every possible scenario that a patient could encounter throughout the rest of their life when health-care decisions have to be made, which is why having both a carefully selected HCPOA and a living will is essential and recommended.

HEALTH-CARE FINANCE

It is impossible to consider options for different settings and services without considering the financial feasibility. A patient's insurance coverage and their ability to afford care are often the determining factors of where, how, and who will provide what is needed to a patient. In the United States, the predominate third-party payers of medically necessary services to older adults are Medicare, Medicaid, and private insurance companies. The Centers for Medicare & Medicaid Services (CMS) sets the rules for these payers and administers some coverage benefits directly.

Medicare

In 1965 Medicare was passed as an amendment to the 1935 Social Security Act. It is a federal insurance program available to adults 65 years of age and older, individuals on disability, and patients with end-stage renal disease. The Medicare program initially included two parts, A and B. Part A is coverage for hospitalization and provided to everyone 65 and older who paid Medicare taxes for at least 10 years. Part B, medical coverage, is offered as an option and requires an additional premium, which is deducted from the individual's Social Security payment.

In 1997, the Balanced Budget Act provided an option for a managed care plan, Medicare Part C. These plans provide an option for those with Medicare Parts A and B to sign up for a private insurance managed care plan. These private insurance plans administer a patient's benefits, often called Medicare Advantage plans. These plans are not bound by the requirements of Medicare Part A, B, or D and can offer benefits such as dental care, eyeglasses, hearing aids, and even health club memberships. By the end of 2020, more than 40% of Medicare beneficiaries had elected to enroll in a managed care plan, increasing the privatization of Medicare. Patients who sign up for Advantage plans must receive services from the plan's network of providers and receive prescriptions from within the Advantage plan's formulary to have them covered.

The decision to keep traditional Medicare Parts A and B versus signing up for an Advantage plan has a crucial impact on the future of the beneficiary's options for care. In Ohio, for example, there are more than 20 Advantage plans available for beneficiaries to choose from. Turning 65 years old and becoming eligible for Medicare can be a daunting experience, and beneficiaries often seek the support of financial advisors to navigate through the sea of options. Because open enrollment occurs every year and changes can be made at that time, Medicare beneficiaries may change their plans. The primary care physician (PCP) may suggest the importance of making sure the current PCP is included in the plan and that the benefits offered will meet the level of care that the patient needs.

In 2003, the Medicare Prescription Drug, Improvement, and Modernization Act (MMA) was passed, establishing prescription drug coverage under Medicare Part D. For the first time the federal government was providing medication coverage. The plan was less than perfect, including a "donut hole" provision that resulted in many older adults toward the end of the year running out of coverage and paying full price for their medications. The Affordable Care Act (ACA) has a provision slowly closing that donut hole, but it can still be a problem for patients. The yearly open enrollment also applies to Medicare Part D plans. PCPs are also important resources to remind patients to select their plans carefully to make sure their medications are covered without requiring prior authorization or excessive copayments. Those with Medicare Advantage plans have their medications covered under that plan and are not required to sign up for Part D and not subject to the "donut hole."

Medicaid

Medicaid is a program for low-income individuals that is jointly administered by the federal and state governments using a system of cost sharing. Of those receiving Medicare, 21% are also receiving Medicaid. Medicaid is available to children, pregnant women, parents, and people with disabilities, as well as older adults. The ACA raised the eligibility requirement to 133% of the federal poverty level. Each state sets the conditions of participation and coverage as well as the income and asset threshold for eligibility, and not all states chose to expand coverage as provided by the ACA. The asset threshold is the criteria that results in some older adults not taking advantage of the benefit out of fear of losing their home and any bequest they hoped to leave to their families. Assets that could be used to pay medical bills cannot be gifted, sold under market value, or transferred without penalty of a period of Medicaid ineligibility. Medicaid has a look-back period of 60 months from the day of application in all states but California, which has a 30-month look-back period. Any assets transferred after that period may affect eligibility for Medicaid. Most long-term care services and, in many states, residential care facility (RCF) services are covered by Medicaid. States offering privatized Medicaid plans

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allow beneficiaries to select a private insurance company to manage their Medicaid benefit.

Older adults can qualify for and receive both Medicare and Medicaid coverage at the same time if they are older than 65 years and have low income and few assets. These beneficiaries are called "dual-eligibles." In this scenario, the payors work together to cover outpatient, acute, subacute care, and prescriptions (Medicare) and long-term care services (Medicaid). Some states administer their Medicaid benefits to beneficiaries directly, while others have transitioned to encouraging dual-eligibles to sign up for an Advantage plan. Older adults may opt out of the recommendation to sign up for an Advantage plan and keep traditional Medicare Parts A and B with Medicaid as a supplement, but many do not realize that opting out is possible. NPs assisting older adults in transitions of care must have knowledge of the benefits and restrictions of each patient's coverage.

Private Pay

Most older adults will at least have traditional Medicare Parts A and B, but there are still many uncovered costs. Medicare Supplement and Advantage plans cover some of these expenses but not everything. Medication copays can be very high if the medication is a third-tier drug. More and more medications are approved for sale without a prescription and plans generally do not cover over-the-counter medications at all. Paying privately for care, particularly long-term care services, can be profoundly expensive and therefore unaffordable for patients. In the United States, the average private pay room and board rate in 2020 was approximately $8,000 per month in a nursing home, $4,300 per month in assisted living, and $4,500 per month for long-term nonskilled home health (Genworth, 2021). The cost of long-term care services will often exhaust a patient's savings and assets and result in the need to apply for Medicaid to continue to receive the care they need. Medicaid is the largest single payer of long-term care services, with a range from 50% to 75% depending on the state. Case examples of various private pay scenarios are shown in Box 5-1.

BOX 5-1
Private Pay Scenarios

- The clinician may want a patient to go to a skilled nursing facility (SNF) for rehabilitation after a hospital stay. Medicare only covers an SNF stay if the patient has been admitted in the hospital for a minimum of 72 hours. If the patient did not meet the 72-hour admission criteria and cannot afford to pay for the SNF stay privately, they would return home with home health agency services instead.
- If a patient is rehabilitating in an SNF and does not meet their treatment goals and needs to stay for long-term care in the nursing home, Medicare stops covering the patient's stay. The patient either needs to pay the daily private pay rate and/or apply for Medicaid if they cannot afford the private pay rates.
- A nurse practitioner may order for a patient to receive skilled home health care by a certain agency, but if the agency is not in the patient's Advantage plan network, a different agency must be found, which can cause delays and communication hazards.
- Acute care providers discharging patients to their homes are often unfamiliar with coverage issues and prescribe medications that patients will not use because of the enormous expense in fulfilling the prescription.

CASE STUDY

You are the PCP for Deborah, an active 88-year-old retired teacher, and her husband, Bill, an 89-year-old with advanced rheumatoid arthritis. They reside together in an independent living community (IL) condo. Deb has well-managed comorbidities of hypertension, type 2 diabetes, and hyperlipidemia. She sustains a fall that fractures her femur and requires surgical repair. While in the hospital, Deb develops pneumonia, which prolongs and complicates her inpatient stay. She goes to a skilled nursing facility (SNF) for rehabilitation for 45 days. While there, her type 2 diabetes management requires escalation, and she is treated for deep vein thrombosis. Bill wants Deb to stay longer in the SNF because she has not returned to her baseline functional status prior to her injury, and he is apprehensive about handling her medical care at home on top of his own problems; however, her insurance will not cover any additional SNF time. They cannot afford to pay the $295 per day privately and do not meet the income level to be eligible for Medicaid, so Deb is discharged home on a Friday afternoon. When Bill goes to pick up her medications from the pharmacy, including new basal insulin and a novel anticoagulant, the cost is over $2,000 because the prescriptions were not in their drug plan formulary, so he does not get them. On Sunday, an unlicensed aide in the IL helps Deb check her blood sugar, which is 390. The aide decides to call 911. A social worker in the emergency room tells Deb and Bill before sending them back home that they should consider assisted living. Hearing this, daughter Susan comes into town, and all three of them are in your office for a transitional care management (TCM) follow-up visit to come up with a plan with your guidance. Susan has her health-care power of attorney (HCPOA) documents with her just in case you need to see them so she can make the decisions for her parents today.

1. What transitional care complications were avoidable in this scenario? How could they have been prevented?
2. What information will you obtain to be able to come up with an effective care plan for Deb and her family?
3. What services could Deb be eligible for today?
4. What conditions are Deb and Bill at high risk for?
5. Do you think that assisted living placement is the answer for this family? Why or why not?
6. Will Susan be making the decisions for her parents? Why or why not?

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unit II

Assessment

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CHAPTER 6

Comprehensive Geriatric Assessment

Evelyn Duffy

The comprehensive geriatric assessment (CGA) has been a cornerstone of the care of older adults. Older individuals represent a richly diverse population. People age at different rates and within one person organ systems age at different rates. In addition to physiological changes with aging, older adults face many psychosocial adaptations, as well as economic and environmental challenges. How these changes impact the functional ability of the older adult is a key to the overall assessment of their health (Tran & Leonard, 2017). These changes can differ dramatically among individuals of the same chronological age. Older individuals who can benefit the most from CGA are those with multimorbidity and the older adult who is already experiencing functional decline. All older adults, but especially those with frailty, have less physiological reserve and are at increased risk of iatrogenic complications, particularly related to the multiple medications prescribed to treat chronic conditions. The disease model that applies differential diagnosis is inadequate in the setting of multimorbidity and frailty. CGA helps not only to diagnose treatable conditions and improve patient outcomes, but also to identify potentially preventable conditions.

CGA has been defined as a multidimensional, interprofessional, diagnostic process to identify care needs, plan care, and improve outcomes for older people (Palmer & Onder, 2018). A Cochrane Systematic Review of inpatient CGA versus usual care of older adults admitted to acute care or inpatient rehabilitation concluded that older adults were more likely to be alive and in their own homes if they received a CGA (Ellis et al., 2017). A systematic review of CGA in primary care (Garrard et al., 2020) concluded that there was improved adherence to medications but no improvement in survival or functional outcomes. The authors note that the interventions were widely accepted by the patients and potentially cost-effective. Garrard, et al. (2020) and Palmer and Onder (2018) suggest that a formal CGA be offered to a select category of patients—those with multimorbidity or frailty—because they may benefit most. Patients with multimorbidity are found to report lower quality of life and well-being and less satisfaction with care. Patient-centered care respects the wishes of the individual, and the result is an increased satisfaction with care and improved outcomes (Kuipers et al., 2019).

Advanced practice nurses may be a part of a team that works together to complete a CGA or may apply the concepts of CGA to their own patients. The nursing model of addressing the biopsychosocial needs of patients is reflected in the concepts of the CGA, which include function, physical health, mobility, psychological well-being, socioeconomic and environmental factors, and quality of life. Several geriatric assessment instruments are focused on these domains. These tools can facilitate the assessment, diagnosis, and evaluation processes, and those with the most clinical utility are highlighted in this chapter. Suggested dimensions within each CGA domain are identified in Table 6-1. Each of these domains is described in greater detail as follows.

PHYSICAL HEALTH

The physical assessment of the older adult includes all the components of a conventional medical history (chief complaint, history of present illness, past medical history, family and social history, and a review of systems), the conventional physical examination, and appropriate diagnostics based on the findings. Assessment begins with the first contact with the patient. Observe the patient's appearance, language, and behaviors and whether they look the stated age. Note if they are appropriately dressed for the occasion and season and if there are any signs of neglect in self-care. What is the quality of their voice and the manner and content of speech? What behaviors are observed, including facial expressions, eye contact, gestures, or abnormal movements? If a family member or caregiver accompanies the patient, how do they interact?

Interviewing begins before the physical examination and typically continues throughout the examination. In a formal CGA, it is common to send a geriatric history-taking form to the patient in advance so that they or their family can complete it and the details can be reviewed and expanded on during the visit. Any impairment in vision, hearing, speech, or cognition may affect the patient's ability to communicate effectively. Impairments should be addressed, and measures taken to accommodate them during the visit, to prevent the trap of talking to the family or caregiver, if present, to facilitate the visit rather than talking directly to the patient. In most cases, the patient's permission should be acquired

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TABLE 6-1 Comprehensive Geriatric Assessment

DOMAINS OF COMPREHENSIVE GERIATRIC ASSESSMENT	DIMENSIONS OF COMPREHENSIVE GERIATRIC ASSESSMENT
Physical health	History taking
	Physical examination
	Diagnostics
	Nutritional assessment
	Medication review
Functional health	Activities of daily living
	Instrumental activities of daily living
	Sensory assessment (hearing, vision)
	Gait and balance
Psychological health	Cognitive disorders (delirium, dementia, mild cognitive impairment)
	Affective disorders (depression, anxiety)
	Spiritual well-being
Socioenvironmental supports	Social network and support
	Living situation
	Environmental safety
	Economic resources
Quality of life measures	Physical conditions
	Social conditions
	Environmental conditions
	Personal resources (mental health, life perspective)
	Preferences for care

before interviewing the family. However, the input of the family or caregiver can provide valuable information about the patient's behavioral or functional changes of which the patient may not be aware or willing to share. A change in function can be a sign of change in the patient's overall health status; it is often the first sign of illness or decompensation of an existing disease. It is important to address what the patient or their family considers significant, which often differs from what the provider considers significant.

Many older adults suffer from multiple chronic conditions that require monitoring. When two or more chronic diseases are present it is described as multimorbidity (Kadambi et al., 2020). There are no good clinical tools for measuring the burden of multimorbidity, although research tools that include the number and severity of chronic diseases, such as the Charlson Comorbidity Index (CCI), do exist (Kadambi et al., 2020). The history of chronic diseases should be identified and updated with any symptoms of decompensation. An older adult may not present with a new chief concern, but if one is reported it is important to put it into the context of the patient's previous health and illness. If a new concern is identified, a history of present illness is recorded using the seven dimensions of symptomatology as a guide (location and radiation, quantity and quality, aggravating and alleviating factors, associated symptoms and signs, absence of associated symptoms and signs, evolution and course of the symptom, and effect of the symptom on normal daily activities). After taking the history, the provider should summarize for the patient what was heard. This gives the patient the opportunity to clarify or deny any parts of the discussion.

Medication

Medication review should be completed at every encounter. Asking a patient to describe how they take a medication rather than asking if they take it is much more informative. Because older adults are the population most likely to suffer from multiple chronic diseases, they are also most likely to take more medications, both prescribed and over-the-counter. The more medications a person is taking, the more likely they are to have an adverse drug event. Polypharmacy is associated with both adverse drug events and frailty. The risk of mortality and disability is higher in patients with polypharmacy and frailty than in polypharmacy alone (Kojima et al., 2020). The most frequently used tool for evaluating drug use is the American Geriatrics Society (AGS) Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults, first published in 1991 and most recently updated in 2019 (American Geriatrics Society [AGS], 2019).

A subsequent scale was developed to address some of the limitations of the Beers criteria, the Medication Appropriateness Index (Hanlon & Schmader, 2013; Hanlon et al., 1992) (Table 6-2). First published in 1992, it is a validated tool that can be used along with the Beers criteria to determine the appropriateness of prescribed medications for older adult patients. While the screening questions in Table 6-2 are applicable in the clinical setting, use of the complete instrument is more appropriate for research.

Appropriate prescribing often means that multiple medications are required for adequate management of chronic disease. Appropriate prescribing may require adding a medication, such as an angiotensin-converting enzyme (ACE) inhibitor for a patient with diabetes or chronic kidney disease. Limitations in the Beers criteria led to the development of more explicit criteria, including the Screening Tool of Older Persons' Prescriptions (STOPP) and the Screening Tool to Alert Doctors to Right Treatment (START) (Gallagher

TABLE 6-2 Medication Appropriateness Index Criteria

Is there an indication for the drug?
Is the medication effective for the condition?
Is the dosage correct?
Are the directions correct?
Are the directions practical?
Are there clinically significant drug-drug interactions?
Are there clinically significant drug-disease/condition interactions?
Is there unnecessary duplication with other drugs?
Is the duration of therapy acceptable?
Is this drug the least expensive alternative compared with others of equal usefulness?

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et al., 2008). The tools address the issue of appropriate prescribing and deprescribing more specifically and are organized by organ system. They were updated in 2015 with the publication, *STOPP/START Criteria for Potentially Inappropriate Prescribing in Older People: Version 2* (O'Mahony et al., 2015). While the STOPP tool lists those that should be assessed for possible elimination the START tool includes medications that may need to be added, which is a unique aspect of STOPP/START. O'Mahony in 2020 reviewed recent research evaluating the integration of the STOPP/START criteria into the electronic medical record (EMR) showing its ongoing value in improving clinical outcomes.

Examination

Objective data collection begins with vital signs. These may be obtained by ancillary staff, but any abnormalities need to be verified by the provider. A common issue is the necessity to rule out orthostatic hypotension, which is prevalent in older adults due to volume depletion and the effects of medications. If concerns indicate the possibility of orthostatic drop, the provider needs to accurately measure the blood pressure (BP). The patient should lie down for 5 minutes and then have the BP and pulse rate measured. Have the patient stand and wait for a full minute, then repeat the BP and pulse rate measurements. Note any symptoms of light-headedness or dizziness and any drop in systolic BP greater than or equal to 20 mm Hg or diastolic BP greater than or equal to 10 mm Hg. An increase of heart rate of at least 30 beats per minute (bpm) is also abnormal. With aging, baroreceptors that are triggered by a change in position become less sensitive and vasoconstriction to maintain blood pressure is slowed, so it is important to repeat the BP and pulse rate measurements 3 minutes after standing if there was a significant drop. If BP and pulse have returned to baseline the patient has not demonstrated true orthostasis, but you may have confirmed the cause of light-headedness or dizziness.

Pulse oximetry provides a measure of oxygen saturation. The right middle finger and thumb may provide the best results. Normal readings range from 95% to 100% and any value less than 90% is considered low. A respiratory rate greater than 20 respirations per minute is classified as tachypnea and may be a sign of infection or sepsis, lung disease, heart failure, or a metabolic disorder. Weight is another measurement in which accuracy is important because it is a marker for both nutritional and fluid status. Pain is the fifth vital sign and quantifying pain can be accomplished in various ways, although older adults may prefer verbally descriptive scales.

A comprehensive physical examination of the older adult should be completed as a part of the CGA. A sample examination is identified in Table 6-3. An examination of the older adult, including a thorough assessment of functional ability, is as important as careful examination of each body system. All five senses impact functional health. Vision and hearing are commonly included in physical examination, but sense of touch, taste, and smell may not be. Among the many lessons learned from COVID-19 was the increased understanding of the importance of both smell and taste to flavor of food and subsequently to a good appetite. Addressing the health of all five senses can improve function in multiple ways because sensory loss often precludes the ability of the older adult to live independently. Both a decline in hearing and vision have been linked to cognitive decline (Ray et al., 2019). Measured visual acuity (corrected with lenses) equal to or worse than 20/40 constitutes a visual impairment. Abnormality in the six cardinal fields of gaze with nystagmus or lack of a downward gaze may reveal a neurological disease, such as progressive supranuclear palsy (PSP). Dilated ophthalmologic examinations are essential to the identification of cataracts, diabetic retinopathy, glaucoma, or macular degeneration. All of these are common diseases of the eye in older adults, and treatment can preserve vision. Although traditional Medicare does not cover routine eye examinations, it does cover examinations to assess for disease.

Screening for hearing loss can be accomplished using a handheld audiometer, which is more accurate than the whispered voice test. Otoscopic examination may reveal a cerumen impaction, which can result in a conductive hearing loss. If hearing loss is suspected, referral to an audiologist for a complete assessment is required. Although Medicare does not pay for hearing aids, it will cover a hearing assessment by an audiologist for suspected hearing loss. Many Medicare managed care plans cover both routine eye examinations and hearing aids.

Thorough neurological and musculoskeletal examinations are particularly important in the older adult. In younger adults, neurological and musculoskeletal examination may be less of a focus because health of those systems is obvious, but older adults may have unrecognized muscle weakness, limitations in range of joint motion, or contractures requiring thorough examination. Hip flexion contractures are common but can obscured by an increase in lumbar curvature. Careful assessment of range of motion of the hip is important because hip flexor contractures can increase the risk of falls. The Thomas test is an assessment technique that can help accurately evaluate the hip.

After completing the examination, discuss the general findings with the patient. Patient teaching should reinforce the positive behaviors taken to improve or maintain health and teach self-assessment and self-care management strategies. A plan for implementing recommended screening tests should be included in the discussion.

Diagnostics

Chapter 1 discusses the changes associated with aging that are reflected in laboratory values. This section provides some general guidelines on when to order testing. The reader is referred to the disease sections of this text for more specific guidelines. There needs to be a distinction between tests used to screen older adults and tests used to aid in diagnosis as these have different objectives. Screening has been defined as the presumptive identification of unrecognized disease or defect by the application of tests, examinations, or other procedures. The screening parameters for those older than 65 years, which include diagnostic testing, are covered in Chapter 2, Health Promotion.

Before ordering a test for diagnostic purposes the provider needs to assess whether the test result will alter the diagnosis, prognosis, or management of a condition. Some guidelines for use of diagnostics in decision making include: What is the prevalence of the disease being screened for with the test? What is the sensitivity and specificity of the test? Will the test

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TABLE 6-3 Sample Focused Geriatric Physical Examination

SIGNS		PHYSICAL SIGN OR SYMPTOM	DIFFERENTIAL DIAGNOSES
Vital signs	Blood pressure	Hypertension	Adverse effects from medication, autonomic dysfunction
		Orthostatic hypotension	Adverse effects from medication, atherosclerosis, coronary artery disease
	Heart rate	Bradycardia	Adverse effects from medication, heart block
		Irregularly irregular heart rate	Atrial fibrillation
	Respiratory rate	Increased respiratory rate >24 breaths per min	Chronic obstructive pulmonary disease, heart failure, pneumonia
	Temperature	Hyperthermia, hypothermia	Hyperthyroidism and hypothyroidism, infection
General		Unintentional weight loss	Cancer, depression
		Weight gain	Adverse effects from heart failure, medication
Head		Asymmetrical facial or extraocular muscle weakness or paralysis	Bell's palsy, stroke, transient ischemic attack
		Frontal bossing	Paget's disease
		Temporal artery tenderness	Temporal arteritis
Eyes		Eye pain	Glaucoma, temporal arteritis
		Impaired visual acuity	Presbyopia
		Loss of central vision	Age-related macular degeneration
		Loss of peripheral vision	Glaucoma, stroke
		Ocular lens opacification	Cataracts
Ears		Hearing loss	Acoustic neuroma, adverse effects from medication, cerumen impaction, faulty or ill-fitting hearing aids, Paget's disease
Mouth, throat		Gum or mouth sores	Dental or periodontal disease, ill-fitting dentures
		Leukoplakia	Cancerous and precancerous lesions
		Xerostomia	Age-related, Sjögren's syndrome
Neck		Carotid bruits	Aortic stenosis, cerebrovascular disease
		Thyroid enlargement and nodularity	Hyperthyroidism and hypothyroidism
Cardiac		Fourth heart sound (S_4)	Left ventricular thickening
		Systolic ejection, regurgitant murmurs	Valvular arteriosclerosis
Pulmonary		Barrel chest	Emphysema
		Shortness of breath	Asthma, cardiomyopathy, chronic obstructive pulmonary disease, heart failure
Breasts		Masses	Cancer, fibroadenoma
Abdomen		Pulsatile mass	Aortic aneurysm
Gastro-intestinal		Constipation	Adverse effects from medication, colorectal cancer, dehydration, hypothyroidism, inactivity, inadequate fiber intake
Genital/rectal		Fecal incontinence	Fecal impaction, rectal cancer, rectal prolapse
		Atrophy of the vaginal mucosa	Estrogen deficiency
		Prostate enlargement	Benign prostatic hypertrophy
		Prostate nodules	Prostate cancer
		Rectal mass, occult blood	Colorectal cancer
Urinary		Urinary incontinence	Bladder or uterine prolapse, detrusor instability, estrogen deficiency

Continued

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TABLE 6-3 Sample Focused Geriatric Physical Examination—cont'd

SIGNS	PHYSICAL SIGN OR SYMPTOM	DIFFERENTIAL DIAGNOSES
Extremities	Abnormalities of the feet	Bunions, onychomycosis
	Diminished or absent lower extremity pulses	Peripheral vascular disease, venous insufficiency
	Heberden nodes	Osteoarthritis
	Swan neck deformity	Rheumatoid arthritis
	Pedal edema	Adverse effects from medication, venous insufficiency, heart failure
Musculo-skeletal	Diminished range of motion, pain	Arthritis, fracture
	Dorsal kyphosis, vertebral tenderness, back pain	Cancer, compression fracture, osteoporosis
	Gait disturbances	Adverse effects from medication, arthritis, deconditioning, foot abnormalities, Parkinson's disease, stroke
	Leg pain	Intermittent claudication, neuropathy, osteoarthritis, radiculopathy, venous insufficiency
	Muscle wasting	Atrophy, malnutrition
Skin	Erythema, ulceration over pressure points, unexplained bruises	Anticoagulant use, elder abuse, idiopathic thrombocytopenic purpura
	Premalignant or malignant lesions	Actinic keratoses, basal cell carcinoma, malignant melanoma, pressure ulcer, squamous cell carcinoma
Neurological	Tremor with rigidity	Parkinson's disease

Source: From Elsay, B., & Higgins, K. E. (2011). The geriatric assessment. American Family Physician, 83*(1), 48–56.*

be accepted and tolerated by the patient? Does the benefit of the test outweigh the risk? Is it the least invasive test available? Will the results change the treatment of the patient? The best tests for screening have high sensitivity to decrease the risk of false negatives. For diagnosis, it is preferred that the test have high specificity to avoid the problem of false positives, which can result in additional testing and expense. This is especially true if the disease has a low prevalence. An excellent resource for providers is the ChoosingWisely.org Web site. Even tests with high sensitivity and specificity produce false results when applied inappropriately and without a firm understanding of the concepts. Most important, consider the test's acceptability to the patient. This is especially significant in the patient who cannot make a choice and give consent. In such individuals, a proxy is needed to gain permission to give the test. Although some patients may be unable to express themselves verbally, their behavior may give nonverbal expression to their feelings toward the test's acceptability.

The physical examination may reveal some indicators of malnutrition, including weight loss, muscle wasting, dry and dull hair, mental impairments, and poor wound healing. The body mass index (BMI) is commonly used to determine whether patients are underweight or obese. The proportion of fat increases with age and muscle mass decreases. Muscle weighs more than fat, so the BMI in older person may be artificially low.

There is no gold standard for biomarkers of nutritional deficiencies in the older adult, but some indicators include prealbumin, transferrin, albumin, chemistries, complete blood count, vitamin B_{12}, folate, 25(OH) vitamin D, and thyroid panel. As the understanding of the role of pro-inflammatory cytokines on the acute phase protein response, albumin cannot be used as the sole indication of malnutrition. The presence of inflammation needs to be considered when interpreting serum albumin results. This is reviewed in detail in Chapter 4.

FUNCTIONAL HEALTH

Although functional decline is common with advanced aging, the two are not synonymous. Functional decline occurs in every system, but the distinction between functional usual aging and functional successful aging remains unclear. The goal in geriatric care is to improve function, if possible, and, if not, to prevent further functional decline or slow down the process of functional deterioration. The parameters of function include both activities of daily living (ADLs) and instrumental activities of daily living (IADLs). Basic ADLs include three components: basic self-care, mobility, and continence. IADLs measure community interactions within the home and outside the home (Table 6-4). Whereas these activities are classic measures of function, physical health, mood, memory, substance use, and medications are also involved in a patient's functional ability.

Two well-established tools used to evaluate function in older adults are the Katz Activities of Daily Living Scale (Katz et al., 1963) and the Lawton and Brody Scale for Instrumental Activities of Daily Living (Lawton & Brody, 1969). It is important to be cautious about self-report of function (rather than direct observation of function) and to ask, "How do you . . .?" or "Show me how you. . . ." instead of "Can you . . .?" in order to determine whether patients actually perform the activity. Bathing is often the first ADL that poses problems for older

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TABLE 6-4 Selected Elements of Functional Independence/Dependence

ACTIVITIES OF DAILY LIVING	INSTRUMENTAL ACTIVITIES OF DAILY LIVING
Bathing	Food preparation
Dressing	Household chores
Toileting	Laundry
Feeding oneself	Managing medications
Moving from bed to a standing position or chair	Using the telephone
Ability to walk with or without assistive device	Managing finances
Continence of urine	Shopping
Continence of stool	Transportation

adults. When function is an issue involving other disciplines, physical therapy, occupational therapy, or social work can add data that will improve the planning. Since 2020 advanced practice registered nurses (APRNs) have been able to certify for Medicare home health care. Referring for a home assessment to a home health agency is an advantage. The home health nurse can assess medications, and the therapists can assess for safety hazards and observe the patient in their own environment. They can also help identify environmental risks for falling. Falls are a leading cause of death and disability in the older adult, and assessment of both intrinsic and extrinsic factors contributing to falls is important. Ask yourself the question, "Why did this patient fall today?" A valid tool for assessment of falls is the Hendrich II Fall Risk Model, which is useful in acute care, ambulatory care, assisted living, and long-term care (Hendrich et al., 2003). In addition to identifying those at risk for falls, it helps to identify appropriate interventions to reduce their fall risk. Mobility can be screened with the Timed Get Up and Go Test. This test involves observing for unsteadiness as the patient gets up from a chair without using the arms, walks 10 feet, turns around, walks back, and resumes a seated position. Timing the process, which should take less than 16 seconds, enhances the sensitivity of this test (Podsiadlo & Richardson, 1991). Patient difficulties performing this test indicate mobility issues, weakness of the extremities, and an increased risk of falling. Tinetti's Performance Oriented Mobility Assessment is a task-oriented test that measures gait and balance abilities (Tinetti, 1986).

PSYCHOLOGICAL HEALTH

Cognitive and affective disorders, specifically dementia, depression, and delirium, are more prevalent in older adults, and clinical definitions of these disorders are addressed in the *Diagnostic and Statistical Manual of Mental Health Disorders (DSM)*, 5th ed. (5th ed.; *DSM-5*; American Psychiatric Association, 2013). The *DSM-5* describes the characteristics of delirium and mild or moderate neurocognitive disorders. There are several validated tools used to screen for cognitive dysfunction. For years the gold standard was the Mini-Mental Status Examination (MMSE), but more recent tools have all been validated against that standard. Three tools used in clinical settings have comparable psychometric properties to the MMSE: the Mini-Cog, Montreal Cognitive Assessment (MoCA), and Saint Louis University Mental Status Examination (SLUMS) (Cummings-Vaugh et al., 2014; Tariq et al., 2006; Tsoi et al., 2015). The Mini-Cog is now copyrighted and details regarding its administration are available on the Web site mini-cog.com. Both the MoCA and SLUMS have comparable specificity and sensitivity to the MMSE and are better at identifying mild neurocognitive disorder. The MoCA, which has the distinction of being the most sensitive screening tool for mild neurocognitive disorder now requires registration and training prior to its use; refer to its Web site, https://www.mocatest.org. Currently the SLUMS is still accessible online, and additional requirements for administration are not preventing its use.

Older adults are at greater risk of delirium, which is underrecognized and underdiagnosed. There are several instruments designed to screen for delirium; however, the best evidence supports the use of the Confusion Assessment Method (CAM), which takes 5 minutes to administer (Inouye et al., 1990). The CAM diagnostic algorithm is based on four cardinal features of delirium: (1) acute onset and fluctuating course, (2) inattention, (3) disorganized thinking, and (4) altered level of consciousness (Shi et al., 2013).

Depression is also underrecognized in older adults. There are several screening tools for depression. The Patient Health Questionnaire (PHQ) has become the universal screen for depression across adult age-groups and is the screen included in the Medicare Wellness examination. It assesses depressive symptoms and functional impairment and screens for symptom severity. The PHQ-2 consists of two items; if positive, it is followed by the PHQ-9, a nine-item depression scale. In a recent meta-analysis by Levis et al. (2020), the combined screening had a higher sensitivity but a comparable specificity than the use of the PHQ-9 alone. In both cases, the specificity and sensitivity exceeded 80% for major depressive disorder. Still widely used in clinical practice is the Geriatric Depression Scale: Short Form (GDS:SF). It consists of 15 questions requiring a "yes" or "no" response, and it can be completed quickly in any setting (Sheikh & Yesavage, 1986).

A program to improve the quality of spiritual care validated the use of three instruments: HOPE, FICA, and SPIRIT. These tools are effective means of determining the older patient's spiritual beliefs and the comfort associated with these beliefs (Piotrowski, 2013). In that program, they chose to use the HOPE questionnaire with one additional question, "Are you at peace?"

HOPE (Anandarajah & Hight, 2001)

- Sources of **H**ope, meaning, comfort, strength, peace, love, and connection
- **O**rganized religion
- **P**ersonal spirituality and practice
- **E**ffects on medical care and end-of-life issues

FICA (Puchalski & Romer, 2000)

- **F**aith or belief
- **I**mportance or influence
- **C**ommunity
- **A**ddress

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SPIRIT (Ambuel, 2005)

- **S**piritual belief system
- **P**ersonal spirituality
- **I**ntegration with a spiritual community
- **R**itualized practice and restrictions
- **I**mplications for medical care
- **T**erminal event planning

SOCIAL DETERMINANTS OF HEALTH

Healthy People 2030 includes an emphasis on the personal, social, economic, and environmental factors that impact health. One of *Healthy People 2030*'s goals is to "Create social, physical, and economic environments that promote attaining the full potential for health and well-being for all." Social determinants of health (SDOH) include conditions and environments that affect health, function, and quality of life. An assessment of key determinants should be included in a comprehensive geriatric assessment (CGA). SDOH include five domains: Economic Stability, Education Access and Quality, Health Care Access and Quality, Neighborhood and Environment, and Social and Community Context. A safe living situation is critical to the health of older adults and includes the neighborhood in which they live, their housing, and access to reliable transportation. Older adults need an income adequate to meet basic needs and access to nutritious foods and physical activity. Literacy skills, especially health literacy, also impact health of older adults. Recently there has been an increased awareness of how racism, discrimination, and violence have a negative impact on health, and many of the most vulnerable older adults are at risk.

In community-dwelling older adults, the risk of social isolation and loneliness are all too common and are a significant health risk, affected by the SDOH. In a report by the National Academies of Science, Engineering, and Medicine (NASEM, 2020) it was noted that 24% of community-dwelling older adults are socially isolated and 35% of adults 45 and older are lonely. Social isolation and loneliness have been shown to affect overall quality of life and to contribute to all-cause mortality. Gardiner et al. (2018) in a review, cited evidence that social isolation and loneliness have been associated with depression, a decline in cognitive function, an increase in cardiovascular disease, and a decrease in overall quality of life. Social isolation and loneliness may not be detected because they are not consistently assessed in the primary care setting (Cotterell et al., 2018). Because of their broad impact on health, assessment of social isolation and loneliness should be an essential component of a CGA.

The use of screening tools in the CGA provides a framework and consistency of assessment. However, it is important to distinguish between tools useful for research and those best used in clinical practice. The NASEM (2020) identified two tools most useful in the clinical setting, the Berrkman-Syme Social Network Index, for measuring social isolation, and the three-item UCLA Loneliness Scale, for measuring loneliness. In 1995, Kane recommended including the following statements in a CGA to help improve understanding of the patient's social support:

- Is there any one special person you could call or contact if you need help? (If yes, identify.)
- In general, other than your children, how many relatives do you feel close to and have contact with at least once a month? (Number.)
- In general, how many friends do you feel close to and have contact with at least once a month? (Number.)

SUMMARY

A comprehensive geriatric assessment (CGA) is a multidimensional process designed to identify care needs, plan care, and improve outcomes for older adults. The domains of CGA include, but are not limited to, physical health, functional status, psychological health, socioenvironmental supports, and measures of quality of life. The evidence of the value of CGA in general has been inconsistent. The evidence is clear that parts of the CGA do improve certain outcomes in older patients, but continued rigorous research is indicated.

Clinical Recommendation	Evidence Rating	References
Both loss of vision and hearing have been linked to cognitive decline.	B	Ray et al., 2019
Evidence shows that the benefit of mammography screening increases with age, with women between 50 and 74 years old benefiting the most. The best balance of benefit to harm is when screening every 2 years. For women older than 75 years, evidence is insufficient; screening decisions should be on an individual basis.	A	Siu for U.S. Preventive Services Task Force (USPSTF), 2016
Patients at higher risk for glaucoma should have a dilated eye examination every 2 years. Blacks 40 years and older. All adults over 60. People with a family history of glaucoma.	B	CDC, 2021
Women aged 65 years and older and younger women whose fracture risk is equal to those 65 years and older who have no additional risk factors should be screened for osteoporosis with dual-energy x-ray absorptiometry of the femoral neck. For men, current evidence is insufficient to assess benefits and harms of screening.	B	USPSTF, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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AGE-FRIENDLY HEALTH SYSTEMS

The prevalence of living with multiple chronic conditions increases with age, requiring long-term treatments, complex management, and reliable continuity of care. The comprehensive geriatric assessment (CGA) requires expertise in the care of older adults and coordination across disciplines. With the rapidly growing, diverse aging population, demand for more efficient, effective, safe, and age-appropriate care of older adults is increasing (Tavares et al., 2021; Fulmer et al., 2018). Tavares and colleagues (2021) emphasize that older adults face challenges related to declining health conditions, autonomy, and independence, which may worsen due to adverse events in the health-care environment. These adverse events can extend a care period and compromise daily routines and function (Tavares et al., 2021). Application of evidence-based, age-friendly care is essential to assessment and management of older adults across health-care settings.

The Evidence for Age-Friendly Health Systems

The Institute for Healthcare Improvement (IHI) developed an approach to improve the performance of health systems. The Triple Aim model was developed by the IHI to address weaknesses in the U.S. health-care system as well as population health, experience of care, and per capita costs (IHI, 2021). When adverse events occur in health-care systems, it is commonly because of a lack of attention to the population or the experience of care, and the result is often increased cost. IHI's expertise in improving the quality of health care resulted in their partnership in 2017 with the John A. Hartford Foundation as well as the American Hospital Association and the Catholic Health Association of the United States to radically change the care received by older adults in the United States. This partnership resulted in the Age-Friendly Health System initiative. The care model focused on efficiency while providing effective, safe care for older adults. Unlike more comprehensive geriatric care models, the Age-Friendly Health System initiative easily translates into a variety of health-care settings, allowing for ease of use and reliability (Fulmer et al., 2018). The understanding is that older adults deserve safe, effective, and patient-centered care in the settings in which they receive their care.

THE 4MS FRAMEWORK

The Age-Friendly Healthcare System's evidenced-based initiative was developed by researchers, clinical geriatric specialists, and health system leaders. Methodologically, geriatric experts were convened to review 17 geriatric care models with level 1 or 2 evidence of impact. They identified 90 care elements, removed redundancies, and found 13 discrete features. That expert meeting led to the selection of a set of four core features now known as the 4Ms Framework (Fig. 6-1). The framework provides a guide for health-care providers so that the care of older adults is organized, manageable, and reliably delivered (Fulmer at al., 2018; IHI, 2021). The 4Ms include:

- What **M**atters: considering what is most important to the older adult, family, and caregivers and goals and preferences
- **M**edication: making sure all medications have clear indications, prescribed at the lowest effective dosages and frequencies
- **M**entation: assessing and managing dementia, delirium, and/or depression
- **M**obility: maintaining or improving mobility and function

The resulting age-friendly care focuses on an older adult's wellness and strengths rather than on disease. The 4Ms apply regardless of the older adult's cultural, racial, ethnic, or religious background, or the number of conditions or functional problems they may have. Many health systems found they already provide care to older adults that align with one or more of the 4Ms. The challenge to those systems is to incorporate the other elements and organize care, so that all 4Ms are used as a set to reliably guide every encounter with an older adult and their family or other caregiver (IHI, 2020).

In Age-Friendly Health Systems, healthcare-related harms to older adults are dramatically reduced and older adults get the best care possible, are satisfied with their care, and value is optimized for everyone (Mate et al., 2021). The provision of age-friendly care means that care follows an essential set of evidence-based practices, causes no harm, and aligns with what matters to the older adult and their family or other caregivers (IHI, 2020). Age-Friendly Health Systems may be applied in acute, ambulatory, long-term care, and convenient care settings.

What Matters

The Age-Friendly Health Systems initiative defines "What Matters" as knowing and aligning care with each older adult's specific health outcome goals and care preferences including, but not limited to, end-of-life care and across settings of care (IHI, 2021). Specifically asking what matters to the patient helps establish a treatment plan and a rapport with the health-care provider and allows their concerns to be the center of the visit. Research shows if what matters to an older adult is identified, it leads to decreases in inpatient utilization by 54% and intensive care unit stays by 80%, and improves patient satisfaction (Mate et al., 2021).

Understanding what matters is an ongoing process. Health-care providers should assess what matters during a series of conversations over time and use what matters as a guide for how care is delivered. What matters conversations about goals and preferences should be included in all points of care such as during annual well visits, acute and chronic disease management visits, as well as life changing events such as the death of a spouse, illness, or new medical diagnoses. What matters may include self-care, visiting family, advance care planning, and any core values of the older adults such as ideas about happiness and fulfillment. Once assessed, providers should align the care plan with what matters most to the older adult, considering their goals and preferences (Mate et al., 2018).

Medication

As adults age, the number of medications they are prescribed increases. Nearly 90% of adults 65 and older report they are currently taking prescription medication. Further, 54% of these adults report taking four or more medications daily. Polypharmacy occurs when people use multiple medications and the harm, or potential harm, of taking those medications

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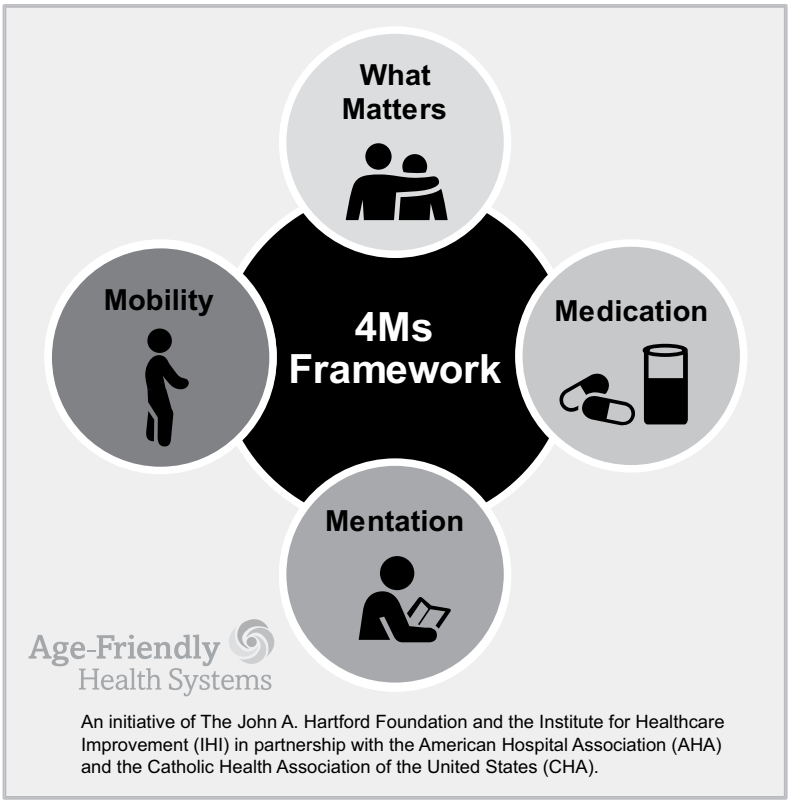

FIGURE 6-1 The 4Ms Framework. (Reprinted with permission from the Institute for Healthcare Improvement.)

outweighs the benefits (Mate et al., 2021). Problems with polypharmacy are affected by the physiological changes that occur with aging. An increase in drug excretion time, for example, may increase risk of effects on mentation and/or mobility, thereby interfering with what matters.

The Age-Friendly Health Systems movement emphasizes that if an older adult needs medication, it should be appropriate for older adults and at the lowest effective dose and frequency. In reviewing or prescribing medications for older adults, assess if any medications are currently listed on the AGS Beers Criteria® list of potentially inappropriate medication for older adults (AGS, 2019) and whether any may be safely deprescribed. These may include anticholinergic medications, benzodiazepines, opioids, muscle relaxants, tricyclic antidepressants, and antipsychotics. Across care settings, health-care providers should ensure that all medications are age-friendly and that any prescribed medications do not affect their mentation, mobility, or what matters to them. Follow-up is needed to assess tolerance to any medication changes.

Mentation

Dementia and depression as well as delirium are common psychiatric and geriatric syndromes that may occur concurrently (Leyhe et al., 2017). These syndromes may be underassessed and undiagnosed in health-care settings. Health-care providers may not be aware of the assessment or screening tools available, may have time restraints for visits depending on the setting, and may not be specialists in care of older adults. Regardless, in Age-Friendly Health Systems, assessment for cognition, delirium, and depression using evidence-based tools is expected and required. This, in turn, leads to appropriate prevention, identification, treatment, and management across all care settings. It is important to note that the Age-Friendly Health Systems movement uses evidence-based practice approaches that are also effective with patients living with dementia (Fulmer & Li, 2018). Further, the 4Ms framework centers around the patient and what matters to them, including those with dementia and their family's wishes regarding care throughout the stages of dementia.

As discussed earlier in this chapter, evidence-based assessment tools for cognition include the Mini-Cog™, SLUMS test, and MoCA. Depression screening tools may include the Patient Health Questionnaire or Geriatric Depression Scale. Delirium screening may be conducted using the Confusion Assessment Method or Ultra Brief-2 (UB-2) Screener. Actions for a positive memory-related screening tool may include assessment or testing of other potential causes or referral to a neuropsychiatrist for a more comprehensive cognitive assessment. Actions for a positive depression screen may include referral to a specialist, support group, community resources and programs, or cognitive behavioral therapy. Further assessment and emergency treatment may be indicated if a person is suicidal. Actions for delirium should focus on the underlying cause of the delirium, which may indicate a medical emergency. A follow-up plan for any abnormalities noted is important to include, and alignment of the mentation treatment plan with what matters, medication, and mobility is key.

Mobility

Mobility is a fundamental part of both basic ADLs and IADLs. Mobility, including the ability to walk and/or climb stairs, is an important predictor of quality of life among older adults

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and a measure of successful aging (Musich et al., 2018). Although increased physical strength, function, and mobility are associated with healthier outcomes, some older adults may lead a more sedentary lifestyle, which may lead to decreased health and increased risk of falls. The Centers for Disease Control and Prevention (CDC) recommend that older adults engage in physical activity of moderate to intense aerobic activity at least 150 minutes per week to have health benefits such as muscle strength (CDC, 2021). As part of age-friendly care, health-care providers should assess if there are any barriers to mobility or participating in physical activities so they may be addressed in the plan of care.

Examples of mobility assessment tools include the Timed Up and Go Test or Stopping Elderly Accidents, Deaths, & Injuries (STEADI). Actions include encouraging older adults to move safely every day and develop or continue a daily mobility goal. Older adults should receive education about appropriate physical activities, fall prevention methods such as wearing supportive, non-slip footwear, maintaining good lighting and clear walking paths in the surrounding area, avoiding use of throw rugs, and using grab bars and non-skid mats in the bathroom. As needed, patients may be encouraged to use an assistive device and/or referred to local community activities, exercise programs, or physical therapy. The mobility plan should align with what matters, medication, and mentation.

Age-Friendly Care Implementation

Becoming an Age-Friendly Health System begins with an interprofessional team developing an aim statement and articulating how it plans to operationalize age-friendly care using the 4Ms framework, including the assessment and action steps for the 4Ms. The choice of evidence-based assessment tools and frequency of use is organization-specific, and implementation of age-friendly care may vary across settings of care. For example, in acute care, assessment of the 4Ms may be done daily with delirium screening possibly every shift or every 12 hours. In ambulatory care, assessment of the 4Ms may occur annually or with a change in condition. Providers in the convenient care setting may assess and act on the 4Ms at every older adult visit, as that may be the only opportunity they have to provide age-friendly care for that patient.

The IHI offers guidebooks and toolkits to support providers in adopting the 4Ms on their Web site (http://ihi.org/agefriendly). These resources include practical guidance for various care settings and electronic health record requirements. To prepare organizations to become Age-Friendly Health Systems, the IHI holds free Action Communities that meet for 7 months and provide educational webinars, coaching, and resources.

The IHI recommends using implementation science methods, such as integrating the 4Ms into care using Plan-Do-Study-Act (PDSA) cycles to test changes to workflows, documentation practices, or other processes, before launching changes health system-wide. The PDSA steps include: (1) understand the current state, (2) describe how the care is consistent with the 4Ms, (3) design or adapt the workflow, (4) provide care, (5) study performance, and (6) improve and sustain care (IHI, 2020).

Initially launched with five pioneering health systems (Trinity Health, Ascension, Providence St. Joseph Health, Anne Arundel Medical Center, and Kaiser Permanente), as of June 2021, there are 2233 Age-Friendly Health System Participants (IHI, 2021). In 2018 CVS Health's Minute Clinic became the first convenient care setting to implement the Age-Friendly Health Systems, 4Ms model. Recognition as an Age-Friendly Health Systems Participant means that these hospitals, ambulatory practices, convenient care clinics, and nursing homes have articulated plans to implement age-friendly care into practice using the 4Ms framework. Additionally, as of June 2021, there are 537 Age-Friendly Health Systems recognized as Committed to Care Excellence, meaning they are exemplar and have at least 3 months of verified data to demonstrate early impact of using the 4Ms. The goal is to continue to scale and spread the Age-Friendly Health Systems movement across the United States and globally.

The Age-Friendly Health Systems movement was developed in response to the crucial need for an efficient, safe, effective, and reliable framework that may be easily adopted across all health-care settings. Health-care providers are expected to provide evidenced-based quality care to older adults. Assessing and acting on all 4Ms as a set in all care settings is a proven method to ensure age-friendly care is provided to all older adults.

Clinical Recommendation	Evidence Rating	References
All care provided to older adults should be age-friendly using the 4Ms framework.	A	Mate et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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CHAPTER 7

Symptoms and Syndromes

Evelyn Duffy

ASSESSMENT

Differential diagnosis begins when the patient presents their chief concern, or a change in condition is identified. Assessment of a symptom is based on the presentation of the concern, change in condition, or an evaluation of a geriatric syndrome in the older adult. In addition to the classic approach to defining a symptom, listening to the patient's story and asking the right questions are necessary to determine an accurate diagnosis as well as inform the development of the plan of care. Using a change in function as a measure of the impact of a symptom on the patient is an effective means of sorting out the differential. Heterogeneity increases with age, and older adults are more likely to present common diseases in uncommon ways. This requires the provider to consider a greater number of possibilities when formulating a diagnosis, and the differential diagnosis can be quite broad. It is important not to form a probable diagnosis before obtaining a full history and considering more uncommon diagnoses (Reinoso et al., 2018). Working up an older adult with a single symptom or cluster of symptoms using typical symptom analysis and clinical decision-making tools can be done, but it is often complicated by the fact that patients may ignore symptoms initially because they do not interfere with functional activities or because they attribute the symptoms to the aging process. Conversely, patients may fear loss of independence related to a subtle decline in functional abilities and thus deliberately choose to conceal certain symptoms, or they may be unaware of a subtle decline until it becomes apparent to others.

Acuity of symptoms may be blunted because of changes in the efficiency of certain physiological mechanisms (Vonnes & El-Rady, 2021). New symptoms often appear in one organ system as an offshoot of pre-existing disease in another organ system. Multiple symptoms may be present because of comorbidities. These factors can result in a delayed or atypical presentation (Vonnes & El-Rady, 2021). In many cases, the first hint of illness may be a change in cognitive function or mental status. In the case of the patient with an underlying dementia, the refusal to eat or drink, or a change in the patient's behavior, may signal an acute illness. The term *geriatric syndrome* refers to conditions that have multiple underlying factors that may involve multiple organ systems; some of the most common are delirium, falls, dizziness, and incontinence. Older adults may present with both an atypical presentation in addition to a pre-existing geriatric syndrome (Vonnes & El-Rady, 2021). The literature reflects that shared risk factors across geriatric syndromes include older age, cognitive impairment, functional impairment, and impaired mobility. For each presenting symptom, the following descriptors should be used to guide the diagnosis:

- Mode of onset of the symptom (events coinciding with onset, similar past episodes, gradual or sudden, total duration)
- Location of the symptom
- Character of the symptom
- Radiation of the symptom
- Precipitating or aggravating factors
- Relieving or ameliorating factors
- Past treatment or evaluation (when, where, who; studies done and results)
- Course of the symptom
- Effect of the symptom on normal daily activities

If the symptom or the patient's demeanor indicates a problem in function or cognition, assess these areas. Perform a thorough medication history, including the use of over-the-counter (OTC) preparations, vitamins, herbal and homeopathic remedies, and any other dietary supplements, and consider their use in formulating diagnostic possibilities. Pharmacotherapeutic or other treatment modalities can complicate or even cause illness in older patients. Diuretics, which are included in almost every older adult's medication list, were found to be the number one cause of adverse drug reactions in older adults (Brandt & Lee, 2021). In developing a differential diagnosis, an adverse drug reaction should always be a consideration. The process of differential diagnosis includes multiple decision points, and at each point, it is important to utilize shared decision making by including the patient and what matters most to them (Pel-Little et al., 2020). The nurse practitioner also should consider who else is involved in the patient's health care and whether they need to be included in these discussions. Outcomes are improved when shared decision making is utilized.

This chapter includes many of the common symptoms presented by older adults. Each section contains multiple

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differentials to consider when evaluating the patient. Regardless of what may seem like a clear presentation, in caring for older adults the compounding factors of medication side effects, geriatric syndromes, and atypical presentation of disease are essential to the final determination of evaluation and plan of care. Including the patient and their informal caregivers increases the possibility that the final plan will be successful.

BOWEL INCONTINENCE

Description: Bowel incontinence or fecal incontinence (FI) is an involuntary passage of stool, either small amount with the expulsion of flatulence or the complete inability to control stool from expulsion. There are three types of FI: (1) urge incontinence: a person feels the need to defecate but cannot make it to the toilet despite attempts to avoid defecation; (2) passive incontinence: involuntary loss of gas or stool without awareness; and (3) fecal seepage-leakage of stool after a normal bowel evacuation, usually presenting as staining of clothing (Nazario, 2020; Shah et al., 2012). On occasion bowel incontinence may be the leakage of liquid stool going around a hard mass of stool in the colon, also known as a fecal impaction. This condition can be costly because of the need to use adult briefs as well as greater incidence of nursing home placement of individuals with FI. It can also be a socially and emotionally devastating situation that interferes with quality of life and leads to diminished self-esteem and depression.

Etiology: Defecation involves a complex series of events and factors: diet, stool consistency, muscle strength and function, anorectal sensation and anal patency, as well as neurological integrity, cognition, and motivation (Nazario, 2020; Shah et al., 2012). The ability to defecate has two components: continence and defecation. Continence is the ability to hold fecal material and is under the control of the autonomic nervous system and spinal cord nerve functioning, including the internal and external anal sphincter. Defecation is the evacuation of feces when a person consciously attempts to have a bowel movement (Shah et al., 2012). FI occurs for various reasons, ranging from gastrointestinal (GI) issues to cognitive or neurological diseases. A greater concern exists in a patient who is continent of urine but incontinent of stool. See Table 7-1 for a review of causes of FI.

Occurrence: Prevalence in community-dwelling older adults is 36% and up to 65% in nursing home residents. In the hospitalized setting, there is reported to be 16% prevalence (Shah et al., 2012). FI occurs more commonly in women than men due to delivery of large babies or from obstetrical trauma related to childbirth (Shah et al., 2012).

Age: FI is found more frequently in older adults than in the general population.

Ethnicity: Not significant.

Contributing Factors: There are certain epidemiological risk factors in the older individual associated with FI. In men, kidney disease and urinary incontinence were associated with FI, and in women, depression, urinary incontinence, and chronic diarrhea were associated with FI (Nazario, 2020; Shah et al., 2012).

Diarrhea from GI disease (colitis, irritable bowel syndrome [IBS]), infectious causes such as viral gastroenteritis or *Clostridioides difficile (C. diff)*, or medication side effects can contribute to acute, short-term bowel incontinence. *C. diff* infections occur when a person is exposed to the pathogen while receiving antibiotic treatment for another illness (Connell, 2019; Keller & Surawicz, 2014). Antibiotics suppress the normal bacteria in the colon, allowing malabsorbed carbohydrates or *C. diff* to flourish, producing toxins

TABLE 7-1 Causes of Bowel/Fecal Incontinence

DISEASE	MECHANISM	COMMENTS
Central Nervous System		
Dementia	Impairs awareness of need to defecate—unable to interpret the sensation of stool in bowels Loss of inhibitory control	Manifestations depend on type and severity of dementia
Stroke	Impaired awareness of anal control Slowed motor processing communication with frontal lobe damage	Dependent on size of infarct or hemorrhage within the brain
Brain tumor	Similar to stroke	Dependent on location of tumor
Multiple sclerosis	Decreased external anal sphincter pressures leading to decreased volumes of rectal distention to inhibit the internal anal sphincter	
Peripheral Nervous System		
Cauda equina syndrome	Compression of spinal nerves	
Polyneuropathies	Various mechanisms leading to destruction of the axon and myelin	Causes include infection, autoimmune disease, hypothyroidism, vitamin B_{12} deficiency, and medications

Continued

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TABLE 7-1 Causes of Bowel/Fecal Incontinence—cont'd

DISEASE	MECHANISM	COMMENTS
Diabetes mellitus	Neuropathy of sensory and motor nerves	
	Internal anal sphincter dysfunction	
Shy Drager syndrome	Multisystem atrophy	
Toxic neuropathy	Destruction of nerve cells leading to loss of sensation or motor control	Chemotherapy and radiation therapy
Traumatic neuropathy	Chronic straining during evacuation	
	External anal sphincter weakness or pudendal nerve neuropathy	
Fecal impaction	Altered rectal sensation	
	Liquid stool escaping around solid feces in colon or higher in bowels	
Gastrointestinal (GI)		
GI disease	GI dysfunction/disease with excessive stool volume and rapid gut transit	Causes include viral or bacterial gastroenteritis, colitis, Crohn's disease, celiac disease, colon cancer, irritable bowel syndrome, rectocele, and other GI diseases
		**Clostridioides difficile* can cause severe diarrhea in the elderly and can lead to death
Rectal sphincter dysfunction	Anal sphincter damage and/or pudendal neuropathy affecting sphincters, puborectalis muscle, and rectal sensation	Common causes include delivery of large baby, traumatic childbirth, anal surgery, rectal prolapse, and prolonged straining
Reservoir incontinence	Loss of compliance of the rectal wall leading to urgency, frequency, and leakage of stool	Associated with colectomy, inflammatory bowel disease, chronic rectal ischemia, and prostate/cervical radiation
		Diminished colonic/rectal capacity is a less common type of FI
Medications		
Laxatives	Medications causing increased gastric motility or increased water in stools	
Fiber products	Increase fluid in the stool to keep it soft and move easier but can lead to diarrhea and FI	
Magnesium	Draws fluid into the bowels through osmosis	Magnesium containing antacids and certain laxatives contain significant amounts of magnesium
Other medications	Antibiotics can cause destruction of the colon's natural flora, leading to diarrhea	
	Other medications that can cause diarrhea include proton pump inhibitors, SSRIs, and NSAIDs	
Other		
Physical deficits	Inability to recognize need to defecate (cognitive problems) or inability to ambulate to toilet without assistance	Common causes of cognitive problems include dementia
		Common causes of mobility problems include debilitating arthritis, hemiplegia, or any condition affecting gait
Dietary causes	Foods in susceptible individuals include a diet high in fiber, spicy foods, fatty/greasy foods, cured meats, smoked meats, dairy products, caffeine, or sorbitol	Sugar-free gum and artificial sweeteners can cause diarrhea and FI
		Avoidance of irritating foods can eliminate the FI
Obesity	Inability to ambulate to defecate	This is usually a reversible condition
Excessive fluid intake	Overhydration can lead to diarrhea and possibly cause FI	

Sources: Connell, 2019; Nazario, 2020; Shah et al., 2012

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that cause a severe diarrhea. Damage to the colon can cause the individual to become septic and possibly cause death, especially in the older patient (Connell, 2019).

Signs and Symptoms: The first step in the clinical appraisal is to inquire about bowel habits, including incidence of diarrhea and fecal continence. Determine the duration, frequency, severity, and character of the incontinence (gas, liquid, solid). Inquire if there is sensation of contents within the bowels, a sensation of rectal fullness, awareness of passing stool or gas, and warning symptoms of cramping or urgency. Associated symptoms of abdominal pain and bloating, anorexia, diarrhea or constipation, nausea and/or vomiting, rectal bleeding, and urinary incontinence should be ascertained. Review prescription and OTC medications carefully. Past medical history may be positive for diabetes, neurological and psychiatric diseases, GI disorders, cancers with radiation, and any condition limiting mobility. Surgical history may include hemorrhoidectomy, anal fissure repair, fistulectomy, anal dilation, or colon resection. Diet review may reveal high fiber intake and excessive fluid intake or foods that may cause irritation and worsen FI such as caffeine, alcohol, chocolate, greasy or spicy foods, dairy products, and various raw fruits and vegetables.

Physical examination includes assessing for significant weight loss. The abdomen should be examined for distention, hyperactive or absent bowel sounds, pain, masses, and bladder distention. The perineum is inspected for gaping of anus, an indication of severe sphincteric dysfunction, hemorrhoids, dermatitis, surgical scars, fissures, and fistulas. The clinician should check the "anal wink" (the reflex contraction of the anal sphincter when the skin around the anus is stroked bilaterally) to test sensation and pudendal nerve function. Asking the patient to bear down will reveal rectal prolapse, if present. The digital rectal examination is performed to detect hemorrhoids or masses, and evaluate baseline and squeeze sphincter tone, as well as the amount and character of stool. Neurological examination includes assessment of gait, general mobility, motor strength, and sensory testing.

Diagnostic Tests: The results of data collected from the history and physical examination will dictate if additional testing is needed. Categorize the diarrhea as inflammatory, fatty, or watery. When an infectious or foodborne cause is suspected, stool tests guided by the clinical presentation are indicated. Exclusion of fecal impaction, particularly in nursing home patients, is essential. Plain abdominal radiograph may show a high impaction when no hardened stool is felt in the rectal vault. If organic bowel disease is suspected (inflammatory disease, ischemic colitis, neoplasm), stools for occult blood, flexible sigmoidoscopy or colonoscopy is indicated. Anorectal manometry tests rectal sensation and compliance through the use of an intrarectal balloon and measures pressure, tone, and reflex contraction of the internal sphincter. It provides comprehensive information about anorectal function and is reasonable in the ambulatory and/or healthy elder who has failed conservative interventions. Other tests that may be considered include colonoscopy, electromyography, anal ultrasound, and magnetic resonance imaging (MRI).

Differential Diagnosis: The differential diagnosis includes fecal impaction, gastroenteritis, foodborne illness, ruptured diverticulum, inflammatory bowel disease, ischemic colitis, IBS, anal fistula, diabetic neuropathy, rectal prolapse, upper motor neuron lesions secondary to cerebrovascular accident (CVA), multiple sclerosis, spinal cord compression, degenerative processes, dementia, depression with self-care deficits, and functional impairment.

Treatment: Underlying causes should be treated when possible, such as administering antibiotics for *C. diff* infection, administering steroids or amino salicylate drugs (5-ASA) for inflammatory bowel disease, or implementing a gluten-free diet for celiac disease (Connell, 2019). Eliminating potentially causative agents is an important first step if diarrhea is caused by a medication or an intolerance of a diet that the individual is unable to digest such as gluten. Fecal impaction requires removal of the impaction (manually, with enemas, and/or osmotic/stimulant laxatives) and establishment of a preventive bowel regimen (see section on constipation). With loose or liquid stools, a supplement of soluble dietary fiber may be beneficial (adding more bulk to stools); the ideal amount and type have yet to be determined, and response varies greatly. Increasing fiber gradually over a period of several days can help reduce symptoms of abdominal bloating and discomfort that may be associated with increased fiber intake. In the setting of fecal reservoir incontinence, avoidance of dietary fiber may be indicated. Bowel training may be effective for elders with dementia and involves frequent and regular toileting on a timed schedule, usually after a meal to take advantage of the gastrocolic reflex and every 2 hours while awake. Once infection is ruled out, fecal impaction is excluded, and no clear cause is determined for FI with diarrhea, the antidiarrheal medication loperamide (Imodium) may be tried. For rectosphincter dysfunction, biofeedback with sphincter-strengthening exercises is an option for motivated, cognitively intact older adults who have some degree of rectal sensation. Sacral nerve stimulation is also a promising, safe, minimally invasive treatment of FI related to rectosphincter dysfunction. Surgical sphincter repair may be considered when incontinence is severe, unresponsive to conservative interventions, and clearly related to anatomical defects, with best outcomes seen with repair of defined defects in the external sphincter.

Follow-Up: Follow-up is indicated to assess resolution of FI, and the time frame will be dictated by the identified cause as well as the severity of the problem. Ongoing monitoring is needed in all cases.

Sequelae: Complications of FI include perineal irritation or dermatitis, pressure injury in the sacral/perineal area, non-healing wounds, recurrent urinary tract infections (UTIs), anxiety, social isolation, and depression. FI, along with urinary incontinence, is a leading cause of institutionalization of older adults.

Prevention/Prophylaxis: Manage constipation. Optimize treatment of underlying medical conditions, such as diabetes and GI disturbances. Adjust diet and laxative use to address loose stools. Consider physical therapy/occupational therapy (PT/OT) intervention to address mobility and toileting ability. Reinforce a regular toileting program for the cognitively impaired and physically frail.

Referral: Consider emergent spinal imaging/neurosurgical consultation for new-onset fecal/urinary incontinence with lower extremity weakness and paresthesia to rule out spinal cord compression. Additional evaluation is needed with "alarm" symptoms (change in bowel habits, rectal bleeding, weight loss) to rule out GI malignancy.

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Education: Provide clear information on normal bowel function, FI cause, and rationale for any diagnostic tests, preventive strategies, and treatments. Instruct in appropriate dilution and need for adequate fluid with fiber supplements. Direct to appropriate resources for incontinence pads and briefs as needed.

Clinical Recommendation	Evidence Rating	References
With loose or liquid stools, a supplement of soluble dietary fiber may be beneficial.	A	Nazario, 2020 Shah et al., 2012
Habit training may be effective for older adults with dementia and involves frequent and regular toileting.	B	Connell, 2019
Antidiarrheal medications, such as loperamide (drug of choice) and diphenoxylate, may be considered.	A	Connell, 2019 Shah et al, 2012
Provide biofeedback with sphincter-strengthening exercises.	B	Connell, 2019
Stimulate the sacral nerve.	A B	Connell, 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CHEST PAIN

Description: Acute, nontraumatic chest discomfort, perceived as pain or as a sensation of tightness, pressure, or squeezing in the chest or thorax area; associated with actual or potential tissue or organ damage.

Etiology: The many different pathologies of chest pain (CP) may be attributed to segmental overlap of neurons of cardiopulmonary and noncardiopulmonary origin. CP may originate from organs within or outside of the thorax; cardiac, pulmonary, esophageal, large vessel, gastric, pancreas, biliary, musculoskeletal, skin, and psychological pathology may be implicated. Life-threatening or high acuity causes include acute coronary syndrome (ACS) (includes acute myocardial infarction [MI] and unstable angina), aortic aneurysm, thoracic aortic dissection, spontaneous tension pneumothorax, pneumonia, pulmonary embolism (PE), esophageal perforation, and esophagitis. Lower acuity causes of CP can be stable angina, pericarditis, myocarditis, gastroesophageal reflux disease/gastro-peptic, biliary disease, costochondritis, rib fracture/trauma, and herpes zoster (Sanchez-Lopez & Paniagua, 2021).

Occurrence: Chest pain accounts for 5% to 10% of all emergency department (ED) visits in the United States and is one of the common complaints worldwide (Laureano-Phillips et al., 2019). Of those 6 million visits, approximately 15% are older than 65 years (Vespa et al., 2020). It is the most common reason that persons older than 65 present to the ED (Sanchez-Lopez & Paniagua, 2021).

Ethnicity: A recent study by Iacoe et al. (2018) found no statistically significant difference in the time to treatment for ACS based on ethnicity of patients seeking care.

Contributing Factors: GI causes of chest pain may mimic ACS. Gastroesophageal reflux disease (GERD) can not only mimic ACS, but in 50% of patients it can also coexist with coronary artery disease (CAD). In a 2020 study (Eisa et al., 2020) patients with GERD controlling for many other factors had a higher risk of acute myocardial infarct than a control group without GERD. Several medications and illicit substances can cause ACS. These include nonsteroidal anti-inflammatory drugs, which can cause endothelial cell damage, most prominent in COX-2 inhibitors. Antiviral therapy and highly active antiretroviral therapy (HAART) increase ACS risk by 26%. Illicit medications, including methamphetamines, LSD, cocaine, and heroin, can all lead to cardiac complications. Recent work has even correlated the use of cannabis with ACS (Richards et al., 2019). Anemia, which is frequently found in the older adult, may predispose the person to cardiac ischemia secondary to supply and demand of oxygen carrying red blood cells (Klabunde, 2020). Atrial arrhythmias, atrial fibrillation and flutter can be associated with pulmonary emboli, as a cause-and-effect relationship, as in recent orthopedic surgery, recent immobilization, deep vein thrombosis (DVT), and cancers (Ptaszynska-Kopczynska et al., 2019).

Signs and Symptoms: Pain of ACS may be midsternal, retrosternal or poorly localized; the pain may radiate to arms, back, neck, or jaw; may occur at rest; may last longer than 20 minutes; and may not be relieved with nitroglycerin. Nausea, vomiting, diaphoresis, dyspnea, weakness, fatigue, light-headedness, and/or anxiety, may accompany chest pain representing an acute coronary event or acute coronary syndrome. Chest pain may be precipitated by stress, exercise, or by mild or severe illness. Stable angina can present as substernal or precordial pressure, a feeling of constricting, or heaviness in the chest, precipitated by exertion, and may be relieved with vasodilator medication such as a nitrate. Older adults or patients with diabetes may have

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altered pain perception or inability to localize the discomfort commonly seen in typical presentations of chest pain. The average age of a patient presenting with their first MI is 65 years old for men and the average age for women is 72 years old. The incidence of MI increases with age and an absence of chest pain with ACS in older adults is common. Dyspnea is a common presenting symptom of acute MI in patients older than 85 years. Anyone older than 65 years of age who presents with the chief complaint of CP must receive an ACS work-up.

Thoracic aortic dissection has abrupt onset and severe, retrosternal tearing pain that usually radiates to the back and both arms. Pulmonary embolism (PE) may present with acute dyspnea, cough, deep pleuritic chest pain that may or may not be severe. Tension pneumothorax is associated with acute unilateral pleuritic chest pain and dyspnea and often is sudden. Esophageal spasm and GERD may mimic the pain of myocardial ischemia, can be associated with eating, consuming alcohol, improves with upright position or antacids, and is accompanied by cough, hoarseness, and dysphagia. Acute pancreatitis may present with knifelike epigastric or lower chest pain radiating to the left shoulder associated with vomiting and relieved by leaning forward. Musculoskeletal pain is usually persistent and is aggravated by movement, cough, or deep respirations and can be associated with a recent fall, or old/chronic spine injury. Musculoskeletal pain may be replicable on examination. Chest pain associated with Herpes zoster is described as sharp pain or paresthesia in the mid-thorax unilaterally and causes a vesicular rash in a unilateral thoracic dermatome. Pain may precede rash by several days.

History may be positive for CAD with or without angina or risk factors thereof, including hypertension, diabetes, and hypercholesterolemia. GI disorders, degenerative joint disease, and anxiety disorders, as well as tobacco and alcohol abuse, can also be clues to the diagnosis.

Signs of serious conditions include acute confusion or anxiety, pallor/cyanosis, diaphoresis, tachycardia, bradycardia, tachypnea, and hypotension and or mean arterial pressure less than 70. A new S_3 or S_4 gallop, new systolic murmur, or signs of HF (jugular venous distention, basilar crackles, or lower extremity edema) suggest myocardial ischemia/injury. Asymmetrical blood pressures, absent or asymmetrical extremity pulses, and aortic bruit may be present with aortic dissection. Cardiac tamponade is more common in the setting of other chronic diseases such as autoimmune disease, malignancy, or recent chest trauma. Tracheal deviation, unilateral diminished or absent breath sounds, and palpable subcutaneous crepitus may reveal pneumothorax. Rapid, irregular apical pulse suggests atrial fibrillation, whereas unilateral lower extremity swelling and tenderness suggests DVT. Fever suggests an infectious cause. Localized abdominal tenderness with guarding and rebound points to GI origins. Costochondritis pain is worse with chest movement, sneezing, or cough and is not associated with fever, shortness of breath, tachycardia, or other cardiopulmonary symptoms. Diffuse tenderness is usually seen over one or more costochondral joints.

In the older adult CP symptoms are less pronounced and may be attributed to symptoms of normal aging. This can lead to delays in care and adverse outcomes or death. Furthermore, the older adult with cognitive impairment, severe depression, delirium, or difficulty in communicating their symptoms are at a higher risk for poor outcomes and potential further debilitating manifestations (Sanchez-Lopez & Paniagua, 2021).

Diagnostic Tests: If myocardial ischemia or injury is suspected, immediate 12-lead electrocardiogram (ECG) is needed and may show ST-segment depression or elevation, T-wave inversion, new left bundle branch block (LBBB), or new Q waves. However, the ECG may not change for hours or sometimes not at all. Elevations in cardiac markers (troponins T and I) taken at hours 0, 3, and 6 after the onset of pain indicate myocardial injury (Gursahani, 2021).

Additional tests include chest x-ray (CXR), which may reveal pulmonary edema, pneumothorax, pleural effusion, pneumonia, or lung mass. A d-dimer blood test and spiral computed tomography or ventilation/perfusion scan may confirm pulmonary emboli. D-dimer levels increase with age (ADJUST-PE study; age adjusted defined as 10 times the age if >50 years old or >00 if <50 years old) and this must be taken into consideration with older aged patients (Blondon et al., 2020). Lower extremity doppler ultrasound can diagnose DVT. Additional testing is guided by the clinical situation, history, and physical findings. Older adult patients with ACS are less likely to have typical ECG findings (i.e., ST-segment elevation). Unstable angina/non-ST elevation MI shows T-wave inversion, absent Q waves, and evolving ST-segment changes.

Differential Diagnosis: The differential diagnosis includes:

Non-Ischemic	Pulmonary	GI	Chest Wall/ Musculoskeletal	Psychiatric
Cardiovascular	Pulmonary embolism	Esophageal	Costochondritis	Anxiety disorder
Aortic dissection	Pneumothorax	Esophagitis	Fibrositis	Hyperventilation
Pericarditis	Pneumonia	Reflux	Rib fracture	Panic disorder
	Pleuritic	Biliary colic	Sternoclavicular arthritis	Primary anxiety
		Cholecystitis	Herpes zoster (before rash)	Affective disorders
		Choledocholithiasis		Thought disorders
		Cholangitis		
		Peptic ulcer		
		Pancreatitis		

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Treatment: If there is high suspicion of emergent conditions such as ACS or aortic dissection, immediate transport to the ED by emergency medical services (EMS) is required. For frail older adults, conservative management of ACS in the facility may be considered. Functional older adults should receive immediate intervention and early hospital care for suspected ACS. Treatment with supplemental oxygen to maintain an oxygen saturation above 91%, aspirin 160 to 325 mg chewed (if no allergy) sublingual or IV nitroglycerin if blood pressure is greater than 90 mm Hg systolic and heart rate is greater than 50 beats per minute (bpm). Nitrates should never be administered to patients with suspected ST elevation MI (STEMI) or non-ST elevation MI (NSTEMI) who received phosphodiesterase inhibitors (sildenafil, tadalafil, vardenafil) within 24 to 48 hours of onset of symptoms. This can cause a precipitous fall in the blood pressure, leading to a potentially fatal outcome. Pursuing further treatments such as coronary artery intervention can be determined on a case-by-case basis (Mechanic et al., 2021).

Analgesic therapy may be recommended for pain control, and morphine IV can be used in a patient when not contraindicated. Treatment of stable angina includes aspirin, beta blockers, angiotensin-converting enzyme (ACE) inhibitors, nitrates, and statins. Long-acting calcium channel blockers may be used for symptom reduction if beta blockers are ineffective or contraindicated. Although only moderately successful, treatment options for esophageal spasm include calcium channel blockers, tricyclic antidepressants (exercise caution with use in older adults), nitrates, botulinum toxin, and dilation. Proton pump inhibitors (PPIs), antihistamine-1 blockers, and/or antacids are the mainstay for GERD. Weight loss is advised for the overweight and obese patient. Costochondritis may respond to conservative treatment of heat, cold, rest, topical or oral analgesics/anti-inflammatory agent. Careful examination of the skin to detect herpes zoster requires oral antiviral medications and appropriate pain management. Reassurance, cognitive-behavioral therapy, and/or antidepressants may be indicated for psychogenic causes.

Follow-Up: Follow-up is guided by diagnosis and response to treatment.

Sequelae: A 20% to 60% rate of unrecognized MI in older adults with inappropriate hospital discharge and delayed treatment results in poor outcomes and increased mortality (Acharya et al., 2019).

Prevention/Prophylaxis: Recognizing and optimizing treatment of diabetes, hypertension, CAD, hyperlipidemia, and arrythmias is essential. Encourage daily exercise and cessation of use of all tobacco products. For reflux symptoms, recommend controlling weight, elevating head of bed on blocks, staying upright after meals, and avoiding or moderating the consumption of caffeine, chocolate, spicy foods, peppermint, tobacco use, and alcohol. Encourage the patient to get age-appropriate vaccinations when indicated.

Referral: Suspected life-threatening conditions or unstable status should be referred to the ED for further evaluation and treatment. End of life and goals of care should be considered/honored per patient's wishes when life-sustaining measures may be futile to maintain one's quality of life. Establishing a person's health-care power of attorney or designee is often overlooked, making medical decisions challenging. Consultation is indicated when pain is uncontrolled, diagnosis is uncertain, and there is a poor response to usual treatment.

Education: Teach patients and families to seek immediate medical care with acute new-onset CP or when a change in chronic CP is experienced. Carefully explain causes of pain, appropriate testing and treatment, prevention strategies, and indications for follow-up. Chest pain is a common symptom found in older adults and if misdiagnosed, untreated, or undertreated, it can be life threatening and lead to high-risk complications that affect the patient's quality of life. Atypical presentations are common in this patient population which may lead to delayed care and missed opportunity to treat. It is essential to do a thorough physical examination, obtain a 12-lead ECG, cardiac isoenzymes, and CXR to establish an initial evaluation of the patient with chest pain of symptoms that may mimic cardiovascular symptoms. A careful stepwise approach is needed to assure the patient's testing is tailored to the individual's best outcome.

Clinical Recommendation	Evidence Rating	References
GERD can mimic ACS but 50% of patients with GERD also have CAD and are higher risk of MI then patients without GERD.	A	Eisa et al., 2020
Immediate EKG is needed if MI is suspected and MI would cause ST depression or elevation, T-wave inversion or new LBBB or Q waves.	A	Gursahani, 2021
Serial high sensitivity cardiac troponin (cTn) I or T tests are preferred to diagnose MI or rule it out more quickly.	B	Gulati et al., 2021
High suspicion of MI or aortic dissection requires immediate transfer to the ED by EMS.	C	Gulati et al., 2021
A 20%–60% rate of unrecognized MI in older adults with inappropriate hospital discharge and delayed treatment resulted in poor outcomes and increased mortality	C	Acharya et al., 2019

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COUGH

Description: Cough is a preventive reflex for expelling air from the lungs involving the use of accessory muscles of the chest and constriction of the glottis (Lai et al., 2018). It is one of the most common complaints that leads people to seek medical care.

Etiology: Cough is the voluntary or involuntary mechanism used to eject aspirants or noxious substances, including fluids, solids, dust, and gases, from the body's upper and lower airways. Cough is also the body's mechanism for removing mucus from the upper or lower respiratory tracts. Involuntary cough is regulated by the vagal afferent nerve, but higher central nervous system (CNS) cortical modulation can inhibit cough or allow for voluntary cough.

Occurrence: Cough is one of the most common complaints for seeking medical attention. It is divided into three categories based on duration: acute, lasting less than 3 weeks; subacute, lasting between 3 and 8 weeks; and chronic, lasting more than 8 weeks. It can further be defined as wet or dry cough, with a wet cough producing a sputum level >10 mL per day (Lai et al., 2018). Women tend to experience heightened cough reflex sensitivity (Lai et al., 2018), and twice as many women develop a cough related to (ACE) inhibitor therapy than men (Alharbi et al., 2017).

Age: Cough occurs at any age, although in European and American countries chronic cough is more prevalent between the ages of 50 and 60 years (Lai et al., 2018). In the older adult population there is a reduced cough reflex, which is related to increased risk for aspiration pneumonia (Song et al., 2019).

Ethnicity: No direct ties to ethnicity have been documented at this time.

Contributing Factors: Any stimulation, chemical or mechanical, that irritates the receptors of the cough reflex are causes of cough. These receptors are located in the upper and lower respiratory tract, esophagus, pericardium, diaphragm, and stomach. Environmental exposure that causes cough includes multiple different types of irritants such as chemicals, dust, and pollen, along with infectious agents such as the common cold, tuberculosis (TB), or *Bordetella pertussis*. Trauma, including assault, motor vehicle accidents, or falls that lead to contusion of the lungs can cause cough. Medications may cause cough, particularly ACE inhibitors (in 5%–35% of users) (Spanevello et al., 2020).

Smoking is a primary cause of chronic cough, but medical services are often not sought by smokers. Cigarette smoking is the most significant preventable cause of disease, and lung cancer is the number one cause of cancer deaths of both men and women in the United States. Cough from chronic obstructive pulmonary disease (COPD) worsens in intensity and duration if the patient continues to smoke. Bronchogenic cancers are often associated with cough, but metastatic cancers to the lungs seldom result in cough until late in the course of the disease.

Signs and Symptoms: A thorough disease history is required because multiple chronic diseases present with cough as a symptom. Risk factors and work and home environment assessment is essential in narrowing the cause of cough. Using a systematic anatomical approach provides ease in identifying the trigger and illness. Risk factors for cough include recent exposure, smoking, stroke, immigrant status, use of ACE inhibitors, HIV-positive status, reflux and heart disease. The cough may be productive or nonproductive, and the sputum may be a variety of colors or tinged with blood. Identify the onset, including if it is episodic, continuous, or occurs only certain times of the day; the duration and character; and if it is associated with other symptoms, including red flag findings such as fever, tachycardia, dyspnea, weight loss, or pain.

The physical examination begins with vital signs that should include temperature, heart rate, respirations, and oxygen saturation. Next is a thorough examination of the nose and oropharyngeal mucosa. A pale or swollen appearance to nasal mucosa with a clear mucus in the bottom of the nasal cavity may indicate allergic rhinitis (Lai et al., 2018). A "cobblestone" appearance to the oropharyngeal mucosa and swollen eyelids are other indicators of a possible allergic origin (Lai et al., 2018). Loss of tooth enamel can indicate GERD. The chest must be assessed for adventitious breath sounds. Expiratory wheezes suggest the possibility of bronchitis or asthma caused by mucus in or constriction of the airways. Inspiratory wheezes may represent a central airway tumor (Lai et al., 2018). Rhonchi or crackles are suspicious for pneumonia or infiltrates. Diminished or absent lung sounds by auscultation and dullness to percussion are highly suggestive of pneumonia's consolidation. Rhonchi or crackles with cardiomegaly on x-ray or hypertrophy on ECG could indicate heart failure (HF) and may not be accompanied by peripheral edema or abnormal heart sounds. A velcro-like sound to the lower lung bases may suggest interstitial lung disease (Lai et al., 2018). However, most patients with chronic cough will have normal findings on physical examination (Lai et al., 2018).

Diagnostic Tests: No specific tests are indicated when the patient has a cough. The selection and extent of testing depends on the findings of the history and physical examination, cough duration (acute, subacute, or chronic), and previous evaluations.

Acute cough associated with upper respiratory infection does not require further diagnostic evaluation unless influenza or COVID-19 is suspected. In such cases, an influenza or COVID-19 diagnostic test may be beneficial. Acute cough with physical findings of life-threatening illness should be appropriately evaluated for the diagnosis of concern. A chest radiograph is appropriate for physical findings consistent with pneumonia (fever, heart rate above 100 bpm, respiratory rate greater than 24 breaths/min, altered mental status, chest examination with findings of local consolidation). Viral cultures, serologic assays, and sputum analysis should not be routinely performed in the diagnosis of acute bronchitis.

Subacute cough that has lasted more than 2 weeks without an apparent cause and is associated with posttussive vomiting, inspiratory whooping, and paroxysms of coughing should have a nasopharyngeal aspirate or polymer swab of the nasopharynx for culture to confirm the presence of

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B. pertussis (whooping cough). Bacterial isolation is the only certain way to confirm the diagnosis. Testing for TB is indicated when there is an increased risk of the population becoming infected, such as in nursing homes or prisons; in a patient with a recent visit to a country with high prevalence of TB; or in an immunocompromised patient.

Chronic cough diagnostic testing in nonsmokers is guided by elimination through treatment of the most common disorders: upper airway cough syndrome (UACS), previously known as postnasal drip syndrome, secondary to rhinosinus diseases; GERD; nonasthmatic eosinophilic bronchitis; and asthma. Medical history is crucial for determining progression of diagnostic tests for chronic cough. A chest radiograph is routinely recommended for chronic cough, though most are negative. An abnormal study would guide further diagnostics. A high-resolution computed tomography (CT) scan can identify lesions, nodules, or interstitial pulmonary disease. Bronchoscopy and biopsy can be performed to determine presence of lung cancer. HF would lead to cardiovascular evaluation via echocardiogram. Evidence of infection such as TB would direct microbiological diagnostics. Pulmonary function tests (PFTs) are valuable in diagnosing asthma or COPD. An allergen skin prick test can be beneficial in determining UACS as the underlying cause of cough (Lai et al., 2018). Chronic rhinosinusitis evaluation includes sinus imaging via sinus CT or performance of flexible nasolaryngoscopy (Michaudet & Malaty, 2017). Scans or films taken during the episode of a common cold are not diagnostic of bacterial sinus infection. Evaluation for asthma-induced chronic cough is bronchoprovocation challenge. GERD evaluation may include a barium swallow or 24-hour esophageal pH monitoring test. An induced sputum sample with eosinophilia identified can be suggestive of eosinophilic bronchitis but may also be seen in patients with cough variant asthma (Lai et al., 2018).

Differential Diagnosis: The most important first step is determining if the acute cough is potentially related to a life-threatening condition such as pneumonia, HF, or PE. Most acute coughs are related to a respiratory tract condition such as the common cold, flu, acute bronchitis, acute exacerbation of COPD, viral syndrome, or exposure to an environmental irritant.

Subacute cough is usually a cough that lingers on from a respiratory tract infection. A postinfectious cough can last 2 to 3 weeks after onset, although COVID-19 associated cough symptoms have at times been lasting longer than this. Consider UACS, transient bronchial hyper-responsiveness, asthma, acute exacerbation of chronic bronchitis, and pertussis. If it appears to be a noninfectious cough, it should be managed and further evaluated as a chronic cough.

Chronic cough most commonly is UACS, asthma, or GERD. Other potential causes may include nonasthmatic eosinophilic bronchitis, COPD, drug-induced cough, fungal infection, and mediastinal masses. A nocturnal cough associated with shortness of breath suggests HF; without shortness of breath it is more indicative of an allergy. Diagnosis of unexplained cough or idiopathic cough requires an exhaustive evaluation by a pulmonary specialist to assess the patient for uncommon causes.

Treatment: Most often the source of the cough is isolated to the respiratory system and the condition is not life threatening. The following treatments are recommended:

Common Cold. Recommendation is symptomatic treatment only; antibiotics are ineffective at decreasing the duration of symptoms and are not recommended (Lai et al., 2018). Use of first generation antihistamines alone is not recommended because of the lack of clinical benefits (Lai et al., 2018). Use of these medications is also contraindicated in patient populations older than age 65 because of the adverse reactions that can present. Combined use of a decongestant and second generation antihistamine can be considered and may significantly improve cough, sneezing, and nasal congestion. Acetaminophen is a beneficial option in those without liver disease to assist with reducing fever and improving myalgias (Lai et al., 2018). Naproxen, an NSAID, may also be used to decrease cough. It is thought to work by inhibiting the inflammatory process; however, use of naproxen should be avoided in older adults especially those with renal impairment or those at risk for stroke or MI. Antitussive agents, such as dextromethorphan, are beneficial for severe cough and come in forms that can be used by patients with diabetes. Dextromethorphan is centrally acting and should be used with caution in older adults. Expectorants, such as guaifenesin, are commonly used to help with cough and have minimal adverse reaction risk in patients older than the age of 65. Strong evidence for its efficacy is lacking, but patients often report symptom relief.

UACS. Second generation antihistamines, including loratadine and cetirizine, can be used in those older than age 65 with minimal adverse reaction risk and can be used in combination with intranasal corticosteroids, such as fluticasone, to help relieve symptoms. Improvement should present clinically within days to up to 2 months (Michaudet & Malaty, 2017). For those with severe UACS symptoms that do not respond to primary treatment, use of leukotriene receptor antagonists, such as montelukast, or immunological therapy for specific allergens is recommended (Lai et al., 2018). Immunological therapy can take a long time to manifest effectiveness (Lai et al., 2018).

Acute Bronchitis. This diagnosis is applicable in persons without signs or symptoms of acute exacerbation of COPD, acute asthma, common cold, or pneumonia. In the older adult, a high suspicion of pneumonia should be considered until proven otherwise because of the risks associated with a reduced cough reflex. Most acute bronchitis is viral and self-limiting; antibiotics do not shorten the course of the disease and should not be used. Beta2-agonists are not recommended for routine treatment unless there is wheezing or an element of pulmonary disease is present. Expectorants such as guaifenesin may be used. Dextromethorphan or codeine may be used for cough suppression for severe coughing, although research has only been done in chronic bronchitis and care must be taken when used in older adults. A cool mist humidifier in the bedroom may be helpful. If daily nicotine use is present, recommend smoking cessation.

Bacterial Pneumonia. Community-acquired pneumonia (CAP) is treated differently than healthcare-associated pneumonia. It is of particular concern in older adult patients and those who are immunocompromised because their symptoms may be less intense. In the outpatient setting, it is recommended not to obtain sputum culture; this is recommended only pretreatment in the adult who is hospitalized with CAP (Metlay et al., 2019). Prior to treatment, it is recommended to use a clinical prediction rule that is validated to aide in determining

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prognosis. The Pneumonia Severity Index (PSI) is preferred (Metlay et al., 2019). This scale assists in determining need for hospitalization versus outpatient treatment. Patients with PSI less than or equal to 90 may be considered for outpatient treatment; however, clinical judgment should also be considered (Metlay et al., 2019). See also Chapter 11 for more information about pneumonia and its treatment.

COPD. COPD embodies a variety of diseases including emphysema and chronic bronchitis (Vogelmeier et al., 2020). Treatment of these is based on the GOLD standards created by the Global Initiative for Chronic Obstructive Pulmonary Disease. Pulmonary function testing is pertinent in treating these disorders because the FEV1 and FEV1/FVC are utilized to determine severity of the airflow obstruction and the step approach to inhaler maintenance and treatment. Inhalers play a key role in the management of COPD (Vogelmeier et al., 2020). When patients with COPD experience an exacerbation they have a sudden change of symptoms with an increase in cough, shortness of breath, purulent sputum, and increase in sputum production. Treatment of exacerbations includes a SABA with or without a SAMA, systemic corticosteroids, and antibiotics for 5 to 7 days. Diagnosis and management of COPD including exacerbations is addressed in Chapter 11.

TB. Antituberculosis drugs should be initiated if the tuberculin skin test is positive, and the patient should be referred to the local health department or local infectious disease specialist.

Drug Reaction. ACE inhibitors should be stopped and only restarted if there is compelling need for the category of drug. It is recommended not to use ACE inhibitors in smokers (Lai et al., 2018). Cough will commonly subside 1 to 4 weeks after discontinuing the ACE inhibitor (Lai et al., 2018). Angiotensin receptor blockers (ARBs) can be used as an alternative treatment in those with ACE inhibitor intolerance and may also be used in smokers who may require them for kidney protection (Ding et al., 2020). ARBs are generally tolerated better and have a lower incidence of cough (Ding et al., 2020). Other medications that may cause cough include opioids, such as fentanyl, statins, omeprazole, leflunomide, interferon, and sitagliptin (Ding et al., 2020).

Postinfectious Cough. A treatment trial of inhaled ipratropium for a cough that is adversely affecting quality of life may be used. If ipratropium alone is not successful, use of inhaled corticosteroids can be considered. Antibiotics are not recommended. Severe symptoms may require use of an oral steroid for a short period while other causes of cough are being considered.

Chronic Cough Treatment. Treatment of UACS, asthma, and GERD in a stepwise, systematic approach is most likely to provide a high rate of success. Because UACS is the most common cause of chronic cough, a trial of second generation antihistamine and decongestant can be tried. Cough should improve in 1 to 2 weeks. If the response is positive, the medication should continue because it may take several weeks for marked improvement. A partial response indicates more than one cause of the cough, and evaluation and treatment for asthma or GERD is reasonable. For an unexplained cough, after evaluation and treatment for all common causes, then a referral to pulmonary medicine or otolaryngologist is recommended (Michaudet & Malaty, 2017). In some trials use of gabapentin or pregabalin along with speech therapy, or speech therapy alone have shown benefit in chronic cough (Michaudet & Malaty, 2017).

Follow-Up: The timing of follow-up depends on the severity of the illness and the impact on the patient's life. For pneumonia or bronchitis with minimal dyspnea, a call or virtual visit to check on the patient is appropriate. Rising temperature or increasing difficulty breathing requires immediate attention or ED evaluation. Patients with resolving pneumonia should be evaluated in 2 to 3 weeks; a repeat chest x-ray may be taken at that time. Chronic cough may take multiple follow-up visits, evaluation, and treatment trials.

Sequelae: If a cough is caused by lung cancer, the prognosis is ominous. Cough from COPD worsens in intensity and duration if the patient continues to smoke. In older adults, chronic cough can contribute to stress incontinence.

Prevention/Prophylaxis: Preventive measures include smoking avoidance or cessation intervention, evaluation of the work and home environment, and humidification of the sleeping area with a cool mist humidifier. Patients should be provided vaccinations following Centers for Disease Control and Prevention (CDC) guidelines, including annual flu shots, Pneumovax, and Tdap.

Referral: A referral to a specialist can be initiated anytime during the evaluation and treatment of a cough. Some results, such as lesions suspicious for cancer on radiography, require referral to a specialist immediately. A cough specialist, allergist, otolaryngologist, or pulmonologist referral is appropriate for a chronic cough that is persistent. Other specialists who may be helpful are a GI specialist for evaluation of GERD, an infectious disease specialist for infections and immunocompromised patients, and a cardiologist for heart conditions.

Education: Recommend smoking cessation classes and allergen avoidance training. Cough can last longer than the patient expects.

Diagnosis	Clinical Recommendation	Evidence Rating	References
Common cold and UACS	Pharmacological treatments include second generation antihistamine, nasal corticosteroids, acetaminophen, and expectorants.	B	Lai et al., 2018 Michaudet & Malaty, 2017
Acute bronchitis without signs or symptoms of pneumonia, COPD exacerbation, acute asthma, or common cold	Most acute bronchitis is viral and self-limiting; antibiotics do not shorten the course of the disease and should not be used.	B	Kinkade & Long, 2016

Continued

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Diagnosis	Clinical Recommendation	Evidence Rating	References
Chronic obstructive pulmonary disease	Combination bronchodilator, beta agonists, and ipratropium as an inhaler or as a nebulizer, antibiotics, and oral steroids; may be used for cough suppression.	A	Vogelmeier et al., 2020
Drug reaction	ACE inhibitor should be stopped	A	Ding et al., 2020
Postinfectious cough with other conditions ruled out	Treatment trial of inhaled ipratropium for cough if affecting quality of life; inhaled corticosteroids or use of prednisone for a limited period may be considered for severe paroxysms. Cough suppression for failure of other treatments. Antibiotics are not recommended.	B	Iyer & Lim, 2013

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

DEHYDRATION

Description: Dehydration, or volume depletion, is a loss of total body water caused by too little fluid intake, sodium loss, or both. It is a common condition in older adults. Balancing solutes and water aids in avoiding dehydration.

Etiology: Total body water decreases with age. Small decreases in fluid intake can cause dehydration in an older adult because of a smaller fluid reserve. Age-related pathophysiological changes make the older adult increasingly vulnerable to disturbances in fluid and electrolyte balance, particularly during periods of ill health or physiological stress (El-Sharkawy et al., 2020). The ability of the kidneys to concentrate urine declines with age, so that even when deprived of water, urination is not significantly reduced. Also, thirst, which is an important self-regulation against dehydration, decreases as a person ages.

Dehydration can be defined as a fluid and electrolyte disturbance arising from either a water depletion or a sodium depletion in which there is accompanying water loss. Volume depletion occurs from loss of sodium and water from third-space sequestration, GI, renal and skin losses. It can be classified into three different types based on the possible causes (see Table 7-2): isotonic, hypotonic, and hypertonic.

Occurrence: Dehydration has been reported to be the most common fluid and electrolyte imbalance in older adults. Estimates of prevalence of dehydration in older adults vary depending on the subgroup being measured: one-third of older adult hospital admissions, 20% to 88% of older adults in care homes and 60% of community-dwelling older adults (Edmonds et al., 2021).

Age: Adults older than 65 continue to have the highest rates of admissions for dehydration as a primary diagnosis, with those older than 75 having the highest rates (Mentes & Gaspar, 2020).

Ethnicity: Not significant.

Contributing Factors: Causes of dehydration are multifactorial and include decreased mobility and the presence of chronic diseases, such as diabetes, cancer, and cardiovascular and renal disease, which make older adults more sensitive to fluid and electrolyte imbalance. Other risk factors in older adults include dependency for eating or drinking, mouth pain, poorly fitted dentures, and difficulty swallowing. Conditions such as vomiting, diarrhea, hemorrhage, and increased metabolic states that result in excess loss of fluids (fever, infection, excess sweating, excess urination) can contribute to volume loss. The use of certain medications, such as diuretics, anticholinergics, psychotropics, or laxatives, also may increase the risk. Dehydration is the most frequent secondary condition resulting from debilitating issues such as fever, confusion, pain, or pneumonia. Cognitive impairment (delirium, dementia, depression) has been associated with dehydration in older adults.

Signs and Symptoms: Clinical diagnosis of dehydration is often based on medical history, body inspection, and blood sampling, but there is no standardized or validated method for this evaluation. Symptoms are usually vague and confounded by

TABLE 7-2 Types of Dehydration

TYPE OF DEHYDRATION	DESCRIPTION
Isotonic	A balanced loss of both sodium and water causes extracellular fluid loss that increases blood viscosity. Common causes: vomiting, diarrhea, osmotic effects of glucose.
Hypertonic	Excessive water loss results in raised sodium levels and shifts from the intracellular space to extracellular space. Common causes: renal tubular disease, osmotic diuresis, resistance to vasopressin.
Hypotonic	Excessive sodium loss results in extracellular fluid loss. Common causes: overuse of diuretics, chronic salt wasting.

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age. A rise in serum osmolality indicates the presence of a water deficit, which causes intracellular dehydration, whereas a rise in serum sodium or hematocrit better indicates extracellular dehydration (Johnson & Hahn, 2018). A dry, furrowed tongue and mucous membranes; sunken eyes; headaches; dizziness on standing; confusion; concentrated or dark urine; weight loss; and upper body muscle weakness may indicate dehydration. Clinical signs may not appear, however, until dehydration is far advanced. In addition, the usual signs of constipation, disorientation, dry mucous membranes, orthostatic hypotension, and weight loss may be caused by other factors. If one or more of these are present or are a change from baseline, dehydration may be the cause. Although poor skin turgor is an expected finding in older adults, it is also a classic sign of dehydration. Signs and symptoms of hypovolemic shock include altered mental status; hypotension; tachycardia; cold, clammy skin; and rapid, deep respirations.

Diagnostic Tests: Serum markers provide the most reliable indicators of dehydration, and these include serum sodium, increased serum osmolality, and blood urea nitrogen (BUN)–creatinine ratio. Hyperosmolar dehydration, defined as serum osmolality >300 mOsm/kg or osmolarity >300 mOsm/L may be more sensitive for the early detection of dehydration because of the challenges in detecting these signs and symptoms in older adults (El-Sharkawy et al., 2020). The serum albumin and hematocrit may be elevated when the patient is dehydrated.

Differential Diagnosis: When dehydration is identified, the clinician must identify the cause and address the contributing factors. Weight gain and edema from heart failure (HF) can conceal a patient's dehydrated status.

Treatment: Individualize treatment depending on the type of dehydration. The route of administration (oral, IV, or subcutaneous) is determined by what is safe and effective. Subcutaneous fluid administration has been shown to be as effective with similar rates of adverse effects to IV infusion (Volkert et al., 2019). Regular presentation of fluids to bedridden individuals, providing continuous verbal cues, and determining the patient's preference can maintain adequate hydration status. Older women should be offered at least 1.6 L of drinks each day, whereas older men should be offered at least 2.0 L of drinks each day unless there is a clinical condition that requires a different approach (Volkert et al., 2019).

Follow-Up: The timing of patient follow-up depends on the seriousness of the identified cause and the response to treatment.

Sequelae: Dehydration has severe consequences for older adults and can have a major impact on quality of life. Dehydration is associated with chronic health problems, including constipation, falls, medication toxicity, increased confusion, and infection. Inadequate fluid intake can have serious medical consequences such as renal failure, hyperthermia, bowel obstructions, delirium, cardiovascular symptoms, and death. Patients admitted with hyperosmolar dehydration have been shown to be four times more likely to develop AKI 12-24 hours after admission and had 60% greater 30-day mortality compared with those who were adequately hydrated (El-Sharkawy et al., 2020).

Prevention/Prophylaxis: Educate patients, families, and caregivers about the need for adequate fluid intake to prevent dehydration. All liquids are not the same in maintaining fluid balance. Water is the best and should be at least half of the daily intake of fluid. Add milk, fruit and vegetable juices, and non-salty soups for variety. Decrease coffee, tea, alcohol, colas, and liquid diet supplements because they may cause dehydration. The use of a 24-hour fluid balance chart can help determine whether the patient is at risk or is dehydrated.

Referral: Refer as indicated by source of symptom. Hospitalization is indicated when the patient has severe signs and symptoms such as dizziness, altered mental status, or lethargy; is hemodynamically unstable; or cannot tolerate oral fluids.

Education: Explain causes of symptoms and measures taken to determine cause and treatment. Allow adequate time for eating at mealtimes. Meals can provide two-thirds of daily fluids. Offer fluids regularly during the day. Encourage consumption of fluids with medications. Staff education is critical; staff should report any significant weight loss, change in fluid consumption, or other relevant symptoms, such as dry mucous membranes.

Clinical Recommendation	Evidence Rating	References
The recommended daily intake of fluids for older women should be at least 1.6 L of drinks each day. Older men should be offered at least 2.0 L of drinks each day unless there is a clinical condition that requires a different approach.	A	Volkert et al., 2019
Hypodermoclysis is as effective as IV rehydration of older adults.	A	Volkert et al., 2019
Verbal prompts have been shown to increase fluid intake in nursing home residents.	A	Oates & Price, 2017
Use evidence-based practice guidelines for hydration management.	A	Mentes & Gaspar, 2020

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DIARRHEA

Description: Diarrhea is the passage of increased stool frequency, liquidity, or volume. It is objectively quantified as passage of three or more loose or watery stools or increased stool weight of greater than 200 g or 200 ml per 24 hours (Connell, 2019). Most episodes of diarrhea are caused by viral gastroenteritis, are short lived (resolving within 7 days), and require no treatment other than maintaining hydration (Connell, 2019). There are three types of diarrhea: Acute diarrhea lasting 1 to 2 days. Persistent diarrhea lasting at least 2 weeks but no longer than 4 weeks. Chronic diarrhea is defined as diarrhea that lasts longer than 3 to 4 weeks and may be continuous or intermittent.

Etiology: In normal bowel motility, water is not actively transported across the intestinal mucosa, it moves passively by osmotic forces generated by solutes such as electrolytes and nutrients. Absorption and secretion take place simultaneously, but when there is either a decrease in absorption or an increase in water within the intestinal lumen, diarrhea occurs. The fundamental cause of diarrhea is the incomplete absorption of water from the intestinal luminal contents. The pathophysiological mechanisms of diarrhea include osmotic, secretory, inflammatory, and altered motility leading to food and liquids being passed too quickly through the body and being excreted through the colon as loose or watery stool. Diarrhea is often accompanied by abdominal cramping, as well as nausea. There are various causes of diarrhea (see Table 7-3). Note that *Clostridiosides difficile* (*C. diff*) infection should be suspected as a cause of diarrhea in patients with watery diarrhea during or shortly after receiving antibiotic

TABLE 7-3 Causes of Diarrhea

DISEASE	MECHANISM	COMMENTS
Physical Causes Contributing to the Incidence of Diarrhea		
Dementia	Impairs awareness of need to defecate, loss of inhibitory control	Manifestations depend on type and severity of dementia.
Stroke	Impaired awareness of anal control, slowed motor processing communication with frontal lobe damage	Dependent on size of infarct or hemorrhage within the brain.
Fecal impaction	Altered rectal sensation, liquid stool escaping around solid feces in colon	
GI disease	GI dysfunction/disease with excessive stool volume and rapid gut transit	Causes include viral or bacterial gastroenteritis, colitis, Crohn disease, celiac disease, colon cancer, irritable bowel syndrome, rectocele, and other GI diseases. *Clostridioides difficile* can cause severe diarrhea in the older adult individual and can lead to death.
Medication Causes		
Laxatives	Medications causing increased gastric motility or increased water in stools	
Fiber products	Increase fluid in the stool to keep it soft and move easier but can lead to diarrhea and FI	
Magnesium	Draws fluid into the bowels through osmosis	Magnesium containing antacids and certain laxatives contain significant amounts of magnesium.
Other medications	Antibiotics can cause destruction of the colon's natural flora, leading to diarrhea Other medications that can cause diarrhea include proton pump inhibitors, SSRIs, and NSAIDs	
Other		
Physical deficits	Inability to recognize need to defecate (cognitive problems) or inability to ambulate to toilet without assistance	Common causes of cognitive problems include dementia. Common causes of mobility problems include debilitating arthritis, hemiplegia, or any condition affecting gait.
Dietary causes	Other foods in susceptible individuals include diet high in fiber, spicy foods, fatty/greasy foods, cured meats, smoked meats, dairy products, caffeine, and sorbitol	Sugar-free gum and artificial sweeteners can cause diarrhea and FI. Avoidance of irritating foods can eliminate the FI.
Excessive fluid intake	Overhydration can lead to diarrhea and possibly cause FI	

Sources: Connell, 2019; Sweetser, 2012.

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therapy or recent hospitalization and can be especially detrimental in older adults, potentially leading to death.

Occurrence: In the United States, an estimated 179 million cases of acute diarrhea occur in the United States each year. An estimated 48 million foodborne diarrheal illnesses occur annually, resulting in more than 128,000 hospitalizations and 3,000 deaths (National Institutes of Health, 2021). The greatest risk factor is contact with another individual with diarrhea.

Age: Diarrhea occurs at any age. The severity of illness and the mortality rate is increased in individuals older than 65 years, especially if the individual has a concurrent medical illness (Khatri, 2019).

Ethnicity: No direct ties to ethnicity have been documented.

Contributing Factors: The following can be contributing factors in the development of diarrhea: recent travel, family history of inflammatory/bowel disorders, recent antibiotic use, exposures to either contacts or foods including tube feedings, whether or not the individual is immunocompromised such as with HIV, recent hospitalization, age of more than 65 years, extended stay in hospital or nursing home, recent chemotherapy, recent GI surgery including post-pyloric tube feeding, and medications. The list of medications that can cause diarrhea include diuretics, beta blockers, NSAIDs, antibiotics, quinidine, chemotherapy, colchicine, metformin, laxatives, digoxin, theophylline, prostaglandins, cholinergic agents, and phenolphthalein.

Signs and Symptoms: The initial clinical assessment is to obtain a detailed history including symptom assessment parameters, onset, frequency, amount, and character of the stool (the presence of blood, mucus, or atypical color) and any associated symptoms such as abdominal pain, cramping, fever, nausea/vomiting, or bloating. Include the patient's baseline bowel pattern, usual dietary intake, food intolerance history, exposure to others with illness, and any recent dining out experiences. A thorough medication review including any over-the-counter herbal remedies or laxatives should be conducted. A dietary history 3 to 5 days before onset of symptoms would be helpful, with particular attention to the ingestion of meat, dairy products, seafood, and products containing gluten. The associated symptoms of fever, abdominal pain and distention, vomiting, myalgias, and headache with abrupt onset suggest acute diarrhea etiology. In contrast, fatigue, muscle weakness, weight loss, alternating diarrhea and constipation, incomplete evacuation, abdominal pain, and protracted or recurring symptoms suggest chronic diarrhea etiologies.

Physical examination should include vital signs, weight, and other symptoms such as dizziness, light-headedness, or syncopal episodes, assessing for the presence of postural hypotension. Assess the skin for turgor and the condition of the tongue and mucous membranes. Check for evidence of jaundice, abdominal tenderness or fullness, rashes, or lesions. Examine the thyroid for enlargement or lesions. Perform a thorough examination of the abdomen for distention, rigidity, tenderness, bowel sounds, masses, hepatomegaly, or splenomegaly. Perform a rectal examination to check for impaction, include hemoccult testing to assess for bleeding, hemorrhoids, polyps, fissures, fistulas, or evidence of malignancy. Include a general inspection for arthritis or lymphadenopathy. Stool should be examined for mucus and the presence of blood. Depending on the results of the exam, an abdominal x-ray may be warranted. Figure 7-1 describes an algorithm to assist in determining the appropriate work-up needed for diarrhea.

Diagnostic Tests: For most cases of diarrhea of acute onset, no diagnostic testing is warranted unless the individual appears acutely ill. Hydration should be maintained. If abnormal findings are observed on physical examination or the individual has additional comorbid conditions, then diagnostic testing may be necessary. A flat plate abdominal x-ray can reveal obstruction, ischemia, or a mass. Complete blood count (CBC) and a complete metabolic panel (CMP) to include electrolytes and renal function will help identify an infectious process, any electrolyte imbalance, and the presence of dehydration. A barium enema can reveal malignancies, polyps, or abnormalities of the mucosal lining. Colonoscopy or sigmoidoscopy may be useful when symptoms are persistent and/or unexplained. If laxative abuse is suspected, consider ordering a stool laxative screen. Send a stool sample to test for occult blood, *Clostridioides difficile*, salmonella, *Escherichia coli*, lactoferrin, campylobacter, leukocytes, ova, and parasites. If the stool tests positive for leukocytes, the sample should be cultured to identify any bacterial etiology.

Differential Diagnosis: Identify the time frame for the episode(s) of diarrhea: acute diarrhea (1 to 2 days), persistent diarrhea (14 to 28 days), and chronic diarrhea (more than 28 days). In acute diarrhea, consider inflammatory bowel disease, fecal impaction, IBS, diverticulitis, antibiotic-associated pseudomembranous colitis, bowel ischemia, drug side effects, food poisoning, and virus or bacteria exposure. In chronic diarrhea consider ulcerative colitis, Crohn disease, microscopic colitis, celiac disease, IBS, bile acid malabsorption, occult neoplasm, post-radiation enterocolitis, and functional problems. A fecal specimen should be obtained for anyone in cases of severe, bloody, inflammatory, or persistent diarrhea or if an outbreak is suspected. A stool for *Clostridioides difficile* may be warranted in the older patient who has recently taken antibiotics.

Treatment: Hydration is a priority regardless of cause or other treatments prescribed. In many cases of diarrhea, replacing lost fluid and electrolytes is the only treatment needed, but treatment is dependent on the cause. Older adults who are frail are at increased risk for dehydration, renal failure, and multisystem failure. If diarrhea is severe, refer the patient for emergent evaluation and treatment. In the hospital, the older adult patient should be treated aggressively with IV fluid therapy with close monitoring of the cardiopulmonary status, renal status, and electrolytes. In cases of acute-onset diarrhea in which a viral cause is likely, provide symptomatic treatment to maintain hydration and electrolyte balance. Use of medications can slow the intestinal motility but may also extend the time frame of the occurrence of diarrhea.

Follow-Up: Scheduling follow-up visits will be determined based on the cause of the diarrhea. In the case of acute diarrhea, reevaluate the patient after 3 to 5 days of following the initial treatment plan. If diarrhea persists, diagnostic studies may be indicated, and the patient's hydration status reevaluated.

Sequelae: Depending on the cause and extent of the diarrhea, complications may include dehydration, sepsis, shock, anemia, fluid and electrolyte imbalance, malnutrition, renal failure, and peritonitis.

Prevention/Prophylaxis: Prevention depends on the cause. Oral replacement of fluids is of highest priority, but in severe cases IV fluid replacement may be warranted. Proper

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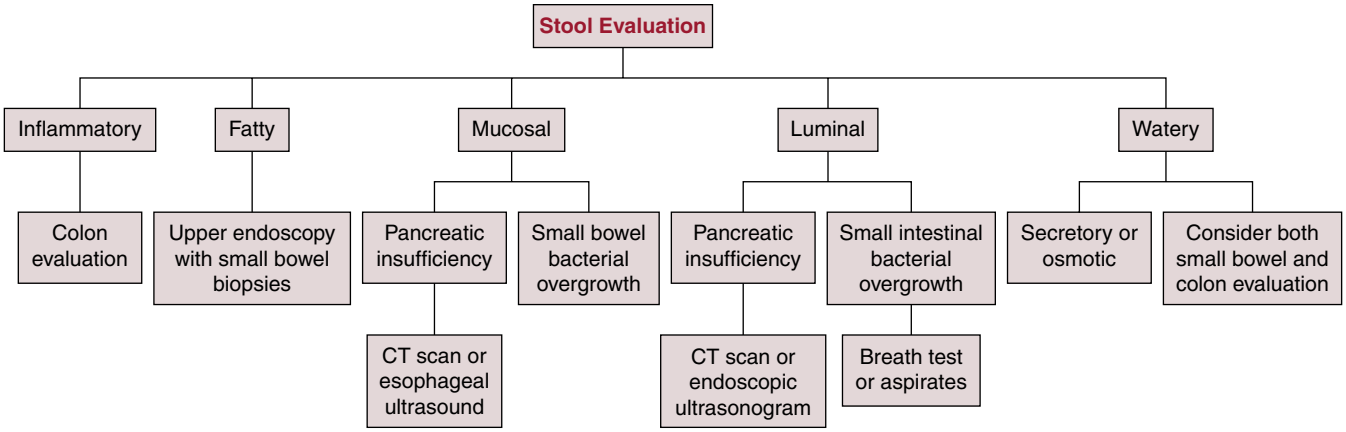

Type of Diarrhea	Assessment	Common Causes
Inflammatory diarrhea	Frequent, small volume, bloody stools, and may be accompanied by fever and severe abdominal cramping May have leukocytes in stool Laboratory tests may demonstrate elevated C-reactive protein level or elevated sed rate (ESR), and low albumin level	Crohn's disease Ulcerative colitis Ischemic colitis Infectious processes including *C. diff*, cytomegalovirus, tuberculosis, and *Entamoeba histolytica*
Fatty diarrhea	History of weight loss Greasy or bulky appearing stools (may be difficult to flush and creates oily toilet requiring a brush to remove)	Malabsorption syndromes Celiac disease Chronic pancreatitis Inadequate bile acid concentration Small intestinal bacterial overgrowth Liver cirrhosis
Watery diarrhea	Classified as osmotic or secretory in origin Differentiate: Fasting decreases stool production in osmotic diarrhea but does not affect secretory diarrhea	Osmotic diarrhea is due to poorly absorbed ions or sugars caused by ingestion of anions such as laxatives and antacids or ions such as magnesium; or carbohydrate malabsorption of poorly absorbed sugars or sugar alcohols such as sorbitol or xylitol Secretory diarrhea is due to disruption of epithelial electrolyte transport caused most commonly by infectious processes—either viral or bacterial, as well as parasitic or peptide-secreting endocrine tumors such as in cancerous processes

FIGURE 7-1. Algorithm to assist in determining the appropriate work-up needed for diarrhea.

nutrition is important; introduce solid foods slowly, the diet should be bland, advancing from clear liquids to full liquids, to soft foods, before graduating to a regular diet. Careful cooking and storage of food is important to avoid spoilage. Check expiration dates on dairy and meat products before using. Clean cutting boards and utensils. Educate about cross-contamination when cooking, such as with raw meats, to prevent exposure to pathogens. For individuals who are traveling to a foreign country, begin appropriate prophylactic treatment (Connell, 2019). Caution travelers about avoiding undercooked foods, raw foods, buffet food, unpasteurized dairy products, untreated water, and ice. Carbonated drinks, bottled water, and boiled water are considered safe for drinking and to use for oral hygiene.

Prevention of transmission of diarrhea to or from others (including young children) in hospitals and in long-term care facilities is extremely important. Frequent hand washing by patients and health-care providers is the key to preventing transmission of infectious diarrhea. Avoidance of long-term laxative use and prudent use of antimicrobial agents are also important in preventing diarrhea.

Referral: Further work-up may be necessary in individuals who are exhibiting prolonged diarrhea, severe dehydration, or recurrent episodes of diarrhea and in individuals who report blood in stools. Refer to the hospital for consideration of an inpatient stay if IV fluids and/or electrolyte replacements are needed or if diarrhea persists. The patient may need to be evaluated by a gastroenterologist or an infectious disease specialist depending on the causative agent of the individual's diarrhea. Complications may include dehydration, malnutrition, peritonitis, sepsis, shock, anemia, renal failure, or electrolyte imbalances, which can be life threatening (such as with hypokalemia).

Education: Explain to the patient, family, and caregivers the cause of symptoms, diagnostic and treatment measures, any follow-up needs, and preventive strategies. Emphasize the need for early intervention to prevent dehydration.

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Clinical Recommendation	Evidence Rating	References
Classify diarrhea into three categories (watery, bloody, or fatty) based on the history, physical examination, and testing.	A	Connell, 2019 Sweetser, 2012
Specific therapy depends on the underlying cause.	C	Connell, 2019 Sweetser, 2012
Teach patients the signs and symptoms of dehydration.	C	Connell, 2019
Vancomycin 125 mg orally 4 times a day for 10 days has been shown to be more efficacious than metronidazole but more costly.	A	Cho et al., 2019

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DIZZINESS AND VERTIGO

Description: Dizziness is an imprecise term commonly used by laypersons, especially older adults to describe various subjective symptoms. Dizziness is an independent predictor of falls, which is the leading cause of accidental death and the leading cause of disability in individuals older than age 65 (Zanotto et al., 2017). A prompt evaluation and development of an appropriate treatment plan is essential to mitigate this risk. The practitioner must first understand the patient's personal meaning of dizziness to guide the diagnostic process to determine etiology of the dizziness. Establishing the time course, provoking or aggravating factors, concurrent symptoms, epidemiological risk factors, pre-existing conditions as well as interpreting physical examination findings are crucial in establishing a diagnosis. Despite a thorough history and physical examination, the final cause of dizziness may not be identified in some patients. For others, multiple practitioner visits may be needed to identify a cause. The ambiguity of patient descriptions as well as the multifactorial etiology of dizziness can result in significant healthcare costs from diagnostic work-up and interrupted daily activities.

The traditional clinical categories of dizziness are vertigo, unsteadiness or gait instability, light-headedness, and disequilibrium. However, there are new diagnostic approaches that do not rely on this traditional classification but rather utilize the patient's responses to determine the classification of dizziness as episodic triggered, spontaneous episodic, or continuous vestibular. This approach is referred to with the pneumonic TiTrATE: **T**iming of the symptom, the **Tr**iggers that provoke the symptom, **A**nd a **T**argeted **E**xamination (Muncie et al., 2017). The practitioner should therefore approach dizziness in the older adult population as a syndrome that requires specific strategies to recognize, evaluate, and manage to reduce significant disability and complications.

Etiology: Dizziness may result from mixed pathologies that include medications; metabolic derangement; infections; toxins; and neurological, otolaryngological, cardiovascular, or psychiatric conditions. These conditions can be divided into peripheral, central, or systemic causes. Benign paroxysmal positional vertigo (BPPV), a disorder arising from the inner ear, is the most common peripheral cause in individuals, including those older than 70 years (Balatsouras et al., 2018). The etiology of BPPV is usually loose calcium crystals in the semicircular ear, which results in the patient having a sensation of movement with any shifts in gravity and movement of the crystals. BPPV can affect the posterior or lateral semicircular canals, but posterior canal BPPV occurs in 85% to 95% of cases (Balatsouras et al., 2018). Risk factors for BPPV include head trauma and recent viral upper respiratory or inner ear infection. Dizziness associated with tinnitus or audiological manifestations is usually from Ménière disease. Individuals with dizziness and associated neurological deficits require evaluation for a central cause as this is usually due to vertebrobasilar system involvement. The most common vertebrobasilar etiologies in older adults include hemorrhagic stroke, transient ischemic attack (TIA), ischemic stroke, and vertebrobasilar insufficiency due to atherosclerotic disease. In younger adults who have a history of migraine with aura and are experiencing dizziness associated with headache but no other neurological deficits, a vestibular migraine diagnosis is high on the differential for a central etiology (Headache Classification Committee of the International Headache Society, 2018). It is not typical for older adults to have a vestibular migraine as an initial presentation of migraine so other common vestibular causes should be investigated first. Individuals with a history of migraine with aura are at increased risk for other neurological manifestations including TIA and the presence of patent foramen ovale. These patients require a referral to neurology for continued management, monitoring of their migraine, and optimization of risk factors and preventative therapy when indicated (Elbadawi et al., 2019). Dizziness associated with loss of pallor, diaphoresis, shortness of breath, or other cardiac manifestations should prompt evaluation for cardiac etiology such as orthostatic hypotension, arrythmias, ischemic heart disease, or heart failure (HF). Psychiatric disorders such as depression and anxiety can result in dizziness either due to medications utilized to treat the disorders or due to symptoms associated with the disorders. In recent years, there has been recognition of a disorder called persistent postural-perceptual dizziness (PPPD), which is a disorder on the spectrum of functional neurological disorders.

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It results in chronic dizziness with symptoms of unsteadiness and hypersensitivity to self-motion or complex visual stimuli, phobic avoidance of provocative situations similar to fear of falling, and functional gait abnormalities in the absence of other identified organic cause for the symptoms. It is believed to be caused by a long-term maladaptation to a medical vestibular event that caused the initial dizziness symptoms. Diagnosis is guided by the Bárány Society's diagnostic criteria for persistent postural-perceptual dizziness, which relies heavily on the patient's history (Popkirov et al., 2018). Individuals older than age 70 can develop presbystasis, an age-related disequilibrium not attributed to any pathology that is characterized by a gradual onset of difficulty walking (Kesser & Tucker Gleason, 2019).

Occurrence: Dizziness is common, with 45% of affected nonhospitalized patients seeking care from primary care providers (Muncie et al., 2017). The most common location to seek care after primary care is in the ED. Referral to specialists, neurologists, otolaryngologists, or cardiologists is also common if etiology is unclear or symptoms do not respond to treatment. More men than women experience BPPV; however, the condition may persist longer in women, which results in their seeking treatment more often (Álvarez-Morujo de Sande et al., 2019).

Age: Vestibular impairment is common in older adults and may affect nearly 50% of those older than 60 years (Agrawal et al., 2019).

Ethnicity: Not significant.

Contributing Factors: Contributory medications include antihypertensives, anticonvulsants, psychotropic drugs, and ototoxic drugs. Physiological changes occurring with age can affect equilibrium. Altered sensitivity of the baroreceptors, as well as diminished sensory and motor pathways over time, increase the vulnerability to syncope and gait instability.

Signs and Symptoms: The patient's description of the symptom helps determine the type of dizziness experienced.

Vertigo. Vertigo is the sensation of movement of the patient or the environment due to central or peripheral causes. Associated symptoms may include nausea, vomiting, unsteadiness, or visual disturbances that occur because of fast-beating nystagmus. The time course of vertigo assists in determining the appropriate diagnosis. Episodic vertigo following a viral illness and lasting days with nausea and no associated symptoms is usually due to vestibular neuritis. Episodic vertigo lasting for seconds and associated with position changes is probably due to BPPV. Vertigo of sudden onset lasting for minutes can be due to migraine or cerebrovascular disease, especially if neurological deficits are present. Vertigo lasting hours and when associated with endolymphatic hydrops symptoms, including tinnitus, dizziness, fluctuating hearing loss, imbalance, and a feeling of fullness/pressure in the ear, is probably caused by Ménière disease. Older adults with head or neck pain post trauma can develop cervicogenic vertigo provoked by movement or sustained positions of the neck. This cervicogenic type of vertigo requires further diagnostic work-up to rule out vascular traumatic injuries such as vertebral artery dissection.

Presyncope. In presyncope, patients have the sensation of nearly fainting. Associated symptoms include perspiration, fatigue, pallor, palpitations, dimming of auditory or visual stimuli.

Light-Headedness. Patients often describe presyncope symptoms as light-headedness. This can also be associated with anxiety or depression.

Disequilibrium. Patients with disequilibrium describe a sense of imbalance. Symptoms improve dramatically by bracing on a stationary object and are exacerbated by vision deficits or uneven surfaces. Associated symptoms may include chronic hearing loss, chronic lower extremity sensation deficits, poor coordination, and generalized weakness. However, patients with acute gait instability need further evaluation for cerebrovascular disease.

Physical Examination: The physical examination should be comprehensive and include the following components:

General. Observe how the patient moves around and any symptom reproduction with activity. Does he or she hold onto the furniture or walls? Any signs or symptoms of fever?

Head, Eyes, Ears, Nose, and Throat. Test for extraocular movement, watching for nystagmus. Rotatory nystagmus suggests a peripheral cause of dizziness, but this alone is not a conclusive finding. Vertical nystagmus suggests a central lesion and needs further investigation. In many clinical situations, rotatory nystagmus is superimposed on horizontal nystagmus. Check the patient's static monocular or binocular visual acuity and dynamic visual acuity. Evaluate visual fields. Perform a funduscopic examination, looking for papilledema and other abnormalities. Inspect the ears for accumulation of fluid, tympanic membrane abnormalities, or presence of cerumen impaction. Examine the neck for range of motion and flexibility.

Cardiovascular. Evaluate central and peripheral function. Auscultate for heart sounds; evaluate for arrhythmias and murmurs. Evaluate the carotid arteries for bruits. Check vital signs, including orthostatic vitals. A drop in systolic blood pressure of 20 mm Hg or diastolic blood pressure of 10 mm Hg is significant, especially if it reproduces the patient's symptoms.

Neurological. Test for coordination deficits with finger to nose, heel to shin, past pointing, and rapid alternating movements. If coordination tests are abnormal, keep vestibular dysfunction or cerebrovascular insufficiency in the differential. Test sensation including pain, temperature, vibration, proprioception, and Romberg. Patients with cerebellar disease have difficulty standing with their feet together. Patients with decreased position sense or other sensory deficits in their lower extremities are able to compensate with eyes open but sway with eyes closed. Perform gait assessment, including tandem gait. Complete a motor examination and evaluate deep tendon reflexes. The inclusion of psychological tests (mental status, depression, anxiety) is appropriate if a functional cause is suspected.

Special Diagnostic and Screening Tests. Forced hyperventilation involves asking the patient to breathe 20 to 30 times per minute for 2 to 3 minutes. This normally causes dizziness and

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finger and perioral numbness. If presenting sensations are reproduced, the dizziness may be related to anxiety or other functional etiology.

Have the patient march in place for 30 seconds with the eyes closed and arms extended in front. Be careful not to orient the patient with any sounds (e.g., your voice or a ticking clock). Patients with absent or reduced vestibular function (from prior vestibular damage) rotate more than 30 to 45 degrees while marching.

For the Dix-Hallpike maneuver, assist the patient to quickly lie down on the examination table with the head hanging over the back of the table at an approximate 30-degree angle with the face turned 45 degrees to the right. While holding the patient's head in place for 1 minute, observe the patient for nystagmus and ask whether this reproduces the dizziness (vertigo) symptoms. Bring the patient back to a sitting position and observe for 1 minute. Repeat the test with the head turned 45 degrees to the left. If vertigo is reproduced, the test should be repeated two or three times on the side that caused the most severe symptoms to determine whether the nystagmus and symptoms begin to disappear. Patients with benign postural vertigo experience severe vertigo 5 to 15 seconds after the head is turned and nystagmus is induced. Position change must be completed in 2 seconds, as the signs typically fade in less than 1 minute, and repeated testing causes the symptoms to disappear. The safety of this test must be considered if the patient is frail or has neck or back problems. The Dix-Hallpike test is underutilized and may be inappropriately utilized causing misdiagnosis or missed diagnosis. Thorough history taking is a key to its appropriate use (Dmitriew et al., 2021).

Diagnostic Tests: Diagnostic tests are dependent on the presenting symptoms, the history and physical examination, as well as comorbid factors. The HINTS (head-impulse, nystagmus, test of skew) examination can help distinguish peripheral from central etiologies, as well as delineate which patients may need diagnostic testing (Muncie et al., 2017). Select testing might include CBC for anemia, serum glucose for hypoglycemia, ECG or Holter monitoring for arrhythmia, audiometry if hearing loss is present, or vestibular function tests (such as videonystagmography or electronystagmography). Neuroimaging (CT, CTA, MRI, or MRA) must be ordered if neurological symptoms are present to evaluate for a central lesion, vascular stenoses or occlusions causing ischemia. For patients with psychiatric disorders or functional neurological disorders, evaluation for anxiety and depression using a standardized scale such as a Generalized Anxiety Disorder-7 for anxiety or Patient Health Questionnaire 2 or 9 to screen for depression.

Differential Diagnosis: Differentiate between vertigo (a sensation of movement), imbalance (gait instability), light-headedness (a sensation of being about to faint), and syncope (an actual loss of consciousness) to help narrow down differential diagnoses. Differential diagnoses for peripheral causes can include BPPV, vestibular neuritis, and Ménière disease. Differential diagnoses for central causes can include TIA, vertebrobasilar insufficiency, ischemic stroke, hemorrhagic stroke, vestibular migraine, and PPPD. Diagnoses for systemic causes can include orthostatic hypotension, arrythmia, HF, ischemic heart disease, infection, depression, anxiety, and other neurological disorders such as ocular myasthenia gravis. If dizziness has a predictable pattern associated with it (e.g., mid to late morning, mid to late afternoon, 2 to 4 hours after eating), suspect hypoglycemia.

Treatment: Treatment is based on the cause of the dizziness. Traditional vestibular rehabilitation is highly effective but requires face-to-face time, resulting in inconsistent completion rates. Recently, however, there are ongoing studies evaluating the efficacy of blended online and face-to-face vestibular rehabilitation protocols in the hope of improving access and promoting consistent completion rates (Van Vugt et al., 2017). Physical therapy (PT) for balance training may supplement other management approaches as well.

Patients with benign positional vertigo (BPV) can perform the Epley maneuver, which loosens and moves particles out of the posterior semicircular canal and back into the utricle. If the cause of light-headedness is medication side effects or volume deficiencies, adjustments are indicated. Support stockings may alleviate symptoms from orthostatic hypotension. Appropriate management of cardiovascular, cerebrovascular, or functional conditions is warranted.

The efficacy and mechanism of action of the common medication meclizine has not always been supported, but a recent study reported by Wibble et al. (2020) concluded that meclizine was effective in treating vertigo in "everyday activities but may not be helpful in high-acceleration environments. Benzodiazepines, despite the risk of somnolence and potential for dependency, are frequently used to treat associated symptoms of vertigo, although recent studies have shown no difference between meclizine and diazepam (Shih et al., 2017). These medications require caution because they can worsen the symptoms of dizziness and have other side effects, which are particularly problematic in older adults.

Follow-Up: Patients should follow up if symptoms worsen, change from one type of dizziness to another, or do not resolve within 2 weeks.

Sequelae: Older adults with dizziness are at high risk for falls and injury, as well as self-induced immobility due to fear of falling.

Prevention/Prophylaxis: Educate older adults to move extremities before rising from positions held for any length of time to compensate for age-related changes in vascularity. Evaluate for medication side effects before adding medications to combat the dizziness.

Referral: Persistent symptoms with unknown etiology require a referral to neurology, cardiology, otolaryngology, or psychiatry as appropriate.

Education: Explain the underlying cause, rationale for treatment, and importance of exercises like the Epley maneuver. Teach the patient the exercises and ask for return demonstration. Explain that this condition may take time to completely resolve, but that it is important to seek care for worsening or persistent symptoms. Encourage the use of assistive devices for safety until the condition resolves.

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Clinical Recommendation	Evidence Rating	References
Balance disorders and presence of dizziness in older adults is a strong predictor of falls.	A	Zanotto et al., 2017
Review medications for adjustment to prevent/resolve medication-related dizziness. Vestibular suppressants for acute vertigo should be limited to the acute phase to avoid negatively affecting functional recovery or central compensation for balance.	A	Casani et al., 2021
No routine neuroimaging tests are indicated in the diagnosis of dizziness unless neurological symptoms are present. However, check glucose levels in patients with diabetes and monitor cardiac rhythm in those >45 years old or those with the appropriate comorbidities.	C	Muncie et al., 2017
A diagnosis of PPPD is guided by the Bárány Society's diagnostic criteria.	A	Popkirov et al., 2018
Vestibular rehabilitation is highly effective for rapid and complete vestibular compensation.	A	Van Vugt et al., 2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

DYSPHAGIA

Description: Dysphagia is a commonly encountered problem in the older adult population and involves the inability to pass food from the mouth to the stomach appropriately. This problem can cause significant impairment in quality of life and even increase mortality risk (Tulunay-Ugar & Eibling, 2018). A problem can arise during any of the three swallowing phases and thus the specific type of dysphagia will be described based on the phase—oral, pharyngeal, or esophageal. Often a deficit exists in more than one phase (Christmas & Rogus-Pulia, 2019).

Etiology: Normal changes in the swallowing process that occur with aging are called presbyphagia. These changes often do not produce symptoms or complications for the individual. Common normal changes include increased residue after swallowing and a slower rise in swallowing pressure (Tulunay-Ugar & Eibling, 2018). Dysphagia, however, is pathological and not a normal part of aging.

Oral dysphagia involves the disruption of the normal process of chewing food, mixing the food with saliva, and moving the food to the back of the mouth. Several functional impairments can produce oral dysphagia: tongue weakness, dry mouth (xerostomia), alerted consciousness, and movement disorders. Medications that cause sedation or dry mouth, as well as presence of dementia and delirium can cause oral dysphagia. Pharyngeal dysphagia involves the disruption of the normal process of moving the food into the pharynx, through the pharynx and to the esophagus. Weakness of the tongue, pharynx, or vocal cords can contribute. Common diseases associated with pharyngeal dysphagia include Parkinson's disease, amyotrophic lateral sclerosis, stroke, or vocal cord tumor. Finally, esophageal dysphagia involves the impairment of the normal process of moving food down the esophagus using peristalsis and gravity. Mechanical obstruction from the food bolus and impairment of the esophageal muscle or lower esophageal muscle tone can contribute. Common disease processes associated with esophageal dysphagia include esophagitis, achalasia, and esophageal obstruction by the presence of a tumor, stricture, or diverticulum (Christmas & Rogus-Pulia, 2019).

Age/Occurrence: Risk of developing dysphagia increases with age. Accurate measurements of the incidence of dysphagia are difficult to quantify due to underreporting of symptoms and lack of awareness of symptoms. However, it is estimated that 10% of people older than the age of 50 have dysphagia. Dysphagia is believed to affect 40% of institutionalized older adults (Tulunay-Ugur & Eibling, 2018).

Ethnicity: Not significant.

Contributing Factors: Considering that the causes and risks of dysphagia are diverse, a multidimensional framework has been proposed for early identification of dysphagia, even in the preclinical (or unidentified) stage (Madhavan, 2021). This framework considers causative, associative, and speculated associative evidence in the development of preclinical dysphagia among community-dwelling older adults. Causative factors for the development of preclinical dysphagia include advanced age and certain diagnoses (Madhavan, 2021). The increased vulnerability to acute illness that older adults face may worsen decline in swallowing function and lead to dysphagia (Namasivayam-MacDonald & Riquelme, 2019). Neurological disease is the most common disease process associated with dysphagia (Hou et al., 2019). Dysphagia may be the first symptom identified by patients suffering from neurodegenerative disease (Tye et al., 2020). Ischemic stroke is also a major risk factor for dysphagia, with one study finding 32% of patients experiencing their first ischemic stroke having a new diagnosis of dysphagia (Stipancic et al., 2019). There are certain medications that can have a causative effect on the development of dysphagia. Anticholinergic drugs, such as those used for urinary incontinence, as well as tricyclic antidepressants can lead to xerostomia. The use of sedatives and neuroleptics often contribute to dysphagia

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because they can reduce attention and affect oral function. Steroids can weaken the strength of the tongue and mouth. Antipsychotic medications can impair the pharyngeal phase of swallowing, whereas bisphosphonate therapy can impair the esophageal phase (Christmas & Rogus-Pulia, 2019).

Risk factors that are associated with the development of dysphagia among older adults include frailty, reduced physical function, poor nutrition, cognitive decline, and poor oral health (Madhavan, 2021). A major component of frailty is sarcopenia, or the loss of skeletal muscle mass and strength, and has also been associated with an increased risk of dysphagia (Madhavan, 2021; Cha et al., 2019). Applying a multidimensional framework to the assessment of dysphagia requires including an assessment of the patient's level of social support or for the presence of sensory loss (Madhavan, 2021).

Signs and Symptoms: Symptoms typically associated with oropharyngeal dysphagia include difficulty initiating swallowing, food sticking in the throat, nasal regurgitation, and coughing during swallowing. Specifically oral dysphagia may present with pocketing or "cheeking" of food, prolonged chewing, and leftover food residue in the oral cavity. Pharyngeal dysphagia often presents with cough, throat clearing, wet sound to the voice after swallowing, nasal regurgitation of food, and even aspiration (Christmas & Rogus-Pulia, 2019). Patients with esophageal dysphagia most commonly present with a complaint that food is stuck in the chest (sternum or suprasternal area) and may report choking or a sensation of pressure and may even regurgitate food (Christmas & Rogus-Pulia, 2019).

For oropharyngeal dysphagia, a trained speech language pathologist (SLP) is an integral component of the evaluation process. Assessment begins with careful history taking through review of medical history, interview with patient and caregivers, examination of the cranial nerves, and administering of various types of foods and liquids (Christmas & Rogus-Pulia, 2019). Patients often feel symptoms of oropharyngeal dysphagia within one second of attempting swallow (Dunlap & Patterson, 2019).

Diagnostic Tests: Diagnostic tests are based on the medical history and initial examination findings (Christmas & Rogus-Pulia, 2019). Videofluoroscopy (VFSS) (modified barium swallow) is most commonly used when evaluating neuromuscular disease but is complicated by the requirement for a separate referral and appointment (Audag et al., 2019; Tye et al., 2020). The VFSS involves the administration of various amounts and viscosities of barium. The oropharyngeal area is visualized with radiography, allowing the SLP to see if swallowing difficulties are present and how well the individual is able to swallow (Christmas & Rogus-Pulia, 2019). Fiberoptic endoscopic evaluation of swallowing (FEES) is an option that can be more easily completed in office, limiting the need for additional visits (Audag et al., 2019; Tye et al., 2020). The FEES diagnostic test involves the insertion of a flexible endoscope into the nose and upper pharynx for the visualization of the swallowing process (Christmas & Rogus-Pulia, 2019).

Differential Diagnosis: It is important to differentiate whether the patient has a feeding problem or a swallowing problem or both. Cognitive impairments are frequently associated with feeding problems. Evaluation for specific motor, neurological, or obstructive causes should be performed. For the patient complaining of burning associated with swallowing, reflux esophagitis, esophageal infection, and gastroesophageal reflux disease (GERD) need to be explored.

Treatment: The purpose of early identification and treatment of dysphagia is prevention of complications such as aspiration, malnutrition, dehydration, choking, pneumonia, and death (Dunlap & Patterson, 2019; Tulunay-Ugar & Eibling, 2018). Many facilities utilize a team-based approach often lead by an SLP with coordination among nutritionists and occupational therapists. (Tulunay-Ugar & Eibling, 2018). Treatment strategies can be divided into two methods: compensatory and rehabilitative (Christmas & Rogus-Pulia, 2019).

Compensatory methods compensate for the impairment to reduce complications. Providing good oral care is one such method. Postural changes are another and can involve the chin-down position (tucking of the chin to the chest) or the head-turn position (the turning of the head toward one shoulder) (Christmas & Rogus-Pulia, 2019).

Another compensatory method of treating dysphagia is through the alteration of the thickness of swallowed foods. For example, patients with difficulty swallowing thin liquids will often be placed on a thickened liquid diet; however, this poses additional risks such as dehydration from decreased oral intake. The use of textured thin liquids can be a potential solution (Howard et al., 2018). The International Dysphagia Diet Standardization Initiative has set standards for defining textured-modified foods and liquids (Cichero et al., 2017). However, the evidence is conflicting on the clinical benefit of textured-modified foods in the treatment of dysphagia, and a patient-centered focus should be taken when determining if this approach is best for each individual (Christmas & Rogus-Pulia, 2019).

The placement of a feeding tube is a common, yet controversial, compensatory practice. The intention is to reduce the risk of aspiration and pneumonia, but the evidence as to the clinical benefit is lacking. Cellulitis and bacteremia are potential complications of gastrostomy tubes. Agitation, sinus infection, and nasal irritation are potential complications of nasogastric feeding tubes. All feeding tubes also increase the risk of diarrhea (Christmas & Rogus-Pulia, 2019). The American Geriatrics Society (AGS) published a position statement cautioning against the placement of feedings tubes in patients with both dementia and dysphagia due to the serious risks of the practice. AGS recommends careful hand feeding rather than placement of a feeding tube (AGS, 2014).

Rehabilitation methods are intended to improve the swallowing process. Exercise and training programs may help improve swallowing planning and coordination. Swallowing maneuvers may be taught to help with dysphagia. The Mendelsohn maneuver involves the patient voluntarily holding the larynx in its higher position for 2 to 3 seconds before swallowing (Christmas & Rogus-Pulia, 2019). There is only low- to very-low-quality evidence that swallowing interventions may reduce the incidence of dysphagia and chest infection or improve swallowing function. Moderate quality evidence suggests that these interventions have reduced hospital length of stay but have not reduced fatality or disability rate (Bath et al., 2018).

Esophageal dysphagia treatment depends on the cause. Esophageal dilation may be helpful for patients with achalasia (Wilkinson & Halland, 2020). Patients with esophageal spasms can be given calcium channel blockers, nitrates, or

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phosphodiesterase-5 inhibitors (Wilikinson & Halland, 2020). Esophagitis and GERD can be treated with antacids, H_2 blockers, or PPIs. More aggressive forms of treatment would involve surgical intervention such as esophageal dilation or feeding tube placement. One study found that by the time of FEES evaluation among patients with neurological disorders, almost 20% were referred for surgical intervention, thus highlighting the importance of early screening and detection to potentially reduce the need for aggressive measures (Tye et al., 2020).

Follow-Up: Patient monitoring depends on the specific etiology of the dysphagia.

Sequelae: Complications from dysphagia are caused by food or liquid penetration or aspiration. Penetration involves the movement of the oral substance—or bolus—into the laryngeal vestibule but not below the vocal cords. Aspiration involves the movement of the bolus into the trachea and lungs. Silent aspiration occurs when the patient lacks the ability to respond to aspiration through throat clearing or cough. Dysphagia in the presence of stroke and dementia is highly associated with decreased survivability (Christmas & Rogus-Pulia, 2019).

Prevention/Prophylaxis: Early detection and treatment are key in preventing complications. Patients with known disorders that are highly associated with dysphagia should be screened for symptoms.

Referral: Initial consultation with speech pathology for evaluation can be essential in deciding on further assessment. Gastroenterology should be consulted if invasive diagnostic tests are indicated.

Education: Patients and caregivers should be encouraged to provide food and fluids at appropriate consistency. Specific education is provided based on the type of dysphagia and treatment regimen used.

Clinical Recommendation	Evidence Rating	References
A team-based approach with the involvement of a trained speech language pathologist should be used for evaluation and treatment of dysphagia.	C	Tulunay-Ugar & Eibling, 2018
Feeding tubes should be avoided in patients with dementia and dysphagia.	B	American Geriatrics Society, 2014
A patient-centered approach should be taken when considering use of textured-modified foods.	C	Christmas & Rogus-Pulia, 2019

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FALLS

Description: According to the World Health Organization (WHO), a fall is an event that results in a person coming to rest inadvertently on the ground, floor, or other lower level (WHO, 2021). In the *International Statistical Classification of Diseases and Related Health Problems (ICD-10)*, falls are coded based on the circumstance that caused an injury, such as slipping, tripping, and stumbling (ICD-10 Data, 2021). Falls are the leading cause of nonfatal injuries, and complications resulting from falls are the leading cause of death in older adults. Of serious injuries, fractures and traumatic brain injury are the most common, with falls as the cause for 95% of hip fractures, which has a 1-year mortality ranging from 12% to 37%. The total medical cost for fall-related injuries in 2015 was more than $50 billion (CDC, 2021).

Etiology: Falls are included in the list of geriatric syndromes because older adults have multiple risk factors that contribute to falls. Most falls are caused by an interaction of several intrinsic and extrinsic risk factors. Intrinsic factors include age, previous falls, weakness, gait/balance problems, poor vision, problems with feet, postural hypotension, chronic medical conditions (e.g., arthritis, dementia, arrhythmia, neuropathies), an occult medical condition (e.g., pneumonia or urinary tract infection (UTI), and fear of falling. Extrinsic factors include conditions in the environment such as lack of handrails, grab bars, improper use of assistive devices, poor lighting, obstacles, slippery or uneven surfaces, medications. Additional risk factors include inactivity and risky behavior (e.g., use of a ladder).

Eight risk factors have been identified and validated as predictors of falls in the inpatient setting using the Hendrich II Fall Risk Model. These risk factors are altered mental status, symptomatic depression, altered elimination, dizziness or vertigo, two medication categories (antiepileptics and benzodiazepines), male sex, and decreased ability to rise from a chair (Hendrich et al., 2020; Hendrich, 2021).

Occurrence: Approximately 25% of persons 65 years and older, 34% of persons older than 80 years and 50% of persons living in long-term care fall each year, although the true incidence of falling is likely to be higher due to the fact that many falls are not reported (CDCa, 2021). Although women and men are equally likely to fall, women are more likely to suffer a fracture from a fall because more women have osteoporosis.

Age: Although many sources report that falls should not be considered a normal part of aging, there are normal physiological changes with aging that can impact risk of falling.

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Age-related changes that affect postural control and increase the risk of falling include proprioceptive sensory loss in the lower extremities, impaired vestibular function, muscle activation patterns that impact balance, and visual impairment. Cognitive impairment and age-related decline in baroreceptor sensitivity, which increases heart rate with decreases in blood pressure, also increase risk of falling in older adults.

Ethnicity: Blacks are less likely to experience initial or recurrent falls than non-Hispanic Whites (Nicklett & Taylor, 2014). Among older women, the risk of having a recent fall was substantially lower for Black and Asian women when compared to White women (Geng et al., 2017).

Contributing Factors: The risk of a fall increases as the number of risk factors increases. Chronic underlying disease that impacts mobility and cognition, visual impairment, alcohol use, and environmental factors (lighting, floor covering, railings) impact the risk of falling. In addition to the assessment of medications potentially associated with falls (psychoactives, hypnotics, opioids, diuretics, vasodilators), complete a thorough inquiry about over-the-counter (OTC) medications (such as antihistamines), herbal supplements, potential drug interactions, dose changes in existing medications and if, when, and how medications are actually taken.

Signs and Symptoms: Every older adult patient or their families/caregivers should be questioned every year about falls, frequency of falling, and difficulties with gait or balance as a core component of geriatric assessment. Half of patients or families may fail to mention a fall unless there was injury. For patients who report a fall, it is important to obtain information about the circumstances of the fall, including location, what the patient was doing, how the fall occurred, symptoms at the time of the fall (e.g., chest pain, shortness of breath, dizziness/light-headedness, vertigo, diaphoresis, numbness and weakness of extremities, loss of consciousness), and presence of pain after the fall. Loss of consciousness is difficult to determine in unwitnessed falls and may not be reported from persons with cognitive impairment and those who did not sustain an injury. When possible, it is important to obtain information from someone who witnessed the fall.

In addition to asking about falling, it is important to assess tripping, slipping, or stumbling but not falling and any fear of falling because these factors increase the risk of falling. For those who report recurrent falls (two or more), difficulties with gait/balance, or presented to the emergency department (ED) because of a fall, a multifactorial risk assessment should be completed which includes history of falls, medications, gait, balance, mobility, visual acuity, neurological impairments, muscle strength, heart rate/rhythm, postural hypotension, footwear, and environmental hazards.

Diagnostic Tests: There is no routine diagnostic evaluation for individuals who fall. A complete blood count (CBC) and electrolyte panel to assess for anemia or electrolyte imbalance could be appropriate. The details about how the fall occurred, symptoms associated with a fall, comorbidities, and the physical examination will determine the need for diagnostic evaluation. Evidence of trauma to the head and loss of consciousness are predictive of intracranial injuries and should guide the decision to obtain diagnostic imaging of the brain. Intracerebral injuries should be considered in any older adult who reports head trauma or any fall in a patient on anticoagulants or antiplatelet drugs. Evaluation of syncope with Holter monitoring should be considered for those with unexplained nonaccidental falls or recurrent falls and when loss of consciousness is reported.

The decision to obtain a plain radiograph should be based on history and physical examination findings and the nature of the fall. Wrist, hip, and vertebral are the most common fractures. Femoral neck fractures should be considered in persons with any of the following: sudden onset of hip pain before or after a fall, pain in the groin region, inability to bear weight, external rotation, and shortened appearance of the leg. A plain anterior-posterior (AP) radiograph can detect fractures in most patients. Obtaining an AP pelvis radiograph allows for comparison with the unaffected hip. For patients with negative fracture on plain radiograph, ongoing pain, and inability to function at a previous level, an occult hip fracture should be suspected and evaluated with a magnetic resonance imaging (MRI) or computed tomography (CT) scan.

Differential Diagnosis: Determining the cause of a fall can be complex because most falls are multifactorial, resulting from intrinsic and extrinsic factors. A differential diagnosis can be narrowed by assessment of these risk factors, along with the history and physical examination findings. Reports of light-headedness, near-fainting, or legs giving out suggest orthostasis, arrhythmias, or other cardiovascular conditions. Difficulty standing from a chair or feeling that legs are not supportive suggests deconditioning or neuromuscular disease.

The physical examination may help narrow a differential diagnosis or identify additional factors related to a fall. It is important to initially assess for injury. The pattern of injury can help sort out the event leading to a fall. For example, a wrist fracture caused by a fall on an outstretched hand suggests that consciousness was preserved while falling. Bilateral wounds on knees could suggest drop attacks. The differential diagnosis can also be narrowed by including assessment of orthostatic vital signs, muscle tone to determine spasticity or rigidity, sensation, proprioception, vibration to determine neuropathy or a somatosensory problem, cognitive status, and visual problems. In older adults, falls are often a commonly presenting symptom of an underlying medical problem or an acute illness such as pneumonia or UTI.

Treatment: Interventions should be tailored to the cause(s) and individualized risks of falling. A framework that can be used to coordinate interventions with falls risk factors is the 4Ms, which include what Matters to the patient (incorporates patients' values and goals), Medication, Mentation, and Mobility (Institute for Healthcare Improvement, 2020). Medications can be an easily modified risk factor for falls, so it is important to consider deprescribing inappropriate medications based on Beers criteria® (American Geriatrics Society Beers Criteria® Update Expert Panel, 2019), decreasing the dosage of medications if possible, and adjusting medication dosage based on creatinine clearance. Bedrails, fall alert bracelets, chair/bed alarms and restraints have not been shown to decrease rates of falls in acute and long-term care settings (Cameron et al., 2018).

Follow-Up: For patients who have fallen and those at risk for falling, ongoing management and monitoring of medical conditions, mobility and medications associated with falling is important. Asking about the home environment and providing resources on safety interventions and exercises to improve gait, strength, and balance, reinforces the importance of decreasing the risk of falling.

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Sequelae: Persons who report a previous fall are at increased risk for subsequent falls. Approximately 20% to 30% of older adults who fall endure serious injury, including fractures and traumatic brain injury (WHO, 2021). Injuries result in decreased functional status, subsequent loss of independence, and possible nursing home placement. Falls can also have psychological and social consequences, such as fear of falling or post-fall anxiety syndrome, which can result in social isolation and loss of self-confidence. Approximately 25% to 50% of older adults will not ambulate at their previous level after a fall (CDCa, 2021).

Prevention/Prophylaxis: A baseline assessment of a patient's extrinsic and intrinsic fall risk factors is helpful for not only tailoring individual interventions but allows for assessment of subtle changes in a patient in subsequent encounters both inpatient and outpatient. Part of the baseline and subsequent evaluations should include assessment of gait, strength, and balance. Some of the most commonly used tests include the Get Up and Go Test, Functional Reach Test, and 4-Stage Balance Test. Each of these tests can be done in less than 30 seconds (CDCa, 2021).

There are many patient- and caregiver-appropriate resources available from the CDC (2021), National Council on Aging (2021), and National Institute on Aging (2017) to assess the risk of falling, safety, and fall prevention for both inpatient and outpatient use. These resources address specific environmental safety issues (e.g., inappropriate lighting, lack of grab bars, ill-fitting footwear, inappropriate assistive devices)

Although vitamin D supplementation is often prescribed for older adults with an intent to prevent falls, it has not been directly associated with decreasing fall risk (Cameron et al., 2018). Exercise in general has been shown to reduce the prevalence of falls, although evidence on specific exercise is lacking. Exercises that address balance, strength, and gait can prevent falls in community-dwelling older adults (Sherrington et al., 2019).

Referral: A home safety assessment is important for patients with falls and identified fall risks (both intrinsic and extrinsic). Based on individualized risk factors, an advanced practice registered nurse (APRN) should consider referrals to home health nursing, physical therapist (PT), occupational therapist (OT), a podiatrist, or subspecialty providers such as a cardiologist or a neurologist.

Education: Patients and their families need to be informed that many falls are preventable, but helping patients, families and caregivers understand their individual risks is important to supporting patient goals for mobility and independence. They need to be encouraged to report all falls, near falls, or fear of falling to their health-care providers so that assessment of risks, identification of appropriate interventions to decrease risk and referrals can be made.

Clinical Recommendation	Evidence Rating	References
Exercises that target balance, gait, and muscle strength can prevent falls in older persons living in the community.	A	Sherrington et al., 2019
Exercise may help reduce fear of falling in community-dwelling adults.	C	Kendrick et al., 2014
Exercise as a single intervention can prevent falls in community-dwelling older adults.	A	Sherrington et al., 2019
Vitamin D supplementation does not reduce risk of falls in older persons.	A	Cameron et al., 2018 Guirguis-Blake et al., 2018 USPSTF, 2018
Multiple component intervention programs do not decrease the rate or risk of falling	A	Bhasin et al., 2020 Hopewell et al., 2018 Guirguis-Blake et al., 2018 USPSTF, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

FATIGUE

Description: Fatigue is a subjective state often described as a feeling of tiredness, weariness, lack of energy, muscle weakness, slowed responses, or exhaustion that is unrelieved or only partially relieved by rest. Fatigue can be differentiated as physical and mental and can be a symptom of or lead to depression. It often results in an inability to initiate normal activity; a reduced capacity to maintain activity; and difficulty with concentration, memory, and emotional stability (Brazier, 2020; Wasserman, 2021). Wasserman (2021) defines three classifications of fatigue:

1. New onset of fatigue or recent fatigue: Fatigue lasting less than 1 month. Occasional fatigue is common, but pathological fatigue may affect quality of life and impair independence.

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2. Prolonged fatigue: Fatigue that lasts longer than 1 month, up to 6 months.
3. Chronic fatigue syndrome: Occurs when fatigue lasts longer than 6 months and is not relieved with rest. Fatigue could also be a symptom of another illness and any older person with this complaint should obtain a medical evaluation and work-up.

Etiology: Physiological fatigue occurs normally with inadequate rest, excess exertion, or insufficient diet. Fatigue that interrupts the individual's activities of daily living (ADLs) may have a physical or psychological cause and may be acute or chronic. Fatigue in older adults may be an early indicator of the aging process, nutritional deficiencies, anemia, fibromyalgia, obstructive sleep apnea, stress, bereavement, emotional exhaustion, as well as debility or another disorder (Kalathil & Akpan, 2020). Certain disease can also cause fatigue including kidney disease, thyroid disease, electrolyte imbalances, and heart failure (HF). See Table 7-4 for common causes of fatigue.

Occurrence: Fatigue occurs in about 21.9% of the U.S. population (Galland-Decker et al., 2019). Underreporting and under recognition make the actual prevalence unknown.

Age: Fatigue is common the general population of older adults, ranging in prevalence from 27% to 50%, but the significance is difficult to quantify due to under reporting and underdiagnosing (Kalathil & Akpan, 2020). Among older adults living in the community and assisted living facilities, more than 50% report mild fatigue and 7% report severe fatigue on a chronic basis. Fatigue is more common in women than in men (Galland-Decker et al., 2019; Kalathil & Akpan, 2020).

Ethnicity: The prevalence of fatigue is more common in Blacks (Kalathil & Akpan, 2020).

Contributing Factors: Poor dietary habits, overexertion, alcohol abuse, smoking, stress, chronic illness, drug interactions,

TABLE 7-4 Common Causes of Fatigue

Infectious causes	Viral infections
	• Hepatitis A, B, C • Epstein-Barr virus (mononucleosis) • HIV
	Bacterial infections
	• Tuberculosis • Lyme disease • Occult endocarditis • Osteomyelitis
	Immunological/rheumatic
	• Rheumatoid arthritis • Systemic lupus erythematous
	Celiac disease
	Fibromyalgia
Medication related	NSAIDs
	Tetracycline
	Antipsychotics
	Antidepressants
	Sleep medications
	Pain medications
	Marijuana/cannabis
	Anxiolytics
	Statin agents
	Illicit drugs
	Alcohol
Chronic fatigue syndrome	No known cause but theories to the cause include viral infections, immune system problems, and hormonal imbalances
Physiological	Inadequate sleep
	Insufficient rest
	Overactivity
	Poor physical conditioning
	Stress
	Changes in diet, including decreased protein intake
	Relocation of one's home or change in job/retirement
	Frailty
	Weight loss
	Sarcopenia
	Parkinson's disease
	Vitamin deficiencies including vitamins B_{12} and D
Endocrine related	Hypothyroidism including subclinical hypothyroidism
	Hyperthyroidism
	Perimenopausal/postmenopausal
	Hypogonadism (low testosterone levels)
Neoplastic-related disorders	Any form of cancer
	Chemotherapy treatments
	Radiation treatments
	Anemia related to cancer, as well as its treatment
Toxin-related disorders	Exposure as well as toxicity to:
	• Carbon monoxide, possibly caused by wood-burning stove, kerosene lamps, automobile exhaust, or coal-burning plants • Lead • Arsenic
Cardiovascular/pulmonary diseases	HF
	Chronic obstructive pulmonary disease
Psychogenic	Depression
	Anxiety
	Somatoform disorders
	Substance abuse (prescribed and nonprescription drugs, alcohol)

Sources: *Brazier, 2020; Galland-Decker et al., 2019.*

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misuse of drugs, and lack of sleep and/or sleep apnea may contribute to fatigue symptoms. In the older adult individual, it is compounded by a decrease in muscle strength, loss of muscle neurons, muscle atrophy, a decrease in hormone levels, increased sedentary lifestyles, and lack of exercise. Certain medications can contribute to fatigue symptoms including antidepressants, anxiolytics, statins, steroids, antihistamines, pain medications, and insomnia agents.

Signs and Symptoms: Obtain a complete medical history and perform a thorough physical examination when an individual complains of fatigue because it may indicate various psychological or physiological illnesses. Conduct a complete symptom assessment, including the onset; duration; severity; and precipitating, aggravating, and relieving factors. Identify other indicators or associated symptoms of fatigue, which may include decreased energy expenditure, decreased endurance, sleep disturbance, attention deficits, somatic complaints (aching body, tired eyes), dyspnea, and weakness. Carefully review the adequacy of the diet, all medications (evaluating for potential medication side effects), activity level (including degree of independence of activities of daily living (ADLs), and potential causes or contributing factors. Identify the impact fatigue is having on the person's ADLs and quality of life and current stressors. The quality and quantity of sleep should always be evaluated. Distinguish between generalized fatigue and actual weakness by testing for muscle strength, range of motion for arms, legs and the spine, and presence of localized tenderness. A thorough physical examination will include a mental status examination for depression and screening for dementia.

Diagnostic Tests: Screening tools are available for assessment of the complaint of fatigue, but there is no standardized assessment tool (Kalathil & Akpan, 2020). The benefits of diagnostic tests are limited when fatigue is the only symptom. Diagnostic tests on all patients with persistent unresolved fatigue should include complete metabolic panel (CMP), complete blood count (CBC) with differential, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), thyroid-stimulating hormone (TSH), and a vitamin D level. These tests are relatively low cost and offer significant screening capacity. Other tests that may be appropriate include urinalysis and pulmonary function tests (PFTs). If symptoms and signs indicate cardiac decompensation, a B-type natriuretic peptide (BNP) may indicate degree of HF, and an electrocardiogram (ECG) may reveal cardiac arrhythmias, enlargement of the heart, myocardial infarction (MI), or abnormalities in the conduction system. Late-life hypothyroidism or masked hyperthyroidism may present with a chief complaint of fatigue (Wasserman, 2021).

Differential Diagnosis: Fatigue can be related to many psychological and physiological etiologies. Depression was shown to be an independent predictor of fatigue in a study by Galland-Decker et al. (2019). Many psychiatric disorders affect sleep and may result in fatigue, including depression, generalized anxiety disorder, obsessive-compulsive disorder, and panic disorder (Holmes, 2021). An underlying cause of fatigue may not be definitively identified in many cases. Fatigue that cannot be relieved by rest or sleep is often a sign of disease, physical or psychological.

Treatment: Treatment depends on the etiology identified in the comprehensive work-up. Symptom management includes regular exercise, attention-restoring activities, psychosocial techniques, energy conservation measures, good sleep hygiene, eating a well-balanced diet, drinking an adequate amount of water intake, and possibly adding nutritional supplements. Pharmacological management is directed at identifying and treating the cause of the fatigue. Changing medications may be considered to diminish side effects of the medications. In extreme cases, clinicians may consider prescribing psychostimulants for opioid-related somnolence, cognitive impairment, and depression.

Follow-Up: Follow-up depends on the findings. Monitor the patient periodically as indicated by diagnosis or symptoms, symptom persistence, and disability associated with the symptom. The symptom may be a subclinical one.

The potential for complications relates to the cause of fatigue and the impact the symptom has on the person's function.

Prevention/Prophylaxis: Optimal health maintenance, including maintaining a healthy diet, adequate hydration, regular exercise, and good sleep hygiene, may prevent or enable early recognition of signs and symptoms of systemic or psychological illness.

Referral: Referral to a specialist may be indicated based on the results of the work-up.

Education: If the fatigue has a physiological cause, teaching should be related to the disease/disorder identified as the cause of the fatigue symptoms. Psychological counseling, changes in the environment, behavior modification, and stress reduction may be needed. The goal of fatigue management is to provide the patient with self-help tools to eliminate or alleviate fatigue.

Clinical Recommendation	Evidence Rating	References
A thorough history and physical examination are crucial in determining the differential diagnosis and identifying the causative agent.	C	Wasserman, 2021 Galland-Decker et al., 2019
A meta-analysis of fatigue and frailty in older adults defines frailty and discusses characteristics of fatigue, causes, frailty, and challenges to managing fatigue.	A	Kalathil & Akpan, 2020
Graded exercise has been shown to improve symptoms and physical function in patients with fatigue.	A	Galland-Decker et al., 2019
Cognitive-behavioral therapy is an effective treatment for adult outpatients with chronic fatigue syndrome.	A	Galland-Decker et al., 2019;

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HEADACHE

Description: Headache refers to a symptom that occurs in the head, neck, or face. Headaches decline with aging. Any new onset of headache in the older adult should be considered serious until proved otherwise.

Etiology: *The International Classification of Headache Disorders (ICHD), 3rd edition*, describes two categories of headache: primary and secondary (International Headache Society [IHS], 2018). Primary headaches include those in which there is an intrinsic dysfunction of the nervous system, often genetic in origin, (Robbins, 2021) which predisposes the older adult to increased vulnerability to headache attacks. Primary headaches include migraine, tension-type headache (TTH), cluster headache, and other trigeminal autonomic cephalgias. In contrast, secondary headaches are those in which the headache is secondary to an organic or physiological process, intracranially or extracranially. Medication overuse headache (MOH) is a unique headache diagnosis defined as headache occurring on 15 or more days per month developing as a consequence of regular overuse of acute or symptomatic headache medication (Berk et al., 2018). There are many possible reasons for secondary headaches. Some to consider are trauma to head or neck, nonvascular intracranial disorder such as neoplasms, substance abuse or withdrawal, infection including fever, disorders of the cranium or face, and psychiatric disorders.

Occurrence: Although the prevalence of headache decreases in the older adult, 75% to 90% of people have headaches at some point in their lives (Robbins, 2021; Taga et al., 2017). Headaches remain a problem for 35.6% of individuals aged 60 to 69 and 17.8% of individuals aged 70 to 79, with frequency decreasing after age 79 (Taga et al., 2017). Most headaches (approximately 50%) are primary, TTH, and migraine. TTH is the most common type of headache in individuals older than age 65 and in the general population, with a prevalence of 50.4% (Robbins, 2021) and 35.8% in the older adult (Berk et al., 2018). Of greater significance is that secondary headaches are more common in older adults older than 65 years, 15% of which are secondary headaches, which is significantly increased from an estimated 1.6% for adults younger than 65 years old (Phu Do et al., 2019).

Age: The prevalence of primary headaches decreases with age. The prevalence of migraine in patients older than 65 years is reported to be 5.7% to 15% (Berk et al., 2018; Burch et al., 2018). New-onset migraine in patients older than age 60 years is rare and is a red flag indicating evaluation for a secondary cause (Robbins, 2021; Starling, 2018). TTHs are generally listed as being more frequent in women (Berk et al., 2018; Feleppa et al., 2017; Taga et al., 2017) but at least one citation indicates that TTHs occur twice as often in men (Robbins, 2021). Migraine headaches, which tend to begin in early adulthood, are more common in women than in men, with 17% to 20% prevalence in women and 5% to 9% prevalence in men (Burch et al., 2018; Robbins, 2021). Cluster headaches are more common in men than in women, with a mean age of onset at age 30 years, although chronic cluster headaches may be more common in women (Berk et al., 2018; Manzoni et al., 2019). Giant cell arteritis is more commonly seen in women (Robblee & Singh, 2020; Starling, 2018).

Ethnicity: Giant cell arteritis is more common in White populations (Starling, 2018). There are some data to indicate a slight prevalence of migraine headaches in Native Americans and Alaskan Natives (Burch et al., 2018).

Contributing Factors: Depending on the type of headache, multiple factors can contribute. Poor posture, cervical osteoarthritis, ill-fitting dentures, tooth pain, and jaw disorders can contribute to tension headaches. Depression, anxiety, sleep disorders, and general pain syndromes can also contribute to most headache types. Medication side effects, particularly with estrogen, calcium channel blockers, nitrates, anti-Parkinson's drugs, indomethacin, and theophylline, can contribute to headaches. Alcohol can trigger or worsen headaches. Dehydration may be a factor. Migraines can be triggered by dietary factors such as aged or smoked cheese, chocolate, caffeine, and monosodium glutamate, as well as changes in sleep pattern, weather changes, and smoking. Genetics may play a role in migraine, cluster headache, and giant cell arteritis (Robbins, 2021; Starling, 2018).

Signs and Symptoms: Headache types, presentation, and treatment options change as patients age. Tension headaches are the most common and are due to mostly extracranial causes, such as muscle tension. Migraine in older adults may appear with sensory or motor phenomenon and may be confused with transient ischemic attack (TIA) or stroke (Burch et al., 2018; Lebedeva et al., 2020; Starling, 2018). The reported symptoms change with age bilaterally or globally with decreasing associated symptoms such as photophobia, phonophobia, nausea, and vomiting. The older adult may complain of increased neck pain, bilateral rhinorrhea, and lacrimation. Migraine in older adults is more often bilateral. In addition, older adults often have an aura without getting the headache; these symptoms need to be differentiated from a cerebrovascular accident (CVA) (Robblee & Singh, 2020). The older adult frequently has a better response to medication as compared with younger adults. Patients who report new-onset auras without a headache; that is, visual, sensory, and/or speech symptoms that may mimic those of migraine headaches, merit immediate referral for evaluation of secondary causes such as TIA, seizure, and intracranial hemorrhage (Berk et al., 2018; Starling, 2018). Two rare primary headaches occurring in older adults are hypnic (developing only during sleep, lasting several hours) and primary cough or Valsalva maneuver headache precipitated by cough or other Valsalva maneuver, lasting up to 2 hours (Berk et al., 2018).

The evaluation of an acute headache in adults is based largely on the history; the physical examination is often normal. Key responses in the history of present illness include the classic, "The worst headache in my life" or "thunderclap headache," which may suggest subarachnoid hemorrhage (SAH), a medical emergency. Ask if the headache is "typical." If the typical headache does not improve with usual treatment, consider a secondary diagnosis. The onset of the headache is very informative, a headache that has an unprovoked, sudden onset may be SAH or CVA. A headache with a sudden onset provoked by agitation, orgasm, cough, or sneeze is usually benign and transient. A subacute headache progressing over weeks may indicate an intracranial lesion, subdural

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hematoma, or hydrocephalus (Berk et al., 2018; Robbins, 2021; Starling, 2018). For the older adult with their first headache, always consider giant cell arteritis (Berk et al., 2018; Starling, 2018) Location, duration, frequency, severity, character, triggering or aggravating factors, and alleviating factors must be considered.

A focused review of systems is important. For example, fever may suggest meningitis, brain abscess, viral syndrome, or dehydration. Vomiting is less common in older adults with migraine; if present, a CVA or SAH should be considered. Visual complaints suggest a possible CVA, acute angle glaucoma, or giant cell arteritis. Other significant findings would be seizures, confusion or change in mental status, dizziness, weakness, neck pain, recent head trauma, recent travel, facial pain, tenderness, and eye pain. Ask if other contacts are ill. Past medical history should address the patient's immune status, recent change in medication, history of cancer, and hypertension. A family history of migraine or brain tumor may be significant. Alcohol consumption and smoking should be examined, as well as caffeine withdrawal. For recurrent/frequent headaches, having the patient keep a headache diary is helpful in identifying patterns and the impact the symptom has on function. Impact of the headaches on the patient's activities of daily living (ADLs) is an essential part of the history. An infection with COVID-19 may present with headache, and long COVID may also include headache.

The physical examination is often normal. Assess vital signs for extremes in blood pressure (suggestive of a neurological event) and temperature elevation, which suggests infection. Observe the patient's general appearance, including facies, and evaluation of mental status. Any sudden change in mental status or mood should be evaluated swiftly. A thorough neurological examination should include assessment of cranial nerves, gait, balance, and tactile sensation. Perform a fundoscopic examination to assess for papilledema, hemorrhages, exudates, and venous pulsations. Check for pupillary size and look at the cornea for haziness. Check extraocular movements and position of the eyelids.

Conduct an examination of the head and neck for lymphadenopathy, thyroid enlargement, carotid bruits, trigger points, meningeal irritation, or limitation in normal range of motion. Palpate the head and neck for tenderness, which may suggest TTH. Tenderness over the frontal and maxillary sinuses suggests sinusitis. Check for enlargement, tenderness, or pulsation of the temporal artery, tenderness suggests giant cell arteritis. Palpate the temporomandibular joint for alignment, mobility, and clicking. Examine the ears, nose, throat, and teeth for contributing problems. Evaluate the patient for postural alignment problems, muscle spasms, or trigger points in the back or shoulders.

Diagnostic Tests: Individualize diagnostic tests according to the suspected cause of the symptom. Neuroimaging sometimes is indicated for emergency evaluation of suspected vascular, neoplastic, or infectious disease. If red flags are present, in addition to a full neurological evaluation, neuroimaging should be considered. There are red flags that should be considered especially in the older adult. These are indicated through a mnemonic, SNOOP, originally proposed by Dodick in 2003, many versions of this are currently seen (Do et al., 2019, Walling, 2020). Dodick identified the following headache red flags: **S**ystemic symptoms including fever or weight loss, or **S**econdary risk factors such as HIV or malignancy; **N**eurological symptoms or abnormal signs such as confusion, impaired attention or consciousness; **O**nset that is sudden, abrupt, thunderclap, or positional; **O**lder age (over 50 years) at onset of a new onset or progressive headache; **P**revious headache pattern has changed in frequency, severity, or presentation. Generally, MRI is preferred to CT scan (Berk et al., 2018; Do et al., 2019). MRI is considered if the headache is of sudden onset, severe, worsening, unresponsive to treatment, and associated with neurological or constitutional symptoms. Laboratory tests generally are not helpful, unless anemia, infection, or electrolyte imbalance is suspected. However, erythrocyte sedimentation rate (ESR) or C-reactive protein (CRP) should be ordered if an inflammatory condition, such as giant cell arteritis, is under consideration. An elevated ESR warrants referral of the patient for temporal artery biopsy to confirm diagnosis. A lumbar puncture may be indicated after a negative CT scan without contrast if the patient has a "thunder-clap headache," suggesting an SAH, fever, or neck stiffness. Sinus or cervical spine x-rays may be indicated.

Differential Diagnosis: There are numerous differential diagnoses to be considered based on the history and examination. Urgent headaches as mentioned in the prior section should be delineated first. Primary headaches include TTHs, which are the most common, and may be triggered by lack of sleep, emotional or physical stress, medications, caffeine withdrawal, alcohol as delineated previously. The patient may complain of constant bilateral tightening pressure that does not worsen with ADLs. The neurological examination will be normal. Migraine headaches, as noted previously, with or without aura, are rarely new onset in the older adult. Medication-induced headache must be considered, especially with medication overuse for the treatment of either TTH or migraine headaches. Medication-induced headaches may also be the result of the misuse of barbiturate-analgesic-caffeine combinations, codeine, opioids, caffeine, acetaminophen, aspirin, and NSAIDs. These patients may present with daily or near-daily headaches. Other potential diagnoses include sinusitis and cervical spine disease.

The cluster headache is characterized by severe unilateral orbital, periorbital, or temporal pain. The attacks are relatively short (15 to 180 minutes) but can recur up to eight times in one day. Autonomic symptoms are also associated with the pain and present as ipsilateral ptosis, miosis, lacrimation, rhinorrhea, nasal congestion, and facial swelling. Cluster headaches tend to occur more often in men except in those older than age 60, when they are more common in women (Berk et al., 2018; Ljubisavljevic & Trajkovic, 2019).

Urgent diagnoses include SAH, giant cell arteritis, stroke/CVA, brain tumor, infection, and acute angle-closure glaucoma. The most common acute cerebral bleed is a subarachnoid hemorrhage, which has its highest incidence in women older than age 70 with a history including smoking, excessive alcohol ingestion, and hypertension. The patient with SAH often presents with a "thunderclap" or the "worst headache of my life," and the pain may be associated with other symptoms, such as confusion, vomiting, and seizures. This represents a medical emergency, and the patient needs to be evaluated in the emergency department with more extensive

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testing including a CT scan and consideration for possible surgery (Starling 2018).

Giant cell arteritis occurs predominantly in females older than 50 years who may also have a history of polymyalgia rheumatica. The patient may present with monocular vision loss, flu-like symptoms, and jaw claudication. On examination, unilateral blindness may be present with tenderness in the temporal area. Headache is the only presenting symptom in 1/3 of the patients with Giant cell arteritis. Optic nerve edema may be seen on funduscopic examination (Robblee & Singh, 2020).

Headache only occurs as a warning of an impending ischemic stroke in about 25% of all cases but occurs in 40% to 60% of all hemorrhagic strokes. Infectious diseases, such as encephalitis and meningitis, may also present with a headache but would include associated symptoms such as fever, altered mental status, and nuchal rigidity. When infectious disease is suspected as the cause of headache, the patient should be immediately transferred for further evaluation.

A patient with acute angle-closure glaucoma presents with acute unilateral eye and/or forehead pain, blurred vision, halos around lights, injected sclera, and nausea/vomiting. On examination, the pupil is mid-position, and the cornea appears hazy. There may be a decreased visual field, and the lack of any sign of exudate or discharge common in conjunctivitis is also significant. This presentation is considered a serious emergency, and the patient should be seen immediately by an ophthalmologist.

Treatment: Treatment of headache depends on the presumed etiology. Regardless, acute and preventive medications must be carefully scrutinized, considering the presence of comorbidities and the pathophysiological aspects of aging. The dearth of research studies including older adults limits best evidence. To avoid polypharmacy in older adults the most parsimonious option is preferred (Soni et al., 2020).

For migraine headaches, acetaminophen, NSAIDs, triptans, as well as combinations, have been established as effective for acute migraine treatment based on available evidence. Combining NSAIDs with triptans improves the efficacy. Vasoactive substances (triptans or dihydroergotamine) are contraindicated in patients with coronary arterial disease, peripheral vascular disease, or cerebral vascular disease (CVD), including a history of stroke. They should not be used in patients with uncontrolled hypertension or severe hepatic impairment, limiting their use in older adults. If the patient is at low cardiovascular risk, triptans could be considered for acute episodes. Side effects must be recognized to include cognitive and autonomic signs/symptoms. Recently, several new classes of medication for the treatment of migraines have been approved. One class of medications are the calcitonin gene-related peptide receptor (CGRP) antagonists, rimegepant (Nortek) and ubrogepant (Ubrelvy). Side effects are minimal and pain relief at 2 hours occurs more than 50% of the time. (Soni et al., 2020) Another class of medications target serotonin and 5HT1p receptors and inhibit trigeminal nerve firing. The first in this class is lasmiditan (Reyvow) (Soni et al., 2020). The mechanism of action of this class is not associated with vasoconstriction. Adjunct measures include antiemetics, hydration, and possibly magnesium. Various forms of the triptans are available in oral, injectable, and nasal forms.

Management of TTHs combines pharmacological and nonpharmacological measures. Analgesics and NSAIDs including cyclooxygenase-2 (COX-2) inhibitors are effective. All NSAIDs must be used with caution in older adults because of the risk of gastrointestinal (GI) ulceration and renal and hepatic impairment. Concomitant use of NSAIDs with aspirin or antiplatelet agents increases the risk of bleeding. Treatment should be limited to 2 days per week to avoid MOH, which is defined as headache on more than 15 days in a month (Walling, 2020). MOH respond to medication but then return when the medication wears off. Prophylactic therapy is advised for patients with MOH. Other considerations for TTH include tricyclic antidepressants (amitriptyline and nortriptyline), but they are listed on *Beers Criteria for Potentially Inappropriate Medication Use in Older Adults* (AGS, 2019) due to their anticholinergic side effects, which are a concern in older adults. Topiramate, Botox, and even corticosteroids have been used in the treatment of TTH (Walling, 2020). Behavioral intervention such as relaxation, cognitive behavioral therapy, biofeedback, and other lifestyle modifications may be helpful as adjunctive therapy.

The goal of therapy for cluster headaches is to abort the attacks after they have started. There is no evidence to support the use of NSAIDs. The uses of inhaled oxygen and subcutaneous sumatriptan 6 mg or sumatriptan nasal spray 20 mg are effective in improving headache response, as is zolmitriptan nasal spray 5 mg (Ljubisavljevic & Trajkovic, 2019). The calcium channel blocker verapamil (with an initial target dose of 240 mg per day), lithium up to 900 mg per day, and galcanezumab (Emgality, a CGRP inhibitor), 300 mg, injected monthly are preventive therapies (Robbins, 2021).

For giant cell arteritis, management requires larger doses of prednisone to prevent visual sequelae (40 to 60 mg and even 80 mg/day). The dose is maintained until remission is reached, which may take 2 to 4 weeks before tapering. The medication tocilizumab (Actemra), a disease-modifying antirheumatic drug, has also been indicated to be effective. (Robblee & Singh, 2020). Monitor blood sugar and other side effects of corticosteroids, such as changes in glucose tolerance, cognition, and mood.

Follow-Up: Monitoring depends on etiology and treatment strategies. After the diagnosis has been made and management strategies identified, patients should be monitored for effectiveness of treatment.

Sequelae: Sequelae depend on cause. Missed diagnosis of acute, life-threatening symptoms can prove fatal. Older adults are at higher risk for life-threatening headaches. Most common causes have recurrence or chronicity, which affects quality of life. Potential for side effects from medications and medication overuse must be considered.

Prevention/Prophylaxis: Preventive measures include avoidance of triggers, early intervention with medication as soon as symptoms present, and stress-reduction techniques as appropriate. Use of alcohol, tobacco, and caffeine in specific types of headaches should be monitored. For recurrent headaches, prophylactic therapy may be indicated. In addition to medication, patients should be advised to avoid triggers and to consider behavioral modification. Regular meals, sleep hygiene, hydration, and regular physical activity should be encouraged. All categories of drugs should be started at low doses and incrementally increased to therapeutic dosing.

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For older adults without predominant depression or aura, the most effective drugs are the same as those for younger adults. Medication is taken daily for a trial period (usually 1 to 2 months) to evaluate the effect on headache frequency and strength.

Anticonvulsants have been found to be among the most effective agents for prophylaxis of migraine headaches including valproic acid (250 to 500 mg in daily divided doses), topiramate (25 to 200 mg in divided doses), and gabapentin (begin with 300 mg increasing to a maximum of 3,600 mg/day). Anticonvulsants can increase fatigue, and baseline liver and kidney function studies should be obtained before initiation. Topiramate can cause kidney stones, so it is important that the patient increase fluids while taking the medication. Although beta blockers (propranolol, 80 mg orally daily; atenolol, 50 to 100 mg orally daily; or nadolol, 40 mg orally daily) have been used prophylactically for migraine and TTH, they are contraindicated in patients with a history of bronchospastic disease, asthma, diabetes, or heart failure (HF). Non-dihydropyridine calcium channel blockers (verapamil, 240 mg orally daily in divided doses, or nifedipine, 30 to 180 mg orally daily) have also been used prophylactically to prevent cluster headaches and are highly effective. Contraindications include HF, heart block, hypotension, sick sinus syndrome, and atrial fibrillation. There is moderate evidence that tricyclic antidepressants may also be effective for headache prophylaxis in low doses (amitriptyline, 25 to 50 mg orally daily, or desipramine, 50 mg orally daily). As noted above they are identified in Beers Criteria and may be contraindicated because of adverse effects on the cardiovascular system.

Referral: Refer patients to the emergency department (ED) for urgent conditions when headaches may be a result of hemorrhage, vasculitis, stroke, infectious disease, or acute angle-closure glaucoma. Any abnormal MRI or CT scan results should be referred to a neurologist. Headache red flag symptoms that indicate an urgent diagnosis, such as SAH, giant cell arteritis, stroke, brain tumor, infection, and acute angle-closure glaucoma, warrant immediate referral to the ED.

Education: Patient and family/caregiver education should be ongoing, specifically nonpharmacological management as well as pharmacological management. Evidence-based resources should be provided, as well as Web-based resources from organizations such as the American Headache Society and International Headache Society. Provide a headache journal (templates available from the American Headache Society and other sources) for the patient and instruct them on how to use it. If medications are prescribed, ensure that the patient understands proper use and safety considerations.

Clinical Recommendation	Evidence Rating	References
Relaxation, biofeedback, and cognitive therapy lead to significant reductions in headache activity.	C	Walling, 2020 Robblee & Singh, 2020
Venlofaxine, amitriptyline, ibuprofen, or naproxen are used for migraine prophylaxis.	B	Starling, 2018 Berk et al., 2018
Botox may be used for prevention of migraine.	A	Starling, 2018
Inderol, topiramate, timolol, valproate may be used for migraine prophylaxis.	A	Starling, 2018 Berk et al., 2018
Carbamazepine, pindolol, lisinopril, clonidine, CoQ10 may be used for migraine prophylaxis.	C	Berk et al., 2018
Oxygen can be used for cluster headaches.	A	Berk et al., 2018
Acetaminophen, ergots, NSAIDs, triptans are established as effective for acute migraine management. Medications must be individualized based on older adult patient's risk factors.	A	Robblee & Singh, 2020 Soni et al., 2020
Rimegepant for treatment of migraine	A	Soni et al., 2020
Red flags for secondary headaches include fever, focal or mental status changes, sudden or thunderclap headache.	B	Starling, 2018

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HEMATURIA

Description: Hematuria is the presence of red blood cells (RBCs) in the urine. It can be classified as either gross or microscopic. Gross hematuria is suspected when the urine appears either red or brown in color to the naked eye. Microscopic hematuria is identified by microscopic laboratory analysis. The American Urological Association (AUA) (Barocas et al., 2020) defines clinically significant microscopic hematuria as three or more RBCs per high-power field on a

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single, properly collected urine specimen. All patients with hematuria require evaluation because 2% to 5% of patients with microscopic hematuria are found to have a malignancy and 10% to 20% of patients with gross hematuria are found to have a malignancy. For patients with microhematuria, the AUA recommends that the clinician perform a history and physical examination to evaluate for risk factors for genitourinary, gynecological, and nonmalignant genitourinary causes as well as malignancy or medical renal disease.

Etiology: Hematuria may be renal or from contamination outside the urinary tract. Renal hematuria may result from glomerular or nonglomerular causes. The source of hematuria may be the upper collection system (e.g., renal, ureter) and/or lower collection system (e.g., bladder, prostrate, urethra). Microscopic hematuria is a common finding on routine urinalysis, and etiologies range from life threatening to benign incidental causes. The pathophysiology depends on the anatomical site from which blood loss occurred. In older adult patients the most common causes are malignancy or benign prostatic hyperplasia.

Occurrence: The prevalence of asymptomatic microscopic hematuria ranges from 2% to 31% in the adult population. In patients older than 50 years, the prevalence is estimated at 13%. There is a slightly higher incidence of hematuria in older women.

Age: Incidence of hematuria increases with age. Younger patients are less likely to have an etiology identified.

Ethnicity: Not significant.

Contributing Factors: Infection, anticoagulation therapy, renal calculi, trauma, anatomical defects such as rectocele, menstruation, atrophic vaginitis, renal disease, or recent urological procedures may all contribute to the presence of hematuria. Risk factors related to the development of a malignancy include age greater than 50 for women and age 40 for men; current or past history of smoking; degree and persistence of microhematuria; history of gross hematuria; occupational exposures to chemicals or dyes (e.g., painters, printers, chemical plant workers), irritative lower urinary tract symptoms; history of pelvic irradiation; any exposures to cytotoxic agents such as cyclophosphamide or ifosfamide; family history of urothelial cancer; or chronic indwelling foreign body, such as a catheter, in the urinary tract.

Signs and Symptoms: A thorough history is important in the assessment of hematuria. Ask all patients about the presence of visible blood in their urine, history of vigorous exercise, recent prostate examination or procedure, recent trauma to the abdomen, recent catheterization, menstruation, renal disease, viral illness, and medications (analgesics, antibiotics, anticoagulants, NSAIDs). Gross hematuria would be recognizable by the red or brownish color of the urine, but there may not be any signs or symptoms related to microscopic hematuria. Symptomatic hematuria with associated flank pain, fever, chills, nausea or vomiting, abdominal pain, or renal colic may represent kidney disease or a kidney stone. A patient may report urinary frequency, lower abdominal pain, or dysuria, which may indicate a urinary tract infection (UTI). Ask about symptoms of prostatic obstruction in males. A physical examination should focus on abdominal or flank pain, urogenital examination, prostate examination, testicular examination, and/or vaginal examination.

Diagnostic Tests: A urinalysis with microscopy should be obtained to confirm hematuria. Urine dipstick evaluation may be misleading because it lacks the ability to distinguish RBCs from myoglobin or hemoglobin. Always confirm a heme-positive dipstick with a microscopic urinalysis. Microscopic hematuria is defined as three or more RBCs per high-power field in a urine collection. The urinalysis should also include evaluation of dysmorphic red blood cells and proteinuria which can be suggestive of glomerular disease. Other analysis may include a comprehensive medical panel (CMP) to identify metabolic abnormalities. An elevated creatinine level may indicate acute or chronic renal disease. Clinicians should refer patients with microhematuria to nephrology for evaluation if medical renal disease is suspected due to an elevated creatinine level or low glomerular filtration rate. If the patient is on anticoagulation therapy, a prothrombin time, International Normalized Ratio, and CBC should be obtained. Note whether the patient is taking any other medications that would affect platelet function or decrease clotting abilities. Based on the initial evaluation, the clinician should classify the patient as low, moderate or high risk as noted on in AUA Guidelines (Barocas et al., 2020) (Table 7-5). Additional urological evaluation is dependent on the AUA risk stratification (Barocas et al.,2020). Adults aged 60 years and older, those with smoking history of more than 30 pack years, more than 25 RBCs per high-power field on a single urinalysis, and history of gross hematuria are classified as high risk for malignancy. Patients with microhematuria at low risk can participate in shared decision making to decide between repeating urinalysis within 6 months or proceeding with urological referral for cystoscopy and renal ultrasound. Evaluation for hematuria, urine cytology, and

TABLE 7-5 American Urological Association's Microhematuria Risk Stratification System

Low (patient meets all criteria)	Intermediate (patients meets any one of these criteria)	High (patients meets any one of these criteria)
Women aged <50 years, Men aged <40 years	Women aged 50–59 years; Men aged 40–59 years	Women or men age ≥60 years
Never smoker or <10 pack years	Smoking 10–30 pack years	Smoking >30 pack years
3–10 RBC/HPF on a single urinalysis	11–35 RBC/HPF on a single urinalysis	>25 RBC/HPF on a single urinalysis
No risk factors for urothelial cancer	Low-risk patient with no prior evaluation and 3–10 RBC/HPF on repeat urinalysis	Hx of gross hematuria
	Additional risk factors for urothelial cancer	

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urine markers for bladder cancer in this low-risk group are not recommended.

Differential Diagnosis: Infection or supratherapeutic anticoagulation should be ruled out as reversible causes of hematuria. More serious causes, such as glomerular disease, renal calculi, trauma, anatomical defects, or malignancy, must be ruled out. Additional benign conditions that can cause microhematuria include benign prostatic enlargement, urethral strictures, exposure to trauma, recent urological procedures, or catheterization.

Treatment: Treatment is directed at the cause. Treatment may not be required for low-risk patients. Appropriate antibiotic therapy for a UTI should resolve the hematuria. If the patient is on anticoagulation therapy, medication adjustment may resolve the problem. If a kidney stone is present, initial treatment may be pain management and oral hydration. The patient with urosepsis, acute kidney injury, anuria, unrelenting nausea, and vomiting should be referred immediately.

Follow-Up: In patients treated for a UTI, a repeat urinalysis with microscopic evaluation must be done following treatment. Referral to a urologist is dependent on patient risk factors (Barocas et al., 2020). When patients have completed the hematuria evaluation and are confirmed to be negative, a urinalysis may be repeated within 12 months for surveillance.

Sequelae: Hematuria may be a sign of a malignancy and should not be ignored, even if it occurs transiently. Hematuria may indicate renal disease, especially when proteinuria is present and, if needed, referral to a nephrologist for a second opinion. A diagnosis of a kidney stone does not rule out the coexistence of a malignancy.

Prevention/Prophylaxis: The U.S. Preventive Services Task Force does not endorse routine screening for asymptomatic hematuria due to lack of evidence. *"No major health organization recommends screening healthy, asymptomatic patients with urinalysis for the purpose of cancer detection."*

Referral: Primary care providers can initiate testing to verify the presence of hematuria and treat if diagnosis is clear. Referral to a nephrologist is indicated if medical renal disease is suspected as evidenced by presence of proteinuria, RBC casts, dysmorphic RBCs, and/or elevated serum creatinine levels. 5% to 40% of patients referred for evaluation of hematuria or specialty care have a urological malignancy.

Education: Counsel patients and family members to seek medical advice about signs and symptoms they should report including gross hematuria, urinary frequency, dysuria, flank pain, and abdominal pain. Educate patients and families about side effects of over-the-counter (OTC) medications and prescribed medications. Educate the patient about the effects of anticoagulation therapy and to call immediately if the patient notices any hematuria which may mean drug levels are too high. Educate the patient about risk factors and recommend tobacco cessation as appropriate.

Clinical Recommendation	Evidence Rating	References
Clinicians should define microhematuria as ≥3 red blood cells per high-power field on microscopic evaluation of a single, properly collected urine specimen.	C	Barocas et al., 2020
In patients with hematuria attributed to a urinary tract infection, clinicians should obtain a urinalysis with microscopic evaluation following treatment to ensure resolution of the hematuria.	C	Barocas et al., 2020
Following initial evaluation, clinicians should categorize patients presenting with microhematuria as low-, intermediate- or high-risk for genitourinary malignancy based on the identified risk factors.	C	Barocas et al., 2020
In low-risk patients with microhematuria, clinicians should engage patients in shared decision making to decide between repeating urinalysis within 6 months or proceeding with cystoscopy and renal ultrasound.	C	Barocas et al., 2020
Clinicians should perform cystoscopy and renal ultrasound in patients with microhematuria categorized as intermediate risk for malignancy.	C	Barocas et al., 2020
Clinicians should not define microhematuria by positive dipstick testing alone. A positive urine dipstick test (trace blood or greater) should prompt formal microscopic evaluation of the urine.	C	Barocas et al., 2020
Clinicians should perform cystoscopy and axial upper tract imaging in patients with microhematuria categorized as high-risk for malignancy.	C	Barocas et al., 2020
For patients with a prior negative hematuria evaluation who develop gross hematuria, significant increase in degree of microhematuria, or new urological symptoms, clinicians should initiate further evaluation.	C	Barocas et al., 2020

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HEMOPTYSIS

Description: Hemoptysis is coughing or spitting blood from the respiratory tract. This can range from blood-streaked sputum to frank bleeding. Massive hemoptysis, which is life threatening, is no longer defined quantitatively. Instead, more important is the briskness of bleeding, ability of a patient to maintain a patent airway and expectorate blood, availability of therapeutic options, and the patient's comorbidities (Davidson & Sojahaee, 2020). These more significant variables underscore the concept of the magnitude of effect definition for massive hemoptysis.

Etiology: Hemoptysis refers specifically to bleeding from the lower respiratory tract, but sometimes bleeding from the upper respiratory tract or the upper gastrointestinal (GI) tract may mimic hemoptysis (pseudohemoptysis). There are multiple potential causes for hemoptysis including, but not limited to, airway disease and trauma, pulmonary infections or inflammation, bronchiectasis, lung neoplasms, cardiac disease, cocaine use, pulmonary embolism (PE), and medication use (anticoagulants, antithrombotics, NSAIDs). Massive hemoptysis is uncommon, and causes include tuberculosis (TB), bronchiectasis, mycetoma, and cancer (Davidson & Sojahaee, 2020).

The lungs receive blood from the pulmonary and bronchial arterial systems. Bleeding involving the low-pressure pulmonary system produces small-volume hemoptysis, whereas the high-pressure bronchial system produces more profuse bleeding. Infection causes mucosal inflammation that can lead to blood vessel rupture. Neoplasms can cause mucosal invasion, eroding into the blood vessels. In the primary care setting the most common causes of hemoptysis are acute and chronic bronchitis, pneumonia, TB, and lung cancer.

Occurrence: The most common cause of hemoptysis is airway disease. There is a strong seasonal trend with peak incidence in the spring and decreased incidence in late summer. The most common causes of life-threatening hemoptysis include bronchiectasis from infectious and noninfectious etiologies, bronchogenic carcinoma, and lung infections including TB (Kathuria et al., 2020).

Age: Hemoptysis may occur at any age, although the age range can vary based on etiology of the hemoptysis. The mean age of occurrence is 62 years.

Ethnicity: No direct ties to ethnicity have been documented, but immigrants and persons living in poverty are at higher risk for TB and other pulmonary infections.

Contributing Factors: Smoking history (active or passive exposure), alcohol use, cocaine use, any history of trauma, environmental exposures, hypertension, comorbidities including diabetes or immunocompromised status. Medications such as aspirin, NSAIDs, or anticoagulants can either be causative or contributing factors. Risk factors associated with an increased risk of lung malignancy include male sex, older than 40 years, greater than 40-pack-per-year smoking history, and duration of hemoptysis longer than 1 week.

Signs and Symptoms: The quantity, characteristics, and duration of the hemoptysis should be established first when assessing the patient. It is important to know if it has increased in severity, if the cough is worse at night, and if there are any other associated symptoms. The amount of hemoptysis is potentially overestimated or underestimated by patients and practitioners, but it is important to at least attempt to determine the volume and rate of blood loss. Hemoptysis of more than 100 mL in less than 24 hours is potentially life threatening and requires immediate assessment in an emergency department. Any sudden onset of hemoptysis with or without associated symptoms can be caused by a PE and needs emergency assessment. A comprehensive history, including the patient's known risk factors and work and home environment, is helpful in narrowing the cause of the hemoptysis. Establish if there are any signs and symptoms of infection (fever, cough, sputum production), malignancy (cachexia, weight loss, smoking history), trauma or foreign body aspiration, or any history of immune deficiency. A thorough medication review should also be completed.

Assess any risk factors such as smoking, cocaine use, long-term alcohol abuse, stroke, older age, immigrant status, immunocompromise, and heart disease when trying to identify the cause of bleeding. Use of tobacco with long-standing or increasingly severe hoarseness may indicate cancer of the mouth or throat. A history of persistent "heartburn" may be a clue to possible esophageal erosion as the source of bleeding. Chronic cough, dyspnea, and/or sputum production may suggest pulmonary disease.

Vital signs should include oxygen saturation. Tachypnea, tachycardia, use of accessory muscles, cyanosis, fatigue, or altered mentation are signs of respiratory distress and should be treated as a medical emergency regardless of the amount of hemoptysis described or observed. The physical examination should begin with a thorough examination of the nose and oropharyngeal mucosa. The neck, supraclavicular area, and axillae should be palpated for any enlarged lymph nodes, a possible sign of infection, lymphoma, or other malignancies. Auscultation of the lungs may reveal a focal abnormality consistent with pneumonia (crackles, rhonchi, wheezing); egophony is suggestive of consolidation and is often present in pneumonia. Heart sounds should be auscultated specifically for a murmur because mitral regurgitation or mitral stenosis can be associated with pulmonary edema or decompensated HF, especially in the setting of clinically apparent volume overload; this sputum is classically described as pink and frothy rather than frank bleeding. An abdomen distended with ascites may be accompanied by esophageal varices.

Diagnostic Tests: The initial test of choice is the chest x-ray or chest computed tomography (CT) scan (Davidson & Sojahaee, 2020). Diagnostic work-up may also include these laboratory tests: complete blood count (CBC) with differential, prothrombin time/partial thromboplastin time/International Normalized Ratio, comprehensive medical panel (CMP), arterial blood gas, sputum culture and smear, TB skin testing or quantiferon gold panel, d-dimer, and ESR. If initial imaging suggests the need for further testing, a CT angiogram or bronchoscopy may be the next step. If no cause of hemoptysis can be isolated and the radiographic

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studies are normal, a flexible bronchoscopy for airway examination is still useful to rule out an endobronchial source of bleeding.

Differential Diagnosis: Determine first whether the blood is coming from the respiratory tract (hemoptysis) or from the GI tract (hematemesis). Patients with hematemesis typically have nausea and vomiting and a history of gastric or liver disease, and the sputum more likely will be coffee ground in texture and a brown-black color. In hemoptysis, however, the sputum is bright red or pink and a frothy liquid or clotted, and the patient may have a history of lung disease. If the source of bleeding is determined to be the lung, possibilities include infection, inflammation, malignancy, trauma, autoimmune disease, cardiovascular disease, and coagulation disorders.

Treatment: The goals of management include bleeding cessation, aspiration prevention, and treatment of the underlying cause. If the source of the bleeding has been reasonably isolated to the respiratory system, the condition is not life threatening, and if an infectious or inflammatory etiology is diagnosed, the following diagnoses might be considered:

Acute Bronchitis. Acute bronchitis is predominantly viral, and antibiotics do not shorten the course of the disease. If the patient smokes, they should be counseled to quit or to cut back significantly. Bronchodilators help open the airways; expectorants such as guaifenesin used to mobilize secretions are about as effective as drinking two additional glasses of water per day. Cough suppressants should be avoided except to help the patient sleep. A cool mist humidifier in the bedroom is useful for loosening secretions.

Chronic Bronchitis. Chronic bronchitis needs a combination bronchodilator as an inhaler or as a nebulizer. Because chronic bronchitis is usually a result of smoking, the patient should be counseled to stop. A short course of prednisone is often helpful to treat an acute exacerbation of chronic bronchitis. Antibiotics should be reserved for acute exacerbations heralded by increasing shortness of breath, change in color of the sputum to dark yellow or green, or fever.

Bronchiectasis. Permanent enlargement of some of the airways in the lungs caused by chronic infections, trauma, or immune system problems can cause intermittent hemoptysis. The hemoptysis usually results from dilation of bronchial arteries. Because this is a chronic illness, antibiotic selection is generally based on previous sputum culture/susceptibility results.

Bacterial Pneumonia. Community-acquired pneumonia is most often caused by *Streptococcus pneumoniae. Hemophilus influenza, Chlamydia pneumoniae, Mycoplasma pneumoniae*, and *Legionella pneumophila* are other major bacteria that cause pneumonia in the otherwise healthy individual. If pneumonia is suspected, a chest x-ray should be obtained, and broad-spectrum antibiotics should be initiated empirically. Immunocompromised patients, patients with any respiratory distress, and older adult patients with significantly elevated or decreased white blood cell (WBC) counts may need to be hospitalized.

Fungal Infection. A fungal infection should be suspected if the pneumonia does not respond to conventional antibiotic therapy. The provider should attempt to collect a sputum specimen for analysis and culture. Appropriate antifungal therapy may be initiated, and the patient should be referred to a pulmonologist and/or infectious disease specialist.

TB. If TB is suspected based on history, signs/symptoms, and chest imaging, the diagnostic work-up should focus both on detecting the bacteria in sputum (acid-fast bacteria culture and smear) and on protecting other individuals from contracting the infection. This may include admission to a negative pressure hospital room with airborne isolation for the diagnostic work-up. Treatment with an antituberculosis regimen can be started by the hospital or outpatient clinic; however, these patients need to be referred to the health department who will often manage treatment through directly observed administration of the antituberculosis regimen.

Follow-Up: Follow-up depends on the severity of the illness. For pneumonia or bronchitis with minimal dyspnea, a call to check on the patient is appropriate. Worsening temperature, bleeding, or difficulty breathing requires immediate attention or emergency department evaluation. Patients with resolving pneumonia should be evaluated in 2 to 3 weeks, radiographic resolution may take 6 to 8 weeks, especially in older adult patients or those with underlying lung disease. Mild hemoptysis recurring sporadically over a few years is common in smokers who have chronic bronchitis punctuated with superimposed acute bronchitis.

Sequelae: Death can occur if the etiology is not identified quickly and treated, particularly if it causes cardiovascular collapse or acute respiratory insufficiency. The mortality rate depends on the etiology, and in patients with a malignancy and massive hemoptysis (more than 1,000 mL per 24 hours) the rate is 80%. Chronic lung disease may also result.

Prevention/Prophylaxis: Counseling patients and their families about the benefits of smoking cessation and decreasing alcohol intake are worthwhile. Discussions to promote a healthy lifestyle are important, stressing activity and weight loss.

Referral: Massive hemoptysis requires treatment in the intensive care unit including pulmonary and cardiovascular/cardiothoracic surgery consultation. In cases of non-massive hemoptysis when bleeding persists or increases, the patient should be referred to a pulmonologist for bronchoscopy or to an otolaryngologist for direct laryngoscopy. If diagnostic imaging such as chest CT suggests malignancy, the next step would include a biopsy, requiring referral to a pulmonologist or cardiothoracic surgeon. In the setting of known or prior malignancy, referral to an oncologist, if not already established, is an important consideration.

Education: Discuss risk factors associated with PE, such as immobility or hormone replacement therapies. Provide patient education related to smoking cessation and cessation of street drugs and/or alcohol abuse. Patients with chronic obstructive pulmonary disease (COPD) or bronchiectasis should be aware of their own clinical signs/symptoms of worsening or acute exacerbation and have an action plan should any of these symptoms occur.

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Clinical Recommendation	Evidence Rating	References
Moderate hemoptysis has shown similar prognosis of recurrent hemoptysis, and mortality to massive hemoptysis; therefore, the more aggressive flexible bronchoscopy and bronchial artery embolization should be considered in moderate hemoptysis.	A	Quigley et al., 2020
The initial test of choice is a chest x-ray. Contrast-enhanced CT with angiography adds additional information and is the method of choice.	A	Ittrich et al., 2017
Patients with a mass on CT and those at risk for cancer should have a flexible bronchoscopy.	A	Davidson & Shojaee, 2020
Massive hemoptysis is a respiratory emergency. CT angiography (CTA) can play a crucial role in assessing the cause and origin of hemoptysis and directing the interventional radiologist before treatment.	A	Ittrich et al., 2017
Lung cancer and bronchiectasis are most common causes of hemoptosis.	A	Quigley et al., 2020

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INVOLUNTARY WEIGHT LOSS

Description: Weight loss is common among older adults and is associated with poor health outcomes and functional decline. Involuntary or unintentional weight loss is a condition in which the patient does not purposefully set out to lose weight for any reason (Kim et al., 2018). It may be a presenting concern of the patient, reported by the family, or first noted by the provider. There is a well-established association between weight loss and mortality in older adults (Cox et al., 2019). The Centers for Medicare and Medicaid Services (CMS) defines involuntary weight loss (IWL) that must be clinically investigated as 5% in 1 month, 7.5% in 3 months, or 10% in 6 months.

Etiology: The causes of IWL are not always clear. With aging there is a decline in bone mass and a decrease in muscle mass, which is responsible for a small decline in weight after the seventh decade of life (0.2 to 0.4 pounds per year). Another age-related phenomenon is a reduction in appetite called anorexia of aging (Cox et al., 2019). Sarcopenia is a geriatric syndrome that includes decrease in muscle mass and strength and decline in physical performance related to aging. The resulting increased ratio of fat to muscle may contribute to further weight loss because of the relationship of adipose tissue to inflammatory cytokines, which have been linked to cachexia and weight loss, including tumor necrosis factor-α (TNF-α), interleukin-1β, and interleukin-6. Cachexia is a metabolic disease characterized by the loss of muscle mass with or without the loss of fat. It may be difficult to distinguish cachexia from sarcopenia, and the two may coexist. Causes of weight loss may be the result of physiological factors, psychological factors, social factors, or a combination of these (see Table 7-6). While often the primary concern is an undiagnosed malignancy, nonmalignant causes are the most common. Many medications can interfere with appetite and result in weight loss, but often medications are added as treatment rather than removed.

Occurrence: Involuntary or unintentional weight loss occurs in 15% to 20% of older adults (Kim et al., 2018). Using the CMS criteria, the yearly incidence of weight loss is about 7% in the community. From 30% to 50% of long-term care residents have below-average body weight, but CMS nursing home data using their criteria reported a 6% incidence when patients with end-stage disease or on hospice were excluded (CMS, 2021).

Age: Old age is a risk factor for IWL because of the normal physiological changes with aging combined with a higher prevalence of physiological, psychological, and social factors associated with involuntary weight loss.

Ethnicity: Not significant.

Contributing Factors: When considering all causes of IWL, nonmalignant causes are most common, but in up to 38% the cause is a malignancy. Nonmalignant gastrointestinal (GI) disease is next, followed by psychiatric, endocrine, and cardiopulmonary conditions; alcoholism; dementia; medications; loss of taste and smell; decreased functional status; chronic infection; dentition; and smoking. Social factors such as isolation, abuse or neglect, location of residence (food deserts, safety concerns), lack of transportation, and financial issues have an influence on adequate nutrition with resulting weight loss as well. Many medications contribute to factors related to weight loss and a careful review should be initiated (see Table 7-7). Because weight loss can cause skeletal muscle loss there is an increased risk for falls, functional impairment, protein calorie malnutrition, immune system compromise, anemia, and decreased cognition, all of which increase morbidity and mortality.

Signs and Symptoms: Weight loss may be reported by the patient, their family, or noted by the provider. If clinical documentation is not available, a classic guideline introduced by Martson et al. (1981) suggests that a change in clothing size, confirmation of history by a family member, or ability of the patient to report exact weight change can be substituted. A thorough history and complete physical examination are required to identify any treatable underlying cause of the weight loss. History should include a review of cardiac,

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TABLE 7-6 Causes of Unintentional Weight Loss

PHYSIOLOGICAL FACTORS	
Disease	
Malignancy	Lung, GI, pancreatic, hematological, prostate
Acute illness	Influenza, pneumonia, *Clostridioides difficile*
GI disease	Malabsorption, autoimmune, oral health
Endocrine	Diabetes, hyperthyroidism
Cardiovascular	HF
Respiratory	COPD, interstitial lung disease
Infectious disease	HIV, TB
Neurological disease	Dementia, stroke, Parkinson's disease
Rheumatological disease	RA, sarcoidosis, inflammation
Renal disease	Uremic cachexia
Previous surgery	Malabsorption, pain
Chronic pain	
Medications	
See Table 7-7	
Functional Issues	
Decline in ADLs and IADLs	Feeding, purchasing, and preparing food
Dysphagia	Food avoidance, dietary restrictions
Sarcopenia	Muscle weakness, decreased mobility
Falls	Fracture, fear of falling
Psychological Factors	
Depression	
Anxiety	
Grief	
Substance abuse and dependence	Alcoholism, tobacco, cocaine
Social Factors	
Social isolation	
Limited income	
Abuse or neglect	
Environment	Food desert, transportation, safety

TABLE 7-7 Medications That May Cause Weight Loss

MEDICATION	EXAMPLES
Neurological Psychiatric	Antidepressants, lithium, anticonvulsants, stimulants, levodopa, dopamine agonists, selegiline, phenothiazines, haloperidol, benzodiazepines, cholinesterase inhibitors, NMDA receptor antagonists
Cardiovascular	Digoxin, ACE inhibitors, CCB, β blockers, α agonists, hydralazine, statins, diuretics, amiodarone, procainamide, spironolactone
GI	Cimetidine, interferon, diphenoxylate-atropine, proton pump inhibitors, laxatives
Anti-infective	Metronidazole, griseofulvin, most antibiotics, amantadine
Nutritional	Calcium carbonate, iron, potassium, bile acid sequestrants
Musculoskeletal (including pain)	NSAIDs, bisphosphonates, colchicine, penicillamine, aspirin, opiates, allopurinol, colchicine, gold, hydroxychloroquine, methotrexate
Pulmonary	Theophylline, pseudoephedrine, antihistamines
Endocrine	Levothyroxine, Armour thyroid, metformin
Other	Anticholinergics

respiratory, GI, genitourinary, endocrine, hematological, or infectious disease symptoms. An assessment of depression, anxiety, cognitive impairment, substance abuse, and functional decline begin with the history. There should be a focus on oral concerns such as poor dentition, new dentures, mouth lesions, dry mouth, dysphagia, or loss of taste. A review of medications both prescribed and over-the-counter (OTC), including supplements, is necessary.

A functional cause of weight loss may be primary or secondary to a physiological or psychological etiology. Determine whether the patient has functional limitations that affect the ability to prepare and eat an appropriate diet and if adequate help is consistently available to assist with activities of daily living (ADLs) if necessary. The Mini-Nutritional Assessment (MNA) is supported by evidence as useful in measuring nutritional risk. The tool is accessible at www.mna-elderly.com where you can download the forms and the user guides at no charge. There is a training video and the possibility of integrating it into the electronic medical record. There are three versions of the MNA: Self MNA, the MNA for clinical use, and the original full MNA. They all include anthropometric measurements and general, dietary, and functional assessments.

Physical examination should include the cardiovascular, respiratory, GI, genitourinary, dermatological, and musculoskeletal systems. A comprehensive neurological examination and a mental status examination that includes assessment of mood, cognitive ability, and substance use are essential components. Patients with significant weight loss appear pale and cachectic, with signs of malnutrition such as hair loss, muscle wasting, and loss of subcutaneous fat. Look for evidence of loose skin, petechiae, cyanosis, clubbing of the fingers, and edema. There may be temporal wasting, icterus, dry mucous membranes, and flattened papillae of the tongue. The oral examination should note denture fit; tooth and gum disease; and oral lesions such as ulcers, stomatitis, and candidiasis. Examination of the cardiorespiratory system may reveal loud or palpable murmurs and diminished breath sounds. The liver or spleen may be palpable. Check for masses in the abdomen, breasts, and rectum. Muscle wasting may be apparent on the extremities, and deep tendon reflexes may have a prolonged

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relaxation phase. Patients may have diminished position and vibratory sense. Check women for ovarian masses, cervical lesions, and any obvious neoplasia. In men, examine the prostate gland for enlargement.

Diagnostic Tests: History and physical examination findings guide the choice of diagnostic tests. It has been shown that 70% of the diagnosis can be made with history alone and the physical examination increases this rate to 90%. Emphasis is placed on evidence-based practice and testing that supports findings from the history and physical examination.

Additional diagnostic tests serve to confirm the assumptions. A nutritional or diet history and calorie counts add objective data to evaluate the amount and quality of food intake. After the results of the diagnostic work-up are available, consider a neoplastic origin when benign causes of weight loss appear unlikely. Malignant and nonmalignant GI disorders are the most prevalent cause of involuntary weight loss. Evidence of microcytic anemia on the complete blood count (CBC) or a positive fecal occult blood result is a reason to refer for colonoscopy. With frail older adults it is important to address the question of treatment options with the patient and family before further invasive and expensive work-up is initiated. If the cause of weight loss is not clear from the diagnostic evaluation, watchful waiting is recommended; watch for further weight loss or specific symptoms and reconsider a functional cause of weight loss. If no abnormalities are detected from the history, physical examination, and diagnostic tests, an organic cause is unlikely (less than 5%). When the findings from the initial work-up are negative, psychological problems, particularly depression and anxiety, are among the most common reasons for weight loss.

Differential Diagnosis: For weight loss that occurs with increased food intake, consider diabetes, thyrotoxicosis, malabsorption, leukemia, lymphoma, and adrenal insufficiency. For weight loss that occurs with normal or decreased food intake, consider alcoholism; malignancy; infection; GI, hepatic, renal, dental, endocrine, respiratory, cardiac, or psychological causes; anorexia nervosa; malnutrition; or a functional origin. After investigation, the cause of weight loss remains unknown in 16% to 28% of patients. Table 7-8 lists causes of weight loss in the older adult.

Treatment: Treat or manage the identified underlying cause. This will likely involve the inclusion of other disciplines. Regardless of the cause, a referral to a nutritionist should be a priority. Medicare offers specific nutritional benefits to patients with diabetes or chronic kidney disease. Dentistry to assess oral health, speech to evaluate swallowing, occupational therapy (OT) or physical therapy (PT), and social work are all key to addressing the problem of IWL. Nonpharmacological options should be initiated first. Diet modifications should minimize dietary restrictions, address patient preferences, and accommodate problems of dentition or swallowing. Smaller, more frequent meals can be useful if the patient reports early satiety. Patients with dementia tend to consume most of their daily energy at breakfast, so high-energy foods should be served at this meal, and varying dietary texture can be helpful. Eating with assistance and in the company of others increases calorie intake. For older adults in the community, home delivered meal programs are beneficial. Oral nutritional supplements, such as high-energy and high-protein drinks, if initiated, should be consumed between meals. Evidence supports that their short-term use improves weight and diagnostic parameters, but data in support of their long-term use is lacking. Regular exercise, especially resistance training, stimulates appetite and can prevent increasing sarcopenia. Use of a multivitamin supplement should not be a first-line intervention; nutrient-dense foods and improving intake are preferable. Oral supplements are rich in micronutrients and when added to the treatment plan are superior to a multivitamin. Multivitamins are preferred over individual vitamin supplements.

It is common in clinical practice for clinicians to order mirtazapine and other pharmacological agents to stimulate appetite; however, evidence underlying their use is limited, particularly in older adults, and none has gained approval from the U.S. Food and Drug Administration (FDA). Megestrol acetate has evidence for use in cancer or HIV, but studies in older adults have had equivocal results. The risk of deep vein thrombosis (DVT) and pulmonary embolus is alarming and increasing in patients who are sedentary. Dronabinol is a synthetic form of tetrahydrocannabinol (THC), a naturally occurring component of cannabis sativa (marijuana), which is FDA approved for chemotherapy-induced nausea and vomiting, and anorexia from AIDS or cancer. Only one study has been conducted in older adults, patients with dementia who were refusing food. The central nervous system (CNS) side effects are a major risk in a population who has a more vulnerable CNS.

TABLE 7-8 Meals-on-Wheels Mnemonic for Causes of Weight Loss in the Older Adult

MNEMONIC	CAUSES OF WEIGHT LOSS
M	Medications
E	Emotional problems (depression, anxiety)
A	Alcoholism, anorexia tardive, abuse
L	Late life paranoia
S	Swallowing disorders (dysphagia)
O	Oral problems
N	Nosocomial infections
	No money (poverty)
W	Wandering and other dementia-related behaviors
H	Hyperthyroidism, hypercalcemia, hypoadrenalism
E	Enteric problems (malabsorption)
E	Eating problems (inability to feed oneself)
L	Low-salt, low-cholesterol diet
S	Social problems
	Shopping and meal preparation
	Stones (cholecystitis)

Source: *Morley & Silver, 1995.*

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Follow-Up: If results of the standard tests listed earlier are negative, and the history and physical examination are negative, the recommended approach is to watch for further weight loss and to reconsider functional causes. Have the patient or caregiver keep a daily record of food intake, activity levels, and symptoms, and schedule a return visit in 2 to 4 weeks. Supplements may be added with the emphasis that they should be used between meals.

Sequelae: Malnutrition (Sanchez-Rodriguez et al., 2017) is the first complication to consider in IWL. Long-term unexplained weight loss may indicate failure to thrive and the beginning of a downward spiral in health and function. Many patients in acute and long-term care have unrecognized protein-calorie malnutrition. Protein-calorie malnutrition is a common iatrogenic complication of hospitalization.

Prevention/Prophylaxis: Discuss proper nutrition and the need for dental care, if appropriate. Address functional, financial, and social issues that may affect nutrition (e.g., address depression; arrange for socialization at mealtime, if feasible; arrange home delivered meals).

Referral: IWL often has multiple factors and may require the assessment of multiple specialties to derive a diagnosis and plan for treatment. Include the patient and their family in discussions about goals of care. Referral for palliative care may be appropriate. Adult failure to thrive can no longer be used as the primary diagnosis for hospice admission; however, consultation with hospice teams can help in determining the primary diagnosis. Always consult a specialist for rapid or acute decline; for positive diagnostic test results indicating malignancy, thyrotoxicosis, or other acute organic illnesses requiring sophisticated diagnostic work-up or management; or for a patient condition beyond your current scope of practice. Refer patients for assistance if social or functional issues may be contributing to weight loss. Refer to an appropriate specialist as noted previously.

Education: Instruct patients about proper nutrition and hydration. Encourage exercise to improve strength or function and to stimulate appetite. Teach patients about medication side effects that may affect nutrition and about signs or symptoms of overmedication or undermedication.

Clinical Recommendation	Evidence Rating	References
There is a relationship between depressive symptoms and weight loss. Patients with weight loss should be screened for depression.	A	Ji et al., 2020
Oral nutritional supplementation is associated with weight gain and reduced mortality, and should be given between meals.	A	Morley, 2018
Loss of weight in obese older adults is associated with greater morbidity than in non-obese older adults	A	De Stefani et al., 2018
If clinically documented weight loss is not available, a change in clothing size, confirmation of history by a family member, or ability of the patient to report exact weight change can be substituted.	B	Martson et al., 1981 (classic study)
Optimize caloric intake, minimize dietary restrictions, eat in the company of others.	B	Gaddey & Holder, 2021 Morley, 2018
No medications have been shown to reduce mortality. Few studies have been done to determine effectiveness in older adults with involuntary weight loss, and all have considerable side effects.	B	Gaddey & Holder, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

JOINT PAIN

Description: Joint pain can be inflammation, irritation, pain, or discomfort from any joint and/or the surrounding structures including bone, muscle, cartilage, bursa, tendons, or ligaments. Joint pain is commonly referred to as arthralgia or arthritis, which is more specifically pain or inflammation within the joint.

Etiology: Joint pain can be the result of many different causes including injury, infection, inflammation, degenerative, autoimmune, cancer, or genetic. It can be an acute, chronic, or a recurring problem. The description, location, onset, and associated symptoms are important to diagnosing the cause of joint pain. Clarifying the etiology of the pain depends on the clinical presentation, history of illness, findings from physical examination, and appropriate diagnostic testing. Joint pain can be mild (e.g., sprain or strain), chronic (lasting more than 3 months), inflammatory (e.g., joint effusion, inflammatory arthritis), or severe and/or acute (e.g., trauma or infection). Acute joint pain may become a chronic pain if exacerbating factors are not relieved such as overuse, inflammation, or physical activity contributing to joint deterioration. For example, knee pain from osteoarthritis (OA) may initially occur intermittently with weight-bearing and evolve into chronic pain. Systemic causes of joint pain include autoimmune diseases such as type 1 diabetes, rheumatoid arthritis (RA), psoriatic arthritis, and inflammatory bowel disease

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as well as infectious causes such as hepatitis and Lyme disease. Drug-induced arthralgia can occur with some medications, such as antibiotics, statins, and breast cancer and osteoporosis treatments (Havelin & King, 2018; Treede et al., 2019; Villa-Forte, 2021).

Occurrence: Pain is one of the leading reasons patients seek medical attention, particularly for low back pain as well as other musculoskeletal pain (Treede et al., 2019). It is estimated that 54 to 92 million U.S. adults have either provider-diagnosed arthritis or report symptoms consistent with arthritis (Arthritis Foundation, 2019; Guglielmo et al., 2019). In the United States, arthritis reportedly limits the activities of approximately 24 million adults and more than 25% of individuals with arthritis consider the pain to be severe (Guglielmo et al., 2019). Chronic low back pain is the greatest contributor for years lived with disability (Treede et al., 2019).

Age: In older adults, the most common cause of acute nontraumatic monoarticular joint pain is osteoarthritis (Villa-Forte, 2021). Approximately 33% of men and women 18 to 64 years old, report having symptoms of joint pain consistent with an arthritis diagnosis and/or have provider-diagnosed arthritis (Arthritis Foundation, 2019). Prevalence of age-specific arthritis increases with each decade of life, ranging from 8.1% for those 18 to 44 years old to 50.4% of those 65 years and older (Guglielmo et al., 2019). RA typically affects adults between 30 and 40 years of age, but in approximately 33% of cases the patient is older than 60 years. Polymyalgia rheumatica (PMR) should be considered in any adult 50 years and older who is experiencing hip and/or shoulder girdle pain and stiffness often with acute onset and particularly notable in the morning (Villa-Forte, 2021). Rates of age-standardized arthritis among women are significantly higher at 25.4% compared to men at 19.1% (Guglielmo et al., 2019). For people older than the age of 65, more than 50% of men and 66% of women may have arthritis (Arthritis Foundation, 2019). Older women with distal interphalangeal (DIP) joint pain should be screened for gout as well as nodular OA (Villa-Forte, 2021).

Ethnicity: Prevalence of joint pain and arthritis varies based on specific etiology. Generally, the prevalence of joint pain and arthritis among Hispanics and non-Hispanic Asians is lower than other racial/ethnic groups. Conversely, the incidence of age-standardized arthritis, at 29.7%, was significantly higher among non-Hispanic American Indian/Alaskan Natives compared to other racial/ethnic groups. Incidence of arthritis is inversely related to the federal poverty level and education. Additionally, rates of arthritis are higher amongst those living in rural areas versus in urban settings (Guglielmo et al., 2019).

Contributing Factors: Factors that may lead to joint pain include overuse or strain, past injury or trauma to the joint, alterations in gait or balance, known history of joint disease, or past surgery. In a younger individual or an athlete, injury, obesity, or occupational activities are the main factors that contribute toward developing osteoarthritis (Arthritis Foundation, 2019). Injury, obesity, and occupation as well as infection and smoking are modifiable risk factors. Genetics, age, and sex are non-modifiable risk factors for joint pain and arthritis (Centers for Disease Control and Prevention [CDC], 2020).

Signs and Symptoms: Assessment of joint pain requires the history of present illness (HPI), review of systems, past medical, social, and family history; and a thorough physical examination. It is important that the HPI include a pain assessment tool such as the PQRSTU assessment that addresses the following measures regarding pain: provocative/palliative, quality/quantity, region/radiation, severity, timing/treatment, and understanding (Gregory, 2019). Questions on timing should elicit if there is prolonged morning stiffness, which would possibly indicate an inflammatory nature or if pain is worse later in the day or with increased activity, which may indicate a degenerative cause. Evaluation of joint pain should include the "red flags" of joint warmth and/or erythema, open skin areas, fatigue, weight loss, fever or other systemic or extra-articular symptoms and any use of anticoagulants or underlying bleeding disorder (Villa-Forte, 2021).

Both the HPI and examination should assess for any swelling, deformity, decreased range of motion (ROM), crepitus or popping/ clicking of the joint and whether there is one or multiple joints involved. The physical examination should include inspection and palpation of each joint, assessing range of motion, noting any pain, limitations in movement or contractures. Additional diagnostic maneuvers, if indicated, should be performed such as the drawer test for ligament injury of the knee, the McMurray test for meniscal tear, or the Thomas test for hip flexion contracture. The patient's posture, gait, and balance should be assessed for any guarding, compensatory mechanisms, or deficits.

Diagnostic Tests: X-rays are useful to detect arthritic changes such as joint space narrowing or destruction, erosions, or degenerative changes as well as to diagnose pseudogout or fracture or to rule them out. For swelling and painful soft tissues surrounding the joint, ultrasound can be beneficial. In the setting of new acute monoarticular joint pain with a joint effusion, arthrocentesis is necessary to distinguish between a noninflammatory and an inflammatory process to rule out infection and to help diagnose a crystalline arthropathy. The specimen should be sent for synovial fluid analysis that includes cell count, crystal analysis, and culture (He et al., 2020). Joint aspiration likely will also offer symptomatic relief. If examination, x-rays, and arthrocentesis fail to adequately diagnose joint pain, then a magnetic resonance imaging (MRI) scan may be needed to rule out uncommon etiologies such as osteonecrosis, occult fracture, metastasis or other musculoskeletal anomalies (Villa-Forte, 2021).

Laboratory testing can help diagnose infection, inflammation, and metabolic problems. A complete metabolic panel (CMP) and complete blood count (CBC) will detect abnormal calcium, alkaline phosphatase, glucose levels as well as an elevated white blood cell (WBC) count. Hypercalcemia and elevated alkaline phosphatase levels can be seen with malignancy and Paget disease. Undiagnosed or poorly controlled diabetes causes more musculoskeletal injuries, joint pain, and fibroproliferative disorders than for those without diabetes (Sözen et al., 2018). Serum creatine kinase (CK) isoenzymes can be elevated with musculoskeletal trauma and myositis. If the joint pain is polyarticular, it may be reasonable to check inflammatory markers such as C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR). More specific laboratory tests would depend on suspected etiology. Checking uric acid during a gout flare is not useful because it is likely that urate will be sequestered in the affected joint and the laboratory level may result artificially low (Villa-Forte, 2021).

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Differential Diagnosis: The diagnosis of joint pain can best be narrowed by considering if it is monoarticular (injury, infection/cellulitis/septic arthritis) or polyarthricular (RA, PMR), if it appears to be infectious (hepatitis, Lyme disease), inflammatory (gout, pseudogout, psoriatic arthritis), or mechanical (OA, spinal stenosis) in nature; if the pain is from the actual joint or from surrounding soft tissue structures (bursitis, tendonitis, ligament injury). The differential diagnoses can further be narrowed by considering whether joint distribution is symmetric (RA, PMR), and if any extra-articular symptoms (sarcoidosis, spondyloarthropathy, connective tissue diseases) are present. Acute polyarticular joint pain is most often due to a systemic inflammatory disease flare, an infectious cause or in some cases severe gout; however, malignancy should be ruled out. If persistent weakness is present the differential should include degenerative and radicular causes; in inflammatory diseases joint weakness tends to improve through the day. Fibromyalgia should be considered for clinical presentation of pain that is more generalized and muscle related (myalgia) than specifically joint pain (Villa-Forte, 2021).

Treatment: Treatment of joint pain is directed toward the underlying cause, first ruling out acute injury/fracture or infection and if suspected treating accordingly. In the process of working up joint pain, it is reasonable and necessary to address pain however glucocorticoids should not be initiated until inflammatory markers are tested if pertinent to the differential. Management of joint pain is multifactorial, utilizing oral, topical, and intra-articular medications as well as physical, surgical, behavioral, educational, and psychosocial interventions (Kolasinski et al., 2020).

Both acute and chronic joint pain can benefit from nonpharmacological treatment modalities such as intermittent cold or heat therapies and short-term wrapping/splinting. It is important, however, to avoid prolonged splinting, which can result in contractures such as of the elbow or adhesive capsulitis (frozen shoulder). PT/OT can assist patients with splints, braces, assistive devices and help to maintain joint function, flexibility, and reduce risk of falls in older adults. Exercise and PT are first-line treatments for chronic and persistent joint pain. Other than gout and pseudogout, most inflammatory joint pain is worse with extended rest as opposed to injury and mechanical joint pain, which improve with rest (Kolasinski et al., 2020; Rice et al., 2019).

Acetaminophen can be useful to alleviate noninflammatory joint pain, particularly at higher therapeutic doses (3 g/day); however, it is important to avoid alcohol and other medications that contain acetaminophen due to possible liver toxicity. Oral NSAIDs can be particularly effective at reducing pain and inflammation; however, caution is advised due to risk of renal and cardiovascular side effects and gastrointestinal toxicity/bleeding. NSAIDs are best prescribed at the lowest effective dose, used symptomatically instead of scheduled, and with routine monitoring. As a selective NSAID, cyclooxygenase type 2 (COX-2) inhibitors offer the anti-inflammatory benefits with a better gastrointestinal (GI) risk profile; however, they carry a higher cardiovascular risk and still require routine labs. Duloxetine, tramadol, and opioids are only conditionally recommended by the American College of Rheumatology although duloxetine can help with different types of pain (Kolasinski, 2020). As with any opioid, patients should be closely monitored due to the increased risk of falls and the lowest dose and shortest duration should be prescribed to avoid complications. Topical NSAIDs are not quite as effective, but they offer a better safety profile. Over-the-counter (OTC) topical preparations include lidocaine 4% and capsaicin, both of which offer variable patient responses (Villa-Forte, 2021).

Any joint with suspected infection should never be injected, only arthrocentesis should be performed; and a joint with surgical hardware should not be punctured with a needle (Sen & Hurley, 2021). Intra-articular (IA) joint injections can offer localized relief without extensive systemic effects. Corticosteroid injections work well in the setting of acute OA pain, and they are relatively low cost and low risk. As with any injection, the risk of infection is possible and intra-articular glucocorticoids can briefly elevate blood glucose (Kloppenburg & Berenbaum, 2020). Systemic inflammatory joint pain will likely require immunosuppression (Villa-Forte, 2021).

Follow-Up: Monitoring of patients depends on etiology and the course of the disease/condition. If joint pain persists for longer than a couple weeks, the patient should be seen for further work-up and referrals as appropriate. Management of chronic joint pain requires routine visits to monitor the effectiveness of treatments and for follow-up laboratory testing if necessary. Providers should also monitor patients for depression, poor sleep, and impaired coping skills as joint pain and possible subsequent disability contribute to these (Deveza et al., 2019).

Sequelae: The prognosis of joint pain is affected by the etiology. Falls are always a concern for older adults and any damage from injury or disease can potentially affect movement as well as cause pain.

Prevention/Prophylaxis: The best prevention of joint pain is to reduce or eliminate modifiable risks, including injury, infection, obesity, smoking, and occupation hazards (CDC, 2020). Weight loss is recommended when appropriate. It is also important to participate in a moderate level of exercise throughout one's life; doing so helps to maintain physical fitness and muscle strength, which helps to ensure proper joint function and flexibility. Tai chi is strongly recommended for older adults because it helps to maintain function and flexibility while also reducing risk of falls (Kolasinski et al., 2020; Rice et al., 2019).

Referral: For acute joint pain related to injury or infection, refer the patient for needed treatment. For joint pain that requires further work-up, specialized treatment, or is resistant to treatment modalities already tried, a referral to a specialist such as rheumatology or orthopedics may be necessary. Many patients with joint pain benefit from referral to PT/OT.

Education: It is important to educate patients on proper follow-up and to have them report any new or persistent problems related to joint pain or any systemic/extra-articular symptoms. Patients also require understanding of medications prescribed, avoidance of duplicate therapy, the necessary monitoring, and possible adverse effects. Patients will have the best outcome by incorporating nonpharmacological modalities, so the importance of these need to be emphasized. Patient participation in the plan of care will offer the best chance of recovery or minimizing the impact of joint pain including slowing progression, avoiding disability, and preventing falls. This includes the use of assistive devices, which some older adults are hesitant to use.

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Clinical Recommendation	Evidence Rating	References
Exercise using a combination of low-impact aerobic and resistance training tailored to the impairments, functional requirements, and patient preferences. Use water therapy when land physical therapy is not tolerated. Tai chi is strongly recommended for knee and/or hip OA.	A	Rice et al., 2019 Kolasinski et al., 2020
For weight loss use a combination of strategies: regular weight monitoring, increased physical activity, social support, meal plans, limiting portion size, reducing fat and sugar intake, time-restricted feeding, and addressing behavioral triggers to eating.	A	Rice et al., 2019 Kolasinski et al., 2020
Topical capsaicin is conditionally recommended for knee OA (and conditionally recommended *against* for hand OA due to possibly of then touching one's eyes/face).	B	Kolasinski et al., 2020
Thermal modalities such as local hot or cold may provide short-term positive effects on pain.	B	Rice et al., 2019
Intra-articular glucocorticoid injections are strongly recommended for knee and/or hip OA and conditionally recommended for hand OA.	A	Kolasinski et al., 2020
Cane use is strongly recommended for patients with knee and/or hip OA in whom disease in one or more joints is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant use of an assistive device.	A	Kolasinski et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

MUSCLE CRAMPS

Description: Muscle cramps are unintentional, and often painful, sudden contractions of a muscle or muscle group. They can range from intermittent and mild to frequent and severe, at times debilitating. There is often gradual resolution after seconds to minutes and most often muscle cramps present in calf and foot muscles. Muscle cramps can reduce quality of life.

Etiology: Muscle cramps present when the body's motor system is stressed by either a physiological stress, such as dehydration, electrolyte imbalance, or extreme exercise, or by a neuromuscular disease (Katzberg, 2020). They are caused by abnormal discharges from nerves or nerve terminals (Katzberg, 2020).

Occurrence: It is a common outpatient complaint with as many as 50% of older adults reporting frequent cramps, more than three times per week, and sleep disturbance from cramps (Katzberg, 2015, Lorenzo et al., 2018). Muscle cramps are 1.5 times more likely to present in women (Lorenzo et al., 2018), and they are at higher risk for muscle cramps related to statin therapy (Thompson et al., 2016).

Age: Muscle cramps can occur at any age, although in the younger population it is more often related to vigorous exercise and in the older population reported more at bedtime or related to an underlying disease process (Swash et al., 2019).

Ethnicity: No direct ties to ethnicity have been documented at this time.

Contributing Factors: A variety of neuropathic conditions are associated with muscles cramps, such as amyotrophic lateral sclerosis (ALS), peripheral neuropathies, and cramp-fasciculation syndrome. Medical conditions can also be associated with muscle cramps and can include hypothyroidism, hypocalcemia, hypomagnesemia, hypokalemia, deep vein thrombosis (DVT), restless leg syndrome (RLS), and renal and liver disorders. Some medications can cause muscle cramps, including statins, furosemide, hydrochlorothiazide, donepezil, nifedipine, and raloxifene. If no underlying cause is found for recurrent muscle cramps, then they are referred to as idiopathic muscle cramps.

Signs and Symptoms: A comprehensive disease history is key to identifying underlying differentials because multiple chronic diseases and medications can cause muscle cramps. A detailed assessment of risk factors, history, current illnesses, and medications must be obtained. Use of a systematic approach facilitates in identifying the underlying causes and disease processes present. Risk factors for muscle cramps include military exposures, liver or kidney disease, vigorous exercise, electrolyte imbalances, smoking, diabetes, use of statins, venous insufficiency, cancer treatments, pregnancy. A thorough review of systems should take place. Muscle cramps can be unilateral or bilateral, localized or generalized, painful or nonpainful, intermittent or consistent, present with other symptoms such as fatigue and red flag symptoms such as swelling, pain with movement, muscle wasting, or weakness. The description of cramp symptoms helps to differentiate from other underlying conditions. Claudication may be described as aching with occasional cramping, noted more during exercise and activity, then relieved with rest. Those with RLS may describe an irresistible urge to move their legs with a cramp-like feeling noted more at night. Intolerance to statin therapy may present as deep aching cramps and can present in any muscle group. In peripheral neuropathy a

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person may complain of numbness and tingling and possible secondary cramps (Allen & Kirby, 2012). Patients with ALS may present with muscles cramps and weakness to extremities, along with loss of muscle mass. A person with exercise-induced cramps or electrolyte imbalances may complain of discomfort after the activity, which then improves with rest and hydration. A patient with DVT can present with unilateral cramping to an extremity, often with pain along a major vessel and possible edema and erythema to area.

Most often cramps will not be present at time of visit, so it is important to assess all physical areas that may be included in differentials (Allen & Kirby, 2012). The physical examination can start when patient enters exam room, by assessing their posture and gait, looking for any muscle imbalances. Vital signs should be obtained, including temperature, heart rate, respirations, and oxygen saturation. If capability is present in office setting, then a blood pressure should be obtained on all extremities, if a weak pulse or low ankle: brachial pressure ratio is present then ischemia needs to be considered. Next is a complete examination, starting with the head and neck, assessing for decreased hair pattern or loss of eyebrow hair and palpating thyroid assessing for enlargement. Assess for changes in skin turgor or moisture of skin, examining for increased dryness of skin which can appear with hypothyroidism. Cardiovascular examination should include palpation of all extremity pulses. Examination of the gastrointestinal (GI) system may include assessing for liver enlargement or jaundice, which may present in cirrhosis. Thorough neurological and musculoskeletal physical examinations must be obtained in patients presenting with muscle cramps, this should include assessing reflexes, strength testing, and sensation to extremities. Two clinical signs may present in those with low calcium, Chvostek and Trousseau, and these should be assessed. The Trousseau sign is more specific because in healthy individuals it is only positive about 1% of the time (Pepe et al., 2020). The provider should be on alert for red flag findings such as muscle weakness, loss of sensation, hyperreflexia, tenderness along area of major veins, or significant incongruency in calf diameter. Homan sign is not considered a reliable test to assess for DVT. Lower extremities should be assessed for skin discoloration, decreased hair pattern, or edema, which may indicate venous insufficiency.

Diagnostic Tests: The testing obtained for muscle cramps depends on the suspected underlying causes, associated differentials, and pertinent findings on physical examination.

When electrolyte imbalance is a concern, pertinent laboratory studies may include a comprehensive metabolic panel (CMP) to look at potassium, sodium, and calcium, plus checking magnesium level. Low levels of these electrolytes can lead to subsequent muscle cramps presenting. An imbalance may be a differential when a patient is undergoing dialysis, vigorously exercises, was out in extreme heat, has poor nutritional status, had recent fluid loss via diarrhea or vomiting, or is taking certain medications, like a diuretic or a proton pump inhibitor (PPI). Severe hypocalcemia, hyponatremia, or hypokalemia frequently require admission to the emergency department (ED) setting and would benefit from an electrocardiogram (ECG) to ensure no life-threatening arrythmias are present (Pepe et al., 2020). A CMP can also assess functional status of the liver, as underlying liver disease can cause muscle cramps.

If concern for peripheral neuropathy is present, then obtaining glycosylated hemoglobin (A1c), HIV antibody, B_{12} level with a methylmalonic acid, and a complete blood count (CBC) may assist in determining whether this is an underlying cause of muscle cramps (Allen & Kirby, 2012). In patients with symptoms concerning for hypothyroid, a thyroid-stimulating hormone (TSH) test would offer value. A d-dimer assay can be obtained on those in whom there is concern for DVT, although this test varies in sensitivity it is a recommended test, with the enzyme-linked immunosorbent assay (ELISA) offering 94% sensitivity (Linkins & Takach Lapner, 2017).

Imaging studies can offer benefit. Venous doppler ultrasounds are obtained to assess circulation in patients in whom there is concern for DVT or venous or arterial insufficiency. In patients who present with muscle weakness, wasting, and cramps, where there is concern for ALS, there remains to be no specific diagnostic test for this disease, and it continues to be primarily a clinical diagnosis (Oskarsson et al., 2018). For ALS the clinical standard for diagnosis remains the revised El Escorial World Federation of Neurology criteria (de Carvalho et al., 2008). Electromyography (EMG) testing is used to assess for abnormalities within the muscle, by recording electrical activity of muscle tissue. It is a cornerstone in assessment of underlying neuromuscular disease (Whittaker, 2012). This testing can be utilized to determine the presence of underlying disease, such as ALS or polyneuropathy, by showing abnormal nerve activity and reduced recruitment of motor units (Chung et al., 2014). Neuroimaging, such as magnetic resonance imaging (MRI), can be obtained to assist in ruling out other possible causes for muscle cramps, such as cervical or lumbar spine degeneration. Specialists may obtain other testing to further determine diagnosis for muscle cramps, these include single-fiber electromyography (EMG) and transcranial magnetic stimulation, both which look at nerve and muscle response with stimulation. The diagnosis of underlying cause for muscle cramps can be a lengthy process and may require a multidisciplinary approach.

Differential Diagnosis: When assessing a patient who complains of muscle cramps it is important to immediately assess those who have red flag symptoms, such as swelling, pain with movement, muscle wasting, chest pain, or weakness. In older adults, an alteration in mental status may also present with an acute illness or electrolyte imbalance; this should immediately be examined.

Some of the most prevalent electrolyte imbalances seen are hypocalcemia, hypokalemia, hyponatremia, and hypomagnesemia (Table 7-9). Diagnosis of electrolyte imbalance is determined by obtaining blood work and assessing levels.

TABLE 7-9 Electrolyte Balances Related to Muscle Cramps

Calcium	*Hypocalcemia:* Below 8/5 mg/dL
Potassium	*Hypokalemia:* Less than 3.5 mmol/L
	Moderate hypokalemia: 2.5 to 3.0 mmol/L
	Severe hypokalemia: <2.5 mmol/L
Sodium	*Hyponatremia:* serum sodium <135 mEq/L
Magnesium	*Hypomagnesemia:* Below 1.6 mg/dL

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Each electrolyte imbalance has a variance in presentation from asymptomatic to life-threatening, this presentation will guide the practitioner's treatment as more serious symptoms may need further evaluation in an emergency room setting. Other causes include amyotrophic lateral sclerosis, chronic venous insufficiency, peripheral neuropathy, restless leg syndrome, and some medications (primarily statins).

Treatment: Treatment of electrolyte imbalances is dependent on the severity and type of imbalance that is present. Treatments for other disorders listed as differential diagnoses are discussed in their respective chapters.

Follow-Up: Follow-up depends on the severity of the muscle cramps and the impact on the patient's quality of life. For electrolyte imbalance, it is important to follow-up within a week to recheck levels or after discharge from hospital. If you have been treating imbalance on an outpatient basis and the patient becomes symptomatic, it is important for them to be seen sooner. With underlying chronic disease such as ALS, RLS, and neuropathy, comanaging with a specialist is important. If medication changes are made to help improve muscle cramps, a 4-week follow-up after changes is reasonable.

Sequelae: ALS has an ominous prognosis and requires a multidisciplinary approach, including hospice involvement as disease progresses. Neuropathy, venous insufficiency, and RLS may take several months to find a beneficial treatment regimen. Good outcomes can be expected when muscle cramps are the result of a medication side effect or an electrolyte imbalance and those problems are corrected.

Prevention/Prophylaxis: Preventive measures include frequent medication reviews to screen for medications that can cause muscle cramps and laboratory testing to check for imbalances. Neuropathy and venous insufficiency can be caused by diabetes. Good diabetic control can help prevent these from developing or worsening. Smoking cessation can aid those with venous insufficiency to help prevent disease or slow down progression.

Referral: A referral to a specialist can be initiated anytime during the evaluation and treatment of muscle cramps. Referral to a nutritionist can facilitate an assessment of dietary deficiencies and recommend improvements. If concern is present for the diagnosis of ALS, then immediate referral to neurology should take place as a multidisciplinary approach is important early on. For those with neuropathy a referral to podiatry for annual foot exams can help with wound prevention and regular foot care. A referral to vascular medicine can be of help to those with venous insufficiency to aide in further assessment and obtaining proper compression stockings. Consultation with a dietitian may aid those with chronic electrolyte imbalances, to assist in understanding dietary supplement needs. Pain management may be needed in patients who fail conservative or initial treatment for pain relief.

Education: Recommend smoking cessation support and discuss options to aide in quitting. If there is risk for electrolytes imbalances, then teach about dietary supplementation. It is important to educate patients on all prescribed medications and side effects, such as muscle cramps and statins, ensuring they present to office if these effects present.

Diagnosis	Clinical Recommendation	Evidence Rating	References
Electrolyte imbalances	Correct the imbalance either via outpatient oral supplements or, if imbalance is severe or the patient is symptomatic, hospitalization with IV replacement. Discontinue medications that may be causing imbalances.	B	Ahmed & Mohammed, 2019 Hoorn & Zietse, 2017 Pepe et al., 2020 Van Laecke, 2019
Amyotrophic lateral sclerosis	Symptom management is key, including use of muscle relaxers for cramps	A	Oskarsson et al., 2018
Chronic venous insufficiency	Risk reduction is initial treatment, including weight loss, smoking cessation, and good diabetes control. Compression hose and Tylenol for discomfort and prevention of worsening are recommended. If poor response with initial treatment, then referral to vascular for more invasive therapy may be needed.	A	Youn & Lee, 2019
Peripheral neuropathy	Prevention is key initial treatment, including good diabetes control. If B_{12} deficiency, replace B_{12} via supplement. If initial treatments do not work then use of gabapentin, pregabalin, duloxetine, amitriptyline, and venlafaxine offer benefit, but for some of these attention must be given to renal function and age of patient. Poor response to initial treatments may require a referral to pain management and discussion of opioid treatment.	A	Katzberg, 2020

Continued

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Diagnosis	Clinical Recommendation	Evidence Rating	References
Restless leg syndrome	Nonpharmacological treatment includes deep tissue massage and passive stretching. Medications for treatment that have been shown to offer benefit include ropinirole, rotigotine, gabapentin, and pregabalin. If ferritin level is low, iron replacement via oral or IV therapy is recommended. Physical measures include pneumatic compression, transcranial direct current stimulation, and repetitive transcranial magnetic stimulus.	A	Gonzalez-Latapi & Malkani, 2019 Tipton & Wszołek, 2017
Medication-induced cramping	Statin therapy may need to be stopped or reduced with rechallenge with two different statins or ezetimibe. Consideration to Repatha or Praluent (PCSK9 inhibitors) if cholesterol control is needed, but statin intolerance is present.	B	Tomaszewski et al., 2011 Thompson et al., 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PERIPHERAL EDEMA

Description: Peripheral edema is swelling due to an increase in the interstitial fluid volume and may not be evident until the interstitial volume has increased by 2.5 to 3 L. This is generally associated with an increase in weight of up to 10% (Goyal et al., 2021). Lymphedema, or lymphatic obstruction, occurs when a compromised lymphatic system causes localized fluid retention and tissue swelling. There are numerous etiologies for peripheral edema ranging from benign to life-threatening clinical conditions.

Etiology: Normally, the distribution of water between the blood and interstitial tissues is maintained by hydrostatic and oncotic pressures in each compartment. Starling's principle—the osmotic pressure of the plasma proteins balances the hydrostatic pressure in the capillaries—helps in the understanding of fluid dynamics (Michel et al., 2020). Fluid flows from the vessels to the interstitial area in response to intravascular hydrostatic pressure and the colloid osmotic pressure of the interstitial fluid. In the opposite direction, fluid enters the blood because of the interstitial tissue tension and the oncotic pressure of the plasma proteins. Interstitial fluid also is returned to the blood as lymph. Under steady-state conditions, net fluid flux out of the capillary is balanced by lymph flow back into circulation. Alteration in any of these compartments (intravascular, extravascular, lymphatic) upsets the equilibrium, and edema occurs. Two basic steps occur in edema formation: sodium and water are retained, and capillary hemodynamics are altered.

Peripheral edema may be due to increased capillary hydrostatic pressure, decreased plasma oncotic pressure, increased capillary permeability or lymphatic obstruction. An increase in capillary hydrostatic pressure may be the result of an increase in localized venous pressure (e.g., deep vein thrombosis [DVT]), a systemic increase in venous pressure (e.g., heart failure [HF], liver failure), or an increase in plasma volume (e.g., pregnancy, renal failure, or certain medications). A decrease in plasma oncotic pressure may be the result of protein loss (e.g., pre-eclampsia nephrotic syndrome), decrease in protein synthesis (malabsorption, malnutrition, or liver disease). Capillary permeability increases in burns, cellulitis, or allergic reactions. Lymphatic obstruction may be the result of malignancy or postoperative effects on lymphatic drainage (Goyal et al., 2021). The swelling that results from lymphedema is nonpitting. It may be primary due to congenital or inherited conditions, or secondary caused by damage to the lymphatic system; cancers (especially breast, ovarian, and prostate); infection; inflammation; or obesity.

Occurrence: The frequency of occurrence depends on the underlying etiology. Lymphedema and venous insufficiency are more common in women.

Age: Edema can occur in any age, but is more common in older adults, has diverse etiologies, and more than one disorder can be causing edema in the same patient. In patients older than age 50, venous insufficiency is the most common cause of peripheral edema (Goyal et al., 2021)

Ethnicity: While moderate edema does not have a notable ethnic difference, severe venous insufficiency is most common in Whites (Pappas et al., 2020).

Contributing Factors: Physiological age-related changes increase the vulnerability to fluid retention. The older adult has a smaller amount of total body water overall (75% to 85% of body weight for an infant, 60% to 65% for an adult male, 50% to 55% for an adult female, less than 40% for an older adult) (Khatun et al., 2020), and of this, two-thirds of the fluid is intracellular and one-third is extracellular. As more intracellular fluid is lost over time, extracellular fluid volume starts to comprise more body water. Risk factors for peripheral edema from age-related changes include a decrease in:

- Serum albumin—less than 2 g/dL can cause edema
- Glomerular filtration rate
- Hepatic blood flow

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- Sodium-concentrating ability of the kidney
- Myocardial contractility and cardiac output
- Baroreceptor sensitivity
- Medications that are used to treat conditions common in older adults can cause peripheral edema:
- NSAIDs cause increased sodium absorption in the kidney due to the blockage of prostaglandin (Trayes et al., 2013).
- Thiazolidinediones are used as treatment for diabetes (pioglitazone or rosiglitazone) and stimulate sodium reabsorption in the kidney; worsening HF is a known side effect (Lebovitz, 2019).
- Antihypertensives with mechanisms that cause vasodilation or activation of the renin-angiotensin-aldosterone sympathetic nervous system may increase peripheral edema (e.g., hydralazine, dihydropyridine calcium channel blockers, and alpha blockers) (Vouri et al., 2019).

Additional contributing factors include dependent positioning of the lower extremities, excessive intake of sodium, and hot weather. Patients who normally live at high altitude may develop lower extremity edema when they transition to lower altitudes. This differs from those who move from sea level to higher altitudes who may develop pulmonary or cerebral edema (Zubieta-Calleja & Zubieta-DeUrioste, 2017).

Signs and Symptoms: The patient may complain of swelling, fullness, discomfort, aching pain, shoes that are too tight, wounds, gait disturbance, self-image issues, or weight gain. The history should elicit the seven dimensions of the signs and symptoms of edema, emphasizing location (unilateral or bilateral) and chronological evolution (acute or chronic progression). Associated symptoms need to be elicited, particularly shortness of breath or awakening at night with difficulty breathing. The presence or absence of pain is helpful in determining the differential diagnosis. Ask about aggravating and alleviating factors, including positional changes, the effect of prolonged sitting or standing, and determine the effect of passive leg elevation. A history of malignancy, pulmonary, cardiac, renal, hepatic, endocrine disorders, or peripheral vascular disease is important. Ask about recent weight loss or gain, changes in diet, salt intake, and alcohol use. A thorough review of medications (both prescribed and over-the-counter [OTC]), particularly new medications or a recent change in dosage is essential. Has the patient been on a trip recently or had periods of prolonged standing or sitting?

The physical examination begins with general appearance, assessing for any distress or apparent discomfort. evaluate the patient's weight for change. Assess skin changes, including pigmentation and thickening, lesions, discoloration, texture, temperature, and induration. Evaluate the venous and arterial circulation, checking pulses throughout; capillary refill; and dependent rubor. Varicose veins are usually readily apparent with the inspection of the legs while the patient stands. Assess the extremity for local or diffuse tenderness and for pitting or nonpitting edema. Measure and compare the circumference bilaterally from a fixed reference point above the ankle to the area of maximal edema (e.g., patella, calf, midcalf). Assess any localized enlargement.

Pitting edema has no universal scale for measurement. When assessing for edema of the lower extremity, the provider applies pressure anterior to the tibia to check for pitting. If pitting is present, this is a positive Godet sign. (Zubieta-Calleja & Zubieta-DeUrioste, 2017). It is generally defined on a scale of 1+ to 4+ or brawny edema (which is chronic and may not be pitting). Edema is assessed by applying firm pressure with your thumb over the area of swelling. A commonly used scale for grading edema refers to the depth of the impression: 2 mm = 1+, 4 mm = 2+, 6 mm = 3+, and 8 mm = 4+ (Brodovicz et al., 2009). Another method adds the amount of time it takes for the impression to return to normal: 30 seconds or less = 1+, 30 to 60 seconds = 2+, 60 to 90 seconds = 3+, and 90 to 120 seconds = 4+. To assess whether nonpitting edema represents the presence of lymphedema, a technique that is recommended was defined by Kaposi and later by Stemmer. The Kaposi-Stemmer sign suggests lymphedema when there is an inability to tent the skin over the dorsum of the foot at the base of the second toe. This sign has high specificity but not sensitivity (Jayarah et al., 2019).

The examination should also include body systems as indicated by the history, particularly pulmonary, cardiac, peripheral vascular, hepatic, renal, and endocrine. If arterial insufficiency is suspected, an ankle-brachial index (ABI) measurement should be performed. In unilateral edema, a 1-cm difference in size above the ankle or a 2-cm difference at the calf is significant and should lead to further investigation.

Diagnostic Tests: Diagnostic tests depend on the probable etiology of peripheral edema. Cardiac causes may warrant a chest x-ray, electrocardiogram (ECG), or echocardiogram. Laboratory studies also depend on the diagnostic considerations: complete blood count (CBC) for suspected anemia, with a differential if infection is a possibility; complete metabolic panel (CMP), which includes electrolytes, glucose, blood urea nitrogen (BUN), creatinine, albumin, phosphorus, aspartate aminotransferase (AST), alanine aminotransferase (ALT), and bilirubin. More targeted chemistries may be reasonable—for example, a basic metabolic, renal, or hepatic panel. Thyroid function can be assessed with a high sensitivity thyroid-stimulating hormone (TSH) with a reflexive addition of free thyroxine if abnormal. Additional studies could include ultrasound, venogram, venous Doppler studies, lymphoscintigraphy, or the more invasive lymphangiography. Computed tomography (CT) scans or ultrasound for pelvic masses and lymphoma may be indicated, as well as a cancer antigen 125 (CA-125) test. Urine studies quantify protein losses and urine electrolytes.

Differential Diagnosis: Peripheral edema is an important clinical sign, and its causes are diverse. The differential diagnosis is facilitated in part by noting if edema is unilateral or bilateral and recognizing distinctions between lymphedema, lipedema, and venous stasis. Lipedema is a bilateral, symmetrical deposition of fat in the lower extremities that spares the feet (a distinguishing feature) and occurs exclusively in obese women. A multisystem approach that excludes major organ system dysfunction is useful, especially pulmonary, cardiac, endocrine, hepatic, and renal disease. An accurate diagnosis is important because the mainstay of treatment is reversing the underlying disorder, if possible.

Treatment: Always direct treatment at the cause of peripheral edema: diuretics for HF, a high-protein diet for hypoalbuminemia, angiotensin-converting enzyme (ACE) inhibitors for proteinuria, and thrombolytics for acute DVT. Any drugs known to cause edema should be discontinued or decreased

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in dosage. Adding a diuretic to manage edema due to medications such as dihydropyridine calcium blockers may result in polypharmacy; consider deprescribing the offending agent, if possible (Vouri et al., 2019). Many patients expect that any edema should be treated with a diuretic, but if fluid overload is not the issue, diuresis can cause tissue death. Edema due to venous stasis, for example, should focus on that specific etiology, which may not require diuretics.

Compression Stockings. Compression stockings decrease the capillary filtration rate, thus decreasing edema. They are especially useful in patients with venous insufficiency. There is no evidence to indicate that high compression (30 to 40 mm Hg) is clinically more advantageous than medium compression (20 to 30 mm Hg), and patients are more compliant with medium compression. The stockings can be difficult to pull on, and a stocking donner can be helpful. Give the patient a prescription for two sets to allow for laundering. They need to be replaced every 6 months because the compression properties decrease with wear. Stockings that zip are available. Send the patient to the medical supply store where trained fitters will ensure the proper fit. Compression stockings are not recommended for patients with peripheral artery disease (PAD), and if suspected, an ABI can be ordered to screen for PAD.

Behavioral modifications include intermittent periods of recumbency, the avoidance of environmental heat, exercise, weight loss, and sodium and water restriction as indicated (Tennison et al., 2018). Exercise improves the muscle pump action and strengthens leg muscles.

Follow-Up: Closely monitor patients for effectiveness of therapy and adverse events. Monitor the weight and limb circumference measurements using the same reference points because a patient's weight may increase 10% before pitting edema is clinically evident.

Sequelae: When administering diuretics, the health-care professional must be alert to potential volume depletion. Older adult patients are very sensitive to diuretics, and their administration may result in falls, weakness, confusion secondary to sodium and other electrolyte abnormalities, urinary incontinence, gout attacks, volume depletion, and acute renal failure. Patients with edema as a result of deep venous insufficiency are prone to recurrent ulceration.

Prevention/Prophylaxis: For patients with recurrent lymphangitis and cellulitis, prescribe intermittent long-term antibiotic prophylaxis. For patients with leg swelling secondary to DVT, thrombolytics may limit the tissue loss, pulmonary embolus, and more extensive thrombosis of the deep venous system.

Referral: Referral to specialists depends on the diagnosis. It would be rare to hospitalize a patient for most causes of peripheral edema, thus treatment is almost always outpatient. Even DVTs can be treated in consultation with a vascular medicine specialist in the outpatient setting with low-molecular-weight heparin (enoxaparin), warfarin, or direct oral anticoagulants (DOAC) (rivaroxaban, dabigatran, apixaban, and edoxaban). The DOACs offer benefits above warfarin because they do not require routine monitoring, have predictable pharmacokinetics, fewer drug-drug interactions, and limited drug-food interactions.

Education: Patients need specific information related to the edema and the management of symptoms. Typically, the patient with edema is instructed to avoid highly salted foods (follow a 2 to 3 g sodium diet). If compression stockings are recommended, emphasize the importance of proper sizing and application technique to avoid excessive pressure. Instruct patients to elevate the legs above heart level to decrease peripheral vascular pressure for 10 to 15 minutes three to four times a day. Periodic active muscle contraction exercises are important for individuals who must sit for long periods. Teach patients with peripheral vascular disorders to avoid excessive heat and reduce weight if indicated. Special care of the skin, including proper shoes and prevention of trauma, is important.

Clinical Recommendation	Evidence Rating	References
When deep vein thrombosis is suspected, use the Wells Clinical Rule, d-dimer and selective use of imaging to confirm the diagnosis.	A	van Dam et al., 2020
Leg edema in immobile patients due to venous insufficiency can be adequately managed with compression and physical therapy alone.	B	Santler & Goerge, 2017
Brain natriuretic peptide is helpful for distinguishing HF from other causes of leg edema.	B	Goyal et al., 2021
Leg lymphoscintigraphy should be the primary method for diagnosis of lymphedema when diagnosis is unclear.	C	O'Donnell, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PRURITUS

Description: Pruritus is a localized or generalized unpleasant, irritating, or itching sensation on the surface of the skin that may lead to the desire to scratch. Pruritus may be acute or chronic (>6 weeks) and is a symptom of an underlying disease process.

Etiology: Pruritus does not always present with visible inflammation or skin lesions. Other causes associated with pruritus include systemic illness, neuropathic and psychogenic processes, and the aging process itself (Butler, 2020; Chung et al., 2020). The itch sensation is a result of immune and neural

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dysfunction. The sensation begins in the dermal layer through triggering the inflammatory immune response. This creates a signal transmitted to the dorsal horn through C fibers. This signal travels up to the thalamus and then it is transmitted to several areas of the brain. The route of pruritus pathways is similar to pain pathways, but the specific pathways differ. The cause of pruritus in older adults is often multifactorial due to aging of the skin and neurological, immunological, and psychological changes associated with aging. In fact, stress can exacerbate itch and vice versa (Golpanian et al., 2020). Additionally, medications are a common exogenous trigger of pruritus, including antihypertensives, antibiotics, opioids, and psychotropics. Drug-induced pruritus may be localized or generalized and may start after the first dose of a drug or many weeks or months after being on the drug.

Occurrence: Pruritus is the most common symptom seen in dermatology and is caused by various skin and systemic diseases. Women are likely to experience and have more intense chronic pruritus symptoms compared to men (Kursewicz et al., 2020; Whang et al., 2019). Additionally, women are more likely to have comorbid autoimmune and psychiatric conditions and for pruritus to have a more negative impact on quality of life (Kursewicz et al., 2020; Whang et al., 2019).

Age: Pruritus is relatively common but increases with age. In older adults, chronic itch is a distressing and debilitating condition associated with a decreased quality of life (Butler, 2020; Chung et al., 2020; Kremer et al., 2020).

Patients who are Black are more likely to experience pruritus and use special lotions, soaps, and clothes than patients who are White (Shaw et al., 2017; Whang et al., 2019). Patients who are Black also report more significant emotional distress from pruritus, but are less likely to seek specialty care (Huang et al., 2019; Shaw et al., 2017).

Contributing Factors: Once a pattern for pruritus has been initiated, continued scratching causes a cascade of inflammatory mediators that provoke the itch sensation and repeat scratching. Additional factors that contribute to dryness include winter weather with low humidity, daily use of cleansers, and bathing without replacement emollients. Sleep deprivation can cause an increase in the release of an inflammatory mediator which results in and contributes to pruritus.

Signs and Symptoms: A thorough history following OLD CARTS (Onset, Location/radiation, Duration, Character, Aggravating factors, Relieving factors, Timing, and Severity) format and physical examination should be done in all patients with pruritus. Find out about allergies and if there was an exposure to new creams or detergents. Ask about systemic-associated symptoms such as weight loss, fever, heat/cold intolerance (thyroid or hepatic disease), nausea and vomiting (chronic renal failure), and polyuria/polydipsia (diabetes). Document past medical history including previous skin conditions, skin care routine, and current medications. A complete physical examination is warranted, examining all surfaces of the skin, including the hair and nails. Assess texture, temperature, moisture, and turgor of the skin. Assess lesions and document the location, shape, and characteristics. A thorough physical examination is required to identify potential systemic causes and contributors to pruritus.

Diagnostic Tests: Skin biopsy or scraping may be needed to establish a diagnosis for a non-recognizable skin lesion. Depending on the results of the history and physical exam appropriate tests might include a comprehensive metabolic panel, complete blood count (CBC), erythrocyte sedimentation rate (ESR), C-reactive protein, thyroid-stimulating hormone (TSH), and HIV. If paraneoplastic itch is suspected, a chest x-ray and/or and computed tomographic scan of the chest and abdomen should be considered. Magnetic resonance imaging may be helpful when addressing itch found along a particular dermatome. Psychiatric assessment can be considered after cutaneous, systemic, and neuropathic causes of itch have been ruled out.

Differential Diagnosis: The differential diagnosis is broad and includes dermatological causes, hypersensitivities, allergic reactions, mite infestation, neuropathic and neurogenic causes, and psychiatric causes, including pruritus associated with systemic diseases. There may be more than one cause, and frequently a cause is never determined.

Treatment: Goals of treatment include alleviating the itch and maintaining skin integrity. Treatment is aimed at the cause. For example, xerosis (dry skin), a common cause of itch in older adults, is treated with emollients that rehydrate the skin and reduce inflammation, and some may include a mild anesthetic or menthol that helps decrease the sense of itching.

Topical Treatments. Most useful with localized forms of pruritus. Topical steroids reduce inflammation, though are avoided for generalized itching or prolonged periods because they cause thinning of the skin. An antihistamine topical cream may be used for localized urticaria. Topical immunomodulators (calcineurin inhibitors) have good evidence to treatment of atopic dermatitis and recently, ceramide emollients and pine tar preparations have been shown useful for itch relief (Harrison & Spada, 2019). Local anesthetics or capsaicin cream can decrease transmission in sensory fibers.

Systemic. These treatments are frequently used for generalized pruritus. Systemic medications with antipruritic properties can be very useful and include serotonin and norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), and tricyclic antidepressants. Mirtazapine, paroxetine, and doxepin have antihistaminic and serotonergic effects. Mirtazapine may be particularly useful for underweight patients with nighttime itch because it may also enhance appetite (Khanna et al., 2019). The antidepressants may also be helpful in psychogenic causes. Depending on the cause, antihistamines, neuroleptics, and opioid agonists and antagonists can help. First generation antihistamines may help patients experiencing nocturnal pruritus to sleep better because of their soporific effects. These medications are included in the Beers list of Potentially Inappropriate Medications because of their anticholinergic properties; therefore, second generation antihistamines are recommended as first line. Gabapentin/pregabalin and opiate antagonists has been shown to be useful for neuropathic or systemic causes of pruritus (Chung et al., 2020).

Nonpharmacological Measures. Remove any identified environmental allergens. Consider occlusive dressing (reduces scratching), cool compresses, psychotherapy, and acupuncture.

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Phototherapy has been used for decades to treat various pruritic dermatoses.

Follow-Up: Monitor the patient frequently to evaluate the effectiveness of treatment and reinforce adherence. Assess for secondary complications.

Sequelae: Secondary infection is a risk when the skin is broken. Neglecting pruritus can have a negative effect on the patient's quality of life and lead to anxiety, depression, and insomnia.

Prevention/Prophylaxis: Avoid triggering or exacerbating factors. Additional recommendations regardless of the cause of pruritus include increasing the humidity in the home, drinking plenty of water, and eliminating triggering food. Bathe less often, use warm (not hot) water, and use a soft towel to gently pat skin dry rather than vigorously rubbing. After bathing, apply emollients gently to avoid overstimulating the nerve endings.

Referral: Depending on the result of your assessment, refer to a specialist to manage systemic disease if indicated. If no specific diagnosis is identified and first-line treatments are ineffective, refer to a dermatologist or an allergist.

Education: Includes an explanation of the diagnosis plus triggering/exacerbating factors. Discuss bathing techniques and use of moisturizers. Counsel to keep fingernails short, wear light/loose clothing, avoid alkaline and alcohol-based cleansers, maintain comfortable temperature and humidification, and alleviate stress. Discussion about breaking the itch-scratch cycle is important.

Clinical Recommendation	Evidence Rating	References
Keep cool, use emollients with or without topical anesthetics, capsaicin, antihistamines, camphor, and menthol lotion. Take oatmeal baths. Take short, tepid showers. Avoid soaking and use moisturizing, gentle, nonfragranced soaps.	C	Chung et al., 2020 Butler, 2020 Shevchenko et al., 2018
Use gabapentin/pregabalin for neuropathic mediated itch.	C	Butler, 2020
First generation and second generation antihistamines have an anti-pruritus effect for urticaria.	B	Butler, 2020
Calcineurin inhibitors are safe and effective for atopic dermatitis.	A	Butler, 2020
Use mirtazapine or serotonin and norepinephrine reuptake inhibitors to treat chronic itch refractory to conventional treatment.	C	Boozalis et al., 2018 Khanna et al., 2019
Topical steroids can be used short-term for localized causes of itch.	B	Harrison & Spada, 2019
In patients with chronic atopic dermatitis, exacerbating factors and appropriate treatment options are important, and interventions that include educational interventions show significant benefits.	A	Butler, 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

SYNCOPE

Description: Syncope is a sudden and transient loss of consciousness and postural tone resulting from a reduction in oxygen to the brain with immediate spontaneous recovery. Although of short duration, it can result in physical injury, accidents, and a decreased quality of life.

Etiology: Etiologies for syncope range from trivial to lethal. In most instances, the loss of consciousness reflects a temporary decrease in cerebral blood flow that is usually secondary to a fall in the systemic arterial blood pressure influenced by metabolic regulation, chemical regulation, and autoregulation. Syncope is categorized as reflex or neurally mediated in 45% of cases, cardiac related in 20% of cases, and orthostatic hypotension (hypotension occurring after standing up) in 10% of cases. Reflex or neurally mediated and orthostatic causes are usually more benign, whereas cardiac and neurological causes are more concerning. Vasovagal syncope is the most common type of reflex syncope and commonly has prodromal symptoms such as sweating, nausea, vomiting and pallor. The second most common reflex syncope that has the highest incidence in older adults is carotid sinus syncope, which is more common in men and reproducible with carotid massage. Other reflex syncope is more situational, triggered by cough, micturition, or defecation. Cardiovascular syncope is associated with underlying cardiac conditions such as arrythmias or structural heart disease. Heart failure (HF) has been associated with syncope in 12% to 14% of patients. Cardiac syncope is associated with increased mortality. Orthostatic hypotension, which is particularly common in older adults, is associated with antihypertensive medications and dehydration. Studies show that the cause of syncope remains elusive in 30% of cases of patients admitted for syncope (Geer, 2021; Runser et al., 2017; Shen et al., 2017).

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Occurrence: Syncope prevalence has been reported as high as 40% and recurrent syncope occurring 13.5%. Syncope accounts for 1% to 1.5% of all emergency room visits and of those experiencing a syncopal episode 30% to 50% will be hospitalized for further evaluation (Runser et al., 2017; Shen et al., 2017). Among younger adults, women have nearly twice the rate of syncope as men; among older adults, men have the greater incidence. This likely reflects the most common etiologies in the different age-groups.

Age: Syncope incidence is increased in older adults. Among patients older than 80 years of age presenting with syncope, 58% were hospitalized. Among older adults, syncope is associated with increased falls. The lifetime incidence of syncope may be 25% in older adults, and 80% of all emergency department (ED) admissions for syncope are individuals older than 65 years of age. Some forms of syncope (i.e., vasovagal, carotid sinus hypersensitivity) are more common in younger persons than in older persons; other forms of syncope (i.e., cardiac, orthostatic, micturition related) occur more often in older than in younger individuals.

Ethnicity: Not significant.

Contributing Factors: Cerebral blood flow has been reported to decline 25% with physiological aging, which is thought to be related to vascular stiffening. Hormonal regulation of extracellular volume may become impaired with age. Cardiac reflexes and baroreceptor sensitivity also may become impaired. The kidneys' ability to conserve sodium and water declines. Chronic diseases, such as heart disease, diabetes, renal insufficiency, hypertension, and chronic pulmonary disease, are predisposing conditions. Medications used to treat these chronic diseases, such as diuretics, beta blockers, vasodilators, nitrates, antiarrhythmics, and antihypertensives, also may be offenders. Alcohol is a contributing factor in vasovagal syncope. An emotional response can cause neurally mediated syncope in susceptible individuals in stressful circumstances. Dehydration and orthostatic hypotension may be factors. Autonomic nervous system dysfunction, such as Parkinson's disease can cause orthostatic symptoms. Situational syncope can occur when the Valsalva maneuver is produced (micturition, defecation, cough, lifting heavy objects, or after meals related to postprandial hypotension). Prolonged recumbency can contribute to micturition syncope, especially in men with prostate enlargement who awaken from a supine sleep and stand to urinate.

Signs and Symptoms: Sudden collapse with loss of motor tone, with or without injury, is the most common presentation of syncope. The American College of Cardiology (ACC), the American Heart Association, and Heart Rhythm Society (2017) developed recommendations for risk stratification to evaluate the syncope type and each individual's risk factors for future cardiac events. The initial syncope evaluation includes history, physical examination, and resting 12-lead electrocardiogram (ECG). Risk categories are low, intermediate, and high risk (Shen et al., 2017). Standardized risk stratification tools guide appropriate evaluation and management of syncope. Helpful risk stratification tools include the Boston Syncope Pathway, CHADS2 score, the FAINT score, and the San Francisco Syncope Rule (Geer, 2021).

Self-report and eyewitness accounts of transient loss of consciousness are often unreliable—even when the eyewitness is a health-care professional. The most important first step is determining if it is true syncope. Obtain the patient's description of symptoms preceding the event and of activities that may have precipitated the event. Cardiac-related syncope may be sudden and without warning. A brief prodrome of symptoms, such as nausea, pallor, or diaphoresis, may suggest a vasovagal episode or a seizure. Many older adult patients report presyncopal episodes along with true syncopal events. In adults older than age 65, only 5% of the causes of syncope can be determined by history alone as compared to 25% of cases in patients below age 65. Determine whether any focal neurological symptoms were present (i.e., diplopia, motor and sensory symptoms). Review significant past medical history, prior history of an event, all medications being used, and alcohol intake. Evaluating the timing of the syncopal event to meals, physical activities, and length of the prodromal symptoms help in determining neurally mediated syncope from cardiac etiology. Ask about family history for sudden cardiac events. Rapid onset and complete recovery are key diagnostic symptoms along with loss of motor tone. If any one of these symptoms is absent, nonsyncopal causes must be considered. It is possible to have generalized jerking movements with syncope that occur after the loss of consciousness. Rapid reorientation can distinguish this presentation of syncope from a seizure disorder. The physical examination should start with checking the patient for evidence of trauma, then focus on the cardiovascular and neurological components. Check blood pressure in both arms and positionally. Determine the compensatory pulse rate. Check the carotids for bruits. Carotid sinus compression sometimes is used to provoke symptoms, but this should be done cautiously and selectively and is contraindicated in patients with a bruit or a history of stroke or myocardial infarction. Examine the heart, assessing for murmurs, signs of arrhythmia, vascular disease, and left ventricular dysfunction. Check oxygen saturation rates. Perform a thorough neurological examination, paying particular attention to focal abnormalities that may suggest neurological syncope. Generalized anxiety disorders can cause hyperventilation and trigger a vasodepressor reaction; this should be evaluated during the physical examination.

Diagnostic Tests: The ECG is the most important diagnostic test with a focus on the rate and rhythm. Diagnosis of cause from the ECG is very low at 2% to 9%, but it is inexpensive and when positive for disease, critical to proper intervention. Positive findings may include sinus bradycardia, prolonged PR interval, a bundle branch block, or ventricular ectopy. Additional laboratory and imaging studies should be ordered only if clinically indicated by the history and physical examination. Extensive diagnostic testing of patients with syncope contributes to increased health-care costs with low diagnostic yield. Additional diagnostic work-up frequently is required in older adult patients (Geer, 2021; Runser et al., 2017; Shen et al., 2017). Cardiac diagnostic studies may include echocardiogram (valuable in estimating ejection fraction and valvular heart disease), ambulatory ECG monitoring, particularly implantable loop recorders, and electrophysiological studies. A stress test is not indicated unless the event occurred during exercise or was accompanied by chest pain. A chest x-ray, which may reveal cardiomyopathy, is indicated in patients with new abnormal findings and in patients with dyspnea. Electroencephalogram and computed tomography (CT) scan of the head are reserved for patients with focal neurological abnormalities. Vasovagal syncope may be induced with tilt-table testing, which may be done with or without isoproterenol.

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It is useful in patients with syncope of unknown etiology or patients with recurrent syncope. Laboratory evaluation is generally of low yield but may include a complete blood count (CBC) with differential if infection or anemia is suspected. Renal function studies and electrolytes may also be considered.

Differential Diagnosis: Distinguish syncope from seizures, dizziness, drop attacks, orthostasis, postprandial hypotension, carotid sinus sensitivity, and arrhythmias. Atypical presentations include myocardial infarction (MI) and pulmonary embolism (PE). Dizziness does not involve a loss of consciousness and is often characterized further as vertigo, light-headedness, disequilibrium, or presyncope (sensation of impending loss of consciousness). Drop attacks are sudden drops without warning and may be due to transient basilar artery insufficiency at times precipitated by head movement or neck hyperextension. Metabolic disorders (hypoglycemia, hypoxemia) cause coma/somnolence rather than syncope. Orthostatic hypotension reflects a drop in blood pressure of 20 mm Hg systolic or 10 mm Hg diastolic after changing from a lying to a standing position and is taken 1 minute after standing and again 3 minutes after standing. Consider the relationship to meals with a drop in blood pressure. Carotid sinus sensitivity and arrhythmias (atrioventricular block, sick sinus syndrome, and supraventricular arrhythmias) increase with age. Supraventricular arrhythmias rarely cause syncope, but ventricular tachyarrhythmias, especially those with decreased ejection fraction, are a major concern.

Treatment: When you identify the specific cause of syncope, you can initiate the appropriate treatment. Hospitalization may be required when there is a high risk of death, recurrence, or injury. Twenty-four-hour observation may be an option for patients with confusing presentation. Vasodepressor syncope is best addressed with volume expansion. Six factors predictive of adverse outcomes were noted in almost all research focused on risk stratification: acute coronary syndrome, HF, structural heart disease, abnormal ECG, anemia, or hemodynamic instability. Antiarrhythmic therapy is initiated, if indicated, and drug-induced or idiopathic orthostatic hypotension is treated appropriately. Cardiac pacing may be appropriate. Cardiac surgery is the treatment of choice for obstructive heart disease. Always correct underlying anemia and metabolic imbalance and optimize cardiac and pulmonary status in the older adult patient. Address any age-related, disease-related, or disuse-related changes that impair the patient's compensation for hypotensive stressors, such as dehydration, deconditioning, and orthostatic hypotension. Nonpharmacological approaches to vasodepressor syncope include tilt-table training and lower extremity muscle tensing.

Follow-Up: Unknown causes precipitate a high incidence of syncopal events and in one-third of patients, syncope is a recurring event. Because recurrences may reflect lack of effective therapy or a failure to diagnose correctly, close monitoring is indicated.

Sequelae: Syncope from cardiovascular causes tends to be more dangerous. Sudden death with syncope has been attributed to arrhythmia. Patients with syncope are at risk for fall-related injury (fracture, subdural hematoma) and reduced functional capacity.

Prevention/Prophylaxis: Patients with vasovagal syncope are taught to avoid triggers and, if premonitory symptoms occur, to lie down immediately and elevate the feet higher than the chest. Adequate fluid intake is a precaution, and for selected individuals with vasovagal syncope, a higher salt intake may be advised. Support hose may help prevent reduction in central plasma volume. Patients are encouraged to avoid a sudden change in position. For syncope caused by atrial fibrillation, low-dose warfarin or aspirin therapy may be prescribed. Micturition syncope can be avoided by advising men to sit down to urinate.

Referral: Hospitalization is necessary for patients in whom you suspect an arrhythmia or MI as the cause of the syncope and for patients who sustain significant injury during the syncopal event. Consultation may be appropriate with a cardiologist for managing cardiac syncope and with a neurologist for managing neurally mediated syncope. Primary care providers can facilitate urgent referrals for patients to specialists for further syncope evaluation (Shen et al., 2017).

Education: In addition to teaching preventive strategies and the avoidance of triggering events, teach individuals with recurrent syncope safety precautions related to driving or the use of dangerous machinery. It is prudent for the health-care professional to understand the driving laws of the state relative to loss of consciousness/syncope.

Clinical Recommendation	Evidence Rating	References
In the initial evaluation of patients with syncope, a resting 12-lead electrocardiogram is useful.	B	Shen et al., 2017
Evaluation of the cause and assessment for the short- and long-term morbidity and mortality risk of syncope are recommended.	B	Shen et al., 2017
Laboratory and imaging studies should be ordered for patients with syncope only if clinically indicated by the history and physical examination.	B, C	Geer, 2021 Runser et al., 2017 Shen et al., 2017
It may be reasonable to manage selected patients with suspected cardiac or reflex-mediated syncope in the outpatient setting in the absence of serious medical conditions.	C	Shen et al., 2017
Implantable loop recorders increase diagnostic yield, reduce time to diagnosis, and are cost effective for suspected cardiac syncope and unexplained syncope.	B	Runser et al., 2017 Shen et al., 2017

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TREMOR

Description: Tremor is the most common form of involuntary movement and is characterized by an intermittent or continuous rhythmic oscillation of a body part that can be classified according to the circumstances under which it occurs. Tremors may result from physiological or pathological processes.

Etiology: Tremor can be classified as genetic, acquired, or idiopathic. It can be an isolated symptom such as a physiological tremor or a symptom associated with a neurological or medical disorder. Although many people experience a physiological tremor or enhanced physiological tremor, they often do not seek medical care. Therefore, the two most commonly diagnosed causes of tremor are essential tremor (ET) followed by tremor related to Parkinson's disease (PD). Other causes of tremor include but are not limited to multiple sclerosis, Wilson's disease, dystonia, brain injury from stroke or trauma, hyperthyroidism, alcohol abuse or withdrawal, some medications, and liver or kidney failure. Some individuals may also experience a functional tremor, not to be confused with malingering.

Occurrence: Tremor is the most common movement disorder encountered in clinical practice. Enhanced physiological tremor is very common and may surface with anxiety, fatigue, caffeine, or other medications and normalizes when the contributing cause is removed or managed (Bhatia et al., 2018). Eight times more common than PD, essential tremor affects 10 million Americans (International Essential Tremor Foundation, 2021).

In 50% of those with ET, the disease is familial (autosomal dominant, meaning their child has a 50% chance of also having ET). Approximately 1 million Americans have PD (Parkinson's Foundation, 2021), but not all people with PD have a tremor. Less common types of tremor are cerebellar tremor, functional tremor, dystonic tremor, and tremor associated with Wilson's disease or other medical conditions or diseases. Essential tremor occurs in both sexes equally, with Parkinson's disease more common in men than in women.

Age: Most studies report a significant age-associated increase in the prevalence of essential tremor. It may start at any age with a median age of 45 years old (International Essential Tremor Foundation, 2021) and will most likely intensify with age. Tremor in older adults is more likely to be of the essential or parkinsonian type than other tremor types noted. While the average age of onset is 62, 4% of individuals with PD are younger than 50 (Parkinson's Foundation, 2021).

Ethnicity: Tremor is most prevalent in Whites, followed by Black, Asian, and Hispanic individuals, though the latter ethnic groups are often underrepresented.

Contributing Factors: During times of stress, the amplitude of a tremor may increase. Fatigue, anxiety, hyperthyroidism, systemic illness, use of medications, drug withdrawal (especially from alcohol), use of methylxanthines, and excess caffeine intake can exaggerate tremors of all types as well. Medications that can cause or exacerbate tremors include those that stimulate the sympathetic nervous system and psychoactive medications.

Signs and Symptoms: Terms used to describe the clinical phenomenology of tremors include rest tremor and action tremor. *Rest tremor* occurs when a muscle is not activated voluntarily, and the relevant body part is fully supported against gravity, whereas *action tremor* is present with voluntary contraction of a muscle. Action tremors can be subclassified further into postural, kinetic, and isometric tremor. *Postural tremor* is present while voluntarily maintaining a position against gravity. *Kinetic tremor* may occur during any form of voluntary movement of the affected body part. *Isometric tremor* occurs with muscle contraction against a rigid stationary object. The first step in evaluating tremors is categorizing the tremor based on activation conditions, distribution, and frequency. Determine the duration and age of onset of symptoms, exacerbating or alleviating factors such as alcohol (some individuals with essential tremor have a temporary improvement when drinking alcohol), and any family history of tremor or other neurological disorders. Include any associated symptoms, such as bradykinesia or rigidity (suggesting PD) or ataxia and nystagmus (suggesting cerebellar disease). The patient's medication history, any exposure to toxins, and the presence of illness should be noted. The impact of the tremor on the patients' ability to perform their ADLs and IADLs, as well as their self-assessment of their quality-of-life, will further help quantify the impact of the tremor.

It is critical to conduct a thorough tremor-focused neurological physical examination. When assessing for rest tremor, patients should be evaluated while supine and seated with the hands dangling or in a relaxed position with the forearms fully supported. (If patients are in a position that does not provide complete support, certain muscles may be active against gravity, producing a tremor that may be classified improperly as a resting tremor.) After rest tremor is identified or ruled out, the patient performs other maneuvers to assess for action tremor.

The upper extremities are examined in an outstretched position with the hands supine (palms up), sideways (semiprone), and then prone (palms down). Having the patient spread their fingers can help to identify myoclonus, a symptom that is often mistaken for tremor. In the wing-beating position (i.e., with opposing fingers held close to each other but not touching in front of the mouth), proximal tremor may be identified. Goal-directed activities are performed, such as finger-to-nose, heel-to-shin, pouring water between cups, writing, and drawing. The latter is done by obtaining handwriting and drawing samples (e.g., script, numbers, Archimedes spirals). Patients with essential tremor typically have shaky and large handwriting, whereas the handwriting of patients with PD initially may be of average size and progressively becomes smaller (micrographia). Archimedes spirals drawn by individuals with essential tremor tend to illustrate natural fluctuations in tremor magnitude. Cranial structures (including the mouth and jaw) are examined at rest and in action, and the tongue is observed during rest and protrusion to assess for vocal tremor. This can be done with normal conversation, or the patient is asked to recite a standard paragraph and enunciate a sustained vowel. Abrupt changes in tremor, entrainment and distractibility are signs the tremor may be functional.

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Careful evaluation is also performed, looking for signs associated with tremor syndromes. Muscle tone is checked throughout the body. Bradykinesia and postural abnormalities are evaluated by observing difficulty rising from a seated position, decreased arm swing, and masked facies. Gait is evaluated for shuffling and unsteadiness, and Romberg (station) and balance testing are conducted.

Diagnostic Tests: The diagnosis of tremor is primarily clinical; however, laboratory testing may be necessary to exclude certain conditions associated with tremor, such as metabolic disturbances, including hyperthyroidism (e.g., through thyroid function tests) and Wilson's disease. Brain imaging may be indicated for select patients, particularly patients with unilateral tremor, sudden onset, or atypical clinical features. For complex cases, nuclear imaging such as a DaT-SPECT scan or, more rarely, an F-DOPA PET scan can differentiate essential tremor from PD, but these tests do not always differentiate PD from atypical parkinsonism.

Electromyography can be but is not frequently used to subdivide tremors according to their rate and relationship to the posture of limbs and volitional movement. Genetic testing may be done if indicated.

Differential Diagnosis: The differential diagnosis, in general practice, is often between PD and essential tremor, but there are many causes of tremor as previously noted, and a few are discussed further below. Other symptoms such as myoclonus, dystonia, and ataxia may be mistaken for tremor.

Physiological Tremor. A normal phenomenon, physiological tremor may occur in all contracting muscle groups. Although seldom visible to the naked eye, physiological tremor often may be detected when the fingers are firmly outstretched with a piece of paper placed over the hands.

Enhanced Physiological Tremor (or an Intensification of Physiological Tremor to Detectable Levels) (8–12 Hz). Physiological tremor may be enhanced under conditions of stress, anxiety, fatigue, exercise, cold, hunger, stimulant use, alcohol withdrawal, or metabolic disturbances such as hypoglycemia or hyperthyroidism. It is often difficult to distinguish it from essential tremor clinically.

Essential Tremor (4–12 Hz). Essential tremor is a persistent postural and kinetic tremor that predominantly affects the hands and forearms. A resting component is present only rarely and typically occurs in the most advanced cases. Although less frequently involved than the hands, tremor in the head or voice is a strong indication of essential tremor and is especially useful in differentiating the syndrome from PD. Head tremor, which is also postural, disappears when the head is supported. Listening to the patient speak or holding a musical note as long as possible may reveal a quivering intonation. The legs are affected less often.

Parkinsonian Tremor Syndromes (4–7 Hz). Parkinsonian tremor syndromes involve resting tremor that is often asymmetrical. Tremor may be observed when muscles are relaxed, such as when the hands are resting on the lap, and may affect the upper and lower extremities, the mandible, and lips. Tremor may disappear during sleep. Typical is an alternating tremor of the thumb against the index finger—*pill-rolling tremor.* Although rest tremor is a diagnostic criterion for Parkinson's disease, tremor in other positions may also be present.

Treatment: Only a small fraction of persons with tremor seek medical attention. However, tremor should be treated if it causes disability or affects their emotional well-being, as, for many, tremor can cause significant social distress. When there is a lack of response to medical treatment or when tremor results in severe disability, a patient may be considered for a referral to neurosurgery. Specific treatments for the most common causes are noted next.

Physiological Tremor. Usually, no treatment is required for physiological tremor. When exaggerated, however, it may interfere with activities requiring extreme precision or cause social embarrassment. Identify and remove precipitating and contributing causes. If the precipitating cause cannot be removed, propranolol may be effective.

Essential Tremor. According to the 2019 International Parkinson and Movement Disorder Society commissioned task force's evidence-based review of treatment for essential tremor, primidone, propranolol, and topiramate (greater than 200 mg daily) are the only medications considered efficacious (Ferreira et al., 2019). Alprazolam and Botulinum toxin type injections for certain types of tremors were found to be likely efficacious. Many other medications are often tried, but the task force found them either inefficacious or with insufficient evidence to determine the effectiveness.

If a medication is documented to be beneficial, it may be continued at the regulated doses, and the subsequent medication may be added to the drug regimen. If the response to a drug is adequate and the dose is well tolerated, monitor tolerance and possibly increase the dose. If the medication is of no benefit at a dose that causes adverse effects, dose levels should be tapered down gradually and eventually discontinued. Although the response to alcohol may help diagnose essential tremor, alcohol should not be used as a treatment. Not only does it cause a rebound tremor, but tolerance can be developed, and it can cause alcoholism, accidents, and damage to the body.

Parkinsonian Tremor. The tremor of PD results from a loss of striatal dopamine, and this is the rationale for treatment with either the dopamine precursor levodopa or dopamine receptor agonists. Anticholinergic medications such as trihexyphenidyl (Artane) are also used but may have undesirable cognitive and other side effects in older adults. The combination of carbidopa with levodopa reduces levodopa-induced nausea. There are other formulations of levodopa, including a levodopa-carbidopa intestinal gel (brand name Duopa) that is dosed for 16 hours during wakefulness. It is administered via a PEG-J tube supplied by an external pump. This dosing route decreases tremor by reducing plasma fluctuations that patients on oral levodopa and carbidopa might experience. See Chapter 17 for further discussion on the treatment of PD.

Functional Tremor. A comprehensive approach involving a movement disorders neurologist, a psychologist, and a physical therapist (PT) provides the best treatment for those experiencing a functional tremor. Patients with severe tremors resistant to pharmacotherapy may benefit from deep brain stimulation (DBS), or magnetic resonance imaging-guided focused ultrasound thalamotomy (product name ExAblate Neuro) is successful in treating essential tremor. Many consider this approach noninvasive because it is incisionless, but it creates an irreversible lesion in the brain.

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Follow-Up: Patients should be evaluated for therapeutic effects and side effects within one week of starting treatment. Routine monitoring for weight loss, depression, and decline in functional status are necessary.

Sequelae: Functional disabilities may occur in activities of daily living (ADLs), including compromised eating, drinking, and preparing food. Decreased caloric intake and weight loss may be observed. Ambulation, especially on stairs, maybe hazardous as many people with tremors also have balance problems. Withdrawal from social situations may occur, and depression is common.

Prevention/Prophylaxis: Reduce factors that can exacerbate the tremor. Continue medication regimen.

Referral: A neurologist, specifically a movement disorder specialist, should be consulted for cerebellar tremors, mixed tremors, parkinsonian tremors, challenging to treat essential tremor, or when a focal neurological deficit is identified. Physical therapy and occupational therapy (OT) should be initiated early on and may continue to be helpful throughout all stages. These specialists often make recommendations to improve functionality and quality of life, such as weighted silverware, special writing tools, and other adaptive devices. Some patients may experience benefits with biofeedback, relaxation methods, and other behavioral techniques by alleviating anxiety or stress that may exacerbate tremors.

Education: When a diagnosis has been established, the natural history of the condition should be explained to patients. They should be encouraged to learn as much as possible about their disease to empower them throughout the progression of the disease. Referral to appropriate disease-specific support organizations is helpful for many patients. It also may be appropriate to recommend counseling. Appropriate coping strategies may reduce stress substantially, preventing possible augmentation of tremor owing to anxiety and may also prevent depression.

Clinical Recommendation	Evidence Rating	References
The diagnosis and classification of tremor is based on clinical information from the history and physical examination.	C	Bhatia et al., 2018
Propranolol, primidone, and topiramate are efficacious treatments for essential tremor.	A	Ferreira et al., 2019
Alprazolam, botulinum toxin type A, unilateral DBS of the ventral intermediate (VIM) nucleus, and unilateral focused ultrasound thalamotomy are likely efficacious.	A	Ferreira et al., 2019
Levodopa-carbidopa intestinal gel improves tremor at rest.	B	Fernandez et al., 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

URINARY INCONTINENCE

Description: Urinary incontinence (UI) is an involuntary loss of urine (Davis et al., 2020). It is common in the older adult. Urinary incontinence is often underreported and can lead to significant consequences, such as falls from attempting to reach the toilet before incontinence occurs or slipping on a wet floor from the incontinence, dermatitis and skin breakdown due to constant moisture, social isolation due to trying to stay near a toilet, depression, and increased caregiver stress. It can be distressing and affect a person's overall quality of life (Batmani et al., 2021; Davis et al 2020).

The detrusor muscle of the bladder is an interlacing bundle of smooth muscle. It relaxes to store urine and contracts to empty the bladder. Alpha-adrenergic activity causes the urethral sphincter to contract (sympathetic activity) and beta-adrenergic innervation causes relaxation of the urethral sphincter (parasympathetic activity). The person's anatomical position can assist in bladder control and is another factor to consider.

There are five types of urinary incontinence: stress, urge, overflow, mixed, and transient (sometimes referred to as functional) (Kolodynska et al., 2019). The most common type is stress incontinence, or outlet incompetence, which occurs in a reported 55% to 88% of all types of incontinence. Urge incontinence, or detrusor overactivity, results when there is an imbalance of inhibitory and excitatory activity and affects 17.4% of women and 15.6% of men (Kolodynska et al., 2019). Overflow incontinence, commonly due to outlet obstruction or detrusor underactivity, results in a loss of urine when the amount of urine exceeds the capacity of the bladder. Mixed incontinence is a combination of UI and overactive bladder and is not uncommon in older adults which can make management more challenging. When there is a normal urinary system but incontinence occurs, it is often due to problems with immobility or cognitive impairment and is referred to as transient or functional UI. It may also be a result of acute illness or the effects of medications and is self-limiting when the cause is determined and addressed. Table 7-10 describes the various types of UI and management strategies.

Etiology: The causes and management of UI are multifactorial, depending on the type of incontinence and the severity

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TABLE 7-10 Types of Urinary Incontinence

TYPE OF URINARY INCONTINENCE	DESCRIPTION/SYMPTOMS	PATHOPHYSIOLOGICAL CHANGES CAUSE UI	COMMON CAUSES	
Stress Incontinence [accounts for up to 88% of all UI]	Leakage of urine caused by increased abdominal pressure associated with standing, bending, lifting heavy objects, sneezing, coughing, laughing, etc.	Weakening of the pelvic floor muscles and failure of complex musculo-ligamentous-fasciocutaneous tissues	Childbirth, trauma, hormonal disorders and a reduction in reproductive organs in abdominal cavity (uterine shrinkage or absence), and surgeries	Lifestyle interventions Behavioral therapies
Urge Incontinence [affects 17.4% of women and 15.6% of men]	A result of an imbalance between inhibitory and excitatory mechanisms' detrusor activity which results in a disorder of micturition Urine leakage associated by or immediately preceded by the feeling of an urgent need to void.	a) CNS damage above bridge – causing detrusor overactivity while reducing the capacity of the bladder b) Spinal cord at the level of S_2–S_4 – at this level there is a micturition center-the bladder is autonomous in relation to the nervous system and has lost the ability to effectively cause shrinkage of residual urine c) Damage to the spinal cord above the level of S_2–S_4 – urination reflex depends on the Parasympathetic nervous system, and the bladder compresses effectively, but is done rather unexpectedly and involuntarily	a) Stroke, dementia, Parkinson's disease b) S_2–S_4 spinal cord damage causing the individual to lose the capacity for reflex emptying c) Spinal cord damage above the level of S_2–S_4 affecting the parasympathetic nervous system	Lifestyle interventions Behavioral therapies Consider trial of antimuscarinic medications
Overflow Incontinence (OI)	The bladder accumulates a urine volume greater than the maximum capacity of the bladder Urine leakage occurs when the bladder is over-distended and may result in incomplete bladder emptying Symptoms can present as constant dribbling, frequency, hesitation when initiating urination, and nocturia	Increased pressure in the bladder causes the urine to flow through the urethra-may occur as a result of the presence of an outflow obstruction (such as prostate hypertrophy)	Associated with bladder outlet obstruction, such as benign prostatic hypertrophy in men and pelvic organ prolapse in women. Neurogenic bladder can also present as overflow UI	Assess for the cause such as medications and fluid intake Double voiding to empty residual urine from bladder
Mixed Incontinence (MI)	A combination of symptoms of UI with stress and urge incontinence, marked by involuntary leakage associated with urgency and also with exertion, effort, sneezing, or coughing.	Same mechanisms as SI & UI	see SI & UI	See Management of Stress Incontinence and Urge Incontinence
Transient Incontinence (TI) and Functional Incontinence	Acute onset of urinary incontinence associated with an illness, an injury, or a new medication. The inability to hold urine due to reasons other than neurological and lower urinary tract dysfunction including delirium, psychiatric disorders, UTI, or impaired mobility	Any temporary change in the patient's ability to identify the sensation of a full bladder and the need to urinate, such as an acute delirium or the result of a medication	Acute confusion, a side effect of a medication such as diuretics, or damage to the nerves affecting muscle control of the urination process	Treat the underlying cause.

Sources: Davis et al., 2020; Kolodynska et al., 2019

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and impact on quality of life for the individual. Anatomical changes, factors related to the individual's medical history, lifestyle, and acute and chronic illnesses, in addition to medications, can result in incontinence that can be either reversible or evolve into a permanent condition. Cognitive as well as chronic mental illness, depression, and functional barriers to continence can also affect an individual's ability to maintain urinary continence.

Occurrence: Urinary incontinence affects 43.8% of Americans older than 65 living in the community and 70.3% of long-term care residents (Davis et al., 2020). It is often underreported because it is accepted as a normal part of the aging process (Kolodynska et al., 2019).

Age: Urinary incontinence affects all age-groups, with the highest prevalence in older adults who live in residential facilities, have cognitive impairment, and have functional limitations including but not limited to frailty. UI is twice as prevalent in women as in men, and the incidence increases with age, with those living in residential facilities, and those who have at least one deficit in activities of daily living (ADLs) (Davis et al., 2020; Kolodynska et al., 2019). In males, prostate enlargement may cause urinary obstruction and a weaker bladder stream due to a partial outflow obstruction leading to urinary retention and overflow incontinence. In males who have had a radical prostatectomy, frequently there is a transient UI for up to 12 weeks with an average of 7% having long-lasting UI (Cleveland Clinic, 2021). In females there are decreased estrogen levels which weakens bladder muscles and increases more space in the pelvic cavity as the uterus atrophies or has been surgically removed. Women are at higher risk for stress incontinence and overflow incontinence is more prevalent in men.

Ethnicity: In a meta-analysis of multiple studies in older adults who experience UI in the age range of 55 to 106 years, the highest prevalence of UI was among women in Asia with 45.1% (Batmani et al., 2021).

Contributing Factors: There are many physical changes that occur with aging, and these changes may contribute to the predisposition for UI including decreased bladder capacity, increased involuntary bladder muscle contractions, increased nighttime urine production, and alterations in immune function. Cognitive losses that frequently present in this population can affect a person's ability to recognize bladder distention and determine the appropriateness of voiding at a specific time and place. The many contributing factors for UI include pelvic muscle weakness, multiparity, estrogen depletion, pelvic organ prolapse, diabetes, stroke, multiple sclerosis, Parkinson's disease (PD), spinal cord injury, benign prostatic hyperplasia, urinary tract infection (UTI), fecal impaction, poor fluid intake or excessive fluid intake, smoking, cognitive impairment, depression, immobility or impaired mobility, environmental barriers, impaired dexterity, visual impairment, obesity, and high-impact physical activities. Incontinence can be a side effect of many medications, including cholinergics, anticholinergics, diuretics, antispasmodics, opiates, hypnotics, calcium channel blockers, angiotensin-converting enzyme (ACE) inhibitors, alcohol, and caffeine.

Signs and Symptoms: In screening for UI it is important to evaluate whether symptoms are transient or persistent in nature. A thorough history should include:

- The severity and quantity of urine lost, including use of pads or adult briefs
- Onset and duration of the problem and whether the UI is worsening
- Triggering factors or events, including sneezing, coughing, laughing, or during activity
- Constant versus intermittent urine loss
- Associated frequency, urgency, dysuria, pain with a full bladder
- History of UTIs
- Association with fecal incontinence or pelvic organ prolapse
- Additional medical problems, including current or past cancers of the pelvic organs (prostate or uterus), congestive heart failure (HF), chronic obstructive pulmonary disease (COPD), cognitive impairment, and connective tissue disorders
- Obstetrical history, including difficult deliveries, multiparity, and large babies
- History of pelvic surgeries or other urological procedures, including use of indwelling urinary catheters
- History of spinal or central nervous system (CNS) problems and/or surgeries
- Lifestyle issues, including use of tobacco, alcohol, or caffeine; occupational or recreational factors causing severe or repetitive increases in intra-abdominal pressure
- Medications, including use of the following medications that have been associated with UI: cholinergic or anticholinergic agents, alpha blockers, over-the-counter (OTC) allergy medications, estrogen replacement, beta-mimetics, sedatives, muscle relaxants, diuretics, and ACE inhibitors
- Effect of these symptoms on ADLs, socialization, and relationships, including sexual activity

Considering that approximately 10% of nursing home admissions are a result of UI, discussion with patients and caregivers before long-term care placement about symptoms has the potential to prolong the individual's ability to remain at home for a longer period of time.

Physical examination should include functional assessment with special attention to mobility, including ability to ambulate to the toilet, and dexterity, including the person's ability to remove necessary clothing in time to use the toilet. Vital signs should be assessed, looking for the presence of an elevated temperature. Respiratory rate and the presence of dyspnea on exertion may affect continence due to limited stamina to complete necessary tasks for maintaining continence. Mental status, including cognition and evidence of depression, should be assessed. The abdomen should be examined for clues such as bladder distention, pelvic masses, inguinal lymphadenopathy, or tenderness in the suprapubic region. Bladder distention can be found in overflow incontinence secondary to obstruction. In women, malignancy, uterine fibroids, or organ prolapse in the pelvic region creates pressure on the bladder seen in urge, stress, or mixed incontinence. A vaginal examination may also reveal poor perineal hygiene, skin breakdown from urine soaking, or redness and thinning of tissue typical of atrophic changes. Prolapse of genitourinary structures or the rectum may also be seen.

To assess for pelvic floor muscle strength and relaxation, instruct the patient to bear down as though having a bowel

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movement, then tighten or squeeze by pulling up with the pelvic floor muscles. In patients with pelvic floor relaxation, you can see the inability to contract or weak contractions and feel a lack of muscle tone when testing during the vaginal examination. Have the patient cough and determine whether leakage occurs. Urethral discharge in male patients should also be assessed. Positive neurological findings in the perineal area include hypersensation, hyposensation, or absence of the bulbocavernosus (anal wink) reflex. A rectal examination may reveal fecal impaction, rectal prolapse, hemorrhoids, masses, or, in men, prostatic enlargement. Whenever possible, the examiner should observe the patient voiding, having the patient void into a measurable receptacle. This should be followed by evaluation of a post-void residual (PVR) urine by ultrasound of the bladder or catheterization. Studies are inconclusive with respect to the amount of PVR that is significant, with values ranging from greater than 50 mL to greater than 200 mL.

Diagnostic Tests: Initial evaluation for UI should include a urinalysis to rule out UTI and renal abnormalities. This has great significance when UI has an acute onset. Older adults have a high rate of asymptomatic bacteriuria. Referring to the McGeer definitions for UTI can increase accurate diagnosis and avoid antibiotic misuse or overuse (Ryan et al., 2018). In addition to the presence of nitrites and leukocyte esterase in the urinalysis, the McGeer definition includes new-onset incontinence and the presence of symptoms including hematuria, pain and or fever. When a UTI is suspected, a culture and sensitivity should be ordered to assess if the bacterial colony count is high enough to qualify as a UTI and to ensure appropriate antimicrobial therapy. Hematuria may indicate a number of diagnostic possibilities including infection, obstruction, kidney stones, or malignancy. Proteinuria is revealing for renal disease and is often associated with poorly controlled diabetes. When renal, metabolic, or obstructive causes of urinary tract dysfunction are suspected, a basic metabolic panel is recommended to evaluate elevated blood urea nitrogen (BUN) and creatinine levels and calculate estimated glomerular filtration rate (eGFR) to evaluate for renal disease. Measurement of PVR may reveal incomplete bladder emptying.

When symptoms and basic noninvasive evaluation does not clearly indicate the type of urinary tract dysfunction, and the individual indicates that UI is problematic enough to warrant further treatment, referral to a urologist or urogynecologist for urodynamic testing is indicated. Urodynamic testing evaluates all stages of lower urinary tract function, including filling and storage, as well as bladder outlet abnormalities. Subjective reporting by the patient of sensation such as urgency can also be evaluated with respect to bladder wall compliance, detrusor overactivity, pressure, and flow measurements during testing. Cystoscopy is indicated for evaluation of hematuria to visualize the bladder wall when cancer is suspected, or when a stricture or prostate enlargement is suspected with symptoms of urinary retention.

Differential Diagnosis: UI is a symptom, not a diagnosis. The two mnemonics DRIP and DIAPERS often are used to differentiate transient (acute) from persistent urinary incontinence:

Mnemonic: DRIP
- **D**elirium
- **R**estricted mobility
- **I**nfection
- **P**harmaceuticals, polyuria

Mnemonic: DIAPERS
- **D**elirium
- **I**nfection, impaction, inflammation
- **A**trophic vaginitis
- **P**sychological, pharmaceuticals, psychotropics
- **E**ndocrine problem
- **R**estricted mobility
- **S**tool impaction

Treatment: Management of UI will depend on the type of incontinence; the patient's preference regarding their perception of how UI affects their lifestyle; and the patient's ability to tolerate treatments, surgical procedures, and risk for adverse effects, as well as complications of medications or treatment regimens. For transient UI, treating, eliminating, or modifying the cause usually alleviates the symptom. Delirium or a mild elevation in temperature from the patient's baseline, rather than a fever, may be the first indication of a UTI in the older adult. Appropriate treatment includes increasing water intake and examining a urinalysis with a culture and sensitivity if indicated (i.e., if the bacterial colony count is greater than 10,000, antimicrobial treatment may be indicated if symptoms persist after increasing water intake, it is warranted that assessing the bacteria's sensitivity to antibiotics guide antibiotic therapy choices due to widespread antibiotic sensitivity).

Lifestyle management using behavioral therapies and pelvic muscle exercises (Kegel exercises) can be an effective treatment for stress and urge incontinence, performed alone or in combination with biofeedback, to help strengthen periurethral muscles. A referral to a physical therapist (PT) who specializes in pelvic floor exercises is an excellent choice to support treatment. Toileting programs (see Table 7-11) can be effective interventions for decreasing the impact of or controlling UI, even in patients with cognitive impairment. Nocturia can be a very annoying problem and cause significant issues where quality of life is concerned. Control of comorbidities and symptoms of fluid overload such as HF and other causes of edema, in addition to limiting fluids before bedtime, can be helpful to improve sleep hygiene.

Pharmacological treatment for urge incontinence with anticholinergic drugs is effective for symptoms; however, they are not without potential side effects, especially constipation, blurred vision, gait abnormalities, and cognitive changes in older adults. These medications, such as tolterodine (Detrol) and oxybutynin (Ditropan), seem to be better tolerated in long acting and transdermal forms. Drugs that are more selective for muscarinic-3 receptors, such as darifenacin (Enablex), solifenacin (Vesicare), and trospium (Sanctura), which do not appear to cross the blood-brain barrier, appear to have a better side-effect profile, and are better tolerated in the older adult population. Patients need to be informed that these medications may take 4 to 6 weeks to experience the full benefit.

Comorbidities such as narrow-angle glaucoma and potential interactions with other medications are always a concern in the older adult population and should be considered before prescribing a drug regimen for UI. In certain situations, estrogen replacement therapy may be considered in women younger than age 65 but caution should be used due to the potential for increasing the risks of developing or worsening

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TABLE 7-11 Lifestyle Measures and Behavioral Therapies for UI Management

Lifestyle measures	Weight loss
	Fluid management-restricting fluids
	Avoiding alcohol, caffeine, and carbonated beverages
	Avoiding constipation
Behavioral therapies	Pelvic floor exercises including Kegel exercises: • Identify the muscle that starts and stops urination through attempts to start and stop urinating • Contract the identified muscle for approximately 8–10 seconds, and then relax the muscles • Perform 8 to 12 contractions • Repeat 3–4 sets of repetitions daily
	Bladder training: • Prompted toileting: Ask the individual to void more often • Habit training: Identifying the toileting pattern including UI episodes, schedule toileting routine to prevent UI episodes • Timed toileting: Scheduled toileting at fixed intervals • Combined toileting and exercise therapy: Incorporates pelvic floor strengthening exercises and bladder training interventions • Double voiding: Empty bladder, relax for 1–2 minutes, then lean forward and/or press on bladder and attempt to void again, emptying the remaining urine from the bladder

Source: *Batmani et al., 2021.*

dementia and increasing the risks of breast cancer. Vaginal or topical estrogen therapy can be an effective remedy for UI as a result of vaginal atrophy. It has a low systemic absorption, but still should be used with caution in women who have a history of breast cancer. Studies have also indicated that the antidepressant duloxetine (Cymbalta) when used in combination with pelvic floor exercises can be an effective treatment for stress UI (Davis et al., 2020).

For patients with overflow incontinence secondary to prostatic hypertrophy, 5-alpha-reductase inhibitors, finasteride (Proscar), or dutasteride (Avodart) are effective to reduce prostate volume by preventing the conversion of testosterone to dihydrotestosterone. These medications take up to 6 months to achieve their maximum benefit. A baseline prostate-specific antigen (PSA) is recommended because the reduction in size of the prostate decreases the PSA and may mask an actual increase. These drugs should not be handled by women of childbearing age because they can be harmful to the development of a male fetus. Selective alpha-adrenergic antagonists such as tamsulosin (Flomax) relax smooth muscle to reduce urethral resistance and improve urine flow. Nonselective alpha-1 blockers such as doxazosin (Cardura) and terazosin (Hytrin) are effective for UI and can also be used in patients who also require antihypertensive therapy. The provider should consider, however, the cardiovascular side effects due to their nonselectivity. Orthostatic hypotension is an adverse reaction that can have serious consequences, such as increased fall risk and injuries, in the older adult patient. Daily tadalafil (Cialis) 5 mg was approved for the treatment of benign prostatic hypertrophy in 2011. It works by increasing the blood flow to the prostate and improving lower urinary tract symptoms. It should not be taken with an alpha adrenergic antagonist, but it may be used with a 5-alpha-reductase inhibitor.

Other treatments for UI include bulking agents such as collagen for stress incontinence, botulinum toxin, sacral nerve stimulation for urge incontinence, and surgical interventions for stress incontinence in women and for prostatic hypertrophy in men. Referral to urology or urogynecology for surgical intervention is appropriate if the patient is inclined to consider surgical intervention and is physically able to tolerate the procedure. Surgical management for pelvic organ prolapse to improve organ support, such as retropubic suspension, sling procedures, and vaginal mesh, are viable options; however, patient education with regard to the high failure rate (10% to 20%) should be discussed when considering these options. In 2008, the FDA warned of potentially serious complications associated with the use of surgical mesh, and in July 2018 they placed it on a "High Vigilance Pause" for pelvic organ prolapse, a frequent cause of stress incontinence (Dawson et al., 2020). When surgical treatment for UI because of pelvic organ prolapse is contraindicated, a pessary is a viable option. In addition to incontinence pads and briefs, pessaries, when properly fitted within the vaginal vault to correct organ prolapse and reduce stress UI, can typically be managed by the patient or cared for by a qualified nurse at regular intervals. Nonsurgical management of persistent urinary overflow incontinence includes clean intermittent catheterization initially and ultimately may require an indwelling suprapubic catheter. Although the Centers for Medicare and Medicaid Services now reimburses for a single-use sterile catheter, there is no evidence to support a reduction in UTIs with the use of sterile versus clean urinary catheters.

Follow-Up: Follow-up visits will depend on the acuity and severity of symptoms. Treatment of infection and symptoms related to urinary retention requires closer and more frequent follow-up due to renal complications that can result. Initially, medication management should be attempted but monitored closely for adverse effects, especially with anticholinergic medications. These medications can increase the risk of falls and side effects can result in other significant complications such as blurred vision, dizziness, acute delirium, and somnolence. Long-acting medications appear to have a lower risk profile, but individual monitoring is necessary to ensure patient safety. Additionally, cognitive impairment and dementia exacerbation can occur with the use of anticholinergic medications, resulting in hallucinations, psychosis, or changes in behavior that can lead to injury to the individual or others. Constipation, a common adverse effect of anticholinergics, can exacerbate UI by causing a fecal impaction. Polypharmacy issues also need to be monitored closely with any medication change, requiring close follow-up when starting a new drug regimen.

Sequelae: Possible complications include UTI, hydronephrosis (with overflow or obstruction), renal failure, adverse drug events, or failure of behavioral therapy. Skin breakdown is a significant complication with persistent UI. Falls due to UI result from environmental factors or as a side effect of medication management. Social isolation may be a result of uncontrolled UI having a significant impact on quality of life and may lead to depression.

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Prevention/Prophylaxis: Ways to help prevent incontinence include:

- Early identification of acute or transient UI
- Teaching patients and family members/caregivers that UI is not a normal part of the aging process and that treatment options are available
- Referral to appropriate specialists for treatment options
- Regular rectal examination in men to detect and treat early prostatic hypertrophy
- Recognition of polypharmacy and adverse reactions when initiating new medications in the geriatric population

Referral: Referral to urogynecology for the female patient to explore treatment options is appropriate if behavioral interventions and medication management are unsuccessful. It is also appropriate to refer to a specialty practice if the diagnosis is uncertain. Refer men with overflow incontinence for urological evaluation urgently if PVR urine volume is significant, to prevent renal complications, and for surgical intervention, if indicated. Referral to certified continence nurse specialists or PT may be appropriate for behavioral therapies, such as biofeedback or for electrical stimulation treatments to improve continence. Further work-up and referral to urology would be indicated if abnormalities in the urinalysis do not resolve after treatment for infection, such as persistent hematuria or proteinuria, and if the patient has a past medical history that includes surgeries for genitourinary diagnoses or a history of pelvic cancer with or without radiation therapy. Patients with neurogenic bladder because of injury or a chronic neurological condition should be followed by a neurologist in collaboration with the primary care provider.

Education: Teach patients, family, caregivers, and health-care providers, as well as the community, that UI is *not* a normal part of aging, and it is a treatable medical problem in many individuals. Behavioral therapy can be provided in the primary care setting, such as Kegel exercises, as well as self-catheterization techniques. When starting a new medication, the patient should be given written instructions that include details regarding possible adverse drug effects to prevent serious consequences of complications. Also, it is important to teach patients with bladder outlet obstruction the signs and symptoms of a UTI, including delirium as an indication of acute illness, and that a fever may not occur with infections in an older adult. Additional topics to address include having an adequate fluid intake, limiting bladder irritants such as caffeine and alcohol, and prevention of constipation to avoid fecal impaction and help to avoid bladder symptoms and infections. The importance of good perineal hygiene, especially for women and patients who do self-catheterization, should be emphasized. When incontinence cannot be completely avoided, attention to skin care and instruction in the use of skin barriers such as zinc oxide or dimethicone-based products should be taught to the patient or caregivers to prevent skin breakdown.

Diagnosis	Clinical Recommendation	Evidence Rating	References
Urinary incontinence	Combination behavioral therapy and medication management	A	Davis et al., 2020 Sung et al., 2019 Kolodynska et al., 2019
Stress urinary incontinence	Alpha-adrenergic medications, serotonin-norepinephrine reuptake inhibitors	A	Lin et al., 2019
Stress urinary incontinence	Surgical procedures	A	Dawson et al., 2020
Urge urinary incontinence	Anticholinergic medications (antimuscarinic agents)	A	Lin et al., 2019
Overflow urinary incontinence	Treatment of underlying cause of bladder outlet obstruction, urinary catheterization	C	Davis et al., 2020
Functional urinary incontinence	Scheduled toileting	A	Sung et al., 2019
Mixed urinary incontinence	Anticholinergic medications (antimuscarinic agents)	A	Lin et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

WANDERING

Description: Wandering in older individuals, whether it appearing to be intentional to a specific destination or aimless, often occurs in individuals who have disorders that cause cognitive impairment. It is characterized as locomotion either ambulation or propelling in a wheelchair. The wandering behavior is often described as having observable patterns such as lapping, pacing, or random movements. The wandering behavior may be frequent, repetitive, temporally disordered, and possibly spatially disordered in nature. A more recent definition, critical wandering, includes elopement which can

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lead to the individual getting lost either in or outside the person's living setting. Once lost, the wandering older adult is at risk for injury from falls, fatigue, and even death from head injury, hip fractures, other accidents, and exposure to the elements of the environment (e.g., temperature extremes, moving vehicles, or injury from animals) (Adekoya & Guse, 2019; Neubauer et al., 2018; Silverstein & Flaherty, 2021). Moser (2019), however, cites statistics that show injury or death due to wandering is actually a rare event.

Etiology: Although poorly understood, there are many hypotheses regarding the causes of wandering behaviors. A medical hypothesis suggested right parietal dysfunction, which leads to spatial perception and memory lapses resulting in these types of behaviors. Another theory is the individual has unmet needs or environmental triggers leading to wandering behaviors (Neubauer et al., 2018) (Table 7-12).

Wandering behaviors occur in individuals who experience confusion—either temporary in states of delirium or in individuals with a dementia, most commonly during the middle to later stages of the dementia process. Delirium is an extreme confusion, an acute episode of fluctuating attention, worsening of cognition, and change in level of consciousness, which frequently results in agitated and wandering behaviors (Neubauer et al., 2018). Most delirium is reversible but occurs more often in individuals with dementia. Common causes of delirium include illness, medications, and environmental factors (Table 7-13).

Occurrence: Wandering behaviors occur in one out of every five individuals with dementia at some point during their illness (Neubauer et al., 2018). In 2016, 46.6 million people globally were living with dementia, and this number is projected to increase to 75 million by 2030 (Neubauer et al., 2018).

Age: Wanderers do not differ in age (although some studies suggested it occurs more frequently in the younger old) or sex (although some reports suggested it occurs more frequently in males) (Cipriani et al., 2014). Women are diagnosed more often with Alzheimer's disease. Women generally live longer than men and therefore are more likely to live to the age when Alzheimer's disease is more common.

Ethnicity: Numerous studies have documented differences in dementia prevalence among racial and ethnic groups in the United States. African Americans and Hispanics are found to have a higher risk of dementia compared to European Americans (Chen & Zissimopoulos, 2018). Prevalence related to ethnicity showed frequency of occurrence to be 58% in European Americans, 67% in African Americans, and 63% in Hispanics.

TABLE 7-12 Potential Causes of Wandering Behaviors

Unmet personal needs	• Internal discomfort: need for toileting, hunger, thirst • Loneliness • Perceived threat to the individual's safety • Past history of walking behaviors
Environmental triggers	• Noisy environment • Increased visual distractors • Visualizing other individuals leaving • Shadowing a caregiver

Source: *Neubauer et al., 2018.*

TABLE 7-13 Common Causes of Delirium in the Older Individual

Illness	• Urinary tract infection • Upper respiratory infections including pneumonia • Sepsis • Severe constipation as well as intestinal obstruction • Meningitis • Dehydration • Electrolyte imbalances, especially low sodium and low calcium levels • Severe malnutrition • Hypoxia • Terminal illness
Medications*	• Medications with anticholinergic properties • Certain antipsychotics • Pain medications, especially when the individual is toxic
Overstimulation	• Loud noises or multiple conversations • Bright or blinking lights • Large number of people • Change in routine of an individual with cognitive impairment • Overly tired individual with a diagnosis of dementia

Sources: AGS, 2019; Neubauer et al., 2018.
**See the Beer's list of potentially inappropriate medications frequently prescribed in the older patient*

Contributing Factors: Wandering behaviors occur in more than one-half of individuals with a diagnosis of dementia in the moderate to late stage of this cognitive impairment process. The greatest percentage of wandering occurrence has been reported in older adults residing in a nursing home setting or during hospitalization when the patient is experiencing an episode of delirium (Adekoya & Guse, 2019; Neubauer et al., 2018). The most frequent occurrence is between 5:00 and 7:00 p.m., which is often referred to as "sundowning," but occurrence has also been reported as early as 2:00 p.m. and late into the night (Neubauer et al., 2018).

Signs and Symptoms: The older adult may be anxious or agitated or exhibit symptoms prior to an episode of wandering, causing the individual to be difficult to redirect. Individuals who are anxious and those who are delusional appear to exhibit wandering behaviors more frequently. The consequences of wandering may include falls, exhaustion, malnutrition, anxiety and aggression, elopement, and becoming lost from the individual's home environment (Adekoye & Guse, 2019; Cipriani et al., 2014; Lin et al., 2019; Tilly, 2015).

Diagnostic Tests: In an older person who seems to wander aimlessly or become confused or lost, a full medical evaluation should be conducted, including an evaluation for dementia,

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particularly Alzheimer's disease. A work-up includes a review of the individual's medications; diet, nutrition, and use of alcohol; as well as medications (prescription and nonprescription/street drugs); vital signs and pain level; laboratory tests (blood and urine); and a thorough physical examination including an in-depth geriatric neurological examination. Although no singular test is available for dementia, multiple cognitive assessments are recommended, including the Mini-Mental State Exam (MMSE), the Montreal Cognitive Assessment, the St. Louis University Mental Status Exam, Mini-Cog test, Clock Drawing test, and Memory Impairment Screening. The Mini-Cog test is a short screening test that incorporates a three-item recall within 5 minutes and a clock drawing test. Although used less often now because the MMSE is proprietary, it had been the most widely used to assess an individual's level of cognitive functioning. In one study wandering behaviors were noted to be common in individuals who scored a 13 or less on the MMSE (Cipriani et al., 2014).

Treatment: Determine whether the wandering behaviors are troublesome or placing the individual at risk for harm. If wandering is benign—consider providing a safe environment for the individual to wander. If intervention is warranted—a person-centered approach to assessment, planning, and delivery of care is the key to managing wandering behaviors (Tilly, 2015). Examine the frequency of wandering occurrences, the time of day, and any triggers that may be the cause of the wandering behavior. When possible, attempt to identify why the person is wandering, and when developing a plan of care, involve the person with dementia in decision making. If able to identify triggers to the behavior, attempt to modify the individual's routine to minimize these triggers; decrease distractions, especially in the afternoon and evening hours or when the person is tired; and do not vary the day-to-day routine. Attempt to engage the individual in nondemanding activities during the time of day the wandering behaviors most frequently occur. Nonpharmacological interventions should be attempted, but when the individual is severely agitated, aggressive, exhausted, or otherwise at risk for harm to self or others, and distraction and redirection are unsuccessful, pharmacological intervention may become necessary.

Sequelae: Consequences of wandering behaviors include accidents, getting lost, fatigue, sleep disturbances, social isolation, falls, injury, and death (Neubauer et al., 2018). Falling with hip fractures and head injuries are common consequences in these individuals. Malnutrition can also occur as a result of an inability to sit for a meal or excessively wandering, which increases caloric requirements and leads to weight loss. Wandering behaviors often lead to early admission to a dementia facility when families are unable to manage the individual in the community setting. Disruptive activities are associated with wandering including agitation, screaming, physical aggression, and disturbed nighttime sleep.

Prevention/Prophylaxis: Care is aimed at balancing a person's need for autonomy with the need to minimize risks. The goal is to provide a pleasant and safe environment where an individual will not wander away, fall, or become exhausted. Wandering is not always problematic if the person is able to ambulate without falling, the behavior does not lead to aggression, or the person does not wander away and become lost. To maximize safety, the living environment needs to be surveyed and modifications made, when necessary, and the area is familiar (minimize changes) and uncluttered. Assure ample lighting, maintain clutter-free walkways, and keep harmful objects out of reach from the confused individual. Other considerations may include putting locks on cabinets and ovens, unplugging dangerous appliances when necessary, removing wall hanging mirrors (the confused individual may misinterpret the reflection as another person in the room), and providing exits with safety mechanisms. Wandering behavior can be diminished with the installation of simple childproof doorknob covers, possibly more complex door locks, or even in-house alarms or bells.

If an individual wanders, identify to where the person usually wanders, what activity the person is usually engaged in when wandering occurs, and at what time of day it usually occurs. Identification bracelets or necklaces may help minimize the hazardous consequences if wandering off does occur and the individual becomes lost. Many Medical Alert necklaces/bracelets have GPS tracking and can be of assistance in locating an older adult who has wandered away. Also include identification in clothing and keep a recent photograph of the individual when assistance is needed to locate the person (Moser, 2019). When wandering occurs, caregivers should approach the individual slowly, speaking softly, in a monotonous and nonthreatening manner. Act in a nonjudgmental, matter-of-fact manner. Validate the person's feeling with positive, open statements or questions such as "You look concerned" or "What can I do to help?" Distract the individual by refocusing the person's attention on something different, such as looking at old pictures or discussing the weather. Redirect the person in a reassuring manner by saying, "I know you are concerned; let's sit and talk and have a cup of coffee." Possibly suggest going for a walk in the direction you wish the person to go instead of the individual leaving that environment. Avoid asking the person to explain the behavior. In summary, validate, redirect, distract, and redirect the wandering or confused person to abort the behavior (Sollito, 2021).

Referral: Caregivers need to determine the abilities of the wandering individual and create an environment that provides for autonomy as much as possible and ensures safety. Referrals may be made to geriatric care specialists for evaluation and management, home health agencies for assistance in the home setting, and community resources for support groups and available educational resources. When necessary, consideration for a more structured living arrangement may be advised when safety becomes a major concern. Options include sitters in the home setting, adult day cares, assisted living facilities, and nursing homes. In extreme situations, when the elder is at risk for harming self or others, referral to a psychiatrist may be indicated for evaluation.

Education: Educating caregivers, both family and friends, of the wanderer, as well as paid caregivers (nurses, aides, staff), is essential to provide optimal care. The essential information includes the causes of dementia and wandering behaviors and how to identify triggers of this behavior, create a safe environment, and manage wandering individuals while promoting quality of life and patient autonomy.

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Clinical Recommendation	Evidence Rating	References
Older adults with dementia frequently engage in wandering behaviors and attempt to exhibit exit-leaving behaviors leading to elopement or becoming lost.	B	Adekoya & Guse, 2019
Focus on the person who wanders rather than the wandering behavior.	A	Adekoya & Guse, 2019
Redirect the individual to a suitable activity.	C	Sollito, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

WEAKNESS

Description: Weakness is "loss of strength" (Cortes-Vicente et al., 2020), but this definition can further be qualified by objective and subjective characteristics. Complaints of weakness could be localized muscle weakness or overall weakness, which is better described as malaise or frailty. Weakness is described usually as an extremity that will not move to its full potential against gravity. Weakness is a risk factor in the decline of independence in instrumental activities of daily living (IADLs) and activities of daily living (ADLs) (McGrath et al,2020).

Etiology: Infections, such as the flu or urinary tract infection, are the most common cause of acute generalized weakness. Acute extremity weakness is most commonly from trauma and typically associated with pain (Levin, 2019). Post-surgery or procedure pain can also result in weakness. Neurological issues, such as multiple sclerosis, myasthenia gravis, or stroke, can cause unilateral weakness or weakness in cranial nerves that can be acute or generalized and even wax and wane (Cortes-Vicente et al., 2020). Hormone levels, such as thyroid levels, or electrolyte imbalances can occur with dehydration and can also cause weakness (Levin, 2019). Weakness may be experienced as the result of an acute infection such as polio, Lyme disease, or other tick-borne illnesses.

Occurrence: Weakness can be acute (seconds to minutes) resulting from an injury, trauma, or stroke. Subacute weakness (hours to days) can result from an infection, inflammatory process, or autoimmune condition such as multiple sclerosis or myasthenia gravis. Chronic weakness may result from a previous injury or trauma, a metabolic or muscle disorder, or a congenital or degenerative condition. Weakness due to multiple sclerosis, myasthenia gravis, or thyroid dysfunction is higher in women because these conditions are generally more predominant in women. Weakness related to stroke is higher in older women (Bushnell et al., 2018).

Age: Weakness can occur at any age. At birth it could be related to trauma, congenital issues, or cerebral palsy. Some types of muscular dystrophy can progress as one ages. Lack of regular exercise, injuries, degenerative changes, obesity, and comorbidities that occur as one ages can also contribute. Neurological causes of weakness such as multiple sclerosis and myasthenia gravis are usually diagnosed between ages 20 to 40 (Cortes-Vicente et al., 2020). Strokes can occur at any age, but incidence doubles for each decade between ages 55 and 85 (National Institute of Neurological Disorders and Stroke, n.d.).

Ethnicity: Certain neurological conditions can be related to ethnicity, and stroke may be seen more in people of color (Hooman et al., 2020).

Contributing Factors: Having a compromised cardiopulmonary system can cause acute or chronic weakness depending on degree of issues and activity level/cardiac demand of patient. Vitamin B_{12} deficiencies, alcoholism, and certain medications such as statins can also cause muscle weakness and/or nerve damage. Obesity and diabetes can contribute to weakness due to glucose levels or calories needed for expenditure.

Signs and Symptoms: Weakness is described as an extremity that will not move to its full potential against gravity. Over time atrophy of the muscle can be visualized or measured. Weight gain or loss may be seen in subacute or chronic weakness. Weight gain may occur because of a lack of calorie expenditure and injury, pain, or hormonal issues can cause weight loss (Levin, 2019).

Generalized weakness is described as trouble moving from point A to B or even the inability to get out of bed or perform ADLs. Cognitive fatigue from poor sleep quality, obstructive sleep apnea, or mental health issues can also result in generalized weakness.

Physical examination should first start with evaluating distress of the patient, especially in an acute situation such as a stroke where facial droop or slurred speech may occur. If not in an acute setting, use of the reported weak extremity should be witnessed during initial intake. Additional factors to consider include:

- Does the patient need assistance with ambulation? Did they require a wheelchair when usually they are fully ambulatory?
- Are they guarding the extremity if having pain?
- Does the patient report or show signs of pain with ambulation or palpation of the extremity?
- Is hygiene compromised because they are unable to get into the shower or bath? Do they spill food or drink on themselves due to upper extremity weakness?
- Is there increased tone or lack of tone? Hyporeflexia or hyperreflexia?
- Is swelling or atrophy present?

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When considering the scale of weakness in isolated muscle groups, motor strength is commonly rated as:

- 0/5: No visible muscle contraction
- 1/5: Visible muscle contraction with no limb movement
- 2/5: Limb movement but not against gravity
- 3/5: Movement against gravity but not resistance
- 4/5: Weakness against resistance
- 5/5: Full strength

Measurement of handgrip strength (HGS) can be done in any setting. HGS provides and assessment of overall muscle strength, and low HGS is associated several poor health outcomes (McGrath et al., 2020).

Diagnostic Tests: The patient's report of acute, subacute, or chronic weakness helps establish next steps for testing. Determination of localized weakness or generalized weakness will further differentiate appropriate testing (Table 7-14).

Differential Diagnosis: Differential Diagnosis is broad for weakness, which is why the patient's reported history of their symptom is crucial. *Acute or subacute:* Injury or reinjury, infection, neurological cause, cancer, electrolyte disturbance. *Chronic:* Nerve damage, alcoholism, eating disorder, cancer.

TABLE 7-14 Diagnostic Testing for Weakness

STAGE	LOCALIZED	GENERALIZED
Acute	• X-ray of extremity if injury occurred • Computed tomography (CT) or magnetic resonance imaging (MRI) of head if stroke causing unilateral weakness is suspected • CT or MRI of extremity, if warranted	• Laboratory tests: complete blood count (CBC), complete metabolic panel (CMP), urine • Consider swabbing for flu, strep infection, or COVID-19. • Head CT
Subacute	• Review of medications and recent activities (excessive exercise) that could cause rhabdomyolysis • Labs: CBC, CMP, AChR antibodies • Electromyography (EMG) or nerve conduction test to help evaluate health of muscles and nerves.	• Laboratory tests: vitamin B_{12}, thyroid-stimulating hormone (TSH), CBC, CMP, urine, erythrocyte sedimentation rate ESR, CRP, ferritin, Hgb A1c, AChR antibodies • Check medication list
Chronic	• EMG or nerve conduction of extremity • Muscle biopsy if indicated	• Laboratory tests: vitamin B_{12}, TSH, ferritin, Hgb A1c, AChR antibodies • Monitor weight. • Screen for depression. • Consider a sleep study. • Determine whether the patient is up to date on cancer screenings, including low dose CT if patient is smoker.

Treatment: Treatment for most types of weakness will likely involve exercise or physical therapy (PT). Locating a physical therapist who specializes in the etiology of the problem can increase success of recovery.

Medications for chronic generalized weakness or fatigue include stimulants or wakefulness medications. These will not help with muscle strength, but they may help the patient feel more energized. There are no medications to make muscles stronger. Sometimes B vitamins have been prescribed to help with weakness or fatigue, but clinical trials have been mixed in terms of true benefit (Levin, 2019). There is one medication with proven efficacy for patients with multiple sclerosis, dalfampridine (Ampyra), a potassium channel blocker that in clinical trials helped patients improve their walking by increasing nerve conduction. If the patient is diagnosed with multiple sclerosis or myasthenia gravis, there are a variety of medications available to stabilize the disease process.

Assistive devices such as canes, rollators or various braces can help with extremity weakness. These may help a patient maintain ambulation to avoid further sequelae from their weakness. A physical or occupational therapist would be the best resource to outfit a patient with the correct device. Diet should be evaluated for nutritional value as well as appropriate caloric intake. Hydration needs to be emphasized especially in certain climates and times of the year.

Follow-Up: Follow up depends on the etiology and treatment and the level of patient distress. Follow up in weeks or months should be determined with the patient in shared decision making.

Sequalae: Sequelae from weakness, even when treated, can still result in atrophy of muscles, pain, falls, deep vein thrombosis (DVT), and osteoporosis. Sequalae can cause poor sleep due to pain or positioning. Weakness can lead to social isolation.

Prevention/Prophylaxis: Weakness from neurological or congenital issues cannot be prevented but can often be improved with therapy and assistive devices. The best prevention for weakness is regular, safe exercise and avoidance of injuries or falls. Eliminating use of tobacco and limiting alcohol use can be beneficial. Risk factors for stroke, such as obesity, hypertension, and diabetes, should also be addressed.

Referral: After the etiology of weakness if diagnosed, the patient should be referred to a specialist in that field as appropriate, such as neurology or orthopedics. Referrals can also be made to PT, occupational therapy (OT), or physical medicine and rehabilitation. Referral to an endocrinologist should be made for management of thyroid disorders. For generalized chronic weakness it may be helpful to refer to a mental health provider.

Education: Patients should be educated on the etiology of their weakness as well as preventive measures. Expectations of treatment should be outlined. Discuss realistic treatment outcomes with the patients, understanding that they may not return to their baseline strength depending on the etiology of their weakness. Education should be done regarding the benefits of a regular exercise program. If initiating medication therapy that has risk of rhabdomyolysis or an electrolyte disturbance that could cause weakness (such as diuretics), patients should be educated on symptoms and what to do immediately should they experience issues.

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Clinical Recommendation	Evidence Rating	References
Measurement of hand grip strength (HGS) is a measure of overall muscle strength.	B	McGrath et al., 2020
Low HGS measurement is associated with poor health outcomes.	A	McGrath et al., 2020
Weakness is an independent factor associated with a decline in independence in IADLs and ADLs.	A	McGrath et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

J. B. is a 77-year-old man who is known to your practice. He is brought in today by his daughter, who reports a new onset of confusion accompanied by UI (first noticed bed was wet a few nights ago). When you see the patient today, he is oriented to place and person (knows you and your office), but not to time, and does not recall much about events of the past few days. He says that he is eating and drinking as usual (but daughter is shaking her head to the contrary). He denies any change in bowel function, but is fearful of sleeping because he might "wet the bed." Daughter states that he has been drinking a lot more water than usual and urinating more frequently. He denies any pain, other than arthritis. He was a regular attendee at the local senior center but has not been there for a week and seems to have forgotten about it.

Past medical history: Known CAD, hypertension, hyperlipidemia, impaired fasting glucose, osteoarthritis of knees.

Medications: Lisinopril 20 mg orally PO once daily in evening; hydrochlorothiazide 12.5 mg PO once daily in morning; metoprolol 50 mg PO once daily in morning; simvastatin 20 mg PO once daily. OTC medications include Aleve, 2 tablets every 12 hours when needed for severe knee pain (infrequent use); topical Icy Hot for knee pain daily; glucosamine-chondroitin preparation daily for joint health; multivitamin for male more than 50 years daily.

Vital signs: Blood pressure (BP) 130/84 mm Hg; heart rate (HR) 60 beats per min, regular; respiratory rate 16 breaths/min; temperature 99.2°F orally; BMI 38.

Physical findings are unremarkable.

Using the guide to characterizing a symptom located in this chapter, focus on the following questions:

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What national guidelines are appropriate to consider?
4. What tests will you order? How will you decide on prioritizing in this patient with multiple symptoms?
5. What are the differential diagnoses that you are considering? For each one, map out your clinical reasoning for and against it and make a tentative plan to confirm it or rule it out.
6. Will you be looking for a consultation?

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unit III

Treating Disorders

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CHAPTER 8

Dermatological Disorders

Laurie Kennedy-Malone

CHANGES WITH AGING

The largest organ of the body, the skin, undergoes certain normal changes with age. The number of cells in the epidermis, such as Langerhans cells, which are responsible for immune surveillance, begin to decline. Melanocytes also decrease, thereby reducing the skin's natural protection from the sun (Russell-Goldman & Murphy, 2020). As people age, the skin tends to be very thin, fragile, and often transparent (Burr, 2018). Skin renewal turnover time increases to approximately 87 days in older adults, compared with 20 days during youth. This fact becomes an important consideration in surgical and dermatological healing. The subcutaneous tissue that houses the eccrine, sebaceous, and apocrine glands thins, thereby providing less protection from heat exposure and less insulation, energy storage, and shock absorption (Golpanian & Yosipovitch 2020; Russell-Goldman & Murphy 2020). Secretions aiding temperature control, moisturization, and odor production are also reduced. The skin of older adults therefore tends to be very dry (xerosis) and with accompanying pruritis (Russell-Goldman & Murphy, 2020). Fat is generally redistributed to the abdomen and thighs, leaving bony surfaces, such as the face, hands, and sacrum, exposed to potential injury, especially skin tears from shearing and friction forces and pressure injury development (Farage et al., 2013). The skin's repair system becomes impaired, with delayed cell regeneration and poor circulation (Russell-Goldman & Murphy, 2020).

Common benign skins lesions in older adults include seborrheic keratoses, cherry angiomas, acrochorda (skin tags), and senile lentigo (Russell-Goldman & Murphy, 2020). Aging skin is also susceptible to develop contact and allergic dermatitis, eczema, and nonmalignant skin cancers and malignant melanoma (Farage et al., 2013). Older adults are also prone to developing many pigmentary disorders not common in younger adults (solar lentigo, lentigo maligna, stasis dermatitis, purpura, poikiloderma) (Armenta et al., 2019).

Although the capillaries in older adults tend to be fragile, making the skin of older adults more susceptible to bruising, it is important to discern the cause of the ecchymosis, whether it is trauma-, pressure-, or medication-induced, as in patients taking anticoagulants or corticosteroids. It is important to note, however, that sudden appearance of numerous seborrheic keratoses, telangiectasia, or pigmented warty lesions (known as Leser-Trelat sign) may suggest internal malignancy (Bernett & Schmieder, 2020).

All of these tissue changes represent a near-catastrophic scenario of aged skin poorly protected from the environment (especially the sun, heat, and cold) and slow to respond to immunological challenges, producing minimal or delayed urticaria and swelling (Shah & Kennedy, 2018). Changes to the skin that occur at the end of life during the dying process (loss of tissue and declining organ function) increase the risk of patients developing pressure injuries (Burr, 2018).

ASSESSMENT

A thorough dermatological assessment should include the presenting concern/compliant with the skin, history of the presenting concern/compliant, past medical history, family history, social history, medicines (including topical treatment, over-the-counter [OTC]), and known allergies. Also determine the patient's routine exposure to ultraviolet (UV) light (Burr, 2018; Czerkasij, 2010). Equally import it to determine the impact of the dermatological concern on the patient's quality of life (Linos et al., 2018). Family history should address any familial tendencies for dermatological conditions, including any predispositions for psoriasis or eczema, or familial atypical multiple mole melanoma (FAMMM) (Lynch & Shaw, 2016). Concurrent and recent conditions experienced by family members may reveal a contagious or environmental etiology. Patients should be questioned about occupation and/or hobbies to consider exposure to chemicals, travel to include exposure to insects (bites, stings), past dermatological allergic reactions (plant-based, food, drug, environmental, animal dander), whether or not the patient smokes (to include prior history), alcohol consumption, medications (including any new prescription or OTC medications. Review with the patient any current psychological stressors that may have triggered a new dermatological response or an exacerbation of a previously diagnosed condition (Willacy, 2019).

When exploring the chief complaint and history with the patient, review the dermatological problem's onset, duration, location, size of lesion, color, associated pain, or itching, and lost or heightened sensation to touch. Has there been a

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previous episode of the lesion in the past that resolved (Burr, 2018; Czerkasij, 2010; Willacy, 2019)?

- Investigate associated symptoms such as wheezing, loss of appetite, fever, malaise, joint pain, headaches, and change in temperature perception. Skin conditions can be clinical signs of underlying malignancies with the most common to metastasize to the skin are "breast, lung, colon, stomach, sinus laryngeal, oral, thyroid, renal, and uterine" (Hall, 2017, p. e287).
- Question current and chronic medication history, complete a focused nutritional assessment, and ask about relevant childhood diseases (especially asthma, atopic dermatitis, and varicella).
- Ask about contact with chemicals, lifetime occupations, hobbies, level of lifetime UV light exposure, family history of skin cancer, contact with animals, change in environmental habits (e.g., exposure to plants, insects, or water) or internal habits (e.g., change in soap or laundry detergents, use of any lotions or creams, recent travel, change in diet and cooking products, and exposure to new clothing items or metals such as nickel).
- Question about smoking history and alcohol use.
- Ask whether the person has been treated for a similar condition in the past and, if so, ask about the treatment (self-administered or provider prescribed).
- Note whether the patient appears uncomfortable or pruritic.
- Observe overall hygiene and grooming
- Is the patient incontinent?
- Has the patient had two doses of the Shingrix? Did they have the Zostavax vaccine?
- Is the patient taking any anticoagulation medications?

To conduct a thorough skin assessment, patients should be asked to gown except for underwear (Wheatley, 2018). Proper equipment for inspection includes good overhead and tangential lighting, a magnifying glass, blades, and collection devices for biopsies and microscopic study. Gloves should be readily available. A total body skin examination is warranted to assess the skin for skin cancers (Linos et al., 2018). During the examination, inspect the skin for possible signs of neglect, abuse, or decreased function. Poorly healing wounds or chronic pressure injuries may signal a problem not only with the patient but with the caregiver's ability to provide adequate care. Welts, lacerations, burns, and distinctive markings may indicate a need for intervention (Earlam et al., 2018).

Inspect the hair and nails. The hair may be graying and thinner than in youth. Normally, nails start to form ridges after age 80. A recent (in the past year) change in quality of hair and nails is a significant finding. For example, the hair may have become dryer, duller, and thinner or the nails pitted or brittle, which may be indicative of a systemic condition or nutritional deficiency (Burr, 2018).

Inspection of the skin for even color and overall quality and care is important. Lesions require close scrutiny, description, and classification. Description by type, shape, arrangement, and distribution is a widely accepted and usable format.

- Type: Is the lesion a macule or papule? Is it a nodule? Is it vesicular? Is it eroded, excoriated, or hyperpigmented or hypopigmented?
- Shape: Is the periphery of the lesion round, ulcerated, or linear?
- Arrangement: Are multiple lesions grouped (serpiginous, zosteriform, arciform, iris, or bull's-eye pattern) with or without definable borders (Suneja et al., 2020)?
- Distribution: Is the extent of the lesions isolated, regional, or generalized? Is the pattern symmetrical or over pressure sites, hairline, or sun-exposed areas? Is the distribution characteristic of scabies, seborrheic dermatitis, contact dermatitis, herpes zoster, or lupus?
- Is there any inflammation around the lesion? Is the lesion or surrounding area tender to the touch?
- Is there bleeding or discharge? (Bleeding may be indicative of a malignancy; discharge may be a sign of an infection.)
- Any noted fluctuation in the presence of the lesion?
- Is there any unexplained bruising that could be indicative of elder abuse or neglect (Earlam, 2018)?

The lesion may be classified as primary or secondary. Primary lesions (vesicles, tumors, burrows) arise from normal tissue. Secondary lesions (infections, crusts, and lichenification) arise from changes to the primary lesion and may be the result of trauma, scratching, or infections (Suneja et al., 2020). Palpate for moisture, temperature, mobility, and turgor. Testing skin turgor in older patients can be done by pinching the skin on the sternum or forehead. The skin should move easily and return back to place after release; a slower return of the skin may be indicative of dehydration. Lax skin may indicate weight loss, whereas fixed skin may be associated with sclerotic or scarred tissue. Lesions should also be palpated to check whether they are fluctuant, hard, or fixed. "Lesions that are crusting, changing, itching, bleeding, burning or otherwise new in recent months require immediate attention" (Czerkasij, 2010, p. 646).

At the end of the examination, consider associated pathology, especially thyroid disorders, diabetes, autoimmune conditions, anemia, and malignancies. Provide wellness instructions, including those concerning proper nutrition, moisturizing, and year-round UV light protection. Awareness of the high susceptibility of the older adults to hyperthermia and hypothermia secondary to reduced thermoregulation in the skin should be emphasized (Farage et al., 2018).

Lesions that concern you or the patient should be examined through biopsy. Lesions that warrant biopsy are those that have changed, bleed, or are painful. Treatment for skin lesions must take impaired absorption, duration, dosage, and delivery method (e.g., cream, powder, ointment, lotion) into consideration. Patients for whom treatment plans fail initially should be referred to a dermatologist.

Guidelines for Prescribing Topical Medications

When prescribing topical treatments, it can be a challenge to determine the quantity necessary to dispense. A guideline for determining the quantity was first described by Long and Finlay in 1991 with the introduction of the "fingertip unit." One fingertip unit (FTU) is the amount of ointment or cream dispensed from a tube with a 5-mm opening from the tip of the finger to the first crease. One FTU is equal to approximately 0.5 g. Along with the concept of FTUs, the "Rule of Hand" was developed. This rule says that the body surface of the front and

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back of an adult hand requires 1 FTU for coverage. Each body part is described by its equivalent surface area in hands. Each arm is equal to three hands, the front torso is seven hands, and so are the back and buttocks. Each leg is equal to six hands, and each foot is two hands. So, if you are treating lesions on one foot, a total of 2 FTUs will be required, or 1 g per treatment. For treatments that are prescribed as twice a day (bid) for 2 weeks, a total of 28 g will be necessary. This guideline results in a more quantitative prescription than writing "dispense 1 week's supply" (Long & Finlay, 1991).

BURNS

Signal Symptoms: Erythema, edema, blistering, serous exudate, eschar, pain, pruritis; carbonaceous sputum, singed nasal hairs, hoarseness, dyspnea (for inhalation injury).

Description: Burns are tissue injuries caused by heat. Beyond the classic thermal injury definition, "burns" may refer more broadly to tissue injury caused by exposure to chemicals, electricity, friction, or radiation. Given the integumentary system's role as the primary physical barrier to the external environment, burns most often affect skin and other superficial tissues. However, burn injuries may extend to deeper tissues, may evolve over time, may be concomitant with inhalation injury and/or multisystem trauma (polytrauma), and may be compounded by significant comorbidities. Optimal long-term outcomes depend upon appropriate referral for definitive care and specialized resources for ongoing recovery and rehabilitation.

Etiology: According to the American Burn Association (ABA) National Burn Repository (2019), flame burns remain the dominant cause of burn injury in the United States, followed by scalds, contact burns (direct exposure to a hot object), electrical burns, and chemical injuries. However, the relative frequency distribution of burn cause and severity varies by age, sex, ethnicity, and numerous other demographic and/or contributory risk factors. Some vulnerable subgroups are at greater risk of burn injury and/or worse outcomes from burn injury.

It must be emphasized that etiology of the original thermal injury to tissue is only part of the equation. Dysregulated host response to injury is a hallmark of burn injury. Severe burns often elicit a heightened and sustained inflammatory response and hypermetabolic state that may exacerbate the original injury, prolong time required for wound healing, and lead to additional tissue damage and/or organ dysfunction (Nielson et al., 2017).

Occurrence: Most burns occur in the home (72.5%), in industrial settings (6.6%), or on street/highway (5.5%) (ABA, 2019). The setting of initial medical treatment may vary (e.g., emergency department [ED], urgent care, private medical office, specialty clinic, hospital), and reporting systems are not integrated. As a result, burn injury incidence estimates vary, but rates may approach 2.5 million injuries annually. Approximately 500,000 individuals receive medical treatment, and approximately 10% of those treated require hospitalization (ABA, 2019). Mortality rate for all cases was 3.0%, though mortality increases with advancing age, burn size, and presence of inhalation injury (ABA, 2019). Annual fire deaths in the United States have fallen steadily from nearly 6,000 in the 1980s to fewer than 3,500 by 2020 (Ahrens & Messerschmidt, 2021).

Age: The overall number of fire fatalities in the United States has fallen substantially over the past 40 years, but the reduction has not been uniform across all age-groups. The greatest reductions have been among younger age-groups, but the annual number of home fire fatalities among those 50 and older has remained largely unchanged; this has caused the percentage of home fire fatalities in those who are 65 or older to increase from 19% to 36% (Ahrens & Messerschmidt, 2021). Worldwide, the incidence of burn injury in older adults is increasing (Jeschke et al., 2020).

Age-related changes to the skin, such as thinner skin, decreased vascularity, and diminished nerve function often result in a higher incidence of deeper burns. Advanced age also imposes an increased burden of comorbidities, weakens the immune system, and prolongs or delays wound healing. Thus, older adults are at particular risk for burns.

Males sustain a higher rate of burn injury than women across all age-groups, except for those individuals 80 years and older (ABA, 2019). Conversely, female sex was related to higher mortality (Bedri et al., 2017). There are some differences in cause of burn injury and location of occurrence; compared to women, a greater proportion of burn injuries for men occur outside or in the workplace.

Ethnicity: National Burn Registry data (ABA, 2019) outlines the following distribution of reported ethnicity in burn injuries: 60.3% White, 20.6% Black, 9.5% Hispanic, 6.0% other, 2.7% Asian, and 1.0% Native American. Race/ethnicity factors may influence injury risk differently across age-groups: people of color younger than age 16 (especially those younger than age 5) are overrepresented among those with burn injuries, but this phenomenon is not observed in older age-groups (ABA, 2019). There are complex interactions between race/ethnicity, gender identity, sex, age, and socioeconomic status—with subsequent effects on burn outcomes. Multivariate analysis by Bedri et al. (2017) found that burn mortality was related to such factors as being Black, being female, and being uninsured in addition to burn severity (total body surface area [TBSA] and depth) and inhalation injury. In addition, people of color were more likely to have complications such as urinary tract infections and septicemia, and they had a higher risk of morbidity and mortality compared with Whites.

Contributing Factors: The major causes of home fires and fire deaths are cooking, home heating, electrical distribution and lighting, and smoking (Ahrens & Messerschmidt, 2021). Smoking is the leading cause of home fire deaths and has been found to increase the risk of burn injury sixfold—even further when compounded by use of home oxygen (Ahrens & Messerschmidt, 2021).

Human judgment plays a large role in activities that are related to burn injury. Older adults may have slower response times and may show impaired judgment due to illness or medications. The ability to sense fire decreases, and disabilities may impede escape. Many older adult individuals live alone or are

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dependent on an aging spouse for support; this isolation further increases the risk of injury. Comorbidities such as cardiac disease, renal disease, diabetes mellitus, dementia, or psychological impairment may complicate outpatient care; these individuals may require initial hospital admission for burn assessment and stabilization (Voight et al., 2018).

Signs and Symptoms: Burn injury constitutes trauma, and as such, the initial evaluation should consist of a primary survey including the ABCs (airway, breathing, circulation), followed by a secondary survey including a comprehensive patient history and thorough head-to-toe examination. Ascertain the time and mechanism of injury, duration of contact with the offending agent, and any steps taken to manage the injury. This will assist in determination of wound depth and suitability for outpatient management.

Skin is the largest organ in the body and performs myriad protective, sensory, and regulatory functions. It is composed of three layers: the epidermis, the dermis, and the subcutaneous tissue or hypodermis. The epidermis is the thin outermost layer of the skin. At this level of the skin, melanocytes produce melanin, which affects skin color and provides protection from UV radiation. The dermis consists of a dense connective tissue that forms the bulk of the skin. This layer is vascular, with its deeper layer containing hair follicles, associated muscle fibers, cutaneous glands, and nerve fibers. The hypodermis is largely composed of adipose tissue, which provides padding and thermal regulation. Burn injury can affect all these skin layers in addition to deeper structures such as muscle and bone. A graduating zone of damage may evolve over time, making it difficult to estimate the depth of a burn when first evaluated.

- First-degree burns involving the epidermis are erythematous and painful, but do not blister. Most sunburns fall into this category and are not considered when estimating total burn size.
- Second-degree (partial-thickness) burns
- Superficial dermal burns involve the dermis and are characterized by blisters. The underlying tissue is pink, moist, and hypersensitive to touch. The tissue will blanch with pressure and is associated with dilation. Superficial dermal burns will often heal within 2 to 3 weeks.
- Deep dermal burns extend further into the dermis, present with blistering, but the tissue surface appears mottled, pink, and white immediately after injury. Capillary refill is slow and usually by the second day from injury the wound bed appears white and dry. Pain is often described more as pressure. Partial-thickness burns that are not healed by 3 weeks should be excised and grafted.
- Third-degree (full-thickness) burns involve the full dermis extending into the subcutaneous tissue. The burn appears dry, white, charred, and leathery. There is no sensation to pinprick in the wound bed. There may be mottling that does not blanch with pressure. There may be visible coagulated vessels on the surface. Full-thickness burns require early excision and autograft.
- Indeterminate burn wounds may hold components of both partial-thickness and full-thickness; they should be evaluated daily over a period of days to determine the need for excision and autograft (Jeschke et al., 2020; Voight et al., 2018).

After determining the depth of tissue injury, estimate the TBSA of second- and third-degree burns. Note that superficial (first-degree) burns are not included when calculating TBSA. The Lund and Browder technique, first published in 1944, considers body surface area relative to age. The estimated surface area stabilizes by 15 years of age through adulthood (Table 8-1). An adjunct method used for scattered or irregularly shaped burns is the Palmar method: the patient's palmar surface (palm, digits, and thumb in adduction) correlates to approximately 1% of TBSA.

Emergency care for burns greater than 20% TBSA should include IV fluid resuscitation to correct ongoing fluid and electrolyte losses and to prevent further tissue injury secondary to hypovolemia and tissue hypoperfusion. Advanced Burn Life Support (ABLS) guidelines recommend use of the Modified Brooke/Parkland Formula to estimate 24-hour fluid volume of Lactated Ringer to be administered: 2 mL × %TBSA × weight in kilograms (Woodson et al., 2018). However, in practice, IV fluid rates are titrated to

TABLE 8-1 Adult Burn Size Estimation

AREA	ADULT (>15 YR)	SECOND-DEGREE INJURY	THIRD-DEGREE INJURY	TOTAL
Head	7			
Neck	2			
Anterior trunk	13			
Posterior trunk	13			
Right buttock	2.5			
Left buttock	2.5			
Genitalia	1			
Right upper arm	4			
Right lower arm	3			
Right hand	2.5			
Left upper arm	4			
Left lower arm	3			
Left hand	2.5			
Right thigh	9.5			
Right lower leg	7			
Right foot	3.5			
Left thigh	9.5			
Left lower leg	7			
Left foot	3.5			
	TOTAL			

Note: Modified Lund and Browder technique for those greater than 15 years of age. Adapted from Anesthesia for burned patients *by L. C. Woodson, E. R. Sherwood, M. P. Kinsky, M. Talon, C. Martinello, and S. M. Woodson (2018), in D. N. Herndon (Ed.),* Total burn care *(5th ed., pp. 130–157). Saunders Elsevier.*

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achieve adequate perfusion as indicated by physical examination, vital signs, and urinary output of 30 to 50 mL/hr (Jeschke et al., 2020). Effective fluid resuscitation of acute burns is best accomplished in consultation with the nearest burn center or trauma center.

After initial patient assessment is completed, a decision must be made to transfer to a higher level of care or to continue management in the outpatient setting. The ABA has established criteria for burn center referral to improve patient outcomes (Table 8-2). An important caveat is that any case of suspected elder abuse should be transferred via the emergency medical system (EMS) to the appropriate emergency department to ensure proper follow-up and reporting. Suspicion of abuse should be triggered by any of the following:

- Burn patterns that do not match the reported event
- Straight or smooth transitions between the area burned and healthy skin, resulting in a stocking- or glove-like appearance
- A long delay between burn injury and request for treatment

Diagnostic Tests/Tools: Laboratory and diagnostic testing should be guided by patient presentation and, if warranted, may be an indication for hospital-based evaluation. Of note, standard pulse oximetry devices may fail to detect smoke inhalation injury; many devices cannot differentiate between saturation of hemoglobin by oxygen versus carbon monoxide, resulting in misleading saturation levels (Jeschke et al., 2020). When in doubt, or if inhalation injury is suspected, obtain an arterial blood gas (ABG) including a carboxyhemoglobin (COHb) level.

Differential Diagnosis: Many exfoliative and necrotizing skin disorders can present in a similar fashion and must be ruled out. Although these skin disorders are not true burns, they are often referred to burn care facilities for definitive treatment. These may include but are not limited to:

- Erythema multiforme
- Necrotizing fasciitis
- Purpura fulminans
- Stevens-Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN)
- Staphylococcal scalded skin syndrome (SSSS)

TABLE 8-2 American Burn Association Referral Criteria

1. Second-degree (partial-thickness) burns greater than 10% of Total Body Surface Area (TBSA)
2. Third-degree (full-thickness) burns of any size
3. Burns involving face, hands, feet, genitalia, perineum, or major joints
4. Electrical burns, including lightning injury
5. Chemical burns
6. Inhalation injury
7. Burn injury in patients with preexisting medical disorders that could complicate management, prolong recovery, or affect mortality
8. Any patient with burns and concomitant trauma in which the burn injury poses the greatest risk of mortality or morbidity; if trauma poses the greater immediate risk, the patient may be stabilized in a trauma center before transfer to a burn unit
9. Burned children in hospitals without qualified personnel or equipment for the care of children
10. Burn injury in patients who will require special social, emotional, or rehabilitative intervention

Burn Center Referral Criteria list from Resources for Optimal Care of the Injured Patient, Committee on Trauma, American College of Surgeons, Chicago, IL, p. 101. Copyright © 2014 American College of Surgeons.

Treatment:

Initial Care. First, stop the burn. Remove and isolate the causative agent while protecting the patient and staff. If a scald has occurred, remove all soaked clothing. If chemical exposure is suspected, contact Poison Control for guidance; in industrial or workplace settings, also refer to corresponding Material Safety Data Sheet (MSDS) if available. Unless contraindicated by the MSDS or Poison Control, irrigate wounds with copious amounts of water to dilute and remove contaminants (Jeschke et al., 2020). Isolate clothing to be sure that others are not contaminated.

In evaluating burns in older adult patients, it is imperative to consider their physiological differences from younger adults, along with any associated comorbidities. If transfer to a higher level of care is appropriate, activate the EMS promptly; do not delay for wound debridement. Cover wounds with dry, clean sheets or towels. Maintain a warm environment to minimize the risk of hypothermia. Provide supplemental oxygen as needed to maintain adequate oxygenation. In cases of suspected inhalation injury, administer 100% oxygen via a nonrebreather mask.

Wound Care. Burn wounds are frequently colonized with bacteria from the local environment. These wounds are routinely managed with topical antibiotics; systemic antibiotic therapy is not generally indicated (Table 8-3). Wounds may be doused briefly (30 seconds) with cool water to disperse any remaining heat in the tissue. Continuous use of cool or cold water for pain relief is not advised, because this may cause further tissue damage due to vasoconstriction, as well as hypothermia. Wounds should be cleaned with a mild soap and rinsed. Antibacterial soaps are not necessary. Although small (<2 cm) blisters may be left intact, any loose or devitalized tissue should be removed. Wounds should be washed daily. However, care must be taken to remove exudate and nonviable tissue while also not disturbing the process of reepithelialization.

The goal of wound dressings is threefold: absorb drainage, provide protection, and decrease pain. Dressings used for small burn wounds should be simple, affordable, and manageable by patients and caregivers. For small burns without infection, use simple petroleum-infused mesh with or without antibiotic ointment. When wrapping a burn wound, it is important to consider function. Digits should be wrapped individually to allow for both active and passive range-of-motion exercises. Elevate extremities at rest and utilize compression garments or elastic bandage wraps (lower extremities only) to prevent edema.

Burn wound care utilizes clean rather than sterile technique. Patients and families should be taught proper cleaning techniques, including frequent hand washing and

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TABLE 8-3 Topical Agents and Dressings for Burn Wounds

NAME	USAGE	APPLICATION
Topical antibiotic ointment (bacitracin, mupirocin, triple-antibiotic ointment, Polysporin®)	Small area, partial-thickness burns: prevention and treatment of infection with gram-positive and some gram-negative bacteria. Mupirocin is active against most strains of MRSA.	For facial burns, apply ophthalmic preparations without a dressing and leave open to air (OTA); reapply thin layer as needed to keep wound slightly moist. For burns to other areas, apply a thin layer daily to wound, and cover with a petroleum-impregnated mesh and sufficient outer gauze to absorb exudate. Change outer gauze more often as needed for excess exudate.
Hydrocolloid dressings	Provide a moist protective covering and barrier against exogenous bacteria. Effective for small-area, partial-thickness burns. Not indicated for wounds with large amounts of exudate.	Occlusive dressings may be left in place for 5–7 days for patients with low risk for complication.
Silver sulfadiazine 1%	Prevention and treatment of infection in second- and third-degree burns with eschar burden. Can delay wound healing by impeding epithelialization. Discontinue use once necrotic tissue has sloughed from wound. Contraindicated in those with sulfa allergies or pregnant women.	Do not apply to face. Cover burn area with a layer approximately 1/16-inch thick, wrap with sufficient gauze to absorb exudate, and change daily or more often as needed for excessive exudate.
Petroleum gauze/mesh (Adaptic®, Xeroform®)	Protective covering, 3% bismuth tribro-mophenate in a petrolatum blend (Xeroform®) has bacteriostatic action, can be used with topical antibiotic ointments. May be used in cases of sulfa allergy.	Apply daily, cover with gauze wrapping sufficient to manage exudate. Change external gauze wrapping more often as needed to manage excess exudate.
Aquacel Ag Hydrocolloids Mepitel Ag Silverlon Suprathel TheraBond 3D	Synthetic wound dressings designed to reduce pain, reduce healing time, and manage exudate by either absorbing or transferring exudate to secondary dressing (varies by type). Appropriate for superficial, partial-thickness burns.	Apply primary dressing after thorough wound cleansing, and cover with secondary dressing such as gauze, hydrogel, or foam dressing. Primary dressing may be left in place for 3-7 days between dressing changes (Hydrocolloids, Mepitel Ag, Silverlon) or up to 14 days (Aquacel Ag, Suprathel, TheraBond 3D); change secondary dressing as needed if saturated with exudate.

Adapted from Care of outpatient burns *by C. D. Voight, M. Celis, and D. W. Voight (2018), in D. N. Herndon (Ed.),* Total burn care *(5th ed., pp. 50–57). Saunders Elsevier.*

management of supplies within their environment. Wounds should be examined daily during care for redness, swelling, purulent drainage, or odor. This should be reported promptly to the health-care provider, and the addition of systemic antibiotics should be considered for any signs or symptoms of infection.

Patients should be instructed to minimize exposure to UV light by using protective clothing and applying sunscreen over healed burn wounds. Patients should also be instructed to continue using compression garments in the rehabilitative phase to minimize swelling and scar formation.

Follow-Up: Outpatients should be reevaluated 24 hours after the burn injury. Examine the condition of the wound and surrounding tissues for signs of healing or impending infection. Reexamine respiratory status of patients with an inhalation injury to detect diffuse wheezing and rhonchi. Determine the adequacy of the current pain management regimen. Have the patient or significant other demonstrate proper dressing techniques. Patients should return periodically about every 4 to 6 weeks to determine healing, assess progress/compliance with any physical therapy or occupational therapy if required, and assess coping mechanisms. Depending on the severity of the burn and/or presence of complications, more frequent visits may be necessary at first, until progressive healing is noted.

Sequelae:

Pain. There is benefit in utilizing medications with different mechanisms of action to address pain in burn patients. This is especially true for burn patients undergoing any type of procedure that can include wound care or physical therapy (Romanowski et al., 2020). It should be anticipated that for small burns the need for narcotics will be short lived as the wound heals. With deeper or larger burns, there may be a benefit to adding pharmacological agents that act on neuropathic pain, such as gabapentin and pregabalin. Acetaminophen and NSAIDs have a good safety profile and may help to manage pain and inflammation, if not contraindicated by comorbidities (Romanowski et al., 2020). Evaluation of renal and liver function should be assessed with dosages adjusted accordingly.

Pruritis. The process of healing triggers the mobilization of multiple agents such as cytokines and histamine into the wound bed. Patients may experience intense pruritus, but scratching can cause significant disruption to wound healing. This can be particularly challenging for older adults

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because antipruritic agents, such as diphenhydramine or hydroxyzine, can be sedating. Adequate analgesia in conjunction with these agents can be effective, but care must be taken to avoid oversedation. Consider scheduling agents that selectively block H_1 receptors, such as cetirizine or loratadine, to limit sedating effects. Moisturizers, massage, and pressure garments on healed wounds can aid in management of pruritus and are essential to prevent drying and cracked skin. Pruritus tends to diminish over a period of approximately 6 months as the burn scar begins to mature, but some patients may need additional interventions.

Hypertrophy and Contracture. Collagen production increases during wound healing. This may be more exaggerated with prolonged wound healing, infected wounds, or in individuals prone to keloid formation. Wounds that remain open for 2 weeks or longer tend to be particularly prone to the development of hypertrophic scarring (Jeschke et al., 2020; Voight et al., 2018). Hypertrophy can lead to pain and loss of function through distortion of normal anatomy. The utilization of appropriate topical agents and dressings that act to facilitate timely wound closure will help prevent and/or minimize hypertrophy. In addition, the use of pressure garments over nearly closed or healed wounds will aid normal scar progression.

Hypertrophic scars may compromise the web spaces of the fingers and toes, and contractures and underlying tendon damage in the hands may result in impairments. The resulting loss of function may be restored through surgical intervention, but early and continuous consultation with specialized occupational therapy services is vital for optimal long-term outcomes. Bands and contractures can continue to develop many years after injury, so scars should be monitored periodically for progression.

Prevention/Prophylaxis: Injuries occur when the host, the environment, and vector converge. For example, an older adult falls asleep while smoking, the sheets ignite, and the individual is burned in a house fire. It is the relationship between this person, their environment, and a potentially hazardous agent that can result in injury. The nurse practitioner can affect each of these components (person, environment, agent) and possibly prevent the initial burn injury from occurring. The nurse practitioner, by virtue of education, clinical expertise, and anticipatory guidance, plays a vital role in burn prevention (Grant, 2004).

Primary prevention constitutes product design, regulation, and legislation. This also includes educational programs designed to educate the public on safety. In the previous example, the individual smoking in bed may benefit from a community smoking cessation program. Regulation of product design would affect the combustibility of clothing, linen, and housing materials exposed to the smoldering cigarette. During annual physical examinations, the nurse practitioner should include discussion and education on healthy lifestyle habits (smoking cessation) and home safety priorities such as proper use of smoke alarms, practicing a home escape plan, removal of hazards such as frayed electrical cords, visual aids for those with impaired sight, and the appropriate temperature setting for home hot water heaters.

Secondary prevention includes actions to limit the extent of damage done by an injury, such as cooling wounds initially to mitigate deeper tissue damage. Occupational therapists provide compression garments and ensure proper splitting technique to maintain function. Physical therapists assist with mobilization through stretching and exercise programs.

Lastly, tertiary prevention addresses recovery and rehabilitation. Individuals continue to work with therapists to maximize function. Management of healed burn scars with moisturizers and sunscreen can prevent further skin damage. Through tertiary prevention, the individual optimizes his or her level of functioning and minimizes disability resultant from the burn injury.

Nurse practitioners are instrumental in developing and/or referring clients to community-based programs that promote home safety for older adults (Grant, 2004). Excellent educational programs are available through agencies such as the National Fire Protection Association (NFPA), the Centers for Disease Control and Prevention (CDC), the ABA Prevention Campaign, and verified burn centers.

Referral: Burns often require complex care and the involvement of multiple disciplines. In the older adult population, even a small burn may require complex fluid resuscitation due to extensive comorbidities and influence of polypharmacy. The absence of support systems or the suspicion of elder abuse should prompt considerations for hospitalization and possible referral to a specialized burn care facility. The ABA has developed a list of criteria that should signal the need for referral to a burn center (see Table 8-2). A burn center verified by the ABA can provide services to a burn patient through all phases of the patient's care.

For rehabilitation concerns related to nerve compression, development of scar bands, or contractures, consider referral to a plastic and reconstructive surgeon. Reconstruction after burn injury should also include evaluation of mature scars that have remained hyperemic and hypertrophic for possible photoablation with laser therapy. Occupational therapy and physical therapy are crucial in preserving and maintaining form and function for burn victims (Voight et al., 2018). Referral for these services should be made early in the care of the burn patient. A referral for social services or in-home assistance may be indicated to promote safe return to a living environment. Contact your nearest burn center for referral information. An excellent resource for patient and family support is the Phoenix Society, a national nonprofit organization dedicated to empowering those affected by a burn injury (https://www.phoenix-society.org/).

Education: Education is an ongoing component of patient care. Clinicians should identify who will provide wound care and assist with recovery. The patient or caregiver should demonstrate the ability to perform wound care before leaving the clinic or hospital setting. Provide appropriate written instructions in clear language for wound care, indicators for infection or tissue compromise, and contact information should questions arise. In addition, provide written instructions on medications, including dosing and possible side effects.

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Clinical Recommendation	Evidence Rating	References
Education regarding fire safety and prevention is the most effective intervention to prevent loss of life and injury due to home fires and should be promoted at every visit.	A	Ahrens & Messerschmidt, 2021 Grant, 2004 Jeschke et al., 2020
Initial pain management for burn injuries is with low-dose narcotics sufficient to allow for wound care and therapy. Adjunct therapy with NSAIDs and neuropathic pain modulators is used as indicated.	A	Jeschke et al., 2020 Nielson et al., 2017 Romanowski et al., 2020 Voight et al., 2018
Use topical antibiotics for burn wounds; avoid prophylactic systemic antibiotics.	C	Jeschke et al., 2020 Nielson et al., 2017 Voight et al., 2018
Systematic daily care of burn wounds using clean technique should be performed.	C	Jeschke et al., 2020 Voight et al., 2018
Pressure garments and silicone sheeting prevent swelling, decrease pruritus, and minimize hypertrophic scar formation.	C	Jeschke et al., 2020 Voight et al., 2018
Evaluate for comorbidities, including physical or psychiatric disorders or disabilities.	C	Jeschke et al., 2020 Voight et al., 2018

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CELLULITIS

Signal Symptoms: Erythema, warmth, local tenderness/pain, and edema.

Description: Cellulitis is an infection of the deep dermis and subcutaneous tissues of the skin; most commonly caused by groups A, B, C, and G beta-hemolytic streptococci, *Staphylococcus aureus* (both methicillin-susceptible [MSSA] and methicillin-resistant [MRSA]), and occasionally a gram-negative organism (Bystritsky, 2021; Infectious Disease Society of America [IDSA], 2014). Cellulitis can also be caused by human or animal bite pathogens.

Etiology: Cellulitis usually occurs when an organism enters the skin through an open area. However, a clear site of entry may not be evident in patients with obesity, edema, or lymphedema (Bystritsky, 2021; Silverberg, 2021)

Occurrence: In the United States, the cases and cost of cellulitis have continued to increase; more than 14 million outpatient cases (Silverberg, 2021) and 10% of the infectious disease hospitalizations are related to cellulitis, (Neill et al., 2019). Most cases occur in the summer months (Bystritsky, 2021)

Age: Cellulitis can occur at any age but most commonly in middle-aged and older adults (Bystritsky, 2021). Lower extremity cellulitis is more common in older adults because they may have poor vascular supply masking the common signs of cellulitis (Gbinigie et al., 2019). Cellulitis occurs equally among men and women.

Ethnicity: Cellulitis occurs in all ethnic groups.

Contributing Factors: Predisposing factors include arterial or venous insufficiency, diabetes mellitus, lacerations, obesity, lower extremity edema, lymphedema, human or animal bites (cat bites), tinea infections, recurring cellulitis, burns, trauma, stasis ulceration, ischemia, toe web maceration, IV drug use, and puncture wounds (Bystritsky, 2021; Silverberg, 2021). Any break in the skin or mucous membranes is a port of entry of bacteria (Rrapi et al., 2021). Acute and chronic sinusitis can lead to periorbital or orbital cellulitis. Consider cellulitis in patients who are immunocompromised or on immunosuppressive medications, immunocompetent (HIV infection and AIDS), have drug or alcohol abuse issues, or are prescribed long-term use of corticosteroids or cancer chemotherapy (Silverberg, 2021). The fragile, thinning skin of the older adult can increase the risk of trauma and bacterial infections (Gbinigie, 2019).

Signs and Symptoms: Cellulitis in older adults often presents atypical symptoms, making a diagnosis difficult (Gbinigie et al., 2019). History of trauma or injury to the skin, preexisting skin conditions, recurrent cellulitis, with the signs including warmth, erythema, edema, and localized tenderness/pain of the affected skin (Neill et al., 2019; Rrapi et al., 2021). Cellulitis is typically unilateral. Systemically patients may present with fever, chills or malaise, hypotension, tachycardia, leukocytosis, lymphadenopathy, and lymphangitis (Neill et al., 2019; Bystritsky, 2021). Cellulitis may

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include drainage that can be purulent or nonpurulent (Bystritsky, 2021).

Diagnostic Tests: Unless purulent drainage has formed in the wound, tissue culture is usually not necessary (Silverberg, 2021). In cases of extensive infection or suspected systemic toxicity, blood cultures and a complete blood count (CBC) with differential should be obtained to determine the severity of illness and to identify the organism, including MRSA (Silverberg, 2021). C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR) may be elevated in patients with severe cellulitis (Silverberg, 2021). Patients with diabetes mellitus should have a radiograph of the area and an ESR to rule out the presence of osteomyelitis or necrotizing infection (Bystritsky, 2021). Ultrasounds could detect abscesses or fascial inflammation if strongly suspected (Silverberg, 2021). Skin biopsies may be necessary to rule out the presence of fungal, viral, parasitic, or mycobacterial etiologies if suspected (Silverberg, 2021).

Differential Diagnosis:

- Lipodermatosclerosis (tender red plaque on the medial lower legs with venous stasis or varicosities)
- Stasis dermatitis (bilateral redness, irritation of lower extremities)
- Acute severe contact dermatitis (superficial edema, itching)
- Acute gout (synovial fluid aspiration contains monosodium urate crystals)
- Deep vein thromboses (DVTs) (lower extremity Doppler ultrasound)
- Pseudogout (synovial fluid aspiration contains calcium pyrophosphate crystal deposition)
- Early herpes zoster
- Atypical drug eruptions
- Erysipelas (superficial dermis cellulitis represented by demarcated erythematous area)
- Venous or varicose eczema (limited or localized erythema, absence of systemic symptoms)
- Diagnoses determined by radiographs, magnetic resonance imaging (MRI) or computed tomography (CT)
  - Necrotizing fasciitis (diffuse swelling of an arm or leg with bullae [clear or serosanguineous fluid], crepitus, and intense pain)
  - Osteomyelitis
  - Pyomyositis

(IDSA, 2014; Rrapi et al., 2021; Silverberg, 2021)

Treatment: Ask when the patient's last tetanus toxoid booster was given if an open wound is present. If the most recent booster was 10 years ago and the wound is grossly contaminated, the tetanus immune globulin should be administered immediately followed by the tetanus booster (CDC, 2020). If the wound is grossly contaminated and the patient's last tetanus booster was 5 to 10 years ago, the practitioner should consider giving another booster at this time (CDC, 2020). An older adult who has not had primary immunizations requires tetanus booster and tetanus immune globulin (CDC, 2020).

Patients with mild-moderate cellulitis may be given oral antibiotics (IDSA, 2014; Silverberg, 2021). The drugs of choice (typically for 5 to 7 days) include one of the following: dicloxacillin 500 mg qid; clindamycin 300 mg qid; amoxicillin/clavulanate 875 mg/125 mg bid; and a first-generation cephalosporin such as cephalexin 250 to 500 mg qid. (Bystritsky, 2021; ISDA, 2014). For streptococcal cellulitis, penicillin is the drug of choice (Bystritsky, 2021; IDSA, 2014). Treatment of MRSA (total duration of therapy is 7 to 14 days) should be guided by wound culture results of open wound and/or considered when the patient has higher risk factors for MRSA or cellulitis is nonresponsive to primary choice of treatment (Bystritsky, 2021; ISDA, 2014). Antibiotic choices include one of the following: clindamycin 300 to 600 mg four times daily; doxycycline 200 mg once followed by 100 mg every 12 hours; trimethoprim-sulfamethoxazole 160 mg/800 mg 1 to 2 tablets twice daily; or linezolid 600 mg every 12 hours (Bystritsky, 2021; ISDA, 2014). Newer oral agents are available for treatment of cellulitis but are reserved for when other agents cannot be used (Bystritsky, 2021). Consider the patient's renal function before prescribing any medication. For patients with complications or severe symptoms (especially systemic), hospitalization is recommended for monitoring and to receive IM/IV antibiotics (IDSA, 2014; Silverberg 2021).

Follow-Up: Symptoms of cellulitis may get worse within the first 24 hours to 48 hours after starting treatment but should begin to improve after that time (Bystritsky, 2021). Outpatients should be requested to contact their health-care providers within 1 week if no improvement with antibiotic use or within 48 hours if fever or inflammation continues.

Sequelae: Further issues caused by cellulitis include bacteremia, bullae, lymphangitis, and necrosis of the affected area (Bystritsky, 2021). Older adults have associated increased mortality from cellulitis so appropriate diagnosis and treatment is imperative (Kumar et al., 2020).

Prevention/Prophylaxis: Prevention of cellulitis includes good hand washing, avoidance of injury/trauma, minimizing edema, prevention of peripheral vascular disease, and controlling diabetes. Daily use of compression therapy to lower extremities prone to recurrent cellulitis reduces the risk of recurrence (Webb et al., 2020).

Referral: Patients with high fever, diabetes, alcoholism, HIV, anaerobic cellulitis, necrotizing fasciitis, or cellulitis of the orbit or face, or those experiencing extreme pain should be referred to an infectious disease specialist. A surgical consultation may be required for incision and drainage of abscesses and debridement of necrotic tissue.

Education: Patients with cellulitis must adhere to antibiotic dose, frequency, and duration of antibiotic treatment for optimal results. Avoid trauma to the area, keep the area clean, and elevate the affected area if able (especially if edema is present). If there are no contraindications, patients may use NSAIDs and acetaminophen for pain relief. If there is no DVT, suggest compression bandages to decrease edema (especially if edema causes recurrent cellulitis). As with any infection, blood glucose levels may need to be monitored in those with diabetes. There is an increased risk of DVT associated with cellulitis, and education should include signs and symptoms of DVT (report immediately if they occur). Treat underlying conditions that predispose the cellulitis, such as tinea, maceration, fissuring, chronic venous stasis, or lymphedema (Bystritsky, 2021).

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Clinical Recommendation	Evidence Rating	References
Guidelines were updated to improve diagnosis and treatment of soft tissue and skin infections (cellulitis).	C	IDSA, 2014
Increasing awareness of differential diagnoses associated with erythematous legs improves accuracy of cellulitis diagnosis.	C	Rrapi et al., 2021
Cellulitis is a common skin infection in the older adult. Choosing the right empiric therapy is important.	C	Kumar et al., 2020 Gbinigie et al., 2019
Treatment of cellulitis should cover *Streptococcus* and methicillin-resistant *Staphylococcus aureus* (MRSA). Expand coverage for MRSA if risk factors are present. Five days of treatment is recommended, with extension if no improvement.	A	Bystritsky, 2021

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CORNS AND CALLUSES

Signal Symptoms: Thickened skin or hyperkeratotic area on the foot or hand that is often painful. This section will focus on those occurring on the foot.

Description: Corns and calluses are benign skin lesions on the foot. Corns (helomas) can be soft (heloma molle) or hard (heloma duram). They have distinct borders as compared to callosities. Soft corns are spongy and most often found between the fourth and fifth toes. Hard corns form from calluses over time. They have a central core that is painful with weight-bearing. They occur on the plantar surface of the foot at the metatarsal heads and on the interphalangeal joints. A callus (tyloma) is a hardened area on the foot's plantar surface. Calluses usually are seen at the metatarsal heads, medially to the first metatarsal head and laterally to the fifth metatarsal head. Melo and colleagues (2015) report lesser-toe deformities, including hammer toes, claw toes, and mallet toes, predispose individuals to callus formation on the second through fifth distal surface of the toes.

Etiology: Mechanical forces of compression, shear, and torsion (Hashmi, 2013) put stress on the stratum corneum of the epidermis. This triggers a protective and inflammatory response. The stratum corneum cells form either a plaque (callus) that is superficial or cone shape (corn), which is pointed and deep (Hashmi, 2013).

Occurrence: Corns and calluses, the leading cause of foot pain, are prevalent in older adults with reports of at least 60% of the population experiencing plantar hyperkeratotic lesions (Spink et al., 2009).

Age: Corns and calluses are common with increasing age (Feldman, 2017). Older adults have a higher incidence because the aging process reduces fatty tissue and bones become more prominent (Nordqvist, 2014).

Ethnicity: Blacks report 30% greater occurrence than Whites (Feldman, 2017).

Contributing Factors:

Intrinsic. Bony prominences, foot deformity, mobility alterations, obesity, diabetes, peripheral neuropathy, peripheral arterial disease, anhidrosis, and hyperhidrosis.

Extrinsic. Poor fitting shoes, not wearing socks or wearing socks that fit poorly, high heels, thin-soled shoes, walking barefoot and standing, walking, or running for prolonged periods of time.

Signs and Symptoms: Pain can be the cardinal symptom of both lesions; however, calluses are usually asymptomatic, although they may be of cosmetic concern. Corns are often painful and interfere with daily activities, which is frequently the chief complaint in podiatry practices (Farndon et al., 2015).

Diagnostic Tests: Clinical examination and history taking is usually the method of discovery. A way to distinguish corns from plantar warts is the absence of capillary dotting, known as the Auspitz sign (Al Aboud & Yarrarapu, 2021). Radiographs may be ordered to assess bone anatomy and foot deformity. Hashmi (2013) reported ultrasound has been used but resolution is poor. Dermatology practices are using optical coherence tomography (OCT) to assess before and after treatment (Baillie et al., 2011; Hashmi, 2013). Dermatoscopy may be used to observe and analyze skin lesions. Pressure studies may assist in identifying areas of high pressure on the plantar surface.

Differential Diagnosis:

- Plantar wart
- Poroma
- Warty dyskeratoma
- Gout and pseudogout
- Hypertrophic lichen planus
- Foreign body granuloma
- Porokeratosis
- Underlying ulcer
- Fungal infection (Al Aboud & Yarrarapu, 2021; Feldman, 2017)

Treatment: Self-maintenance of minor calluses can be done by soaking the feet in warm water and sanding the affected area with a pumice stone. Calluses may be softened with emollients (with and without urea). Homeopathic preparations from clove, garlic, aloe vera, barleria prionitis, lantana camera, moringa oleifera, and tecoma capensis provide

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medicinal benefits (anti-inflammatory, antimicrobial, antioxidant, and analgesic properties) for wound healing and can be applied topically (Anil et al., 2020). Barrier creams and occlusive materials, such as silicone sleeves may reduce friction (Hashimi, 2013) and prevent callus and corn formation. Crest pads (off-loading pressure with padding) will reduce pressures (Curran et al., 2015). Salicylic acid plasters and mechanical debridement or paring with a 15-blade scalpel are two successful treatments for removing corns (Farndon et al., 2013). One study of self-perception of pain following three scalpel debridement of painful calluses versus partial debridement was the same in older adults, thus patients need to be aware that there may be a level of pain with debridement (Garcia & Soler, 2020). High-risk patients with some toe deformities may require surgery. Percutaneous digital flexor tendon tenotomy, which is used to straighten a toe when conservative treatment has been unsuccessful (Bus et al., 2016), and electrosurgery (Hashmi, 2013) are two other recognized methods. Ablative laser surgery is available now and is favored by some over sharp debridement (Al Aboud & Yarrarapu, 2021). Microwave therapy has shown positive results for hyperkeratotic lesions (Bristow & Webb, 2020). Patients with diabetes and those with neuropathy should be advised to never use a chemical treatment on their feet. This could damage normal skin without them knowing it (Al Aboud & Yarrarapu, 2021).

Follow-Up: Follow-up is determined by the intervention type. Use of salicylic acid plasters usually demand a follow-up appointment within 1 week to assess the progress of the chemical debridement, the need for mechanical debridement of affected skin, and to assess for any complication (Farndon et al., 2013).

Sequelae: Untreated corns and calluses usually result in extended periods of pain, possible alteration in mobility that could result in falls, and a general decline in quality of life. There is the potential to develop septic arthritis and osteomyelitis (Al Aboud & Yarrarapu, 2021). According to Bus et al. (2016), patients with diabetes are especially at risk as these lesions may ulcerate, become infected, and worst-case scenario, require amputation.

Prevention/Prophylaxis: Encourage self-awareness and inspection of the feet as a basic self-care measure. Providers should inspect the feet of patients with diabetes at every visit. Proper footwear is essential. The shoe must be the proper size and not cause any friction. If a problem area is identified, inspect the inside of the shoe for problems. Lamb's wool and toe pads of felt or silicone may be used to protect the affected area. Prescribed orthotic inserts or therapeutic shoes may be necessary.

Referral: Primary care providers can address the problems associated with corns and calluses; however, podiatric, orthopedic, or neurology referral for patients with complicated corns and calluses should be made when treatment prescribed has not alleviated or improved the problem (Al Aboud & Yarrarapu, 2021).

It is recommended that patients with diabetes see a podiatrist annually (Bus et al., 2015) and with more frequency if high risk factors or problems exist.

Education: Advise patients to maintain good foot hygiene: washing feet regularly, keeping toenails clipped, and wearing clean socks and shoes that fit properly. Diabetic patients should be instructed to wash and inspect their feet daily, looking for problematic areas, and to seek medical assistance when lesions are apparent. Counsel patients on the prevention measures mentioned previously.

Clinical Recommendation	Evidence Rating	References
There was no significant difference in pain perception when patients were treated with full versus partial debridement of plantar hyperkeratoses.	A	Garcia & Soler, 2020
Crest pads offload pressure from the distal area of the toes in patients with lesser toe deformities, improving, minimizing, and preventing callus formation.	A	Melo et al., 2015
Seven mm felt padding reduces plantar pressure as compared to lesser depth felt padding.	B	Curran et al., 2015
Corn plasters are an effective treatment to reduce and resolve corns as compared to scalpel debridement on appropriate patients.	A	Farndon et al., 2013
Gold standard treatment to reduce corns and calluses is scalpel debridement.	C	Hashmi et al., 2016

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HERPES ZOSTER

Signal Symptoms: Cutaneous eruption of a dermatome distribution; burning, itching, or tingling skin sensation.

Description: Herpes zoster (HZ) is an acute vesicular eruption caused by a virus histologically identical to the varicella (chickenpox) virus—human (alpha) herpes virus 3 (varicella-zoster virus [VZV]), a member of the herpes virus group.

Etiology: Recurrent VZV infection causes herpes zoster. All patients with HZ have incurred some version of primary VZV exposure, usually in childhood, either from contact with a

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person who is sick with the virus or from the primary vaccination (Rosamilia, 2020). The DNA virus resides within the neurons. VZV migrates to adjacent sensory dermatomes. Vesicles with pustulation begin to form within 7 days of the rash onset. Pustulated vesicles form scabs/crusting within 10 days of onset (Le & Rothberg, 2019). Older adults have a decrease in cell-mediated immunity, which contributes to the risk of developing herpes zoster and postherpetic neuralgia (PHN). The incidence of HZ increases with age in persons older than 80 years (Dooling et al., 2018).

Although chickenpox is one of the most readily communicable diseases, HZ has a much lower rate of transmission. Nonimmune persons are considered contagious 8 to 21 days after exposure to VZV. Transmission occurs upon contact with the vesicle fluid. Patients with herpes zoster may be sources of infection for 1 week after the appearance of vesicle lesions.

Occurrence: HZ occurs worldwide, more commonly in older adults. Incidence increases markedly in those 60 years old or older as a result of impaired cell-mediated immunity. One case of herpes zoster occurs for every 100 older adults (Centers for Disease Control and Prevention [CDC], 2020). In the United States, more women are diagnosed with HZ than men (CDC, 2020).

Age: This infection is most common in adults older than 55 years old. It is estimated that the risk of contracting HZ is greater than 50% for those 85 years of age or older. (CDC, 2020).

Ethnicity: Herpes zoster is 50% less common in the African American population (CDC, 2020).

Contributing Factors: Individuals are more likely to develop herpes zoster if they are more than 55 years old, have diabetes mellitus, have had an organ transplant, are immunosuppressed (e.g., patients infected with HIV), have certain malignancies, are receiving long-term corticosteroids, are receiving chemotherapy, or are taking radiation treatments (CDC, 2020).

Signs and Symptoms: Patients usually experience hyperesthesia with an itching, burning, or tingling pain at the site 4 to 5 days before the eruption appears. Pain in a dermatomal pattern may precede the appearance of the vesicles by weeks, however. Allodynia, the presence of pain without a painful stimulus applied to the area, may also be experienced (Ganty, 2014). Patients often experience a sense of anxiety, malaise, headache, fever, and flu-like symptoms with the onset of HZ. Patients may report sleep disturbances, decreased appetite, and depression. There may be reported pain around the eye if ophthalmic HZ later develops. A rash, initially erythematous, forms into vesicular lesion when the VZV reactivates in the dorsal ganglia. The vesicles are clear at first and then become cloudy within 3 to 5 days. T1 to L2 are the most common vertebral dermatomes involved, followed by cervical and sacral dermatomes (Le & Rothberg, 2019). As vesicles age, they become pustular, then crust over after 7 to 10 days, finally healing in 2 to 4 weeks (CDC, 2020; Ganty, 2014).

Lesions may appear in irregular crops and are typically unilateral. Scarring and change in pigmentation may occur following the healing of the crusted vesicles. The most common distributions are on the trunk or face in elderly. The pain can last 6 to 12 months after disappearance of the rash (PHN). Ocular complications occur in about one-half of patients with involvement of the ophthalmic division of the trigeminal nerve. These complications may include keratitis, anterior uveitis, and corneal ulceration. Vesicles on the tip of the nose, known as Hutchinson sign, have been found to be a precursor to ocular involvement in HZ (Sampathkumar et al., 2009). Cutaneous or visceral dissemination, the appearance of numerous varicella-like lesions in extradermatomal sites, may cause pneumonitis, encephalitis, meningitis, myelitis, and hepatitis (CDC, 2020; Fashner & Bell, 2011). The reactivation of VZV in the geniculate ganglion produces vesicles in the mucocutaneous distribution of the peripheral nerves. Known as Ramsey-Hunt syndrome, patients may experience vesicles in the pharynx and external auditory canal, tinnitus, vertigo, one-sided hearing loss, nausea and vomiting, involuntary eye movements and often paralysis on one side of the face (Sampathkumar et al., 2009).

Diagnostic Tests: Diagnosis usually is based on clinical appearance and distribution of the eruption and on a careful history of when the rash appeared. The direct immunofluorescence with fluorescein-tagged antibody (DFA) or polymerase chain reaction (PCR) is preferred over the old standard Tzanck smear. The PCR has the highest sensitivity and specificity. It detects DNA in fluids and tissues (Le & Rothberg, 2019).

Differential Diagnosis:

Pain
- Migraine
- Trigeminal neuralgia
- Myocardial infarction
- Acute abdomen
- Renal colic
- Pericarditis
- Pleuritis
- Pulmonary embolism
- Cholecystitis

Rash
- Contact allergic dermatitis
- Herpes simplex (Le & Rothberg, 2019)

Eye Symptoms
- Ulcerative keratitis
- Acute angle closure glaucoma

Treatment: Antiviral agents are recommended in the presence of significant pain, serious HZ, or involvement near the eye. PHN is not prevented by antiviral therapy, but these agents may decrease PHN duration. Give acyclovir 800 mg five times a day for 7 days: famciclovir 500 mg orally every 8 hours for 7 days, or valacyclovir 1,000 mg orally every 8 hours for 7 days (Saguil et al., 2017). These drugs must be given within 72 hours after onset of rash to be effective, and their use must be monitored in patients with reduced renal function (Beuscher et al., 2017; Tyring et al., 2000). Patients with disseminated disease and those who are immunocompromised may need IV antiviral medications.

Glucocorticoids are used at times as an adjunct to antiviral therapy; these agents have been said to reduce acute pain and can speed healing (Saguil et al., 2017). However, in three adequately powered random controlled studies, evidence was insufficient to support this (Dvorin & Ebell, 2020). Topical

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agents are also effective in treating the initial symptoms of herpes zoster. The use of cool compresses with 1:20 Burrow's solution, calamine lotion, and topical lidocaine (Xylocaine) is recommended for the soothing local effect. Topical antivirals are not recommended (Le & Rothberg, 2019).

Analgesics may be necessary for the initial prodromal pain associated with HZ. Acetaminophen and NSAIDs are recommended initially, but around-the-clock dosing is needed for optimal pain control. Tramadol may be used for moderate pain, and stronger opioids are used for severe pain.

The capsaicin 8% cream and 5% lidocaine patch have been recommended for first-line pain management of PHN. Capsaicin cream is not recommended for acute HZ but is more economical compared to the lidocaine patch. Both are available over the counter (Derry et al., 2017; Saguil et al., 2017; Schmader, 2018).

Gabapentin and pregabalin are also recommended for the treatment of PHN. The initial dose of gabapentin is 300 mg on the first day and is titrated up gradually until pain relief is safely reached. The maximum does of gabapentin is 3,600 mg per day (Chou et al., 2009).

Pregabalin is also recommended for the treatment of PHN and can be administered 50 mg three times a day or 75 mg twice a day. The dosage can be increased to 300 mg daily after 3 to 7 days as tolerated, followed by 150 mg every 3 to 7 days. The maximum recommended dose is 600 mg per day. Caution is advised when prescribing gabapentin and pregabalin to older adults, given probably reduced renal function and the side effects of dizziness and ataxia.

The secondary amine tricyclic antidepressants, nortriptyline 10 mg orally or desipramine 10 to 25 mg orally, have been used in the past; however, because of the anticholinergic side effects in the older population, caution is warranted. Studies show that pain relief with gabapentin and tricyclic antidepressants were the same (Chou et al., 2009). The use of Magnesium sulfate for chronic PHN has proven to be as effective as ketamine. (Shin et al., 2020). Alternative methods of pain management include transcutaneous electrical nerve stimulation, acupuncture, cupping, and meditation.

Follow-Up: Patients should be reexamined in 2 to 4 weeks to monitor progression of rash and as needed for follow-up of PHN.

Sequelae: PHN is the primary complication, occurring almost exclusively in people over 60 years old. Twenty percent of people older than the age of 85 years diagnosed with HZ develop PHN (Ganty, 2014). This pain persists at least 6 weeks after skin lesions. The pain, characterized as constant, severe, sharp, or burning, may develop into a long-standing, debilitating problem. PHN usually lasts 1 year or less. Another possible consequence of HZ is a secondary bacterial infection leading to cellulitis. There is also an increased risk of an acute cardiovascular event, such as a cerebrovascular accident or myocardial infarction in the weeks to months after an episode of HZ (Kim et al., 2017).

Prevention/Prophylaxis: The newest vaccine for herpes zoster (Shingrix) is available and is recommended for patients aged 50 years and older (CDC, 2020; Dooling et al., 2018). People who have had HZ should receive the vaccine to help prevent future occurrences of the disease. The immunization is also recommended without any serologic testing, history of varicella, or history of HZ. The vaccine is given in two doses, with the second dose to be given 2 to 6 months after the first dose. Patients should be scheduled for the second visit (Dooling et al., 2018; Resnick, 2017). With the protection of the Zostavax vaccination waning within the first 5 years and protection uncertain (CDC, 2019; Dooling et al., 2018), it is recommended that patients be protected with the Shingrix vaccination even if they have had the Zostavax vaccine in the past (Dooling et al., 2018; Resnick, 2017). Practitioners are advised to review the listed contraindications before administering the HZ vaccine. High-risk individuals, such as immunosuppressed patients and individuals who may not be able to receive the Shingrix vaccine or have not had chickenpox, may benefit from low-dose acyclovir which could prevent HZ (Schmader, 2018). These individuals should also distance themselves from patients with HZ.

Referral: Because of probable ocular involvement, patients with lesions on the nose or in the eye area should be referred to an ophthalmologist. Patients with disseminated HZ in need of IV antivirals should be referred to an infectious disease specialist. Patients with severe uncontrollable PHN should be referred to a pain management clinic, and a neurology referral may be necessary for HZ with neurological complications such as vasculopathy or neuritis (Schmader, 2018).

Education: Emphasize to the patient the need to stay home and get plenty of rest. Patients are to be advised to keep area clean and dry to prevent superimposed infections that may be caused by excessive scratching. Proper infection control measures and proper disposal of dressings should be encouraged, especially in regard to items of clothing that contain vesicle fluid. This fluid may infect known contacts that are vulnerable for developing varicella; therefore, patients should avoid direct body contact with individuals who are immunocompromised or have not had chickenpox. Covering open, wet lesions may decrease transmission. The respiratory tract of infected people may also shed virus from the respiratory tract (Le & Rothberg, 2019).

Clinical Recommendation	Evidence Rating	References
Antiviral therapy should be initiated within 72 hours of onset of the maculopapular lesions to increase the healing of the herpes zoster (HZ) and decrease the duration of postherpetic neuralgia (PHN).	A	Tyring et al., 2000 Beuscher et al., 2017
Non-drug measures for acute HZ symptoms include applying cool, astringent compresses, keeping the rash clean and dry, and wearing loose clothing.	B	Schmader, 2018 Le & Rothberg, 2019

Continued

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Clinical Recommendation	Evidence Rating	References
The HZ vaccine (Shingrix), unless contraindicated, should be given to persons ≥50 years old to prevent an outbreak of HZ and subsequent development of PHN.	A	CDC, 2019 Dooling et al., 2018
The use of 8% capsaicin cream or patch provided sustained relief from post-acute pain in patients with PHN.	A	Derry et al., 2017
NSAIDs alone or in combination with a weak opioid tramadol may be valuable in the treatment of PHN. For those intolerant of opioids, one or a combination of anticonvulsants, tricyclic antidepressants, or corticosteroids may be appropriate but should be used with caution in the older adult.	B	Song et al., 2018 Shin et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PRESSURE INJURIES

Pressure injuries are classified through the use of staging systems. These systems describe the degree of tissue loss and the clinical presentation of the injury caused by pressure and/or shear. Pressure injury staging has become the basis for treatment, comparison of outcomes, and, if applicable, reimbursement. It is noteworthy that in April 2016 the National Pressure Ulcer Advisory Panel (NPUAP, now National Pressure Injury Advisory Panel, NPIAP) updated the Pressure Injury Classification System after a rigorous literature review by an appointed task force, soliciting input from stakeholders and the public, and hosting the consensus conference with over 400 stakeholders in attendance. The revisions reflect current scientific and clinical understanding of the etiology of pressure injuries, as well as clarify and make the system more accurate and easier to use (Edsberg et al., 2016).

Only pressure injuries should be staged with the NPIAP Staging System. Non–pressure-related ulcers and wounds are subject to unique staging or classification systems based on wound type; these include diabetic foot ulcers (Wagner Classification System), venous leg ulcers (Clinical Etiology Anatomy Pathophysiology [CEAP]), skin tears (International Skin Tear Advisory Panel [ISTAP]), medical adhesive or tape injuries (Medical Adhesive Related Skin Injury [MARSI] categories) and burn classification (TBSA). It is essential to confirm the presence of pressure and/or shear as a causative factor prior to using the NPIAP Staging System for an injury. Because the NPIAP Staging System is based on the extent of tissue damage, an understanding of anatomy is required prior to evaluating tissue types found in wounds. Finally, to ensure an accurate assessment, pressure injury staging should take place only after a wound has been thoroughly cleansed. In 2016, several revisions, which follow, were made to the NPIAP Staging System.

Signal Symptoms: Intact skin with a localized area of nonblanchable erythema may be present, which may appear differently in darkly pigmented skin. It is usually over a bony prominence or related to a medical device. Presence of blanchable erythema or changes in sensation, temperature, or firmness may precede visual changes. Partial-thickness involves loss of skin with exposed dermis, intact serum-filled blister. Full-thickness loss of skin with visible adipose (fat) tissue and/or deeper structures such as fascia, muscle, tendon, ligament, cartilage, or bone may be exposed. Wound edges may be open or present with epiboly (closed or rolled edges). Depth may be obscured by the presence of necrotic tissue, resulting in an unstageable pressure injury until such time when the wound bed becomes visible, and the degree of tissue damage can be determined. Intact or nonintact skin may be present with a purple or maroon discoloration and/or an epidermal separation revealing a dark wound bed or blood-filled blister (European Pressure Ulcer Advisory Panel, National Pressure Injury Advisory Panel, and Pan Pacific Pressure Injury Advisory Panel [EPUAP/NPIAP/PPPIAP], 2019)

Description: A pressure injury is localized damage to the skin and underlying soft tissue usually over a bony prominence or related to a medical device. The injury can present as intact skin or an open ulcer and may be painful. The injury occurs as a result of intense and/or prolonged pressure or pressure in combination with shear. The tolerance of soft tissue for pressure and shear may also be affected by microclimate, nutrition, perfusion, comorbid conditions, and condition of the soft tissue. Common terms for pressure injury include *pressure ulcer, decubitus ulcer, bedsore*, and *pressure sore.* There are six pressure injury stages and two categories pertaining to etiology based on anatomical location (Edsberg et al., 2016):

- Stage 1: Intact skin with a localized area of nonblanchable erythema, which may appear differently in darkly pigmented skin. Presence of blanchable erythema or changes in sensation, temperature, or firmness may precede visual changes. Color changes do not include purple or maroon discoloration; these may indicate DTPI.
- Stage 2: Partial-thickness loss of skin with exposed dermis. The wound bed is visible, pink or red, moist, and may also present as an intact or ruptured serum-filled blister. Adipose (fat) is not visible and deeper tissue is not visible. Granulation tissue, slough, and eschar are not present. These injuries commonly result from

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adverse microclimate and shear in the skin over the pelvis and shear in the heel.

- Stage 3: Full-thickness skin loss in which adipose (fat) is visible in the ulcer and granulation tissue and epibole (rolled wound edges) is often present. Slough and/or eschar may be visible. The depth of tissue damage varies by anatomical location: areas of significant adiposity can develop deep wounds. Undermining and tunneling may occur. Fascia, muscle, tendon, ligament, cartilage, or bone is not exposed. If slough or eschar obscures the extent of tissue loss, this is an unstageable pressure injury.
- Stage 4: Full-thickness skin and tissue loss with exposed or directly palpable fascia, muscle, tendon, ligament, cartilage, or bone in the ulcer. Slough and/or eschar may be visible. Epibole (rolled wound edges), undermining, and/or tunneling often occur. Depth varies by anatomical location. If slough or eschar obscures the extent of tissue loss, this is an unstageable pressure injury.
- Unstageable: Full-thickness skin and tissue loss in which the extent of tissue damage within the ulcer cannot be confirmed because it is obscured by slough or eschar. If slough or eschar is removed, a stage 3 or stage 4 pressure injury will be revealed. Stable eschar (i.e., dry, adherent, intact without erythema or fluctuance) on ischemic limbs or heels should not be softened or removed.
- DTPI: Intact or nonintact skin with localized area of persistent nonblanchable deep red, maroon, purple discoloration, or epidermal separation revealing a dark wound bed or blood-filled blister. Pain and temperature change often precede skin color change. Discoloration may appear differently in darkly pigmented skin. This injury results from intense and/or prolonged pressure and shear forces at the bone-muscle interface. The wound may evolve rapidly to reveal the actual extent of tissue injury or may resolve without tissue loss. If necrotic tissue, subcutaneous tissue, granulation tissue, fascia, muscle, or other underlying structures are visible, this indicates a full-thickness pressure injury (unstageable, stage 3, or stage 4). Do not use DTPI to describe vascular, traumatic, neuropathic, or dermatological conditions.

Ulcer Versus Injury. The 2016 NPUAP Pressure Injury Staging System used the term *injury* instead of *ulcer.* After an intensive review, the panel determined that the term *ulcer* did not accurately describe the clinical presentation of a stage 1 pressure injury or a deep tissue pressure injury (DTPI). In short, an ulcer cannot be present without an injury, but an injury can be present without an ulcer.

Roman Versus Arabic Numerals. Roman numerals were changed to Arabic numerals in each of the numbered stages. This change was made to clarify and reduce the potential for confusion between similar terms used in health care, such as stage IV and intravenous (IV).

Artwork. Artwork was created to illustrate the features of each stage of pressure injury. It is a graphic representation of the tissues present and is to be used for teaching about the extent of injury and the tissues present or absent within each stage of pressure injury. A color version of the artwork is available as a free download on the NPIAP Web site at (https://npiap.com).

Suspected Removed, Pressure Inserted in DTPI. The word *suspected* has been removed from the term *deep tissue injury* and the word *pressure* inserted for consistency with the revisions of the other terms.

Teaching Points. Teaching points (key elements of understanding) have been included with each stage. Educators and those responsible for the accuracy, as well as the interrater reliability of serial assessments, can use these teaching points as elements of an orientation or skills competency program for bedside care providers.

Etiology: Although the science regarding the etiology of pressure injuries has supported the role of tissue deformation, microclimate, nutrition, perfusion, and tissue tolerance, the exact mechanism of pressure injury development is poorly understood (Edsberg et al., 2016). Classic references by Kottner and colleagues (2009) describe four causation theories: ischemia caused by occlusion of the capillaries leading to vascular insufficiency, tissue anoxia, and cell death; reperfusion injury (i.e., cellular injury resulting from the reperfusion of blood to previously ischemic tissue); impairment of lymphatic function leading to a build-up of metabolic waste products; and mechanical deformation of tissue cells (Kottner et al., 2009). The type of tissue involved is also important, with epidermis and dermis being more resilient to the effects of pressure than muscle (Kottner et al., 2009). Also, the type of force or combination of forces (i.e., pressure, shear, friction) exerted on the tissue is important. Pressure and shearing forces mainly affect deeper tissue layers, with moisture, pressure, and friction affecting primarily superficial layers (Kottner et al., 2009). Consequently, pressure is believed to be the major causative factor in pressure injury formation. Several factors play a role, however, in determining whether pressure is sufficient to create an injury. Bergstrom and colleagues (2013) studied the pathological effect of excessive pressure on soft tissue and determined pressure injuries can be attributed to intensity of pressure, duration of pressure, and tissue tolerance (the ability of skin and its supporting structures to endure pressure without adverse sequelae). Injury occurs to the skin and underlying tissues. Ischemia and hypoxia result as the pressure is applied to the area. Waste products accumulate as the ischemia continues, which produces toxins that cause further tissue breakdown.

Medical Device-Related Pressure Injury. Medical device-related pressure injuries result from the use of devices designed and applied for diagnostic or therapeutic purposes. The resultant pressure injury generally conforms to the pattern or shape of the device. The injury *should* be staged using the 2016 NPIAP Pressure Injury Staging System (Delmore & Ayello, 2017).

Mucosal Membrane Pressure Injury. Mucosal membrane pressure injuries (MMPI) are found on mucous membranes with a history of a medical device in use at the location of the injury. Mucosal tissues are especially vulnerable to pressure from medical devices such as oxygen tubing, endotracheal tubes, bite blocks, orogastric and nasogastric tubes,

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indwelling urinary catheters, and fecal containment devices. Because the 2016 NPIAP Pressure Injury Staging System for cutaneous injuries is based on the anatomy of the skin, it *cannot* be used to stage mucosal pressure injury. Development of a classification system for MM pressure injuries has been undertaken with testing of reliability performed in an intensive care setting (ICU). The Reaper Oral Mucosa Pressure Injury Scale (ROMPIS), which described three stages of MM pressure injury, showed moderate interrater reliability. This classification system is undergoing further validation. (Reaper et al., 2017).

Occurrence: Definitive information on the occurrence of pressure injuries is limited. Studies to date have been encumbered by methodological issues such as variability in describing the lesions and in differentiating pressure injuries from lesions of other etiologies. Consequently, pressure injuries are common; increase patient morbidity and mortality; and are costly for patients, their families, and the health-care system (Bauer et al., 2016).

The incidence in hospitalized patients ranges from 2.7% to 29% and the prevalence in hospitalized patients ranges from 3.5% to 69%. Patients in critical care units have an increased risk of pressure injuries, as evidenced by a 33% incidence and 41% prevalence. Older adults admitted to acute care hospitals for nonelective orthopedic procedures, such as hip replacement and treatment of long bone fractures, are at even greater risk, with a 66% incidence (Engels et al., 2016)

In the nursing home environment, the prevalence of pressure injuries is in the range of 2.6% to 24%. The incidence has been as high as 25% in residents admitted from an acute care hospital. Patients with preexisting pressure injuries demonstrate a 26% incidence of additional pressure injury formation over a 6-month period. The incidence in chronic care hospitals is reported to be 10.8%, whereas 33% of those admitted to a chronic care hospital have pressure injuries. Long-term follow-up demonstrates that most injuries healed within a year. Persons with spinal cord injury and associated comorbidity are also at increased risk. The incidence of pressure injuries in this population is in the range of 25% to 66%.

Age: It has long been believed that comorbid conditions are associated with pressure injuries, and age is considered a comorbid state. Recent literature reviews suggest, however, that age is a confounding factor and a general indicator of likely deficits in the main areas of risk, including mobility/activity, skin status, perfusion and oxygenation, nutrition, and skin moisture (EPUAP, 2019). Prevalence of pressure injuries in the older adult population is 11.6% to 27.5%, with the increased risk being assigned to those of advancing age. The incidence in skilled care and nursing home facilities is approximately 25%. Patients admitted to a hospital geriatric unit have similarly high prevalence rates: of patients under 70 years of age, only 6% have pressure injuries; of patients older than 70 years of age, the prevalence almost doubles to 11.6%.

Ethnicity: Cited in the literature and mentioned in the NPIAP 2016 Staging System Update is that there may be some difficulty in detecting stage 1 pressure injuries in persons with darker skin pigmentation because the red-hued changes may appear more subtly in persons with darker skin tones. Thermography has been shown to improve skin assessments in patients with dark skin tones. (Black and Simende, 2020).

Contributing Factors: The main contributing factors to pressure injury development are pressure, shear, adverse microclimate, and malnutrition. Moisture is cited as a related condition because it alters the resiliency of the epidermis to external forces. The primary offending source of moisture is incontinence, and more fecal incontinence than urinary incontinence due to the significantly higher pH of feces (liquid greater than solid) when compared to that of urine. The skin's pH is an acid mantle (i.e., 5.5). Understanding the concept and presentation of moisture associated skin damage (MASD), particularly the two subcategories of incontinence associated dermatitis (IAD) and intertriginous dermatitis (ITD), are essential in the differential diagnosis of pressure injuries from those partial-thickness tissue injuries that are not resultant from pressure (Gray et al., 2011).

Signs and Symptoms: A detailed history of the pressure injury should be obtained from the patient or caregiver, including chronic illness, hygiene, nutritional status, immobility, presence and type of prolonged moisture, ability to perform activities of daily living (ADLs), psychological impact of injury, and sources of available support. Ask the patient if they have pain over or near bony prominences or beneath medical devices.

Clinical presentation can vary from nonblanching erythema to partial-thickness tissue loss and frank tissue necrosis. Nonblanching erythema results from damage to blood vessels and extravasation of blood into the tissue. Its presence suggests that more extensive tissue damage is imminent or has already occurred. The color of the skin can be varying hues of pink to red to darker toned hues of maroon or purple. Pressure-induced nonblanching erythema is occasionally misdiagnosed as a hematoma or ecchymosis. When DTPI is also present, the area is often either indurated or boggy when palpated. Note the injury size; obtain serial measurements of length, width, and depth; note the characteristic of the wound edge (open or epibole [rolled]); note the presence and character of exudate, epithelialization, granulation tissue, deeper structures, and findings such as necrotic tissue, sinus tracts, undermining, tunneling, and other signs of infection, such as induration, warmth, and/or advancing erythema (McNichol et al., 2022)

Diagnostic Tests: General laboratory tests for the patients with a pressure injury include wound culture and sensitivity. Particularly look for any of the following:

- Signs of local infection (erythema, edema, change in exudate to include purulent or foul-smelling drainage, pain, crepitus)
- Signs of systemic infection (fever, leukocytosis); bone involvement (due to risk of osteomyelitis)
- Presence of chronicity to determine whether there is a causative, elusive organism

Evaluation of nutritional status should include total protein, albumin, and prealbumin; in patients with a pressure injury, often these clinical indicators are decreased because of inadequate nutritional stores present for tissue repair. A CBC may reveal increased red blood cell distribution,

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decreased lymphocyte count (malnutrition), and elevated leukocyte count (osteomyelitis). The erythrocyte sedimentation rate will be increased. X-rays of the appropriate area often reveal bony rarefaction (decreased density), periosteal elevation, and new bone formation. New ICD-10-CM diagnosis codes for Moisture-Associated Skin Damage (MASD) have been approved by the ICD-10 Coordination and Maintenance Committee and will take effect on October 1, 2021. These codes will improve patient care and outcomes, resource allocation, clinician education, data collection, and facilitate research.

Differential Diagnosis:

- Skin cancers (neoplasms)
- Fungal or yeast infections
- Herpes simplex (HSV-2)
- HZ (shingles)
- Lower extremity wounds (venous, arterial, mixed etiology, and neuropathic etiology in origin)
- MASD, particularly IAD and ITD
- Burns (thermal injuries) (McNichol et al., 2015)

Treatment: Effective pressure injury treatment with topical dressings requires consideration of numerous factors. Consider use of the mnemonic I DIP A MOP:

- **I**nfection (eliminate, reduce bioburden)
- **D**ebride necrotic tissue (consider surgical/conservative, sharp, mechanical, enzymatic, biologic, autolytic)
- **I**nsulate the wound
- **P**rotect periwound tissue
- **A**bsorb excess exudate
- **M**aintain a constant moisture level
- **O**bliterate dead space
- **P**revent further injury

Pharmacological Management. Most moisture-retentive dressings are available without a prescription. Some antimicrobials (e.g., silver sulfadiazine, mupirocin), some antifungals (e.g., fluconazole), and some enzymatic debriding agents (e.g., collagenase) are prescriptive.

Follow-Up: Practitioners need to objectively evaluate the patient's progress toward healing at least weekly using standardized methods of assessment (e.g., wound measurements in three dimensions, amount of exudate, patient comfort, etc.). Immediate intervention is indicated if wound deterioration is observed sooner. If the wound deteriorates, is it in accordance with a decline in the patient's overall condition? It is important to communicate this decline as an expected result to patient, caregivers, and staff. The patient's general health and nutritional intake, the stability of the comorbid conditions, the need for psychological support, and the patient's comfort level should be monitored. Signs and symptoms of complications need to be reported and recorded accurately (McNichol et al., 2022).

Sequelae: Complications include, but are not limited to, cellulitis, bacteremia, osteomyelitis, and sepsis (secondary to pressure injuries).

Prevention/Prophylaxis: Use a valid and reliable risk assessment tool (e.g., Braden, Norton) at the first encounter and at regular intervals thereafter for patients at risk. Specific interventions are to be directed at the first encounter and at regular intervals following initial appraisal of skin and should be targeted toward improving subscale scores in any areas in which the patient's score falls below normal. Enlist the support of an interdisciplinary care team (e.g., nurse, physician, physical therapist, caregiver, dietitian, pharmacist) to ensure all goals of care are addressed adequately. Consider support surfaces for bed and/or chair when decreased mobility and moisture are risk factors (McNichol et al., 2020).

Referral: Consider referral to a wound care specialist (wound, ostomy, and continence [WOC] nurse, plastic surgeon, infectious disease practitioner, dermatologist) if wounds fail to progress in spite of evidence-based interventions consistent with the overall plan of care.

Education: Practitioners should provide patients and their caregivers with information that highlights the applicable contributing factors to the development of pressure injury formation and information about techniques being used (or those attempted, but not tolerated by the patient) pertaining to mitigation of those contributing factors.

- Review available and appropriate treatment modalities for each identified stage of wound progression, as well as expected outcomes and anticipated time frames for healing.
- Discuss reportable signs and symptoms of infection and complications.
- Discuss advances in technology and dispel myths that may exist regarding wound care.
- Identify informative Web-based resources and explain that information available via electronic means and/or from well-meaning individuals may not be evidence based.
- Discuss hand hygiene and disposal of soiled dressings.
- Review the importance of positioning, sources of dietary protein, and the amount to be consumed during the wound repair process.

Clinical Recommendation	Evidence Rating	References
When conducting a pressure injury risk assessment: • Use a structured approach. • Include a comprehensive skin assessment. • Supplement use of a risk assessment tool with assessment of additional risk factors. • Interpret the assessment outcomes using clinical judgment.	C	EPUAP/NPAIP/PPPIA, 2019

Continued

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Clinical Recommendation	Evidence Rating	References
Consider the impact of the following factors on an individual's risk of pressure injury development: • Skin maturity • Perfusion and oxygenation • Poor nutritional status • Increased skin moisture	B	EPUAP/NPAIP/PPPIAP, 2019
Conduct a comprehensive pain assessment for individuals with a pressure injury.	B	EPUAP/NPAIP/PPPIAP, 2019
Assess the skin under and around medical devices for signs of pressure related injury as part of a routine skin assessment.	C	EPUAP/NPAIP/PPPIAP, 2019
Use a soft silicone multilayered foam dressing to protect the skin for individuals at risk of pressure injuries. Use a prophylactic dressing beneath a medical device to reduce the risk of medical device related pressure injuries.	B B	EPUAP/NPAIP/PPPIAP, 2019
Offer fortified foods and/or high-calorie, high-protein oral nutritional supplements between meals if nutritional requirements cannot be achieved by dietary intake.	B	EPUAP/NPAIP/PPPIAP, 2019
Reposition all individuals with or at risk of pressure injuries on an individualized schedule unless contraindicated.	B	EPUAP/NPAIP/PPPIAP, 2019
Use a high-specification, reactive single layer foam mattress for all individuals assessed for being at risk for pressure injury development.	B	EPUAP/NPAIP/PPPIAP, 2019
Use a pressure redistribution cushion for preventing pressure injuries in people at high risk who are seated in a chair/wheelchair for prolonged periods, particularly if the individual is unable to perform pressure relieving maneuvers.	B	EPUAP/NPAIP/PPPIAP, 2019
Consider the potential impact of older age on the risk for pressure injuries.	C	EPUAP/NPAIP/PPPIAP, 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PSORIASIS

Signal Symptoms: There are several forms of psoriasis. The most common is plaque psoriasis, with erythematous patches, papules, and plaques with silvery scales that may be pruritic. Other forms include inverse psoriasis in intertriginous areas that appears as a smooth plaque; guttate, which is a rare form that presents with pustules; pustular, a rare pustular eruption which can occur in association with another form of psoriasis or independently; and erythrodermic, which can be deadly with generalized rash. Up to 30% of those diagnosed with psoriasis will develop psoriatic arthritis, which shares features of both rheumatoid and spondyloarthritis (Ritchlin et al., 2017).

Description: Psoriasis is a common inflammatory skin disease that results from a combination of environmental triggers and genetics. Well-defined, erythematous plaques with an overlying silvery scale are characteristics of the most common variant, chronic plaque psoriasis (Bolognia et al., 2018). If the scale is removed traumatically, the presence of bleeding points, Auspitz sign, is noted. When the lesion is present in intertriginous areas, the moist environment macerates the scale, so the lesion appears as a smooth plaque. This is referred to as inverse psoriasis. Guttate psoriasis presents as an acute eruption of generalized round or raindrop-like, scaly papules. Pustular psoriasis, in contrast to papular types, include pustular psoriasis of the palms and soles or generalized pustular psoriasis (Zumbusch psoriasis). The least common, yet the most life-threatening variant is erythrodermic psoriasis. It occurs most often as an acute eruption of large, red patches with desquamation in those diagnosed with plaque psoriasis. Less often, it can occur as the first sign of psoriasis (Bolognia et al., 2018). Frequently, those with psoriasis have involvement of either the fingernails or toenails. Fingernail involvement is more common (Habif, 2016; Wolff et al., 2017).

Psoriasis can also affect the joints, causing a seronegative inflammatory arthritis, psoriatic arthritis. It is also associated with other chronic diseases such as cardiovascular disease, metabolic syndrome, and nonalcoholic steatohepatitis (Botelho et al., 2020; Miller et al., 2014). Generally, the symptoms of psoriasis occur in those aged 30 to 39 years and 50 to 69 years. Joint symptoms occur before skin psoriasis in about 15% of cases. Symptoms include early morning stiffness; warm, red joints; and effusions.

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Etiology: Genetic susceptibility, an altered immune response, and a variety of environmental triggers drive the pathogenesis of psoriasis. Interactions between T cells, cytokines, keratinocytes, neutrophils, and dendritic cells play a role in the initial onset and duration of skin inflammation (Armstrong & Read, 2020). Approximately 40% of patients with psoriasis or psoriatic arthritis have a family history of the disease. In addition to the genetics, environmental factors are often the trigger, including skin trauma (Koebner phenomenon), streptococcal or viral infection, stress, medications, smoking, and alcohol consumption (Patterson, 2016).

Occurrence: Psoriasis affects about 2% of the world's population and as high as 4.6% in the United States, or about 15.5 million Americans (Michalek et al., 2016). Chronic stable plaque psoriasis is the most common type, affecting up to 80% of those with psoriasis. Guttate psoriasis most often occurs in younger adults and represents about 8% of patients with psoriasis (National Psoriasis Foundation, 2021). There is an equal incidence of the disease in males and in females.

Age: Psoriasis can have a bimodal age presentation with the peak incidence at age 22.5 with a late onset occurring between 55 to 69 years of age. Women tend to have earlier onset, and earlier onset is associated with more severity of the disease. Psoriatic arthritis occurs most often in those between the ages of 30 and 50 years (National Psoriasis Foundation, 2017).

Ethnicity: Prevalence is highest among Scandinavians, with low incidence in West Africans, Japanese, and Inuits. There is a very low incidence among North and South American Indians. African Americans also have a low incidence of 1.3% compared with 2.5% of European Americans.

Contributing Factors: In addition to genetics, medications, and infections, potential triggers for psoriasis include environmental, medical, and behavioral risk factors. Approximately 40% of those with psoriasis or psoriatic arthritis report a family history of the condition (Lopez-Estebaranz et al., 2015). A streptococcal or viral infection often precedes the onset of guttate psoriasis by 2 weeks. Drugs that may precipitate or exacerbate psoriasis include lithium, beta blockers, antimalarial agents, tetracyclines, and NSAIDs. Several lifestyle factors or behaviors have been associated with a higher rate of psoriasis. The likelihood of developing psoriasis was doubled for smokers compared to nonsmokers (Armstrong et al., 2014). Psoriasis is more prevalent in those who abuse alcohol and may increase the severity of the disease. Multiple studies have noted a relationship between obesity and the development of psoriasis (Menter et al., 2011).

Signs and Symptoms: The characteristic features of psoriasis vary by subtype with chronic plaque psoriasis being most common. Typical findings include symmetrically distributed round or oval well-defined, pink/red plaques with overlying white scale. These plaques are commonly found on elbows, knees, gluteal cleft, and the scalp. Chronic plaque psoriasis may involve a few plaques or may have many plaques scattered over the entire body.

Inguinal folds, umbilicus, axillae, and inframammary folds are often affected areas of inverse psoriasis. Plaques lack scale due to the moist environment, and are typically shiny, thin, and well-defined. This inverse-pattern psoriasis may be difficult to distinguish from *Candida* or tinea. The distinct demarcated border is helpful in differentiation.

The lesions of guttate psoriasis are distinct small papules with overlying fine scale that have a drop-like, or guttate, appearance. The eruption is usually generalized, sparing the palms and soles. The eruption is often preceded by a streptococcal infection and its clinical course is unpredictable.

Most subtypes share other common clinical manifestations. Pruritus is a common complaint of most subtypes. Nail psoriasis may occur concurrently or prior to a cutaneous eruption. Tiny pits scattered in the nailbed, nail plate thickening or crumbling, and tan or brown spots (oil drop sign) are abnormalities associated with psoriasis (Klaassen et al., 2013).

Pustular psoriasis may present as an acute eruption of generalized inflammation, desquamation, and pustules. Similar characteristics are seen in erythrodermic psoriasis, but pustules will not be present. Both can have life-threatening complications.

Diagnostic Tests: The distinct presentation of the lesions of psoriasis makes a clinical diagnosis possible. When fungal infections are a possibility, potassium hydroxide (KOH) tests are the gold standard. There are no laboratory tests to confirm diagnosis. Challenging cases can be confirmed with a skin biopsy. If required, a referral to a dermatologist will ensure accurate testing.

Psoriasis is now considered a chronic inflammatory disease involving multiple systems. In addition to psoriatic arthritis, comorbid conditions should be assessed once diagnosis is confirmed and periodically thereafter. Associated comorbidities include metabolic syndrome, hypertension, atherosclerosis, dyslipidemia, diabetes, and pulmonary disorders (Danielsen et al., 2014; Rodríguez-Zúñiga & García-Perdomo, 2017; Samarasekera et al., 2013; Wu et al., 2020).

Differential Diagnosis:

Plaque Psoriasis:
- Seborrheic dermatitis
- Nummular eczema
- Tinea corporis
- Lichen planus
- Pityriasis rubra pilaris
- Mycosis fungoides
- Atopic dermatitis

Guttate Psoriasis:
- Secondary syphilis
- Pityriasis rosea
- Maculopapular drug eruption

Inverse Psoriasis:
- Candidiasis
- Tinea

Psoriatic Nails:
- Tinea unguium
- Onychomycosis caused by yeast or molds

Treatment: Although treatment decisions will generally be made by the dermatologist or, in the case of psoriatic arthritis, by the rheumatologist, the primary care provider is always responsible for the oversite of the patient's care.

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Knowledge of contraindications, side effects, adverse drug reactions, and drug-drug interactions are all a critical responsibility of the advanced practice nurse provider. Establishing good communication with the specialist is a necessity. It is also crucial that comorbidities that are common with psoriasis are optimally managed.

Treatment options should be evaluated on a case-by-case basis and according to patient preference, type and severity of disease, comorbidities, cost, and medication response. To ensure the appropriate choice of treatment, referral to a dermatologist should be initiated. Dermatologists are the experts who treat and manage the multiple nuances of this disease. Due to comorbidities associated with psoriasis, a multidisciplinary approach to management should be implemented. Team members may include dermatology, rheumatology, cardiology, behavioral health, and nutritionists. Primary care providers are key to ongoing assessment for early recognition of comorbid conditions.

Topical Treatments. For most patients with mild disease, topical treatments are safe and effective (Table 8-4). These treatments are also used as adjunctive therapy for patients with moderate to severe disease who need phototherapy or systemic therapy. Patients may be on concurrent topical therapy with the use of more than one topical agent. Topical agents include corticosteroids, vitamin D analogues, retinoids, calcineurin inhibitors, salicylic acid, anthralin, coal tar, and emollients. A combination of topical corticosteroids (TCS) and corticosteroid-sparing agents are typically used by dermatology (Elmets et al., 2021).

The use of class 1–7 TCS is recommended for twice daily application up to 4 weeks on the body and scalp, not including the intertriginous areas. Low-potency agents (class 6 or 7) should be used on the face and intertriginous areas. Common adverse effects of TCS include striae, atrophy, telangiectasia, and folliculitis. To reduce the risk of adverse effects of TCS, transitioning to lower-strength agents or intermittent use after improvement is recommended. In addition, combining treatment with nonsteroidal agents, such as tacrolimus, pimecrolimus, or crisaborole should be considered (Elmets et al., 2021).

Phototherapy. Phototherapy requires treatment by a dermatologist. Narrow-band ultraviolet B (UVB) is often used in combination with topical therapies and offers the possibility of home therapy. A more aggressive treatment is photochemotherapy with psolaren (an oral medication) and ultraviolet A (PUVA) light. The treatment inhibits mitosis by stopping DNA replication. It increases the risk of squamous cell carcinoma and possibly melanoma. It also induces photoaging. Although it has more risk than UVB, it is more effective (Elmets et al., 2021).

Systemic Therapy. Systemic therapy is reserved for those patients with severe disease and requires management by a dermatologist with expertise in treatment of psoriasis. Common oral medications include methotrexate, cyclosporin, and apremilast. Biologic agents are subcutaneous injections that are well tolerated and have excellent efficacy. Although both oral and injectable medications are effective for treating psoriasis, biologics are costly compared to oral nonbiologic medications. Biologic therapies include etanercept, infliximab, adalimumab, ustekinumab, secukinumab, and ixekizumab, just to name a few.

TABLE 8-4 Topical Treatment for Psoriasis

TOPICAL TREATMENT	MECHANISM OF ACTION	SIDE EFFECTS/ PRECAUTIONS
Corticosteroids	Anti-inflammatory, antiproliferative, immunosuppressive, vasoconstrictive	Skin atrophy, telangiectasia, striae distensai, acne, folliculitis, and purpura
		May exacerbate some superficial skin conditions: rosacea, tinea
		Rebound of psoriasis
		With high potency, possible systemic side effects
Vitamin D analogues	Binds to vitamin D receptors	Burning, pruritus, edema, peeling, dryness, erythema may improve with continued treatment
Calcipotriene topical	Inhibition of keratinocyte proliferation and enhancement of differentiation	Rarely systemic effects of hypercalcemia and parathyroid suppression; apply after UVA therapy
Retinoids Tazarotene topical	Normalizes abnormal keratinocyte differentiation, diminishes hyperproliferation	Local irritation, may be reduced with lower concentrations; combine with moisturizers or topical steroids
	Decreases inflammation	
Calcineurin inhibitors Pimecrolimus topical	Block the synthesis of inflammatory cytokines	Burning and itching reduced with continued therapy
		Cautious use with light therapy
		Not FDA approved for psoriasis
Salicylic acid	Keratolytic; reduce keratinocyte-to-keratinocyte binding	Risk of systemic toxicity; do not use with oral salicylates
	Reduce pH stratum corneum	Use after UVA therapy
Anthralin	Prevent T lymph activation	Skin irritation and staining
	Normalize keratinocyte differentiation	

Methotrexate has direct immunosuppressive effects by its ability to decreases lymphoid cell proliferation. Apremilast reduces the inflammatory response involved in underlying psoriasis. Cyclosporine blocks proinflammatory signaling. Due to its list of serious adverse effects, cyclosporine should not be considered for long-term treatment. Both methotrexate and cyclosporine require close monitoring due to their

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risk factors, the most serious being hepatotoxicity for methotrexate and renal toxicity for cyclosporine. Drug interactions are common with all systemic therapies (Stiff et al., 2018).

Biologics target cytokines including TNF-alpha, interleukin 12 (IL-12), interleukin 17 (IL-17) and interleukin 23 (IL-23). Biologic agents have a high benefit-to-risk ratio and can be used as monotherapy or combination therapy. Baseline and annual screening for latent tuberculosis is mandatory for all biologics due to their potential to activate the disease. Monitoring parameters vary according to drug. All age-appropriate live vaccines should be given at least 2 weeks prior to starting a biologic, inactivated vaccines are safe (Le & Vender, 2021). Coordinating the care of older adults on systemic therapy with the dermatologist is essential to adequate management (Menter et al., 2020).

Follow-Up: Follow-up should be on a case-by-case basis. A key to follow-up is coordination with the dermatologist, who, in other than the mildest cases, should be managing the disease process. It is important to consider the "heartbreak of psoriasis." The incidence of depression and suicidal ideation is higher in psoriasis and may not be directly related to the severity of the disease. All patients should be screened for depression. Patients with psoriasis have a higher incidence of arthritis, heart disease, diabetes, cancer, and hypertension, and all of these are increased in older adults as well (Menter et al., 2020).

Sequelae: Psoriasis is a chronic disease with exacerbations and remissions. In a small percentage of those with psoriasis, more serious types, such as psoriatic erythroderma or generalized acute pustular psoriasis, may occur. These diseases have much higher morbidity and may even result in death. Five percent of those with psoriasis will develop psoriatic arthritis.

Prevention/Prophylaxis: Triggers should be avoided: smoking, excess alcohol use, and skin trauma. Keeping the skin dry but well hydrated may decrease pruritus and the urge to scratch. Drugs known to exacerbate psoriasis should be avoided. Stress management, adequate rest, and a well-balanced diet to achieve ideal body weight are all important.

Referral: Except in the mildest cases of psoriasis, the patient should be comanaged with a dermatologist.

Education: In addition to ways to avoid triggers that can cause exacerbations, patients need to understand the treatment options and partner with providers to make choices that increase adherence. Teaching needs to include information regarding medication side effects and special considerations, such as the importance of not getting live vaccines if currently being treated with biologics. In the current health-care environment, retail clinics and pharmacies are offering vaccines, so patients need to be especially conscious of the recommendations related to their treatments and the guidelines regarding vaccines. The emotional toll of this disease needs to be acknowledged, offering patients connection to support groups. Patients also need to be informed of reputable Internet sources on psoriasis.

Clinical Recommendation	Evidence Rating	References
The use of class 1-5 topical corticosteroids is recommended for up to 4 weeks for plaque psoriasis treatment on all areas not involving the intertriginous areas.	A	Elmets et al., 2021
Methotrexate and apremilast are recommended for the treatment of moderate to severe psoriasis in adults.	A	Menter et al., 2020
Cyclosporine is recommended for patients with severe, recalcitrant psoriasis.	A	Menter et al., 2020
Cyclosporine can be used as short-term intervention in patients who fare well on a preexisting systemic therapy.	C	Menter et al., 2020
Etanercept, infliximab, adalimumab, ustekinumab, secukinumab, and ixekizumab are recommended as treatment options for use in adult patients with moderate-to-severe plaque psoriasis and when associated with psoriatic psoriasis.	A	Menter et al., 2019

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SKIN CANCER

Signal Symptoms: Poikiloderma refers to telangiectasia, reticulate hyperpigmentation, and atrophy. These are signs of long-term sun exposure and indicate significant risk for development of skin cancer. Basal cell carcinoma (BCC) and squamous cell carcinoma (SCC) are common cancers most often found on sun exposed areas of the skin. The SCC type of skin cancer may evolve from actinic keratosis, which present as discrete lesions or a cluster of crusted, scaly papules on sun-exposed skin. These are called actinic keratosis and may be tender or itchy. Melanoma, the fifth most common cancer in the United States is the most serious type of skin cancer (Siegel et al., 2019). Any lesion with changing pigment, abnormal symmetry, crusting, bleeding, or tenderness is a possible skin cancer.

Description: Nonmelanoma skin cancers (NMSCs) include BCCs, which arise from the basal keratinocyte layer of the

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epidermis, and SCC, which originates in the squamous cells of the epithelium. Malignant melanoma (MM) is a tumor arising from pigmented cells. Melanoma causes abnormal proliferation of specialized cells that produce melanin in the skin, eyes, and hair.

Etiology: The major risk factor for the development of nonmelanoma skin cancers is exposure to UV radiation (Bolognia et al., 2018).

Occurrence: Skin cancer is the most common form of cancer in the United States. The worldwide incidence of NMSCs has been rising by 3% to 10% annually for the past 30 years. In the United States, BCC incidence rate has increased between 20% and 80% in the same period (Apalla et al., 2017). Each year, more than 1 million new cases of skin cancer are diagnosed in the United States. SCCs carry a 9% to 14% lifetime risk for men and 4% to 9% for women (Nehal & Bichakjian, 2018). Melanoma occurs less frequently but is responsible for more deaths. It is estimated that over 9,000 persons will die of MM each year (Guy et al., 2015; U.S. Cancer Statistics Working Group, 2016). MM is equally prevalent in men and in women until the age of 40 when incidence nearly triples for males (Apalla et al., 2017). Melanoma, though deadly in the later stages of development, has an excellent prognosis if treated early (Guy et al., 2015).

Age: The incidence of all types of skin cancers increases with age and the degree and intensity of sun exposure.

Ethnicity: Skin cancers are more prevalent in fair-skinned persons who tend to burn instead of tan, reflective of sensitivity to sunlight. In the United States, residents of states where year-round sunshine is abundant and those who live closer to the equator are at a high risk. Although SCC rates are low for those with darker skin types, if they do occur, they tend to arise on skin not exposed to sun. Acral lentiginous melanomas (ALMs) are the most common melanoma subtype in dark skinned persons (Marchetti et al., 2015). They are characterized by location and are found on the palms, plantar surface of feet, and nail matrix (subungual).

Contributing Factors: Skin phenotype and UV exposure, including tanning beds, are major risk factors for all types of skin cancer. Other factors related to the development of BCC include and SCC include age, ionizing radiation, arsenic exposure, genetics, and immunosuppression (Bolognia et al., 2018). Additional risk factors specific to melanoma include a family or prior personal history of melanoma, high numbers of normal nevi (moles), and the multiple atypical nevi (Caini et al., 2009; Pampena et al., 2017). Risk factors for NMSC and MM include skin pigmentation, genetics, age, occupation, chemical exposures, and immunosuppression. BCC is the most common skin cancer in the United States, followed by SCC with a ratio being roughly 4:1.2 (Apalla et al., 2017). Both are treatable with low metastatic potential.

Signs and Symptoms: Question patients about any new or changing lesions. Is the lesion painful? Does it itch or bleed? Has it healed and then reappeared? Ask about past history of any previous actinic keratosis, excised or treated lesions, and prior diagnosed skin of cancer. Question patients about any family history of skin cancers. Ask about their history of sun exposure, severe sunburn, burns, scars, ulcers, radiation dermatitis, use of tanning beds, current and prior occupations, and family history of skin cancer. Palpation can help with subtle skin changes, scale, and depth (firmness) of lesions.

Presentation of the skin cancer will depend on the type of tumor. There are several subtypes of BCCs including nodular, morpheaform, and superficial. Nodular BCCs account for 80% of all subtypes. It often appears on the face favoring the nose, cheeks, nasolabial folds, and forehead. They can present as smooth, pearly papules or nodules with rolled borders with or without central ulceration. Occasionally, brown or black blotchy pigment can be seen. Patients may describe this lesion as a pimple that did not heal. Superficial BCC often appears on the trunk as well-circumscribed, light red or pink patch with slight overlying scale. This type of BCC resembles other chronic skin conditions such as psoriasis, eczema, discoid lupus erythematous, and Bowen disease. The least common type of BCC is the sclerosing or morpheaform tumor. Found on the head and neck and occasionally the trunk of the body and can present as atrophic plaques which may be flesh-colored or light pink (Bolognia et al., 2018). A close examination from several angles with redirection of lighting may help due to the subtle appearance of these types of BCC.

Actinic keratoses, precursors to SCC, appear as round or irregular-shaped erythematous or pink plaques with a scaly or rough surface. Other precursor lesions of SCC include cutaneous horn, leukoplakia, and keratoacanthoma. Clinical presentation can vary from skin colored, pink or red, well-demarcated patch with scale to thick, firm nodules that may be smooth or ulcerated. SCC often originates at sites of chronic inflammation or old scars in individuals with darker skin types. For the immunocompromised, SCC often present with multiple lesions in areas of previous sun damage but can also occur on oral, genital, and anal mucosa. The progression of these lesions varies over time, and they can be painful, pruritic, or tender (Bolognia et al., 2018).

For patients with suspected melanoma, the mnemonic ABCDE guides the clinician in determining if the clinical characteristics of a suspicious lesion warrant close surveillance and/or biopsy for histological evaluation.

- Asymmetry
- Border irregularity
- Color variation
- Diameter greater than 6 mm
- Elevation of a previously flat lesion, evolving, and enlarging (Bibbins-Domingo et al., 2016)

It is important to note that the classic ABCDE pattern of MM development is not always present. The tool is used to alert patients and nondermatologists about suspicious lesions (Rastrelli et al., 2013). Melanoma can appear to have little or no color (amelanotic) and can mimic benign lesions. Approximately 65% to 70% of melanoma lesions arise on normal skin, the remaining from an existing nevus (Pampena et al., 2017)

Major Signs. Change in size, change in shape, change in color. If one or more major signs exist, refer for expeditious biopsy.

Minor Signs. Inflammation, crusting or bleeding, sensory change, diameter of greater than 6 mm. If three or four minor signs exist with a major sign, consider referral.

Patients may be concerned about a new, pigmented lesion or a change in an already existing one. Patients may report associated itching, burning, or pain in a mole. Superficial

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spreading accounts for nearly 70% of all melanoma subtypes. It presents as a flat to slightly raised pigmented lesion with irregular borders, commonly found on the trunk of men and the lower extremities of women. Lentigo maligna melanoma presents as an irregularly light brown, brown, or black pigmented patch with ragged borders on sun-exposed areas, especially on the faces of older adults. Nodular melanoma, the second most common subtype, presents as brown or black papules usually located on the trunk, head, and neck (Elder et al., 2020).

Diagnostic Tests: Skin cancer is diagnosed through biopsy. Biopsy of the suspected lesion is necessary to confirm the diagnosis via histological examination of the tissue. If the lesion is suspicious for melanoma, the entire lesion should be removed. An excisional biopsy is necessary for larger lesions. (Swetter et al., 2019).

Differential Diagnosis:

- Actinic keratoses
- Seborrheic keratoses
- Keratoacanthoma
- Atypical nevi
- Blue nevus
- Dermatofibroma
- Venous lakes
- Pyogenic granulomas
- Intradermal nevus
- Sebaceous hyperplasia
- Molluscum contagiosum
- Psoriasis
- Bowen disease (Nolen et al., 2011)

Treatment: Several factors need to be considered before skin cancer therapy begins: tumor pathology, the patient's age and general health, immune status, size and location of the tumor, and the cosmetic concerns of the patient. BCC and low-risk SCC may be treated by excisional surgery, electrodessication and curettage, cryotherapy, ionizing radiation, and Mohs micrographic surgery. Treatment for high-risk SCC is often guided by clinical and pathological factors. A TNM staging system, which assesses the primary tumor (T), regional lymph nodes (N), metastatic (M) sites, guides melanoma treatment (Elmore et al., 2018).

A number of different treatment options are available for the management of actinic keratosis (AK), including cryotherapy, topical medications, and photodynamic therapy, all of which have been shown to reduce lesion count in patients with AK. Cryotherapy, topical 5-fluorouracil, imiquimod, and photodynamic therapy are the most commonly used treatments for AK (Bolognia et al., 2018). Combination therapies can include both field-directed and lesion-directed therapy (Cornejo et al., 2020).

Follow-Up: Follow-up for a patient with diagnosed skin carcinoma is essential because the recurrence rate of skin cancer is high; 50% to 70% of persons with BCC and SCC have a reappearance of a cancerous lesion within 2 years (Bolognia et al., 2018). A person who is susceptible to skin cancer may develop another cancerous lesion at any time. Precancerous lesions should be examined regularly every 6 to 12 months using a head-to-toe skin examination, including a careful inspection of the previous site of a lesion. In patients with SCC, palpation of regional lymph nodes is suggested. During subsequent visits of patients with malignant melanoma, a thorough review of systems is imperative to elicit clinical signs and symptoms of metastasis.

Sequelae: BCC rarely metastasizes; however, if it is not treated early, the carcinoma may invade the surrounding tissue and bone. Advanced SCC lesions of the lips, ear, and genitalia often recur. Those that occur on the ear, genitalia, within a chronic wound or scar, or on irradiated skin have a higher rate of metastasis. The initial size, depth, and host factors of those diagnosed with NMSC can also influence recurrence and metastasis rate. Five-year prognosis for MM is primarily determined by the thickness of the tumor. Tumors that are thin (<0.8 mm) and caught early are associated with a 97% 5-year survival rate, whereas more advanced melanomas with distant metastasis have a very poor prognosis of 33% for 1-year survival rate (Elmore et al., 2018).

Prevention/Prophylaxis: Because the incidences of all skin cancers increase with age, it is important to discuss sun care protective behaviors with all older adults (Lin et al., 2011). The CDC recommends easy options for sun protection. UV radiation increases the risk for skin cancer with all skin types; therefore, individuals need to seek shade when UV radiation is strongest, during the hours of 10:00 a.m. to 4:00 p.m., and avoid burning. According to the Skin Cancer Foundation, sunscreen should have a sun protective factor (SPF) of at least 30 or higher, broad spectrum, and water resistant for extended outdoor activity. Tanning beds or booths should be avoided, as they pose a significant risk for the development of melanoma and nonmelanoma skin cancers (Boniol et al., 2012; CDC, 2016).

Sunscreen should be applied to sun-exposed skin daily. Approximately 1 teaspoon of sunscreen should be applied to the face and neck, 2 teaspoons to the torso, 1 teaspoon to each arm, and 2 teaspoons to each leg (Isedeh et al., 2013). Sunscreen should be reapplied after toweling off from swimming or exercise and after heavy sweating. Wide-brim hats that shade the face, head, ears, and neck; long-sleeved shirts; and long pants are recommended. Sunglasses that are wraparound type should be worn and can be purchased to block up to 100% of UV radiation (U.S. Cancer Statistics Working Group Department, 2014).

Patients need to be routinely asked about their ability to conduct skin self-examinations. Recommending partner participation can enhance one's thoroughness in examining hard-to-reach areas of the body. Providing individuals with printed directions on how to position mirrors to examine the body, the use of good lighting, and suggesting magnifying lenses for those with impaired eyesight can help ensure a thorough examination has been carried out by the patient. Taking the time to give patients adequate instructions in skin self-examination has been found to be a successful strategy in ensuring older adults routinely conduct or seek assistance in regular skin examinations and the use of sunscreen (Janda et al., 2011). High-risk patients can be provided body maps to record areas of suspicious lesions to bring with them at the time of clinical examinations. These patients should be questioned if they are regularly being followed by a dermatology practice. If not, primary care providers are well positioned to begin triaging (to include referring patients to a dermatologist) patients who present with suspicious skin lesions (Goulart et al., 2011).

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Yearly physical examinations should include assessment of the head, scalp, and skin, and an accurate recording of descriptions of any suspicious lesions. Patients should be fully undressed, to complete an accurate physical. New, unusual, symptomatic, or changing lesions or moles should be evaluated by a dermatologist. Immunosuppressed solid organ transplant recipients are at high risk for developing skin cancer at rates faster than the general patient population and should be scheduled for regular skin examinations.

Referral: When a suspicious lesion is found, referral to a dermatologist for evaluation and possibly biopsy is necessary. Whole-body photographs and dermoscopy may be used to follow patients with suspicious lesions. A tutorial on dermoscopy is available at https://dermoscopedia.org/Main_Page. Oncology referral is needed for metastatic SCC and MM.

Education: Advise older patients that skin cancers are a common occurrence as one ages, especially for patients at risk. Older adults should perform a monthly self-evaluation of the skin. Any suspicious lesion that does not heal in a reasonable time needs to be examined by a primary care provider. Patients also need to report any slow-growing, flesh-colored, or pigmented lesion, noting if the lesion has irregular borders, changes in color, ulceration, bleeding, or horn formation. Sun exposure, especially during the hours of 10:00 a.m. to 4:00 p.m., should be avoided. Year-round broad-spectrum sunscreen that blocks UVA and UVB light is recommended. Vulnerable areas, such as the head and neck, should be covered with protective clothing.

Clinical Recommendation	Evidence Rating	References
Summary of relative risk strongly associated cutaneous melanoma (CM) with high nevus counts. Relative risks for CM also differed by anatomical site for skin and hair color which could be attributed to gene variability.	A	Caini et al., 2009
Melanoma staging in the *American Joint Committee on Cancer (AJCC) Staging Manual*, 8th edition proves greater reproducibility and concordance with the reference standard. Classification improvement of invasive melanoma is expected upon implementation of *AJCC 8*, indicating a positive impact on patients.	B	Elmore et al., 2018
Field therapies address subclinical atypia and visible disease. Patients with widespread field cancerization benefit from combination therapy targeting lesion-directed and field cancerization.	A	Cornejo et al., 2020
Primary care counseling can change sun-protective behaviors and decrease tanning bed use.	A	Lin et al., 2011

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SUPERFICIAL FUNGAL INFECTIONS

Signal Symptoms:

Dermatophyte Infection (Tinea). Erythema, scale, raised border, clearing center, may present with vesicles if inflammatory.

Candidiasis (Moniliasis). Pustules, red, denuded, glistening surface with a scaling border and satellite pustules that often occurs on mucosal surfaces and skinfolds. In the oral cavity candidiasis forms white plaques on the oral mucosa or tongue. Angular cheilitis presents as inflamed skin with crust formation at the angles of the mouth. The scale and inflammatory cells form the classic "cottage cheese curds" within the vagina.

Tinea Versicolor (Pityriasis Versicolor). Hypopigmented macules and patches or scaly red or shades of brown macules or patches may be slightly pruritic. The condition typically occurs on the neck, upper trunk, and proximal arms.

Description: Dermatophytes (*Trichophyton* and *Microsporum*) and yeasts (*Malassezia* and *Candida*) are the primary groups of fungi that cause the most common superficial fungal infections of the skin (Ameen, 2010). Dermatophyte infections are referred to clinically as *tinea* followed by the region of the body that is infected: tinea capitis (the head), tinea barbae (the beard area), tinea facea (the face except for the beard area), tinea manuum (the hand), tinea corporis (the body), tinea cruris (the groin), tinea pedis (the foot), and when there is nail involvement, tinea unguium or onychomycosis. Lay terms for the dermatophytes include ringworm, jock itch, and athlete's foot.

Candidiasis may be termed monilia, yeast, or thrush and generally presents in intertriginous areas or on mucous membranes. Tinea versicolor, often referred to as pityriasis versicolor, is caused by a yeast in the *Malassezia* genus. *Malassezia* is a part of normal skin flora; however, when disrupted tinea versicolor may result. Common factors leading to this disruption include immunosuppression, heat, humidity, oral contraceptives, and genetics (Passeron et al., 2019). Clinical manifestations include macules and patches of varying pigmentation with slight overlying scale on the trunk and upper arms.

Etiology:

Dermatophytes. Dermatophytes are the predominant cause of fungal infections of the skin, hair, and nails. (Ameen, 2010). The dermatophytes are a group of fungi that survive on a protein called keratin which is found in the skin, hair,

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and nails. Patients who are chronically infected may have a genetic predisposition to dermatophyte infection. Dermatophytes are classified by the origin of the infection: anthropophilic, transmission from person to person by fomites or direct contact; zoophilic, transmission from animal to person by fomites or direct contact; or geophilic, from the soil. The latter two sources result in a more rapid and more severe inflammatory response. Clinical subtypes are based on the tissue primarily involved. Epidermal involvement is classified as either tinea corporis, tinea cruris, tinea pedis, tinea faciei, and tinea manuum. Tinea capitis and tinea barbae are infections of the hair and hair shaft, and tinea unguium involves nails. The dermatophytes within the stratum corneum disrupt the horny layer, lead to scaling, and create an inflammatory response. Three fungal species are primarily responsible for the infection: *Trichophyton, Epidermophyton*, and *Microsporum. Trichophyton rubrum* is the most common cause of skin and nail infection, with *Trichophyton* responsible for 80% of infections (Wolff et al., 2017).

Cutaneous Candidiasis. *Candida albicans* is an oval, yeast-like fungus that lives in the normal flora of the mouth and gastrointestinal tract. It reproduces through budding, the development of pseudohyphae, and true hyphae. Conditions that compromise the immune system or alter the normal body flora contribute to the development of *Candida* infections. The yeast infects the outer layer of the skin with the primary lesion, a pustule that dissects under the outer skin layer and peels it away. The result is a glistening surface with a scaling, advancing border and often the presence of satellite lesions. *Candida* grows best in warm, moist environments, and often the lesions end as they meet the area of dry skin.

Tinea Versicolor. Although termed "tinea," this condition is caused by yeasts in the *Malassezia* genus (formerly Pityrosporum, not dermatophytes (Kang et al., 2019). The organisms are lipophilic yeasts that reside in the keratin and hair follicles, areas with increased sebaceous activity (Habif, 2016; Wolff et al., 2017). Tinea versicolor is an overgrowth of normal skin flora and is not contagious. As sebum production declines later in life, the incidence of tinea versicolor also declines.

Occurrence: Immunosuppressed patients are at higher risk for fungal infections of all kinds and are more likely to have infections that do not resolve. Older adults are at higher risk for many fungal infections because of the decline in the immune system with aging, as well as the increased incidence in comorbidities and the use of multiple medications. Functional compromise can lead to a decline in personal hygiene, which also increases the risk factors for fungal infection. Tinea versicolor is more common in young adults due to its link to sebum production (Wolff et al., 2017).

The feet and nails are the most common areas of the body affected by dermatophytes in the older adult. Onychomycosis due to dermatophytes (tinea unguium) account for 60% to 70% of nail infections, the remaining 40% to 30% of nail infections are caused by yeast or nondermatophyte mold (Lipner & Scher, 2019). Incidence of onychomycosis increases with advancing age, while toenail onychomycosis due to *Candida albicans* declines with age. *Candida* most often causes intertriginous infections in those older than 65 years and is also the most common cause of fingernail onychomycosis in this age-group.

When the dermatophytes are inaccurately diagnosed and treated with topical steroids, a phenomenon called tinea incognito may occur. The rash initially disappears, but when treatment with steroids is discontinued, the rash returns with much more extensive involvement and may appear without scale. It is not responsive to subsequent topical steroid treatment, and a thorough history is necessary to make the proper diagnosis of tinea.

Tinea versicolor thrives in heat and humidity. It has an estimated prevalence in the United States population between 2% and 8%; however, the actual prevalence may be much higher because many of those with the disease do not seek medical evaluation.

Tinea barbae is an infection that only occurs in males and is more common in rural areas. Males also more often experience tinea cruris and tinea pedis and are more likely to have toenails infected with dermatophytes than females, whereas females are more likely to have *Candida*-infected fingernails. Differences between sexes have not been found in cases of *Candida* in other parts of the body or in cases of tinea versicolor.

Age: Tinea of the scalp and face (tinea capitis and tinea facialis) are primarily diseases of children. Tinea of the body, trunk, and extremities (tinea corporis) can occur at any age. The initial presentation of tinea pedis (athlete's foot) is most common in adults aged 20 to 50 years, and the initial presentation of tinea unguium (onychomycosis) commonly occurs in those aged 45 to 54 years. Tinea unguium can affect any age, but the incidence in toenails increases with aging and is most common in the oldest old. Approximately 50% of those older than 70 years are affected (Kang et al., 2019)

Candida of the skin occurs more often in older adults because of the decline in immune response with aging, as well as a decline in hygiene among many older adults. Although not a common cause of toenail infection, when it occurs it is more likely in an older adult, whereas fingernail fungus is rarely seen in older adults.

Tinea versicolor is more common when sebaceous glands are most active during puberty and in young adults ages 15 to 24 years. Tinea versicolor is less common in those older than 65 years because sebum production declines with age (Kang et al., 2019).

Ethnicity: African Americans are less likely than other races to be diagnosed with dermatophytosis. Ethnic differences have not been noted for either *Candida* or tinea (pityriasis) versicolor (Habif, 2016; Wolff et al., 2017).

Contributing Factors: Fungal infections are more common in warmer climates. Excessive sweating increases risk. Any of the diseases that compromise the immune system, atopy, and topical and systemic steroids increase risk. Individuals with diabetes are noted to have a higher risk as well as those with abnormalities of the keratin, as in psoriasis and ichthyosis (Nenoff et al., 2014). Age alone increases the risk, particularly of onychomycosis. Tinea manuum is rare in individuals who do not also have tinea pedis. A common presentation is two feet–one hand syndrome, which is believed to be a result of the patient touching or scratching the infected feet. Tinea pedis occurs more frequently in those who wear occlusive

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footwear that promotes warmth and sweating, the perfect environment for fungal growth. Socioeconomic status also appears to contribute to the incidence of dermatophyte infections, with tinea pedis more prevalent in developed countries and tinea capitis more prevalent in countries with fewer resources.

Cutaneous candidiasis is more common in adults with diseases that compromise the immune system, those taking medications that cause immune decline, adults treated with broad-spectrum antibiotics, and those with poor hygiene that results in moisture in intertriginous areas (Habif, 2016; Wolff et al., 2017). Other contributing factors include hot, humid weather; tight underwear; poor hygiene; and inflammatory diseases occurring in skinfolds.

Like other fungal infections, tinea (pityriasis) versicolor is more common in an environment of heat and humidity. It grows best where sebaceous activity is highest and may be more common in those with oily skin. Immune-compromised individuals and those on steroids are also more susceptible. Although the color change may be more noticeable on darker colored skin, there is no noted racial difference (Habif, 2016; Wolff et al., 2017).

Signs and Symptoms: It is not uncommon to have more than one fungal infection simultaneously; therefore, a full examination of hair, skin, and nails is recommended. Well-defined borders with scale are a hallmark of each of the superficial fungal infections. Tinea is often dry and scaly, whereas *Candida* presents with initial pustules that become eroded, confluent, and evolve into patches with sharply demarcated borders and fine scale, surrounded by satellite pustules.

Tinea capitis presents as scaly, round patches with generalized or localized hair loss (alopecia), and broken hairs. Affected areas of the scalp may have inflamed, crusted pustules and papules. Black dot tinea capitis occurs when hairs break off near the surface and give the appearance of dots. The dots may be scattered over the scalp and may not form a classic round patch.

Tinea corporis affects sites other than face, hands, feet, or groin. It presents as the classic ringworm pattern with a clearing center and a raised, scaling leading edge. Tinea cruris presents as an erythematous pruritic rash that begins on the medial upper thigh that centrifugally spreads to the perianal area, gluteal cleft, perineum, and buttocks. The scrotum is often spared, and the rash borders are well-defined. It is usually symmetric, pruritic, and can easily spread from the feet (tinea pedis) to the inguinal folds. The lack of scrotum involvement can help to differentiate tinea from *Candida* of the groin, where scrotum involvement is common (Habif, 2016).

Tinea pedis, athlete's foot, is a common dermatophyte infection and presents with a variety of signs and symptoms. The three main clinical types are interdigital, moccasin type, and vesicular.

- Interdigital tinea pedis results in erythema and scaling present between the third and fourth toes, although any interdigital space can be affected. Secondary infection with bacteria is more common in the macerated toe space.
- Moccasin-type tinea pedis affects the medial and lateral aspects of feet along with the sole. Because of the mild nature of this infection and its subtle presentation, it may be present for years before the patient seeks treatment.
- Vesicular-type tinea pedis often involves the medial foot. It presents as a vesicular, pruritic, and sometimes painful eruption. It may represent a secondary bacterial infection in someone with chronic interdigital tinea pedis and can manifest with interdigital ulcers and erosions.

Toenails are most often infected with dermatophytes, and there are three classic presentations:

- Distal lateral subungual onychomycosis (DLSO) is the most common subtype, which presents with onycholysis (the pulling away of the nail plate from the nailbed), hyperkeratosis, and yellow-brown discoloration.
- Superficial white onychomycosis (SWO), in which the dermatophyte invades the surface of the nail and the dorsal nail plate is chalky white. When lightly scraped it yields a chalky scale.
- Proximal subungual onychomycosis (PSO) is less common than other clinical subtypes that usually affect immunocompromised patients. It appears as a chalky, white color at the base of the nail and extends distally.

When a patient presents with a nail problem it is important to think broadly about the differential because only 50% of nail problems are onychomycosis (Lipner & Scher, 2019). Not every toenail with abnormal appearance is infected with fungus. Other common considerations should be trauma, frequent immersion in water, psoriasis, atopic dermatitis, or HIV infection.

Cutaneous candidiasis may exacerbate or initiate intertrigo. Areas of *Candida* infections include skinfolds, interdigital areas, and nails. Moist, red, macerated patches within skinfolds are hallmark findings of intertrigo. Inflamed satellite pustules and papules suggest *Candida* involvement. Intertriginous candidiasis is most common in bedridden older adults due to immobility. Additional risk factors include incontinence, poor hygiene, obesity, and immune deficiencies.

Tinea (pityriasis) versicolor appears as macules, round patches, and plaques with overlying fine scale. The color varies from light pink to light brown and the condition often manifests on the upper trunk, proximal upper extremities, neck, and face. The lesions vary in size and may become confluent and cover large areas of the body. It is rarely pruritic, and the appearance is the primary concern.

Diagnostic Tests: Although clinical findings raise suspicion of fungal infection, diagnosis should be confirmed with testing due to overlap of other skin disorders that are similar in appearance. Fungal lesions evolve and are typically asymptomatic. Fungal infections are often found coincidentally by the provider on physical examination or presented by the patient when self-treatments have failed.

For fungal skin involvement, the gold standard of diagnosis is direct microscopic examination of a KOH wet mount preparation of skin scrapings (Gupta et al., 2020). Scale is scraped from the affected areas using a surgical blade and placed on a slide. Add one drop of 20% KOH and then place cover glass on top. Examine for hyphae or yeast. It is best to start at 10× (low-power) magnification. Segmented hyphae

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confirm dermatophyte (tinea) infections, whereas pseudohyphae and budding yeasts confirm *Candida* (Kang et al., 2019). Fungal culture is an alternative method for diagnosis, but this may take several weeks to obtain results. Although fungal culture will identify the responsible organism, most antifungal treatments cover most infectious organisms. Only 50% to 60% of nail abnormalities are due to onychomycosis and treatment is lengthy. For these reasons, onychomycosis should be confirmed by laboratory testing (Gupta et al., 2000). Approximately 60% to 70% of nail infections are due to dermatophytes; 30% to 40% are caused by a mold, *Scopulariopsis;* and 10% to 20% are due to a yeast (Lipner & Scher, 2019). *Candida*, often associated with fingernail onychomycosis, may not respond to treatments useful in treating dermatophytes (Habif, 2016; Westerberg & Voyak, 2013). Garcia-Doval and colleagues (2010) present a clinical diagnostic rule for dermatophyte involvement. In their study, they found that if the patient with suspected onychomycosis had greater than 25% involvement of the sole of the foot with plantar desquamation and the presence of interdigital tinea pedis, the positive predictive value of the rule was 81%, which is higher than that of laboratory tests.

Differential Diagnosis:

Scalp Lesions:

- Seborrheic dermatitis – The scale of seborrheic dermatitis appears waxy and yellow compared to the fine, white scale of psoriasis. The patchy alopecia often seen with tinea capitis is not a clinical finding for seborrheic dermatitis.
- Psoriasis – Inflamed, well-defined plaques with coarse white scale. Check for involvement of elbows, knees, and intertriginous areas.
- Atopic dermatitis
- Alopecia areata – Smooth, well-defined, round areas of alopecia.
- Bacterial folliculitis – Gram stain or culture will result with causative bacteria.
- Neoplasia needs to be considered with presence of a kerion

Lesions on the Trunk:

- Allergic contact dermatitis – Tends to be more pruritic than fungal infections.
- Atopic dermatitis – Adults rarely have trunk involvement.
- Nummular eczema – Round plaques with scale, no central clearing.
- Psoriasis – Plaques are thick, appear more inflamed, and have more visible overlying scale.
- Pityriasis rosea – Look for herald patch which may range in size from 3 cm to 10 cm.
- Tinea (pityriasis) versicolor – Involvement usually seen on trunk and neck.
- Early presentation of herpes zoster

Lesions in the Groin:

- Intertrigo – More inflammatory in nature. Check for satellite papules and pustules.
- Psoriasis – Satellite papules and pustules are diagnostic for *Candida*.
- Seborrheic dermatitis
- Erythrasma – Lacks the scale often found with fungal infections.

Lesions on the Feet: Between the Toes:

- Bacterial infections: erythrasma, impetigo, *Pseudomonas*
- *Candida* intertrigo

Moccasin Type:

- Allergic contact dermatitis
- Atopic dermatitis
- Dyshidrotic eczema
- Psoriasis – Often symmetric and limited to soles and palms.

Vesicular:

- Allergic contact dermatitis
- Dyshidrotic eczema
- Bacterial infection
- Bullous disease

Nail Involvement. Distal and Lateral Subungual Onychomycosis (DLSO):

- Psoriatic nails – Randomly scattered deep pits on the nail plate and splinter hemorrhages.
- Onychogryphosis (thickening and hardening)
- Onychauxis (overgrowth or thickening)

Superficial White Onychomycosis (SWO):

- *Candida* onychomycosis – Subungual thickening, redness and swelling of nail folds, and nail plate damage.
- Contact or irritant dermatitis

Tinea Versicolor:

- Vitiligo
- Pityriasis alba – Involves face, often seen in patients with a history of eczema.
- Seborrheic dermatitis – Thicker scale and involvement of scalp, ears, and eyebrows.
- Secondary syphilis
- Pityriasis rosea – Lesions are more inflamed and herald patch is present.

Treatment: In older adults, response to treatment may be decreased due to slower cell turnover and comorbid conditions, particularly diabetes and peripheral vascular disease. Tables 8-5 and 8-6 offer topical and systemic treatment options, respectively (National Library of Medicine National Institutes of Health [NLM-NIH], n.d.). For topical agents, the treatment is once to twice a day for 2 to 6 weeks and should be continued for 1 week after the lesions clear. Application should extend beyond the leading edge of the lesion. Azoles are effective for dermatophytes, *Candida*, and yeasts (tinea versicolor) (Hay, 2018). Within a class of medication, the options are comparable and should be selected based on cost and the preferred base (lotion, cream, ointment). Topical treatments are not useful for tinea capitis, and failure is common in tinea manuum and onychomycosis (tinea unguium).

Newer agents are more likely to cure tinea pedis than the older generation of antifungals, including clotrimazole, which is fungistatic, whereas terbinafine is fungicidal. Terbinafine 1% cream applied twice daily for 1 week has a high cure rate for interdigital tinea pedis and butenafine twice a day for a week is also very effective (Habif, 2016). Econazole and ciclopirox also have antibacterial properties and may be the drugs of choice if bacterial involvement is suspected.

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TABLE 8-5 Topical Treatment for Superficial Fungal Infections

DRUG CLASS	PREPARATION	USE
Azoles	Clotrimazole	Dermatophytes, tinea versicolor, and *Candida*
	Miconazole	Dermatophytes, tinea versicolor, and *Candida*
	Ketoconazole	Dermatophytes, tinea versicolor, and *Candida*
	Econazole	Dermatophytes, tinea versicolor, and *Candida*
	Oxiconizole	Dermatophytes, tinea versicolor, and *Candida*. Other azoles may be more effective against *Candida*.
	Sulconizole	Dermatophytes, tinea versicolor, and *Candida*. Other azoles may be more effective against *Candida*.
Allylamines	Naftifine	Dermatophytes, tinea versicolor, and *Candida*. Less effective than azoles.
	Terbinafine	Dermatophytes, tinea versicolor, and *Candida*. Less effective than azoles.
Naphthionates	Tolnaftate	Dermatophytes, but less effective than other treatment options
Pyridone	Ciclopirox	Dermatophytes, tinea versicolor, onychomycosis SWO, and *Candida*
Polyene	Nystatin	*Candida*

TABLE 8-6 Systemic Treatment for Superficial Fungal Infections

DRUG CLASS	PREPARATION	USE
Allylamines	Terbinafine	Dermatophytes and onychomycosis. More effective than oral azoles for clinical cure.
Azoles	Itraconazole	Dermatophytes, tinea versicolor, onychomycosis, and *Candida*
	Fluconazole	Dermatophytes, tinea versicolor, onychomycosis, and *Candida*
Mitotic inhibitor	Griseofulvin	Dermatophytes and onychomycosis

When tinea pedis is vesicular or has signs of maceration, the use of 1% aluminum acetate solution (Burow solution) compresses applied for 20 minutes several times a day is a helpful drying agent and facilitates the penetration of the topical antifungal treatment. Oral antifungal drugs may be used to treat the acute infection (Bolognia et al., 2018). In hyperkeratotic, moccasin-type tinea, keratolytic agents, such as ammonium lactate lotion or topical urea, can reduce the hyperkeratosis and allow for improved penetration. Applying a plastic occlusive dressing over the keratolytic agents enhances their effectiveness. Oral terbinafine daily for 4 weeks may result in cure rates of 95% (Habif, 2016). For tinea pedis it is important to assess the condition of the nails and treat any reservoir that may be present.

Due to limited penetration of the nail plate, topical antifungals are rarely useful in the treatment of onychomycosis, except for SWO. In the United States, three topical treatments are approved by the Food and Drug Administration. Ciclopirox topical (Penlac Nail Lacquer) is the oldest; new agents include tavaborole (Kerydin) and efinaconazole (Jublia). An intriguing alternative was presented by Derby et al. (2011). In a small study (including only 18 subjects) of the effectiveness of the lay treatment of onychomycosis with Vicks VapoRub applied topically once a day for 48 weeks, 83% of the participants reported satisfactory results, with 27.8% experiencing a complete clinical and mycological cure; 56% had partial clearance, and 17% had no improvement.

An alternative treatment of tinea (pityriasis) versicolor is selenium sulfide 2.5% lotion or shampoo applied for 10 to 15 minutes followed by showering off for 2 weeks. Weekly application for several additional months may prevent recurrence. The skin color alterations may take 1 to 2 months to resolve completely.

Research supports a variety of dosing options for all of the oral antifungal treatments, from daily to once-a-month pulse therapy. The duration of therapy depends on the site of involvement as well as the response. Although oral terbinafine is least toxic of the antifungals, all of the agents have the potential of serious side effects and require lab monitoring (Kreijkamp-Kaspers et al., 2017). Before recommending any oral treatment, consultation is recommended. Mechanical treatments of nails infected with fungus offer another option for resolution of the infection. Partial or total surgical nail removal is an option, but this approach can lead to significant morbidity and is rarely used (Bolognia et al., 2018).

Follow-Up: Follow-up of the patient with superficial fungal infections needs to be addressed on a case-by-case basis. A follow-up in 4 weeks is a reasonable option, especially for those patients on oral therapy, where hepatitis may appear after 4 weeks of treatment (Bolognia et al., 2018). For oral antifungal therapy lasting greater than 4 weeks, a baseline CBC and liver function tests are recommended with retesting every 4 to 6 weeks (Habif, 2016). Infection of the toenails requires 6 weeks or longer to judge results, and in tinea versicolor 1 to 2 months are required before the lesions resolve. Patient education regarding expected outcomes and possible

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side effects can help in the assessment of when or even whether follow-up is necessary.

Sequelae: The superficial fungal infections for the most part do not present a serious health threat to older adults. Their lack of symptoms is one reason they are often chronic before they are addressed. In older adults, onychomycosis can result in cellulitis and foot ulcers. The risk of superinfection with bacteria and resulting severe consequences is greatest in those with diabetes, peripheral vascular disease, or immune compromise. The *Candida* species may have systemic consequences and are often painful; treatment and prevention are key. The side effects of the treatments may be more concerning than the disease, and these risks are important to weigh in decision making. Serious consequences include hepatic toxicity, CYP450 interactions, neutropenia, and agranulocytosis.

Prevention/Prophylaxis: All fungus grows best in warm, humid environments. The key to prevention of all types is to keep the skin cool and dry. Avoiding occlusive footwear, wearing absorbent materials, and practicing good hygiene offer the best primary prevention. Tinea pedis, tinea manuum, and onychomycosis are difficult to completely eradicate; recurrence is common, and the diseases may become chronic in nature. The interdependence of these infections requires the complete resolution of all three in order to prevent recurrence. Tinea versicolor is the result of the conversion of the normal *Malassezia* skin flora to a mycelial form that is pathological and causes the scaly lesions. Older age actually decreases the risk of this disease because sebaceous activity declines with age. Prophylactic therapy with topical or oral antifungals has been effective in preventing recurrence which is common.

The *Candida* species are part of the normal flora in the mouth, gut, and vaginal tract. The key to prevention of recurrence is keeping the skinfolds dry. Use of a hairdryer to thoroughly dry the area after bathing, the use of aluminum acetate solution (Burow solution), and the application of antifungal or absorbent powder have all been shown to prevent recurrence (Habif, 2016; Wolff et al., 2017).

Referral: When definitive diagnosis is needed for suspected fungal infections of the skin, hair, or nails, referral is often necessary to confirm infection based on fungal culture, direct microscopy, PCR, and/or histopathology. This is particularly important for nail involvement given the extensive differential diagnosis of nail infections and adverse effects of oral antifungal treatment.

Education: Patient education should center on the cause of the infection and the risk of reinfection/recurrence. Prevention requires avoidance of situations that cause occlusive, warm, moist environments. This can be accomplished by wearing absorbent materials, loose clothing, and open-toe shoes in the summer, and wearing protective footwear in showers and around pools. Patients can be reassured that tinea versicolor is the result of a change in the normal body flora and not contagious, and that coloration changes will resolve with treatment. Prophylactic antifungal therapy may be required, especially for tinea pedis, tinea manuum, or onychomycosis.

Clinical Recommendation	Evidence Rating	References
A rule for the clinical diagnosis of onychomycosis was developed. Data supported that the rule was at least as accurate as laboratory tests. When dermatologists considered onychomycosis was the most likely diagnosis and plantar desquamation affected >25% of the sole of the foot, treatment could be started without further confirmation. The rule needs to be validated with primary care practitioners.	B	Garcia-Doval et al., 2010
A potassium hydroxide (KOH) preparation with skin scrapings from the affected areas is the primary diagnostic method of confirming epidermal dermatophyte infections.	A	Gupta et al., 2020
Oral ketoconazole is not a recommended treatment for dermatophyte infections. Newer antifungals are more effective, and oral ketoconazole carries a life-threatening risk of hepatotoxicity, drug-drug interactions, and adrenal insufficiency.	A	van Zuuren et al., 2015
A small study of topical Vicks VapoRub applied to nails affected with fungus confirmed by microscopy and culture was found to be as effective as topical ciclopirox 8%, the only FDA-approved treatment for onychomycosis. Participants were followed for 48 weeks, and the outcome measure was clinical and mycological cure. Patient satisfaction was also measured. The cost of treatment is less than one-fourth that of the prescription treatment.	B	Derby et al., 2011
Terbinafine and azoles are effective therapies compared to placebo for resolution of onychomycosis. Cure rates are higher for terbinafine when compared to azoles with equal risk of adverse events.	A	Kreijkamp-Kaspers et al., 2017
Imidazole (azole) topical medications, such as miconazole, econazole, ketoconazole, and clotrimazole are well established as effective treatments for ringworm (tinea) infections with low risk of adverse reactions.	A	Hay, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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CASE STUDY

Mrs. Jones is a 70-year-old woman you are admitting to the skilled nursing facility after a total hip replacement. When you obtain her past medical history, she reports a problem with a chronic rash under her breasts and in her supragluteal fold. She has tried a number of topical antifungal treatments without success. She has never seen a dermatologist. While she finds the rash a nuisance and experiences an occasional increase in itchiness, it is something she can live with. Her primary care provider diagnosed the rash as *Candida* and encouraged her to keep the area clean and dry and to use antifungals. Recently, her 42-year-old daughter was diagnosed with psoriasis and asked about a family history of the disease. Mrs. Jones was unaware of anyone in her or her husband's family with that diagnosis.

On physical examination, you note a shiny, erythematous lesion with symmetrical distribution under both breasts. It is well demarcated without drainage and without the presence of any satellite lesions. Examination of the gluteal fold reveals a similar well-demarcated, shiny, erythematous lesion without drainage. On close inspection of the rest of the body around the umbilicus, you note an erythematous patch with silvery scale. You ask Mrs. Jones about the lesion, and she states that it has been there for years. The lesion is worse in the winter, but she attributes this to the closures on her skirts and pants causing irritation. She reports some improvement when applying OTC hydrocortisone cream, although when she stops using the cream, the lesion returns. For this case, the answers and rationale for your decision making need to be provided.

1. What clues in Mrs. Jones' history can help you determine her diagnosis?
2. What signs on physical examination are most helpful to defend or refute the differential?
3. How would you classify the severity of Mrs. Jones' disease? Be specific in your explanation.
4. What would be the treatment(s) of choice in her case?
5. What are some important points to include in patient education?
6. What would require a referral to a dermatologist?

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CHAPTER 9

Head, Neck, and Face Disorders

Laurie Kennedy-Malone

ASSESSMENT

When approaching the assessment of the head, begin by asking the patient if they have any headaches. If so, are they similar in presentation? Any history of head trauma or stroke? A systematic and thorough examination of the head and neck begins with the inspection of the face, head, and scalp. Assess the shape, size, and symmetry of the patient's features. Examine the shape of the skull, palpating the bones of the head for any anatomical irregularities, masses, or areas of tenderness. Inspect the hair for distribution, quantity, and any balding patterns, noting any uniform alopecia, nits, or seborrhea. Note any changes in the eyebrows, lateral loss of hair can be a sign of thyroid disease (Suchonwanit & Thammarucha, 2020). The scalp should be carefully inspected for any skin lesions on sun-exposed areas, noting pigment changes, tenderness, scales, or lumps. Assess for scars or bruising patterns. Note the symmetry of the patient's features, facial expressions, the presence of involuntary tics or tremors, periorbital edema, or facial drooping; palpate over the temples for any abnormality or tenderness in the temporal arteries. The presence of pain and nodules on palpation is not a normal finding even in very old individuals. Cranial nerve VII (facial nerve) should also be assessed at this time, noting any facial asymmetry, weakness, drooping of the lower eyelid, and unilateral paralysis (Suneja et al., 2020). The temporomandibular joint should be evaluated for degeneration; note if there is any crepitus as the patient lowers and raises their jaw or pain with chewing. Inquire if the patient hears any popping or grating when chewing or opening their mouth (Gauer & Semidey, 2015).

Eyes

Visual impairment is common in older adults, so it is important to review with patients any changes in vision and how they are adjusting to those changes. One will need to distinguish between normal age-related changes (accommodation, color perception, presbyopia, pseudoptosis, enophthalmos, arcus senilis, ectropion, and entropion) from common visual conditions (Besdine, 2019). Ask the patient about any visual changes that impair function and impact quality of life. Has the patient (or a family member) noted any change in cognition as the visual impairment progresses (Swenor et al., 2020)? Does the patient report having floaters, scotomas, diplopia, blurred vision, or glare? If the patient still drives, are they still driving at night? When was the patient's last eye examination, including screening for glaucoma?

Begin the inspection of the eyes by noting the position and symmetry of the surrounding skin and tissue, as well as the presence and position of the eyebrows and eyelashes. Screen visual acuity before proceeding with any other examination of the eye. Using a Snellen chart from 20 feet, or a handheld chart approximately 12 inches from the patient, assess visual acuity in each eye separately, then together; if the patient wears corrective lenses, they should have those lenses on for this test (Tatum III et al., 2018). Note the condition of the skin around the eyes, check the sclera, and note the color of the conjunctiva. Assess the presence of exophthalmos, xanthelasma, pinguecula, ptosis, edema, and skin lesions. The lids should be carefully examined for the presence of hordeolum, chalazion, ectropion, and entropion, which is most common among older adults (Besdine, 2019). Be careful to note any abnormalities in blinking (Parkinson's disease), dull or blank staring (hypothyroidism), residual facial paralysis (Bell's palsy or cerebrovascular accident), and skin changes. Decreased elasticity and turgor is a normal aging pattern; the skin around the eyes becomes thin and wrinkles appear. This is a normal change in older adults and makes skin turgor a poor determinant of hydration status (Suneja et al., 2020).

Note that basal and squamous cell carcinomas are common around the eye. Palpate for any tenderness over the lacrimal gland and assess the patency of the lacrimal duct. Examine the extraocular motions of the eye (cranial nerves III, IV, and VI). Check the visual fields (cranial nerve II), corneal reflexes (cranial nerve V), and pupillary reactions (cranial nerves II and III) with direct and consensual reactions. Examine the cornea for any scarring, presence of pterygium, corneal arcus, and opacities. Carefully perform a funduscopic examination; most older adults need dilation for accurate assessment of the fundus. If you see the fundus, note the narrow, pale appearance of the arterioles common in older adults.

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Sinuses

Inquire about any recent episodes of sinus congestion. Inspect and palpate over the frontal and maxillary sinus areas. Note any gross tenderness or inflammation in the sinus area or around the eyes.

Nose

Disorders of the sense of smell are common in older adults related to the atrophy of the olfactory bulb, history of allergic rhinitis, chronic rhinosinusitis, neurodegenerative conditions such as Parkinson's disease and dementias and certain medications (Malaty & Malaty, 2013). Patients should be questioned about the severity and persistence of hyperosmia or anosmia and how changes in the sense of smell affects their quality of life. Review allergies, history of sinonasal conditions, head trauma, polyps, and any familial history of neurogenerative conditions known to affect the sense of smell (Malaty & Malaty, 2013). Review any recent history of rhinitis, detecting from the patient any indefinable triggers and treatments. Inquire whether the patient has had any episodes of epistaxis especially for patients on anticoagulants medications (Womack et al., 2018).

Inspect the external nose for any asymmetry, inflammation, gross septal deviation, or deformities. Assess the function of the olfactory nerve (cranial nerve I) by having the patient identify familiar-smelling items such as coffee with the eyes closed. Assess for patency of each nostril. Examine the internal nose, noting any discharge, bleeding, or edema. Check the status of the turbinates and position of the septum using a large otoscope speculum. The color and consistency of the inferior and middle turbinates as well as the presence of any polyps should be noted (Suneja et al., 2020).

Ears

While hearing loss is attributed to aging, patients often do not report concerns. Question the patient or, if appropriate, a family member about concerns of decreased hearing and how the patient is compensating for the hearing loss (adaptive equipment, amplifier). Ask whether any auditory testing has been ordered and if hearing aids were recommended or used (Michels et al., 2019). Ask the patient if they are experiencing any tinnitus (buzzing, chirping). If so, when did it begin? Is it interfering with function? How are they compensating? Determine whether the patient is taking any ototoxic medications. Inquire about drainage, itching, and ear hygiene practices.

Carefully examine the external ears, noting their position and symmetry on the head, as well as any abnormal lesions, deformities, and the presence of tophi, keloids, cysts, or skin cancer lesions on the posterior ear and helix. Palpate the tragus for any tenderness, as well as for any preauricular or postauricular adenopathy.

Estimate auditory acuity (cranial nerve VIII) by using the whisper test or finger rub test, testing each ear separately. Use the Weber and Rinne tests to assess for any conductive or sensorineural hearing loss (Michels et al., 2019). If the patient wears an external hearing aid, it should be removed before examining the external canal. When examining the middle ear, note any inflammation, discharge, or erythema. Carefully examine for cerumen in the external auditory canal; if noted, ask the patient about ear hygiene and prior cerumen removal (Croke, 2017). If visible, inspect the tympanic membranes and surrounding landmarks for abnormalities. Note any foreign bodies, dull membranes, alterations in the cone of light reflex, and presence of fluid or scarring.

Oral Cavity

When approaching the examination of the mouth, begin by asking the patient if they have any loose or sensitive teeth. Do they notice any bleeding after mouth care? Explore if the patient wears dentures; ask whether they fit properly. Any noted changes in eating due to mouth pain or discomfort with chewing or swallowing? Does the patient see a dentist? If the patient is dependent for feeding, is oral care regularly performed? Has the patient noted any changes to the sense of taste (Malaty & Malaty, 2013)?

Perform a complete assessment of the lips, mouth, oral mucosa, and pharynx, noting the color, moisture, and presence of any abnormal lesions on and around the lips. Assess for any herpes simplex I, chancres, angular stomatitis, mucous retention cysts, angioedema, xerostomia, and fissures. Check oral mucosa for color, nodules, ulcers, or white patches (Besdine, 2019). If the patient has dentures, these should be removed to do a complete oral examination. Examine the fit of the dentures and assess the consistency of the gums under the dentures. If natural teeth are present, note any loose or broken teeth as well as caries. Because periodontal disease is the primary cause of tooth loss in the adult, do a careful oral and gum examination. Examine the gums for bleeding, discoloration, swelling, and retractions. Note the attrition of the teeth (exposed dentin) and enamel loss from years of chewing (Besdine, 2019).

Note the condition of the hard palate and the presence of torus palatinus, thrush, or other lesions. Assess the gag reflex and rise of the palate (cranial nerves IX and X). Carefully examine the tongue for symmetry, enlargement (hypothyroidism), growths, protrusions, or abnormal movements (cranial nerve XII) and the dorsum for any papillary atrophy. A swollen, red, painful tongue may indicate vitamin B or riboflavin deficiency. Note any inflammation or obstruction in the parotid (Stensen) or submaxillary (Warton) ducts. Thoroughly examine the area underneath the tongue, the floor of the mouth, and the tonsils, soft palate, uvula, and posterior pharynx, noting any lesions, inflammation, or exudate and the color. Examine the strength and movement of the temporal and masseter muscles (cranial nerve V), as well as any crepitus in the mandible junction. Complete assessment should also include evaluation of the voice (cranial nerve X) and speech (cranial nerves V, VII, X, and XII) (Suneja et al., 2020).

Neck

Inspect the neck for symmetry, masses, scars, tracheal position, and deviation. Look for the presence of thyroid inflammation or goiters. Carefully palpate for any lymphadenopathy, noting that loss of lean muscle makes it easier to feel nodes in the cervical region of older adults. Assess supraclavicular, tonsillar, superficial, deep, and posterior cervical chains and submaxillary, submental, occipital, preauricular, and postauricular nodes, noting any inflammation, tenderness, or change in size, position, or shape

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(Besdine, 2019). Hard, fixed nodes imply malignancy; tender nodes are typical of inflammation (Gaddey & Riegel, 2016). Gently palpate and auscultate the carotid arteries one side at a time for any nodularity or bruits. Note any jugular vein distention that occurs when the patient is seated. Check to see whether the patient uses any neck muscles to breathe. Carefully inspect and palpate the thyroid gland, noting any inflammation or nodules (unilateral). Examination of the range of motion of the neck should include flexion, extension, rotation, and lateral bending. Check the strength of the trapezius and sternomastoid muscles (cranial nerve XI) (Besdine, 2019).

A complete and thorough detailed examination of the head and neck has the potential to allow the examiner to discover multiple variants from the normal. Develop a clear and concise pattern of examination to ensure appropriate evaluation of these areas. Keep in mind the normal variants of the older person and how these differ from pathological or abnormal findings.

AGE-RELATED MACULAR DEGENERATION

Signal Symptoms. Age-related macular degeneration (AMD) is the leading cause of blindness in adults. It is a disease that results in a loss of central vision, which is most crucial for activities of daily living (ADLs) and instrumental activities of daily living (IADLs). The severity of central vision loss varies depending on the type of macular degeneration. Most recently, efforts have been made to standardize the terminology and classification of AMD by defining it as one disease with three stages: early, intermediate, and late. Late AMD is characterized by significant vision loss, which may occur with gradual loss due to "dry" macular geographic atrophy, or with rapid onset as a result of the neovascularization of "wet" macular degeneration (Wenick et al., 2018).

Dry, Nonexudative, or Atrophic Macular Degeneration. Gradual loss of central vision in one or both eyes, with complaints of difficulty reading or driving, blurred or fuzzy vision (late), and the concern that straight lines appear wavy. In early dry AMD there is the presence of drusen, yellow deposits under the retina. In the intermediate stage, pigmentary disturbances in the retinal pigment epithelium (RPE) occur, and in the late stage there is geographic atrophy (GA) with severe central vision loss.

Wet, Exudative, or Neovascular Macular Degeneration (NVAMD). This characterizes one form of late AMD with accelerated central vision loss in a period of weeks to a couple of months. The fragility of the neovasculature results in subretinal hemorrhage or fluid accumulation that destroys the visual center. The disease usually presents in one eye initially, but there is a greater than 40% risk of development in the other eye within 5 years.

Description: The macula in the center of the retina comprises millions of photoreceptor cells containing visual pigments for central vision. These are nourished by the RPE, part of a complex basement membrane that becomes sclerotic with age. AMD is defined as early, intermediate, and late, depending on the severity of vision loss and pathological findings. Dry AMD is most common, accounting for 90% of cases. Onset of visual loss is gradual and may not be noticed if only one eye is affected. The cause is unknown, but there is the presence of drusen and disintegration of the RPE and light-sensing cells. Late AMD with neovasculature occurs in 10% of cases of AMD but accounts for 90% of all AMD blindness. Patients with early and intermediate forms of AMD may develop neovascularization of the choroid area with leakage of new blood vessels and fluid into the retinal pigment epithelium, which causes scarring and additional damage to the macula. The risk ranges from 2% to 20% depending on the size of drusen present. The presence of GA does not protect against the development of NVAMD, with an incidence of 16%, which increases to 36% if NVAMD is present in the other eye (Wenick et al., 2018).

Etiology: A challenge in identifying the cause of dry AMD is the difficulty in distinguishing the early form from normal changes with aging and the lack of symptoms at this stage. As the macula ages, the RPE, Bruch membrane, and choroidal vessels are all affected. Hard drusen may be noted in almost all older eyes. It is the increase in size and number of drusen that is one indication of early AMD. Genetic predisposition and risk factors certainly contribute to the development of AMD. The role of inflammation in the development of AMD is the focus of research on the role of the complement pathway (Campbell & Doyle, 2019). NVAMD has been more aggressively studied in attempts to understand the origin of the angiogenesis. As a result of these studies, several pro-angiogenic factors have been identified. The vascular endothelial growth factor (VEGF) is the most important in intraocular angiogenesis, and its role has resulted in new treatment options for NVAMD. The use of anti-VEGF medications has been shown to stabilize visual function and stop progressive loss of vision (Arrigo, 2021). Research on targeted gene expression for both wet and dry AMD may lead to early diagnosis and treatment (Ammar, 2020; Cinici et al., 2021).

Occurrence: Common; macular degeneration is the leading cause of legal blindness in adults older than 55 years. Risk rises with age; occurrence is 30% in adults older than 75 years. In North America, 15 million people have nonexudative AMD, and 1.7 million have NVAMD. These numbers may be an underestimate because those with early AMD may have no visual changes and may not have been diagnosed. Those with early AMD and NVAMD are at low risk for increasing visual loss, with only one-third progressing to intermediate AMD in the next 5 years (Wenick et al., 2018).

Ethnicity: Individuals who are White are more likely to experience visual loss from AMD than individuals who are Black.

Contributing Factors: The primary risk factor for AMD is advancing age. Other risk factors include family history, smoking, exposure to sunlight, nutritional deficits, hyperlipidemia, and cardiovascular disease. History of AMD in one eye is a risk factor for developing it in the other eye (Brady et al., 2018; Thomas et al., 2021).

Signs and Symptoms: In early AMD there may be no symptoms, particularly if it is monocular. Later, patients may note a decrease in visual acuity or blurred vision that improves in bright light. In late NVAMD, straight lines appear wavy, and there may be a hole in central vision. White-yellow drusen spots are seen on funduscopic examination. Until recently, the primary screening device for NVAMD was the Amsler grid

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test, which, when administered, may reveal wavy lines or missing lines in central vision; however, it has low sensitivity (a high number of false negatives). New perimetry devices are now available for both clinical and home monitoring with better sensitivity and specificity for identifying NVAMD (Wenick et al., 2018). On funduscopic examination of those with NVAMD, choroidal neovascular membranes (CNVMs), subretinal fluid, hemorrhage, and subretinal lipid deposits may be present.

Diagnostic Tests: All patients should have a comprehensive eye examination by an ophthalmologist, including visual acuity with best correction, funduscopic examination, Amsler grid or perimetry assessment, fluorescein angiography, and fundus photos, including optical coherence tomography (Brady et al., 2018; Wenick et al., 2018).

Differential Diagnosis:

- Unexplained loss of visual acuity
- Diabetic retinopathy
- Ocular histoplasmosis
- Trauma with scar
- Hypertension

Treatment: The Age-Related Eye Disease Study (AREDS) found that patients at high risk for late AMD lowered their risk by 25% when treated with high doses of vitamin C, vitamin E, beta carotene, zinc oxide, and cupric oxide. This effect was confirmed through 10 years of follow-up. The efficacy of this was demonstrated for those with intermediate AMD or late monocular AMD to prevent further loss or involvement of the other eye. It is not recommended for those without AMD or those with early AMD who have a low 5-year risk of worsening vision. The risk versus benefits of this high-dose vitamin treatment needs to be evaluated for each patient. The AREDS2 evaluated the effect of substituting the carotinoids, lutein and zeaxanthin, as well as omega-3 (DHA) and eicosapentaenoic acid (EPA) for beta carotene and a lower zinc dose on progression of AMD (AREDS2 Research Group, 2013). The conclusion after 5 years was that eliminating beta carotene and lowering zinc did not make a difference in progression to advanced AMD, and the addition of lutein and zeaxanthin, DHA, and EPA did not further reduce progression. However, they concluded that there may be value in substituting lutein and zeaxanthin for beta carotene because beta carotene increased the risk of developing lung cancer, especially in smokers. Two new eye injections for dry AMD that target the complement cascade are in the last clinical trial phases. The use of stem cells to replace damaged retinal cells is also under investigation (Medieros & Mukamal, 2021). Low-vision enhancement aids are available to help patients with dry AMD. For patients with bilateral advanced and end stage untreatable AMD, a visual prosthetic implant may be considered.

First-line therapy for NVAMD includes monoclonal antibodies that have anti-VEGF abilities. These drugs are injected directly into the vitreous area of the eye and bind with the angiogenic VEGF or receptor and interrupt the neovascularization. They are not able to repair the basic defect or attack the source of VEGF, so they must be used repeatedly to suppress the angiogenic process (Brady et al., 2018). Ranibizumab and bevacizumab (off label) are two humanized monoclonal antibodies that are used to treat NVAMD successfully (Brady et al., 2018). They are injected intravitreally at monthly intervals; current focus is on determining optimal spacing and length of treatment for best results. Local side effects include eye pain, uveitis, and endophthalmitis. There are also potential systemic cardiovascular and thrombotic effects from these drugs, although these have proved minimal. Aflibercept is a newer agent that improves visual outcomes with less frequent injections; preliminary studies show it to be as effective as ranibizumab, with better outcomes in visual acuity and less frequent dosing or maintenance; (Arroyo, 2017).

Laser photocoagulation therapy is no longer first-line treatment since the advent of anti-VEGF therapies. Photodynamic therapy is now being studied as a possible combination therapy with anti-VEGF treatment (Arroyo, 2017). Research into surgical options has yielded disappointing results; likewise, use of statins for AMD has not shown positive results, but recent studies with a small number of participants showed some promise (Arroyo, 2017; Leung et al., 2018). Research is currently underway to find safe, effective treatments for both dry and wet AMD.

Follow-Up: All patients with AMD should be seen periodically by an ophthalmologist for reevaluation of disease progression and, where applicable, further treatment. Patients may be given an Amsler grid or the newest option of an at-home perimetry monitor to use weekly or monthly to check for visual changes.

Sequelae: Loss of central vision limits functional capacity and ability to read. Most AMD patients cannot drive. Environmental safety also is compromised; falls and hip fractures can occur in patients with AMD. Patients using high-dose vitamin and mineral therapy may have yellowing of skin. Smokers are at increased risk for lung cancer from beta carotene included in the first AREDS vitamin supplement formula.

Prevention/Prophylaxis: There is no specific prevention. The U.S. Preventive Services Tax Force (USPSTF) has determined that there is not enough evidence to support routine visual screening of older adults for AMD (USPSTF, 2016). Annual eye examinations in persons over 65 years old can facilitate early detection and, in the case of wet AMD, early intervention to limit visual loss. Smokers should be encouraged to quit.

Referral: All patients older than 65 years should be referred to an ophthalmologist for an annual eye examination. Patients younger than 65 years with visual symptoms also should be referred. Patients with AMD should be referred to the local chapter of the Blind Association for services, vision enhancement devices, and support groups.

Education: Teach patients the importance of seeking evaluation for visual symptoms as soon as they occur. Explain disease process and community support services. Educate the family about the need for environmental safety. Caution patients to avoid unproven remedies. Enforce the role of smoking as an independent risk factor in AMD.

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Clinical Recommendation	Evidence Rating	References
Anti-vascular endothelial growth factor injections are first-line agents to treat wet age-related macular degeneration (AMD).	A	Brady et al., 2018 Leung et al., 2018 AAO, 2019 Thomas et al., 2021
Antioxidant formulations as used in the AREDS and AREDS2 trials should be recommended to those with intermediate or advanced AMD.	A	Wenick et al., 2018 Leung et al., 2018
Patients should be advised to achieve/maintain a healthy weight, quit smoking, and control blood pressure and lipids.	A	Thomas et al., 2021
Cessation of antiplatelet/anticoagulation therapy is generally not needed but may be warranted in certain cases.	A	Thomas et al., 2021

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BLEPHARITIS

Signal Symptoms: Redness, itching, burning, scaling of the eyelid margin

Description: Anterior blepharitis affects the eyelids, eyelashes, and follicles. It is chronic, bilateral, with two main types: staphylococcal and seborrheic. Posterior blepharitis is a chronic, bilateral, condition associated with meibomian gland dysfunction (MGD). It is common to see all types of blepharitis occur together (American Academy of Ophthalmology [AAO], 2018; Vagefi, 2017).

Etiology: Anterior blepharitis is associated with a staphylococcal infection or seborrheic dermatitis. Posterior blepharitis is caused by inflammation or infection of the meibomian glands resulting in plugging of the orifices and decreased meibum to the tear film and lid margins. The result can be atrophy and fibrosis of the glands (AAO, 2018; Vagefi, 2018; Watkinson & Seewoodhary, 2017)

Occurrence: Approximately 5% of all ophthalmological conditions in primary care and occurs equally among sexes.

Age: Increased incidence with age.

Ethnicity: No specific association.

Contributing Factors: Other factors include rosacea, dry eye, *Demodex* (mite) infection; viral infections (such as zoster), immunologic conditions (such as lupus or pemphigus), trauma, eyelid tumors, dermatoses, or medication side effects (AAO, 2018; Watkinson & Seewoodhary, 2017).

Signs and Symptoms: Blepharitis due to staphylococcal infection can be associated with scales, dry eye, erythema, ulceration, and loss of eyelashes. Seborrheic blepharitis has greasy scaling on the eyelids and is frequently associated with seborrheic dermatitis of the scalp and eyebrows. Signs of posterior blepharitis include excessive tearing, production of thick "cheese-like" material expressed with pressure on the glands, and hyperemia and telangiectasia of the lid margins, which can roll inward (AAO, 2018; Vagefi, 2018).

Diagnostic Tests: Diagnosis is usually based on patient history. Depending on the chronicity and severity, patients may need a comprehensive eye examination including visual acuity, slit-lamp examination, cultures, or meibomian gland imaging (AAO, 2018).

Differential Diagnosis:

- Discoid lupus erythematosus
- Postoperative endophthalmitis
- Conjunctivitis
- Hordeolum
- Chalazion
- Rosacea
- *Demodex* infection
- Carcinoma (should be considered if unilateral, chronic, and unresponsive to therapy; loss of normal eyelid margin; or focal eyelash loss [AAO, 2018]).

Treatment: Blepharitis is a chronic condition with no cure. The goals of therapy are to provide symptomatic relief and improve quality of life while controlling out-of-pocket costs. Management should be tailored to the patient and include an evaluation of comorbid conditions as well as a review of current medications for potential effects on the eye (AAO, 2018; Charters, 2019; Watkinson & Seewoodhary, 2017). Eyelid hygiene includes warm compresses for several minutes at least once a day. Eyelids can be cleansed once per day with diluted baby shampoo or a commercial eyelid cleaner, which can be applied with a pad, cotton ball, swab, or clean fingertip. Brief, gentle massage can be applied to the meibomian glands but avoid excessive pressure. Artificial tears may help dry eye, but if they are used more than 4 times per day, recommend a product with no preservatives (AAO, 2018; Bitton et al., 2019).

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Topical ophthalmic antibacterial ointments can be applied as directed, usually 1 to 2 times per day for a few weeks if needed. Treatment should be intermittent to avoid microbial resistance. Oral tetracyclines and macrolides may be needed, particularly for MGD. Topical corticosteroid drops or ointment may also be used for severe inflammation. Loteprednol or fluorometholone are preferred. Combination topical antibiotics and corticosteroids are available. Use minimal effective dose and avoid long term use. Topical cyclosporine may be effective in posterior blepharitis (AAO, 2018; Malhotra, 2020; Zhao et al., 2021). If treating possible Demodex (mite infestation), topical or systemic Ivermectin can be prescribed. Studies have shown that products with 50% tea tree oil have also been beneficial (Ergun et al., 2020; Mandal et al., 2017; Periman, 2020). Other treatment modalities for blepharitis, such as intense pulse light therapy, are also available (AAO, 2018; Mandal et al., 2017; Ruan et al., 2019).

Follow-Up: Based on severity, treatment choice, and comorbid conditions.

Sequelae: This is a chronic condition requiring long-term maintenance (AAO, 2018).

Prevention/Prophylaxis: Perform eyelid hygiene on a regular basis. Medications or other treatments are based on response to therapy.

Referral: Refer to ophthalmology with prolonged corticosteroid use to evaluate intraocular pressure. Prompt referral is needed with vision loss, eye pain, recurrent symptoms, or if the patient is unresponsive to therapy.

Education: Emphasize the chronicity of the problem. Develop a plan of care with the patient considering social determinants of health and quality of life with an emphasis on improving symptoms.

Clinical Recommendation	Evidence Rating	References
Blepharitis is a chronic condition that requires frequent eyelid hygiene, including warm compresses, eyelid cleansing, and gentle massage.	A	AAO, 2018 Bitton et al., 2019
Topical ophthalmic antibiotics and corticosteroids can be used alone or in combination but avoid long-term use.	A	AAO, 2018 Zhao et al., 2021
Demodex (mite) infestation is more common in older adults, and diagnosis should be considered if treatment is ineffective. Topical or oral ivermectin or a product with tea tree oil can be used.	C	Ergun et al., 2019 Mandal et al., 2017

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CATARACT

Signal Symptoms: Diminished vision in one or both eyes, poor night vision, sensitivity to glare. Because progression is gradual, changes may go unnoticed until visual loss is advanced.

Description: A cataract is an opacification of the lens that interferes with the passage of light through the lens, decreasing visual acuity. The location, size, and density of this opacity influence the degree of visual impairment (Harper, 2017; Yoo & Zein, 2021). Nuclear sclerotic cataracts affect contrast sensitivity, progress slowly, and tend to preserve functional reading vision while frequently causing nearsightedness. In contrast, posterior subcapsular cataracts progress more rapidly and interfere with reading vision.

Etiology: Most cataracts are related to the aging process. The gradual thickening or hardening in the lens is believed to be caused by oxidative damage to the lens protein.

Occurrence: The rate of visually significant cataracts in persons age 50 to 59 years old is 6.8%. Of persons older than 80 years, 68.3% have cataracts (Harper, 2017). Cataracts tend to be bilateral, although the rate of progression varies between the eyes.

Age: Although subtle changes in visual acuity related to cataract formation occur by age 50, people older than 75 years old experience most visually significant cataracts.

Ethnicity: Not significant.

Contributing Factors: Diabetes mellitus, hypertension, poor nutrition, cigarette smoking, high alcohol intake, trauma to the eye, long-term exposure to ultraviolet (UV) B radiation (sunlight), and a strong family history of cataracts are risk factors. Use of certain substances, including oral glucocorticoids, also contributes to cataracts. An association between cataracts and glaucoma and intraocular inflammation exists (Yoo & Zein, 2021).

Signs and Symptoms: The patient with a cataract initially may present with an improvement in near vision, requiring a new prescription for corrective lenses; distance vision will worsen (Harper, 2017). Patients also may experience blurred vision or sensitivity to glare from bright light or from automobile headlights during night driving. Complaints of having difficulty reading and distinguishing contrast sensitivities and of seeing a yellow tint or washed-out colors are common. Some patients may not seek evaluation of their symptoms by a

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health-care provider owing to denial or fear of loss of independence (driver's license being revoked), whereas other patients seek prompt assessment in the hope of early intervention. A recent history of falls, accidents, or injury is suspicious. On physical examination, visual acuity test results are abnormal for one or both eyes (evaluate near and distance vision). Examine the eye using an opaque light for opacification of the lens. The cataract may be visible to the naked eye. The red reflex may be absent, or the cataract may appear as a black area.

Diagnostic Tests: No diagnostic testing is required other than that for visual acuity and examination of the eye unless other visual problems are suspected. Refer the patient to an ophthalmologist for complete evaluation after initial screening. Pupillary dilation and slit-lamp examination will reveal white, gray, or brownish opacities if the cataract is developed. Dark areas on the red reflex in a dilated eye indicate small cataracts; the red reflex may not be visible if the cataract is large (Harper, 2017).

Differential Diagnosis:

- Corneal scarring
- Retinal detachment
- Macular degeneration
- Chronic glaucoma
- Diabetic retinopathy

Treatment: Treatment is determined after full evaluation by the ophthalmologist. Ultimately, surgical intervention is required with extraction of the cataract and immediate implantation of a plastic intraocular lens (IOL), unless contraindicated by other disease conditions. Phacoemulsification is the most common procedure for removal of cataracts. Laser surgery may also be used particularly for astigmatism with the main disadvantage of higher costs. A variety of types of implantable lenses are used depending on patient vision assessment and lifestyle. These include lenses that adjust for astigmatism and refractive errors. The main IOL used is the monofocal lens, with multifocal used for presbyopia and toric lens and laser for astigmatism (Yoo & Zein, 2021). Patients with posterior capsular opacification may require neodymium:yttrium-aluminum-garnet (Nd:YAG) laser capsulotomy. This should not be performed at the same time as other cataract surgery. Collaboration with the ophthalmologist is indicated for patients with severe cardiac, respiratory, or neuromuscular conditions that may prevent the patient from lying still or supine as required during the surgery. Patients with diabetes and hypertension should be instructed in medication use preoperatively. Patients receiving anticoagulant and antiplatelet therapy also should be managed collaboratively and individually. These medications are not usually discontinued preoperatively since cataract surgery is generally low risk for bleeding. Appropriate laboratory tests should be within therapeutic range within 24 hours of surgery (Yoo & Zein,2021). Patients who are or have been on alpha receptor therapy, such as tamsulosin for prostatic enlargement, may experience intraoperative floppy iris syndrome (IFIS). Discontinuing alpha blockers before surgery has minimal or no effect on preventing IFIS, but surgeons should be aware of their use in case modifications are needed during surgery (Yoo & Zein, 2021). Although still considered an alternate practice pattern, intracameral antibiotic injection during surgery has been shown to reduce rates of the rare complication of endophthalmitis (Durand, 2017; Gower et al., 2017; Hashemian et al., 2017).

The degree of visual impairment and its influence on the patient's activities of daily living determine the need and timing of the surgery (American Academy of Ophthalmology [AAO], 2020; Yoo & Zein, 2021). Initially, a conservative treatment plan may include a prescription for glasses and periodic reevaluation by the ophthalmologist, coupled with a plan for environmental safety and optimization of the patient's functional abilities within his or her visual limitations. Surgery is performed in an outpatient or short procedure unit, with the patient returning home immediately after discharge. With the advent of multifocal implantable lenses and toric lenses for astigmatism, glasses may not be required after surgery, however, insurers currently only support monofocal lenses. Advancements in technology continue for cataract refractive surgery (Alio et al., 2017; de Silva et al., 2016; Harper, 2017; Lawless, et al., 2017; Yoo & Zein, 2021).

Follow-Up: Immediate postsurgical care includes eye protection and application of topical agents prescribed by the ophthalmologist. The patient may be cautioned to avoid straining, lifting, or bending. Postoperative follow-up is usually within 24 to 48 hours. The family or health-care team should heighten precautions for environmental safety to avoid injury. Intensive supervision of mentally compromised patients is required to prevent damage to the operative site. Future follow-up includes a reevaluation of visual acuity, prescription of corrective lenses if indicated, and monitoring of the unaffected eye for cataract development.

Sequelae: Possible sequelae to cataract surgery include faulty wound closure with aqueous humor leakage, blindness secondary to choroidal hemorrhage, endophthalmitis, toxic anterior segment syndrome (TASS), inflammation, retinal detachment, prolapse of the iris into the corneal wound, and secondary glaucoma (AAO, 2016; Williams & Khandelwal, 2019; Yeu, 2021).

Prevention/Prophylaxis: The patient should be protected from exposure to UVB radiation by wearing sunglasses designed for this and by wearing a hat with a wide brim.

Referral: After the initial visual screening, refer the patient to an ophthalmologist for complete examination and treatment, including post-surgery follow-up.

Education: Provide the patient with information on age-related visual changes and the importance of protecting the eyes from sunlight with UV-blocking sunglass lenses; maintaining a nutritionally balanced diet including colorful fruits and vegetables; avoiding tobacco and high alcohol intake; and having regular eye examinations based on the recommendations of the eye specialist. Instruct the patient to seek prompt evaluation of any vision changes (Mayo Clinic, 2018).

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Clinical Recommendation	Evidence Rating	References
There is no evidence from randomized, controlled trials (RCTs) that supplementation with antioxidant vitamins (beta carotene, vitamin A, or vitamin E) prevents or slows the progression of age-related cataract.	A	Olson et al., 2016
The decision to recommend cataract surgery should be based on consideration of the following factors: visual acuity, visual impairment, and the potential for functional benefits that may improve quality of life.	A	AAO, 2021 Yoo & Zein, 2021
Ophthalmologists and other physicians managing patients taking alpha antagonists should be aware of the risks of intraoperative floppy iris syndrome (IFIS).	A	Campbell et al., 2019 Yoo & Zein, 2021
Extracapsular cataract surgery by phacoemulsification with intraocular lens (IOL) implantation provides safe and effective treatment for patients with cataract.	A	AAO, 2021 Yoo & Zein, 2021
Anticoagulation and antiplatelet therapy will usually continue because cataract surgery is a low-risk procedure for bleeding, but the surgeon should be made aware in case surgical modifications are needed.	A	Yoo & Zein, 2021

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EPISTAXIS

Signal Symptoms: Bleeding from the nose or into the posterior nasopharynx.

Etiology: More than 90% of the time the bleeding is the result of a spontaneous rupture of a blood vessel in the anterior septum in the Kiesselbach plexus (Nguyen, 2020; Sowerby et al., 2021; Womack et al., 2018). Local causes of epistaxis include trauma due to digital manipulation, irritation or inflammation of the nasal mucosa, foreign bodies, septal defect, or paranasal tumors. Systemic causes include hematologic, hepatic, renal, genetic, cardiovascular, or hereditary hemorrhagic telangiectasias (Beck et al., 2018; Nguyen, 2020; Tunkel et al., 2020).

Occurrence: Most people have at least one episode of minor, nonrecurring epistaxis (Beck et al., 2018; Sowerby et al., 2021; Tunkel et al., 2020). Several sources indicate a lifetime incidence of 60% with about 6% requiring medical intervention (Nguyen, 2020; Tunkel et al., 2020; Womack et al., 2018). Epistaxis occurs more frequently in males than in females (Tunkel et al., 2020). Patients older than age 65 have an increased risk for emergency department visits due to epistaxis (Tunkel et al., 2020).

Age: Epistaxis occurs most frequently in children under age 10 and in older adults (Tunkel et al., 2020).

Ethnicity: Not significant.

Contributing Factors: Local trauma to the anterior portions of the nose (digital, as in nose picking, and facial trauma) is usually the cause of epistaxis. Low humidity or cold weather, foreign bodies, intranasal neoplasms, septal abnormalities, inflammation from rhinosinusitis, intranasal steroids, and systemic medications, such as NSAIDs, anticoagulants, and antiplatelet therapies, may contribute secondarily to the occurrence of epistaxis. Systemic diseases that contribute include hypertension, hematologic malignancy, coagulopathy, or hereditary hemorrhagic telangiectasia. (Gudis & Soler, 2021; Nguyen, 2020; Tunkel et al., 2020; Womack et al., 2018).

Signs and Symptoms: Usually no signs or symptoms are associated with epistaxis other than external bleeding or an awareness of blood dripping down the posterior nasopharynx (Nguyen, 2020).

Diagnostic Tests: No laboratory studies are indicated for minor and nonrecurring epistaxis. For more substantial or recurrent epistaxis, a complete blood count (CBC), bleeding time, prothrombin time (PT), and partial thromboplastin time may be useful. In a patient who is on warfarin therapy, an international normalized ratio (INR) should be drawn if epistaxis occurs. If bleeding is severe and the need for blood replacement is anticipated, type and crossmatch also should be done (Nguyen, 2020; Tunkel et al., 2020).

Differential Diagnosis:

- Trauma
- Inflammation due to rhinitis or infection
- Vascular disorders
- Clotting disorders and blood dyscrasias
- Intranasal foreign bodies
- Hereditary telangiectasia
- Tumors (Tunkel et al., 2020)

Treatment: Most episodes of epistaxis are mild and self-limited, resolving spontaneously. Epistaxis may be controlled by pinching the nostrils together for 10 to 15 minutes, keeping the patient in an erect sitting position with head tilted forward to prevent blood from going down the posterior nasopharynx to protect the airway (Sowerby et al., 2021; Womack et al., 2018). Anterior bleeding that does not stop with manual pressure alone may be controlled with two sprays of oxymetazoline 0.05% applied directly to the bleeding site followed by 10 to 15 minutes of manual pressure.

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Silver nitrate may also be used for control of bleeding once the site of origin is located. Other devices include nasal tampons, such as Merocel or balloons for packing. If packing is needed, adequate pain management must be prescribed, and it should be removed within 2 to 3 days (Gudis & Soler, 2021; Nguyen, 2020; Tunkel et al., 2020; Womack et al., 2018).

Follow-Up: For recurrent episodes, follow-up visits are recommended as needed. Posterior epistaxis, comorbidities, or recurrent bleeding may necessitate admission or referral to an ear, nose, and throat (ENT) specialist for management (Beck et al., 2018; Gudis & Soler, 2021; Tunkel et al., 2020).

Sequelae: Anemia can be a complication of excessive or frequent bouts of epistaxis. Scarring, infection, or eustachian tube dysfunction can result from nasal packing. Severe blood loss can exacerbate existing diseases. Scarring or septal injury may occur from cauterization (Nguyen, 2020; Tunkel et al., 2020).

Prevention/Prophylaxis: Discourage patients from nose picking and rubbing, and excessive sneezing and forceful blowing of the nose; advise them to increase the humidity in the home, especially in winter months. Some patients may be prescribed bacitracin, saline gel, or petrolatum to apply in the Kiesselbach plexus area. Patients may also need to avoid spicy foods and strenuous activities (Nguyen, 2020; Tunkel et al., 2020).

Referral: Consultation with an ENT specialist is indicated for severe or recurrent epistaxis:

- Bleeding that is not controlled after 15 minutes of compression
- Evidence of massive bleeding
- Recurrent bleeding within the first hour
- Second episode of epistaxis within 1 week
- Uncontrolled bleeding from the posterior nasopharynx

The consulting physician may initiate interventions, such as the insertion of nasal tampons or an intranasal balloon to control bleeding. Intractable epistaxis may require transantral arterial ligation or embolization (Beck et al., 2018; Nguyen, 2020; Tunkel et al., 2020; Womack et al., 2018).

Education: Discourage picking of the nose and advise patients to increase the humidity in the home, especially in winter months, by means of a humidifier. Petrolatum or saline gel may be rubbed over the nasal septum to decrease dryness of mucosa or after treatment for acute epistaxis. Teach the patient how to manage simple epistaxis at home by leaning forward while pinching the soft part of the nose for up to 15 minutes, using oxymetazoline if necessary. Seek medical attention for excessive, persistent, or recurrent epistaxis. Prolonged hot showers and hot, spicy foods should be avoided. Instruct the patient to avoid nose blowing and to open the mouth when sneezing (Gudis & Soler, 2021; Nguyen, 2020; Tunkel et al., 2020).

Clinical Recommendation	Evidence Rating	References
Simple measures are helpful in stopping most nosebleeds: nose blowing to clear clots, pinching the nose for up to 15 minutes, and topical decongestants.	C	Ruhl, 2021
Cauterizing visible bleeding vessels with silver nitrate or electrocautery are equally effective.	B	Ruhl, 2021
Anterior packing with different nasal tampons appears to be equally effective.	B	Ruhl, 2021
Patients with resistant or posterior bleeds are likely to need posterior packing, surgery, or embolization.	C	Ruhl, 2021
Routine coagulation tests for epistaxis are not useful unless the patient is taking an anticoagulant.	B	Ruhl, 2021

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GLAUCOMA, ACUTE AND CHRONIC

Glaucoma is the leading cause of blindness in the world (Kang & Tanna, 2021). Glaucoma encompasses several different eye diseases characterized by progressive neuropathy of the optic disc, leading to loss of vision. The optic disc is composed of vascular, neural, and connective tissue. The axons of the retinal ganglion cells form a rim around a shallow cup in the optic disc. Apoptosis of the ganglion cells of the retina leads to a thinning of the nerve fibers in the inner layer and axons, with atrophy of the disc and the appearance of cupping or expansion of the cup/disc ratio (Kang & Tanna, 2021; Salmon, 2017). The two most common are primary angle closure with acute or chronic closure glaucoma and primary open-angle glaucoma (POAG).

Signal Symptoms: Unilateral eye pain, visual blurring with halos around lights, conjunctival injection, and photophobia; nausea and vomiting may also occur. Approximately two-thirds of patients with angle-closure glaucoma will have vision loss without experiencing an acute episode.

Description: Acute glaucoma, also known as *angle-closure* or *narrow-angle glaucoma,* is an obstruction to the outflow of aqueous humor from the posterior to the anterior

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chamber through the trabecular meshwork, canal of Schlemm, and associated structures. It typically results in an elevation of intraocular pressure, damaging the optic nerve and causing loss of peripheral vision, eye pain, and redness. This type of glaucoma is uncommon but may occur as a primary disease or secondary to other conditions, and constitutes an ophthalmic emergency (Hoffman, 2018; Kang & Tanna, 2021; Salmon, 2017). Associated presenting symptoms may complicate diagnosis or result in misdiagnosis.

Etiology: The precise pathophysiology of angle-closure glaucoma is unknown. It is a disorder of the lens, iris, and retrolenticular system. In the acute form, pupillary blockage limits the progress of the aqueous humor through the trabecular network. The peripheral iris, which blocks the trabecular meshwork, is displaced forward (Kang & Tanna, 2021; Salmon, 2017).

Occurrence: Uncommon; accounts for 10% of all glaucoma. This disorder is more common in families with prior history and occurs more often in women.

Age: The predominant age range for acute glaucoma is 60 to 70 years old.

Ethnicity: Acute and primary angle-closure glaucoma are more common in Inuit and Asian populations.

Contributing Factors: Contributing factors include an anatomically narrow anterior chamber angle, requiring identification with the use of a special examination technique called *gonioscopy*. This examination technique is beyond the scope of the primary care practitioner, but the condition can be evaluated during the comprehensive eye examination. Other risk factors include hyperopia; small cornea; shallow anterior chamber; Asian ancestry; female sex; family history of glaucoma (first-degree relatives have a 2% to 5% risk over a lifetime); and use of antihistamines, adrenergic agonists, tricyclic antidepressants, selective serotonin reuptake inhibitors and serotonin and norepinephrine reuptake inhibitors, anticholinergics, and cholinergic agents—these drugs may precipitate an acute episode (Kang & Tanna, 2021; Salmon, 2017).

Signs and Symptoms: The presentation is often dramatic, but the diagnosis can be missed because of the associated symptoms. The history reveals severe, unilateral eye pain; blurred vision; lacrimation; reports of seeing colored halos around lights; and a red eye. Headache, nausea, and vomiting frequently accompany eye pain, causing eye pain to be overlooked. Emotional stress also is common. Examination reveals circumcorneal, conjunctival injection, tearing, and a fixed mid-dilated pupil that is nonreactive to light; the cornea is steamy or cloudy. Visual acuity, if evaluated, shows a loss in the affected eye.

Diagnostic Tests: Immediately refer patients for a complete ophthalmological examination (Salmon, 2017).

Differential Diagnosis:

- Conjunctivitis
- Hyphema
- Uveitis
- Corneal trauma or infection

Treatment: The patient with acute glaucoma needs an immediate consultation with and referral to an ophthalmologist. Permanent visual loss occurs within 2 to 5 days if this condition is untreated. Surgical treatment includes peripheral iridectomy or laser iridotomy. Intraocular pressure must be lowered preoperatively, which may require the use of an osmotic diuretic intravenously or orally and miotic eye drops. As the primary health-care provider, you must communicate to the specialist any medical conditions that need monitoring with the use of these agents. Bilateral treatment is indicated because patients are at risk for developing the same problem in the other eye (Kang & Tanna, 2021).

Follow-Up: The ophthalmologist treating the patient determines follow-up treatment. Periodic eye examinations are recommended by preventive guidelines.

Sequelae: If treated promptly, acute glaucoma is not associated with sequelae. If untreated, permanent visual loss occurs.

Prevention/Prophylaxis: Knowing the risk factors for acute angle-closure glaucoma, the health-care provider should educate patients about those risk factors (see under Education). Periodic eye examinations are recommended for prevention.

Referral: Refer the patient immediately on presentation and evaluation of symptoms.

Education: Teach patients with known risk factors (see under Contributing Factors) the importance of regular eye examinations and reporting of symptoms.

Clinical Recommendation	Evidence Rating	References
Acute angle-closure glaucoma is an ocular emergency that requires immediate lowering of IOP with topical/oral/parenteral medications. Laser iridotomy or lens extraction is performed for pupillary block.	A	AAO, 2021 Kang & Tanna, 2021 Salmon, 2017
About half of the patients will develop an acute crisis in the opposite eye. Consider prophylactic iridotomy or lens extraction.	A	Kang & Tanna, 2021

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GLAUCOMA, CHRONIC (PRIMARY OPEN-ANGLE)

Signal Symptoms: None initially: silent; blurred vision, tunnel vision, night blindness, halos around lights.

Description: Chronic open-angle or primary open-angle glaucoma is an insidious optic neuropathy characterized by increased intraocular pressure (IOP) severe enough to damage the optic nerve. Progressive over time with a gradual visual field loss, chronic glaucoma is called the *silent blinder* because it often goes unnoticed until the later stages. Variants occur in which IOP does not increase, but the optic nerve still becomes damaged; this is termed *normal tension glaucoma* and is common in Asian populations (Kang & Tanna, 2021; Salmon, 2017). Conversely, some patients have increased IOP but show no optic nerve changes or visual defects; these are referred to as glaucoma suspects (American Academy of Ophthalmology [AAO], 2020a) or those with ocular hypertension (Kass, et al., 2021). Secondary glaucomas are the result of prior or concurrent ocular disease or trauma; they may have open angles caused by steroid-induced pressure increases (Kang & Tanna, 2021).

Etiology: The etiology of chronic glaucoma is unknown, but the disease is associated with increased IOP, optic nerve degeneration, and visual field loss. Because IOP is the one factor that can be measured, most reevaluation and treatment decisions are influenced by this measurement (Sihota et al., 2018).

Occurrence: In 2020, an estimated 76 million people worldwide had glaucoma and by 2040 that number will be 111.8 million (Tham et al., 2014). Prevalence of chronic glaucoma increases in persons older than 40 years, approaching 15% by age 75; 80% of cases are the open-angle type. Primary open-angle glaucoma causes 15% to 20% of all blindness in the United States and is the primary cause of blindness in African Americans (Salmon, 2017). Chronic glaucoma occurs equally in both men and women.

Age: The incidence increases in persons older than 40 years, with another increase in incidence in persons between ages 60 and 75 years. Onset is earlier in African Americans.

Ethnicity: African Americans, Afro-Caribbeans, and Hispanics are at a higher risk than the general population for developing chronic glaucoma (AAO, 2017a; Kang & Tanna, 2021; Salmon, 2017).

Contributing Factors: Risk factors include older age, a positive family history, African American ancestry or Latino/Hispanic ethnicity, type 2 diabetes mellitus, hypertension, myopia, low ocular perfusion, thinner central cornea, and genetic mutations (Kang & Tanna, 2021; Salmon, 2017). Risk factors for secondary open-angle glaucoma include long-term use of topical or oral corticosteroids. It is important to note if the patient had prior LASIK surgery because this can alter corneal thickness. Cataract surgery can also lower IOP, so this history is essential (Salmon, 2017).

Signs and Symptoms: The disease is asymptomatic in the early stages. By the time symptoms develop, significant neural damage has occurred. Eye health specialists frequently discover chronic open-angle glaucoma during routine eye examinations. Patients may present with a complaint of blurred vision, a request for new corrective lenses, or occasionally a report that they see a halo around lights (Kang & Tanna, 2021; Salmon, 2017).

On routine vision screening, visual acuity may be normal or unchanged from previous screening; visual fields may be decreased, however. The skilled examiner may detect changes in the cup-to-disc ratio on funduscopic examination—a cup with a diameter of more than 50% of the vertical disc diameter is highly suspect for glaucoma. Because it is difficult to perform a funduscopic examination on older patients without the benefit of a mydriatic agent, referral for specialized ophthalmological examination is essential. The ophthalmological examination may reveal increased IOP or signs of optic nerve damage without increased pressure (Kang & Tanna, 2021).

Diagnostic Tests: Visual acuity should be measured and compared with prior measurements; pupillary assessment should be included. A dilated funduscopic examination and slit-lamp examination of the anterior segment is conducted, assessing cup-to-disc ratio, asymmetry between discs, or other abnormalities. The most sensitive field testing is done by computerized automated perimeters (Chang, 2017). IOP has a circadian rhythm and is highest in the morning. Time of day, method, and measurements in both eyes are noted and compared with any prior measurements. Target IOP should be individualized with periodic evaluations. Quality of life, comorbid conditions, and social determinants of health, such as costs and adherence, should be considered when setting a target IOP (Sihota et al., 2018).

Gonioscopy is done to rule out other causes of IOP increase, including angle-closure glaucoma. Various imaging modalities, including fundus photography, optical coherence tomography, and scanning laser polarimetry, are used to preserve a permanent visual picture of the optic disc and are to be repeated later for comparison or evidence of disease progression (AAO, 2020b; Salmon, 2017).

Differential Diagnosis:

- Cerebral neoplasia
- Other optic neuropathies
- Vascular occlusive disease
- Trauma

Treatment: Chronic open-angle glaucoma cannot be cured. The goal of treatment is to halt progression of the disease and preserve existing vision as follows:

- IOP control within an identified range
- Stable visual fields
- No further progression of optic nerve damage

Mainstay treatment modalities include:

- Topical eye drops that reduce aqueous production or encourage outflow
- Laser trabeculoplasty
- Trabeculectomy or filtering surgery

Medical treatment with eyedrops is usually first-line therapy unless there are contraindications. Consultation between

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primary care provider and ophthalmologist may be indicated for patient safety and accurate identification of comorbidities and current medications (Kang & Tanna).

If topical ophthalmic agents do not effectively lower IOP, systemic carbonic anhydrase inhibitors can be added. These also may be used before surgery to lower the IOP. If medical therapy is unsuccessful, selective laser trabeculoplasty or filtration surgery (trabeculectomy) to improve aqueous outflow is indicated. The laser treatment is considered for older adults who cannot tolerate surgery, although the outcome is not as desirable as with surgery. In either case, medication still may be required after surgery (AAO, 2017b)

The iStent (one stent) and newer iStent inject (two stents) are available as microinvasive surgery devices. At the conclusion of cataract surgery, this stent is inserted into the canal of Schlemm, allowing the aqueous humor to bypass trabecular obstruction and drain directly from the anterior chamber into Schlemm's canal, lowering IOP. The iStent inject provides superior outflow and increased efficacy.

Follow-Up: Monitor patients for compliance with the treatment regimen. If eyedrops are used, ensure that the patient can instill these, or teach a family member or neighbor to do it. Monitor medications for adverse effects; the range and frequency of side effects to glaucoma medications are significant. Ensure that patients have regular ophthalmological follow-up visits. If visual loss is severe, evaluate the environment for safety and risk of falls or injury. If the patient is still a licensed motor vehicle operator, driver's license retesting may be indicated in the interest of public safety.

Sequelae: If initial presentation is monocular, the other eye may become affected. Changes in the patient's overall health may have implications for the treatment plan.

Prevention/Prophylaxis: The U.S. Preventive Services Task Force (USPSTF) found insufficient evidence to recommend general screening for glaucoma (USPSTF, 2013). Primary care providers need to be aware of risk factors and discuss these with patients who have not been diagnosed but are at risk. Patients who are glaucoma suspects or have actual primary open-angle glaucoma must be reminded of the need for eye examinations, continued monitoring, and adherence to the prescribed regimen. According to the American Academy of Ophthalmology (2020a), patients with known risk factors for glaucoma ages 55 and older should have a comprehensive medical eye examination every 1 to 2 years; ages 40 to 54, every 1 to 3 years; younger than 40 years, every 2 to 5 years. More frequent examinations may be recommended by the eye specialist based on individual risk factors or findings on examination. All adults 65 and older with no risk factors should have an eye examination every 1 to 2 years.

Referral: Refer patients initially for ophthalmological examination and diagnosis. Collaborate on the management plan if the patient has significant medical conditions that affect treatment options, particularly pharmacological choices. Refer patients for periodic follow-up eye examinations or for treatment of complications if they arise.

Education: Educate the patient about the chronic and progressive nature of the disease, the need to follow the treatment regimen as prescribed, and the need for regular follow-up eye examinations and reporting of symptoms, if any. Reassure the patient that, although the disease is not curable, it can be managed. Educate patients with known risk factors about the need for eye examinations despite the absence of symptoms. Asymptomatic patients may question the need for regular treatment. Explain that treatment is preventing disease progression, which is why there are no symptoms. The frequency or complexity of the medication regimen may influence compliance. Reinforce the role of medication in controlling IOP and preventing visual loss.

Clinical Recommendation	Evidence Rating	References
Prostaglandin analogs are effective drugs at lowering IOP and can be considered as initial medical therapy. New medications, comparable to prostaglandins with a different mechanism of action, can overcome some of the limitations of existing medications and improve adherence.	A	Kang & Tanna, 2021 MacIver et al., 2021 Marshall et al., 2018
The goal is a target IOP, based on clinical staging, that would stabilize glaucoma, prevent further visual loss without affecting quality of life.	A	Sihota et al., 2018
The IOP can be lowered by medical treatment, laser therapy, or incisional glaucoma surgery (alone or in combination). The choice of initial therapy depends on numerous considerations, and discussion of treatment with the patient should include the relative risks and benefits of the three options.	A	AAO, 2017b

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

HEARING LOSS

Signal Symptoms: Decreased ability to hear in one or both ears, especially in noisy environments. Because age-related hearing loss is gradual and insidious, hearing loss may go unnoticed until it has progressed. Sudden changes in hearing warrant urgent evaluation (Gross, 2021a, 2021b).

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Description: Hearing loss is the decreased ability or complete inability to hear. The unilateral or bilateral loss may involve the external, middle, or inner ear (Michels et al., 2019).

Etiology:

Sensorineural. Hearing loss that is caused by an abnormal function of the cochlea, auditory nerve, or higher aspects of central auditory perception or processing. Presbycusis, noise-induced hearing loss, and ototoxic drug-related hearing loss are all sensorineural. As there is no cure for this, amplification is usually required.

Conductive. Hearing loss that is caused by an issue with sound wave conduction from the outer ear, tympanic membrane, or middle ear. Structural abnormalities, cerumen impaction, tympanic membrane perforation, middle ear effusion, ossicular damage from trauma or infection, otosclerosis, tympanosclerosis, cholesteatoma, middle ear tumors, temporal bone fractures, injuries related to trauma, and congenital problems are some of the causes.

Mixed. Hearing loss within an ear with both sensorineural and conductive components (Chandrasekhar et al., 2019; Michels et al., 2019).

Occurrence: Occurs in almost 15% of adults of all ages. More than 50% of those older than 70 years old, and 80% of those older than 85 years old have hearing loss (Michels et al., 2019).

Age: Sensorineural hearing loss increases with age (Michels et al., 2019).

Ethnicity: Presbycusis is most common in White men, followed by White women, Black men, and Black women (Cheslock & De Jesus, 2021).

Contributing Factors: Increasing age is the highest risk factor for hearing loss. Exposure to loud noises; heredity; ototoxic drugs, such as aminoglycoside antibiotics, salicylates, loop diuretics, cisplatin, and quinine; eustachian tube obstruction; chronic middle ear infections; and chronic cerumen impaction are contributing factors. Most cases of sudden unilateral hearing loss in older adults are idiopathic (Chandrasekhar et al., 2019; Gross, 2021a; Michels et al., 2019; U.S. Preventive Services Task Force [USPSTF], 2021).

Signs and Symptoms: Decreased ability to hear in one or both ears, especially in noisy environments. There may also be tinnitus, fullness, pressure, vertigo, or loss of balance. A history of noise exposure, prior ear problems, or familial hearing problems is significant. Older adults with hearing loss should also be screened for dementia (Chandrasekhar et al., 2019; Di Stadio, 2021; Michels et al., 2019).

An otoscopic examination of the external auditory canal and middle ear should reveal a clear ear canal with minimal cerumen and an intact tympanic membrane in the case of sensorineural hearing loss. Signs that may indicate other pathology are redness, foreign objects, discharge, odor, scaling, lesions, fluid, or cerumen impaction. Changes in the tympanic membrane may indicate conductive hearing loss (Leedy et al., 2021; Michels et al., 2019; USPSTF, 2021).

Diagnostic Tests: The gold standard for diagnosis is a diagnostic audiogram. Primary care provider awareness requires asking about and screening for hearing loss in older adults. A screening questionnaire could be utilized or asking a single question—"Do you have a hearing problem now?"—can also be effective. Use of a portable pure-tone audiometer in the primary care setting is also a quick screening test. Refer anyone with a hearing threshold of 40 dB or greater to audiology. A history of trauma or sudden hearing loss warrant an urgent otolaryngology consultation, and a computed tomography (CT) scan or magnetic resonance imaging (MRI), respectively, may be ordered. The Weber and Rinne tests can help to differentiate between sensorineural or conductive hearing loss (Chandrasekhar et al., 2019; Cheslock & De Jesus, 2021; Michels et al., 2019; USPSTF, 2021).

Differential Diagnosis:

- Ménière disease
- Acoustic neuroma (unilateral, with tinnitus)
- Cholesteatoma (unilateral)
- Meningioma (unilateral)
- Trauma (often unilateral)
- Otitis media with effusion (retracted tympanic membrane, fluid behind tympanic membrane)
- Acute otitis media (unilateral, ear pain; building, immobile tympanic membrane)
- Central auditory processing disorder (Michels et al., 2019)

Treatment: Treat any reversible or modifiable causes, and refer to audiology and otolaryngology, as appropriate. Amplification, assistive listening devices, and audiological rehabilitation may be helpful. Encouragement, follow-up, and support are important (Chandrasekhar et al., 2019; Di Stadio et al., 2021).

Cerumen Impaction. Cerumen, or earwax, is a naturally occurring substance that cleans, protects, and lubricates the external auditory canals, but obstructs the canals when the self-cleaning mechanism fails. This is most common in older adults; surveillance is recommended for those living in long-term care facilities and in those with developmental delays or hearing aids. Cerumen impactions can cause conductive hearing loss, tinnitus, aural fullness, otalgia, and pruritus. Cerumen disimpaction is only indicated if necessary for otoscopic examination, in young children, or those cognitively impaired who may not be able to express symptoms. Treat patients with cerumenolytic agents, irrigation, or manual removal, and instruct those with hearing aids on proper ear hygiene. Cerumenolytics may be indicated for recurrent cerumen impaction. Patients should be examined for resolution after treatment of impaction, repeating treatment or referring to otolaryngology for persistent or concerning impactions. Ear candling is not recommended to treat or prevent cerumen impactions (Leedy et al., 2021; Schwartz et al., 2017).

Presbycusis. Age-related hearing loss is usually bilateral, symmetric, and slowly progressive with a normal otoscopic examination. It is typical in older adults with a family history. Refer to audiology for diagnosis and amplification, and to otolaryngology if amplification is ineffective (Gross, 2021b; Michels et al., 2019).

Sudden Hearing Loss. This is usually unilateral with an onset of 3 days or less. More than 90% of cases are idiopathic; acoustic neuroma, stroke, or malignancy are the most

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common identified causes. Treatment of choice is oral or intratympanic steroids within 14 days of symptoms onset for best chance of meaningful audiological recovery. Patients should have an MRI to rule out retrocochlear pathology, as well as a formal audiogram and a referral to otolaryngology (Chandrasekhar et al., 2019).

Follow-Up: See patients as indicated by the cause of the symptom (USPSTF, 2021).

Sequelae: Possible complications depend on the cause of the symptom but may include permanent hearing loss. Patients may need hearing aids or assistive listening devices. Middle ear problems may progress to chronic ear problems, such as perforations and cholesteatoma. Social isolation, depression, and dementia may result from inability to communicate (Di Stadio et al., 2021; Michels et al., 2019; USPSTF, 2021).

Prevention/Prophylaxis: Advise patients to use protective devices to limit occupational or recreational noise exposures. Patients should be aware of the potential for barotrauma. Avoid any ototoxic medications. Teach proper techniques for cerumen removal and avoidance of ear swabs or other foreign bodies in the ear. Hearing screening tests are recommended for persons older than 65 years and those reporting hearing difficulty. The USPSTF does not recommend periodic screening for hearing loss in asymptomatic adults (Leedy et al., 2021; Michels et al., 2019; Schwartz et al., 2017; USPSTF, 2021).

Referral: Consult with appropriate specialists as indicated by cause of symptom. Refer to an audiologist for hearing aid evaluation. All patients with hearing loss and tinnitus should be advised of the benefits of audiological rehabilitation. Amplification may prevent and treat cognitive decline in older patients. All patients with unexplained or asymmetric hearing loss should have an otoscopic and audiometric evaluation. Select patients may also be evaluated for bone-anchored hearing devices or cochlear implants (Chandrasekhar et al., 2019; Di Stadio et al., 2021; Michels et al., 2019; USPSTF, 2021).

Education: Explain cause of symptoms, measures taken to determine the cause, and symptomatic treatment, if any. Advise patients when to seek medical care. Teach the importance of using hearing aids, if indicated, because this can make a significant difference in quality of life. It is important for all providers to work together as part of a multidisciplinary team. Patients with hearing loss should directly face others when talking, use adequate lighting, and minimize background noise. There are also auditory, visual, and tactile alerting systems that may be beneficial. Monitor for falls, hospitalizations, social isolation, and cognitive decline, which are all more prevalent with hearing loss (Chandrasekhar et al., 2019; Michels et al., 2019; Schwartz et al., 2017; USPSTF, 2021).

Clinical Recommendation	Evidence Rating	References
The U.S. Preventive Service Task Force found insufficient evidence to assess the balance of benefits and harm of screening for hearing loss in asymptomatic adults ≥50 years.	C	USPSTF, 2021
Thoroughly evaluate clinically and audiometrically any patient who complains of hearing loss if no easily reversible cause is identified (i.e., cerumen or infection)	C	Gross, 2021a
Bedside hearing tests have a good specificity but poor sensitivity for detecting hearing loss; if hearing loss suspected or reported, refer for formal audiometry.	C	Gross, 2021a
Sudden hearing loss warrants urgent evaluation and treatment by a specialist.	C	Gross, 2021a
Patients who report hearing loss should be referred for full audiometry.	C	Gross, 2021b
Order imaging and/or otolaryngology referral if vertigo, sudden onset, neurological symptoms, unilateral loss, or primarily low-frequency loss.	C	Gross, 2021b
Patients with presbycusis may benefit from amplification or assistive listening devices.	C	Gross, 2021b

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HORDEOLUM AND CHALAZION

Signal Symptoms: Increased lacrimation with lump on eyelid.

Description: A hordeolum (stye) is an acute, purulent area of inflammation in the meibomian gland or gland of Zeis, commonly referred to as a "stye." The hordeolum typically contains *Staphylococcus aureus* bacteria; it can occur internally (underside of the eyelid) or externally at the lid margin (Ghosh & Ghosh, 2017); and some styes are sterile. A chalazion is a sterile mass on the eyelid caused by an inflammation and obstruction of a meibomian (oil-secreting) gland of the upper or lower eyelid. Meibomian glands lubricate the lid

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margins. The chalazion is more chronic in nature, painless, and lipogranulomatosis without erythema. It can interfere with vision at times and develops a rubbery consistency (Vagefi, 2018).

Etiology: Blockage in a duct leading to the eyelid surface from the meibomian gland or obstruction of the gland of Zeis results in inflammation or infection (usually from *Staphylococcus*) called hordeolum. If the blockage becomes chronic, progressing to the formation of a hard, granulomatous mass, it is called a chalazion.

Occurrence: Common and occurs equally in men and women.

Age: Can occur at any age.

Ethnicity: Not significant.

Contributing Factors: Previously unresolved blepharitis, poor hygiene, immunosuppression, and skin conditions, such as acne rosacea or seborrheic dermatitis, all are contributing factors to development of hordeolum or chalazion (Fort, 2018; Vagefi, 2018).

Signs and Symptoms: A hordeolum is an acute, erythematous, painful lesion at the hair follicles of the eye lashes (external) or the meibomian glands (internal) (Horak, 2021). A chalazion is a slow-developing, painless nonfluctuant mass, with inflammation of the meibomian gland and possible involvement of the surrounding tissue. It tends to be deeper within the lid than hordeolum. Physical examination with inversion of the eyelid reveals a red, elevated mass that may become large and press against the cornea (Vagefi, 2018).

Diagnostic Tests: None unless recurrent or unusual signs, then biopsy of lesion to rule out malignancy.

Differential Diagnosis:

- Foreign body
- Contact dermatitis
- Rosacea
- Atopic dermatitis
- Blepharitis
- Orbital cellulitis
- Acute dacriocystitis
- Sebaceous cell, meibomian gland, or basal cell carcinoma (Ghosh & Ghosh, 2017; Vagefi, 2018)

Treatment: Warm compresses are applied to the affected eyelid for 10 minutes, four times daily, to facilitate opening and drainage. Allow purulent lesions to drain without squeezing them. Massage of the eyelid after warm compresses may help to soften secretions. Many lesions resolve spontaneously without treatment. In cases of secondary infection, antibiotic eyedrops, or ointment may be used; combination antibiotic and steroid should be used only by an ophthalmologist. If the hordeolum progresses to preseptal cellulitis, prescribe a systemic antibiotic, such as dicloxacillin (Fort, 2018). Treatment of chalazion includes warm compresses for 15 minutes four times a day. Incision and drainage by an ophthalmologist may be needed if there is no resolution after 2 months. Antibiotics are not indicated because it is granulomatous in nature (Ghosh & Ghosh, 2017). A large nondraining hordeolum or chalazion may require emergency treatment if cellulitis occurs (Vagefi, 2018). A Cochrane review on the use of nonsurgical interventions for acute internal hordeolum found no evidence for or against nonsurgical treatment (Lindsley et al., 2017). Most chalazia will resolve with use of conservative measures (Jordan & Beier, 2020).

Follow-Up: See patient in 2 to 4 weeks to evaluate treatment.

Sequelae: Complete resolution may take several weeks to months; frequent recurrence may indicate underlying malignancy (Ghosh & Ghosh, 2017).

Prevention/Prophylaxis: Prevention strategies include advising the patient to perform proper lid hygiene (helps prevent recurrence) by gently scrubbing lids with diluted baby shampoo daily or directly applying baby shampoo with cotton-tipped applicator, then rinsing. Frequent hand washing is advised. Warm compresses should be initiated at the first sign of eyelid irritation or if chalazion starts to return; a clean cloth should be used for each warm compress to eye (Ghosh & Ghosh, 2017).

Referral: Refer to or consult with an ophthalmologist if the patient has a visual change, eye pain, or impairment to the eye, or if the chalazion does not heal spontaneously in 6 weeks, because surgical removal may be necessary.

Education: Explain the problem and treatment. Discuss prevention strategies.

Clinical Recommendation	Evidence Rating	References
Initial treatment includes warm compresses 4 times daily and topical erythromycin ointment for hordeolum.	C	Bragg et al., 2021 Wolter, 2017
Lesions refractory to treatment should be referred for incision and drainage (both hordeolum and chalazion).	C	Jordan & Beier, 2020 Wolter, 2017
Sebaceous carcinoma should be suspected in patients who are middle-aged and older with persistent chalazia. Ulceration, irregular/pearly borders, loss of lashes or eyelid margin, telangiectasia or proximal adenopathy (preauricular nodes): Consider biopsy of lesion.	C	Horak, 2021 Wolter, 2017

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ORAL CANCER

Signal Symptoms: A lesion in the mouth or on the lip that does not heal. A long-lasting sore throat, earaches, swelling in the neck, unintentional weight loss or difficulty chewing or swallowing. There are some patients that have no symptoms at all (Pfister et al., 2020).

Description: Oral cancer includes cancers of the mouth and the back of the throat. These cancers can also arise on or under the tongue, at the base of the tongue, on the lining of the mouth and gums, and the area in the back of the throat (National Institute of Dental and Craniofacial Research, n.d.). The oral cavity includes the lips, the labial and buccal mucosa, the front of the tongue, the retromolar pad, the base of the mouth, the gingiva, and the hard palate (Figure 9-1). The oropharynx includes the palatine and lingual tonsils, base of the tongue, the soft palate, and the posterior pharyngeal wall (CDC, 2020).

Etiology: Alcohol and tobacco are the most common factors in the development of oral cancers. Since the whole aerodigestive tract may be exposed to the carcinogens, patients with head and neck (H&N) cancers are at risk for developing second cancers of the H&N, lung, esophagus, and other sites that share these risk factors (Pfister et al., 2020).

Occurrence: The rate of new cases of oral cavity and pharynx cancer was 11.5 per 100,000 men and women per year (SEER, 2022; Siegel et al., 2022). In 2020, it is estimated that about 65,630 new cases of oral cavity, pharyngeal, and laryngeal cancers will occur, which account for about 3.6% of new cancer cases in the United States. Approximately 14,500 deaths from H&N cancers will occur during the same time period. Squamous cell carcinoma accounts for more than 90% of these tumors (Pfister et al., 2021). More men develop oral cancer then their female counterparts.

Age: Oral cancer rates increase with age, causing the older adult to be at increased risk. The increase becomes more rapid after age 50 and peaks between ages 60 and 70 (Pfister et al., 2020).

Ethnicity: Oral cancer rates are higher in Hispanics and Blacks than for White males (NIDCR, n.d.).

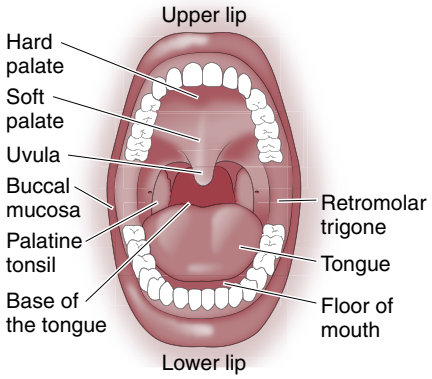

FIGURE 9-1 Oral anatomy.

Contributing Factors: There is an increased risk of oral cancers associated with tobacco use of any type (including smoking or chewing tobacco), and heavy alcohol intake. The combination of both smoking and drinking is synergistic in elevating risk of oral cancer (NIDCR, n.d.). Ultraviolet (UV) light exposure is a major factor in the development of lip cancer. Occupational exposures or being exposed to certain environmental substances, such as those associated with construction work, or working with textiles, ceramics, logging, and food processing industries can expose people to wood dust, formaldehyde, asbestos, nickel, and other chemicals, which can further increase risk. Epstein-Barr virus has been shown to increase the development of cancer in the nose, behind the nose, and cancers of the salivary glands. Human papillomavirus (HPV) has been discovered to have a close relationship to the development of head and neck cancers and is transmitted by oral sex. About 10% of men and 3.6% of women have oral HPV, and oral HPV infection is more common with older age (CDC, 2020).

Signs and Symptoms: A lesion in the mouth can cause a sore that does not heal on the gums, tongue, or lining of the mouth. Patients can also experience swelling of the jaw, unusual bleeding or pain in the mouth, a lump, or problems with ill-fitting dentures. A lesion at the back of the mouth (pharynx) or voice box (larynx) can lead to trouble breathing or speaking. Patients can also experience a lump in their mouth or throat, difficulty chewing or swallowing food, a globus sensation (a feeling that something is caught in the throat), ongoing pain in the throat, pain in the ear, difficulty hearing, or tinnitus (CDC, 2020).

Diagnostic Tests: Screening processes can warn patients about the possible development of the disease before any malignant progression has taken place. Most diagnostic modalities can detect lesions only after they have metastasized. Tissue biopsy followed by histological assessment is still considered as the gold standard for diagnosing oral cancer (Chakraborty et al., 2019). Appropriate selection and use of imaging studies is crucial for proper management of patients with head and neck cancers. CT and/or MRI are often the first diagnostic modalities used (Pfister et al., 2020). A dentist or medical practitioner may check the oral cavity during a routine checkup.

Differential Diagnosis: Differential diagnosis can include: traumatic ulceration, erythroleukoplakia (red or white-red plaques), median rhomboid glossitis (a fungal infection of the dorsal region of the tongue that resolves with treatment), eosinophilic granuloma (self-limiting chronic benign ulcerative lesion of the oral mucosa that it is similar to oral squamous cell carcinoma in its early stages), keratoacanthoma (tumor originating in the pilosebaceous glands and closely resembling oral cancer), or necrotizing sialometaplasia (characterized by salivary gland metaplasia, necrosis, and ulceration). Other differential diagnoses include benign tumors or infection (Bagan & Bagan-Debon, 2020).

Staging. The TNM Staging system is used to describe the amount and spread of cancer in a patient's body, using TNM.

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T describes the size of the tumor and any spread of cancer into nearby tissue (Figure 9-2); N describes spread of cancer to nearby lymph nodes; and M describes metastasis (spread of cancer to other parts of the body) (National Comprehensive Cancer Network [NCCN] 2021).

Treatment: There are three main treatments for oral cancer: surgery, chemotherapy, and/or radiation. The treatment for head and neck malignancies varies greatly based on the primary site and stage of disease. In general, surgery is the first treatment for cancers of the oral cavity and may be followed by radiation or combined chemotherapy and radiation (NCI, n.d.). There are several chemotherapeutic options for oral cancer. A chemotherapy drug may be used alone or combined with other drugs. Combining drugs can often shrink tumors better, but may cause more side effects (American Cancer Society [ACS], 2021). Radiation therapy might be used in a variety of ways. It can be used alone as the main treatment for small cancers or for those patients who are unable to have surgery. It can be used after surgery (adjuvant therapy), either alone or with chemotherapy (chemoradiation), to try to kill any cancer cells that might be lingering after surgery. It can also be used before surgery (neoadjuvant therapy) with chemotherapy (chemoradiation) or after chemotherapy to try to shrink some larger cancers. Radiation can also be used in combination with a targeted drug for larger cancers, if the patient is unable to receive chemotherapy (ACS, 2021). Clinical trials can also offer an alternative or additional treatment option for patients with H&N cancer. Recent, late-phase research clinical trials support the use of immunotherapy for patients with recurrent, unresectable, or metastatic H&N cancer (Pfister et al., 2020).

Sequelae: Patients with oral cancer are at risk of the cancer reoccurring and for developing new cancers in the head and neck area (ACS, 2021).

Prevention/Prophylaxis: People who have been treated for H&N cancers have an increased chance of developing a new cancer, usually in the head, neck, esophagus, or lungs. (NCCN, 2021). The primary intervention in preventing a reoccurrence targets decreasing or eliminating tobacco and alcohol intake. According to the National Cancer Institute (2021), another important intervention for preventing oral cancer includes not chewing betel quid. Chewing betel quid is common in many countries in South Asia and Southeast Asia, especially in China and India. It is a type of smokeless tobacco. Avoiding prolonged sun exposure can help decrease the chance of a sun-related malignancy. HPV has been proven to increase the incidence of oral cancer; therefore, eliminating oral sex or practicing safe sex can prevent HPV-related oral cancers (NCCN, 2021). Figure 9-3 show steps for oral cancer screening.

Referrals: The management of patients with head and neck cancers is challenging. To optimize treatment options and outcomes, oral cancer patients need access to the full range of support services and specialists with experience in managing head and neck cancers. Per the National Comprehensive Cancer Network ([NCCN], 2021), important members of the interdisciplinary team include:

- Head and neck surgery
- Radiation oncology
- Medical oncology
- Plastic and reconstructive surgery
- Specialized nursing care
- Dentistry/Prosthodontics
- Physical medicine and rehabilitation, including therapy for lymphoedema of the neck
- Speech and swallow therapy
- Clinical social work
- Clinical nutrition

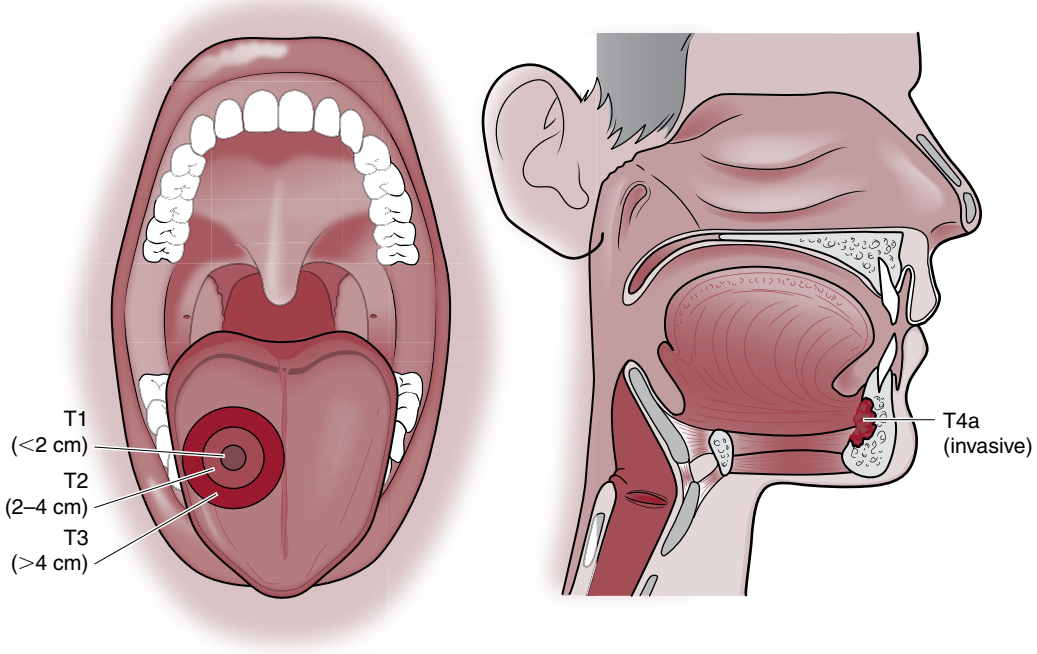

FIGURE 9-2 Oral cancer staging.

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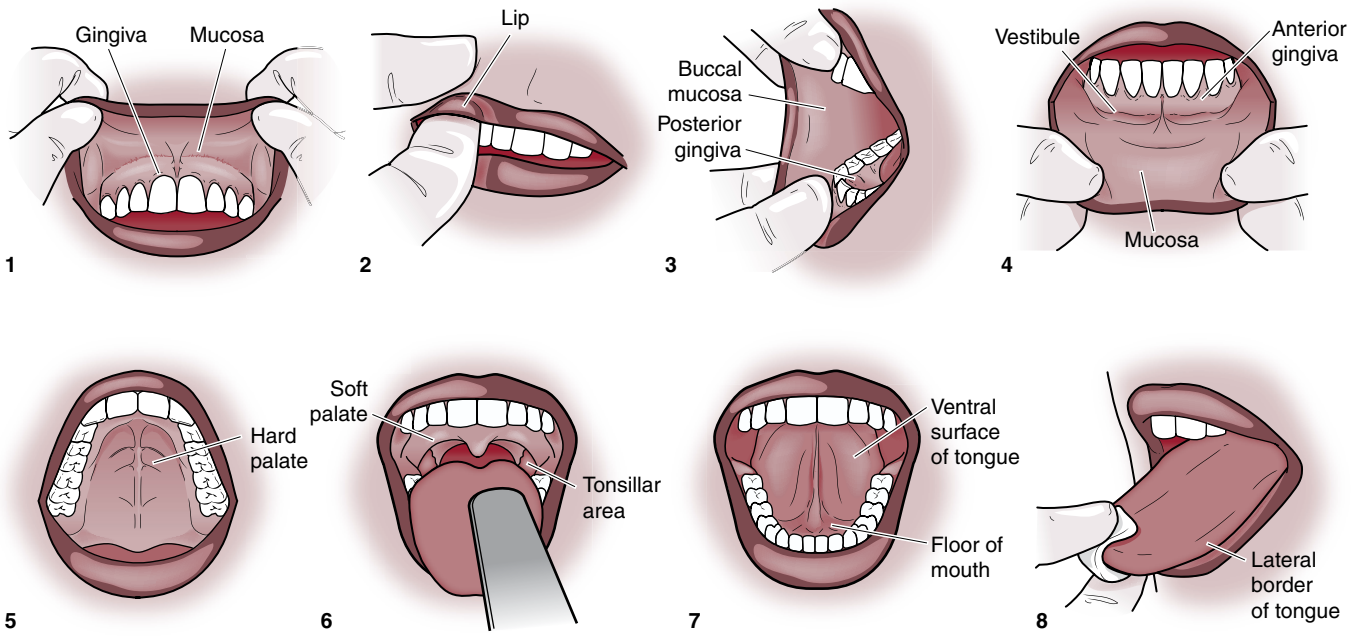

FIGURE 9-3 Oral cancer screening.

- Pathology (including cytopathology)
- Diagnostic and interventional radiology
- Adjunctive services such as neurosurgery, ophthalmology, psychiatry, addiction services, and audiology
- Palliative care

Education: Ongoing education about avoiding factors which increase the risk of oral cancer is critical. Teaching patients how to examination their oral cavity can help to detect reoccurrences. Regular visits to primary care providers, dentists, and specialists are essential.

Clinical Recommendation	Evidence Rating	References
Curative treatment for local oropharyngeal cancer typically consists of resection, which is preferred, or definitive radiation therapy. This surgical intervention consists of resection of primary tumor without neck dissection or resection of primary and ipsilateral or bilateral neck dissection or resection of primary tumor and lymph node biopsy.	A	National Comprehensive Cancer Network Guidelines (NCCN), 2021
Patients with metastatic oral cancer would benefit from either surgery or a clinical trial. For patients with positive margins detected in surgery, systemic therapy would be recommended. Following either surgery or clinical trials, radiation therapy should then be considered.	A	NCCN, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

RETINOPATHY

Signal Symptoms: Blurred vision, painless visual loss, poor night vision, poor color vision, floaters.

Description: Retinopathy, a disease of the retina, includes several types: hypertensive, diabetic, and, less commonly in older adults, sickle cell; polycythemia vera; and infectious causes such as toxoplasmosis or cytomegalovirus in HIV.

Etiology: The pathology of the retinopathy relates to the underlying cause. Systemic causes common to older adults include hypertension (arteriosclerotic retinopathy), diabetes (diabetic retinopathy), and AMD (see previous discussion). Hypertensive or arteriosclerotic retinopathy is related to the severity of the hypertension. Diabetic retinopathy is a highly specific microvascular complication of type 1 and 2 diabetes. It is related directly to the duration of diabetes, the patient's age at onset, and glycemic control. Diabetic retinopathy is either proliferative or nonproliferative. Nonproliferative retinopathy is most common in type 2 diabetics and is characterized by dilation of veins, microaneurysms, retinal edema and hemorrhages, and hard exudates. Proliferative retinopathy is common in type 1 diabetics and includes neovascularization, vitreous hemorrhage, and retinal detachment; secondary

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glaucoma also can occur because of blockage of outflow channels by new vessels. Diabetic retinopathy often coexists with hypertensive retinopathy.

Occurrence: Diabetic retinopathy is the leading cause of new blindness in people 20 to 74 years old. Up to 27% of people with type 1 diabetes have some retinopathy present in 5 to 10 years of diagnosis, and after 10 years the prevalence is 70% to 90% (Yanoff & Cameron, 2016). Nearly 80% people with type 2 diabetes develop retinopathy after 15 to 20 years and it is present in one-third at the time of diagnosis (Hammes et al., 2014). Diabetic retinopathy develops earlier in older patients, but proliferative retinopathy is less common. Proliferative retinopathy is more common with insulin use. According to the National Eye Institute (2020), diabetic retinopathy affects 7.7 million people ages 40 years and older. Hypertensive retinopathy is seen with poorly controlled hypertension.

Age: Older adult patients are more likely to have hypertensive or diabetic retinopathy because of the increase in chronic disease with age. Approximately one-half of all diabetes cases occur in persons older than 55 years. Men develop diabetic retinopathy sooner than women.

Ethnicity: Diabetes is more common in Native Americans, Asian Americans, African Americans, Hispanic Americans, and Pacific Islanders. Rates of diabetic retinopathy are highest among Hispanic Americans. Hypertension is more prevalent among African Americans.

Contributing Factors: Contributing factors in diabetic retinopathy include age at onset, type of diabetes, duration of disease, poor glycemic control (persistent elevated hemoglobin A1c), arterial hypertension, dyslipidemia, nephropathy, smoking, and stage at which retinopathy is detected (early detection of nonproliferative is preferred) (Thomas, et al., 2020). Duration of disease is the best predictive factor for retinopathy (American Academy of Ophthalmology [AAO], Retina/Vitreous Panel, 2020). Causes of other types of retinopathy include poorly controlled hypertension and AMD. Multiple sclerosis, sarcoidosis, and coagulopathies are also associated with proliferative retinopathy (Mathura et al., 2018).

Signs and Symptoms: Retinopathy usually develops without symptoms until advanced stages of the disease. If presenting with symptoms, they may be the insidious painless onset of decreased visual acuity. Patients may report blurred vision, poor night vision, poor color vision, or "floaters and flashers." The ophthalmoscopic examination may be the first point of detection in an asymptomatic patient. All patients with known diabetes or hypertension should have regular comprehensive eye examinations, including a funduscopic examination. The funduscopic changes seen in patients with hypertension include arteriolar narrowing, arteriovenous nicking, changes in arteriolar light reflex, and tortuosity of vessels. Classic nonproliferative changes in patients with diabetes are microaneurysms and hard and soft exudates. Clinical findings in patients with proliferative retinopathy are cotton-wool spots, deep hemorrhages, and neovascularization.

Diagnostic Tests: Dilated funduscopic examination and comprehensive eye examination, fundus photos, ocular coherence tomography (OCT), and fluorescein angiography are used to diagnose diabetic retinopathy (AAO, 2021; Janigian, 2018). Hypertensive retinopathy is a clinical diagnosis based on physical examination findings during slit-lamp examination. Although not specific for the diagnosis of retinopathy, regular monitoring of hypertension, lipids, and blood glucose is essential in disease management and prevention of complications.

Differential Diagnosis:

- Retinal detachment
- Cytomegalovirus retinitis (usually associated with HIV)
- Toxoplasmosis (associated with latent infection)
- Retinal vasculitis
- Retinal vein occlusion
- Hyperviscosity syndromes

Treatment: Prevention and early detection are fundamental to preserving vision. Annual ophthalmological examinations are required. For patients with diabetes, the goal is to optimize glucose control. Patients with hypertension or hypertension and diabetes should be treated to control blood pressure (goal is 130/80 mm Hg for those with diabetes, 140/90 mm Hg without diabetes). Blood pressure reduction should be slow and deliberate to minimize end-organ damage; treatment of the underlying pathology is essential. The parameters and goal of treatment in patients with hypertension and diabetes should be clear and concise.

For patients who have diabetes with nonproliferative retinopathy, macular edema is responsible for most vision loss. If macular edema is clinically significant, treatment with anti-VEGF is superior to laser therapy, but intravitreal steroid injection may also be used. For those with diabetes with severe nonproliferative disease, panretinal laser photocoagulation can lower the risk of progression to proliferative diabetic retinopathy (Crandall & Shamoon, 2016). For patients who have diabetes with vitreous hemorrhage and advanced neovascularization, vitrectomy can be of significant benefit (Mathew & Sivaprasad, 2018).

Follow-Up: Follow-up depends on the findings. A retinal specialist should follow up with patients with retinopathy. The primary care provider is responsible for regular disease management. The staging of retinopathy and the treatment plan require specialty follow-up.

Sequelae: Not all retinopathy is progressive. The condition and its outcome are related to the cause of the retinopathy and the degree of successful disease management. For hypertensive retinopathy, arteriovenous nicking and arteriolar narrowing are irreversible.

Prevention/Prophylaxis: Older adult patients should have an annual ophthalmological examination. During routine office visits, perform a funduscopic examination on the eyes of patients with diabetes and hypertension. Promptly refer the patient to a retinal specialist at the earliest report of vision change or abnormal examination findings. Patients with diabetes and hypertension should be aware of the goals of treatment and the need to control blood pressure and blood glucose. Home monitoring of blood glucose and blood pressure may be advised.

Referral: A retinal specialist should see all patients with retinopathy. All patients with diabetes and hypertension should see an ophthalmologist annually. Communication between

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the specialist and primary care provider is essential for optimal patient treatment.

Education: Patients should report any alteration in vision. Patients should know how the goals of blood pressure and blood glucose control relate to prevention of complications. Finally, patients should understand the importance of follow-up care. The goals of treatment should be a partnership between patient and health-care provider.

Clinical Recommendation	Evidence Rating	References
Refer patients with macular edema, severe nonproliferative retinopathy, or any degree of proliferative retinopathy to an ophthalmologist immediately for treatment.	A	AAO, Retina/Vitreous Panel, 2020
Patients with type 1 diabetes should have annual screenings beginning 5 years after diagnosis. Those with type 2 diabetes should have annual screenings beginning at the time of diagnosis.	A	AAO, 2020
Optimal glycemic, blood pressure, and lipid control reduce the risk and progression of retinopathy.	A	ACCORD Study Group & ACCORD Eye Study Group, 2010 Diabetes Control and Complications Trial (DCCT) Research Group, 1993 Thomas et al., 2020
Laser photocoagulation reduces the risk of vision loss in patients with proliferative retinopathy, clinically significant macular edema, and some cases of severe nonproliferative retinopathy.	A	ACCORD Study Group & ACCORD Eye Study Group, 2010
Intraocular steroids, laser treatment, anti-vascular endothelial growth factor injections or vitrectomy surgery may be utilized alone or in combination for treatment.	A	AAO, 2020 Shah & Gardner, 2017
Aspirin therapy does not prevent the progression of retinopathy, nor is it contraindicated for prevention of cardiovascular disease in the presence of retinopathy, because it does not increase the risk of retinal hemorrhage.	A	AAO, 2020 ACCORD Study Group & ACCORD Eye Study Group, 2010 Early Treatment Diabetic Retinopathy Study Research Group, 2005

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

A 76-year-old woman presents today with complaints of nasal drainage, clearing of throat, and occasional nasal congestion, especially on waking in the morning. She has recently moved into an independent living center after living in her home for 40 years. She states that, although she has had these symptoms before, generally the symptoms appeared in the spring, and she associated the nasal drainage with pollination. Because it is winter, she could not identify the trigger of her symptoms.

Chief complaint: Persistent "runny nose" for 3-week duration, associated clearing of throat, and nasal congestion on awakening in the morning.

Objective data: Blood pressure (BP) 130/84, temperature 98.6, pulse 78, respiratory rate 20.

1. How will you use this information to prepare for today's visit?
2. What additional subjective data are you seeking, to include history of any allergies?
3. What additional objective data will you be assessing for?
4. What are the differential diagnoses that you are considering?
5. What laboratory tests will help you rule out some of the differential diagnoses?
6. What is your treatment, and what specific information about the prescription will you give to this patient?
7. What are the potential complications from the treatment ordered?
8. What additional specific laboratory tests will you consider ordering?
9. What additional patient teaching may be needed?
10. What type of specialist will you be consulting for this patient?

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CHAPTER 10

Cardiovascular Disorders

Evelyn Duffy

ASSESSMENT OF THE CARDIOVASCULAR SYSTEM

Key symptoms for cardiovascular assessment include but are not limited to chest tightness or pressure, shortness of breath or difficulty catching breath, dizziness, syncope or near syncope, edema, abdominal pain, nausea and vomiting, and numbness and claudication of the extremities (Kane et al., 2018). Differentiating normal from abnormal cardiac function in an older adult can be a challenge because one in two older adults has cardiovascular disease (CVD). More specifically, almost one-half of all individuals older than age 60 years have severe coronary artery narrowing with a respective increase in myocardial demand. Of these, less than 50% have clinical signs and symptoms of this process. CVD is the most prominent cause of disability in this age-group and the leading cause of death, accounting for about one-half of all deaths among older adults. Coronary artery disease (CAD) is the most common type of CVD, but CVD also includes valvular disease, cerebrovascular disease that can result in strokes, and peripheral vasculature disease that can result in ischemia or blood clots. More than one in three adults has at least one type of CVD and nearly half of these are age 60 or older. Of those with CVD, nearly 18.2 million Americans have CAD, and the incidence increases with age (Virani et al., 2020).

ASSESSMENT OF RISK FACTORS FOR CARDIOVASCULAR DISEASE

Although some risk factors for CVD can be remedied, others cannot. The most important risk factors that cannot be remedied are advanced age, male sex, and genetic predisposition. The major remediable risk factors are control of hypertension (HTN), managing elevated lipid levels, increasing physical activity, and eliminating harmful habits such as abuse of alcohol or tobacco product. Smoking cigarettes is a dominant risk factor for cardiovascular and non-cardiovascular morbidity and mortality and is one of the most preventable risk factors with the greatest contributions to the development of CVD (Francula-Zaninovic & Nola, 2018). There has been a consistent decline in adult cigarette use between 2011 and 2018 (Virani et al., 2020). Since the 1970s, the mortality rate from CAD has shown a pronounced decline in the United States. Most of this decline can be attributed to changes in lifestyle and improved technologies such as thrombolytic drugs. The decline in CVD has occurred in older as well as younger age-groups, suggesting that the effects of risk factor modification persist well into later life (Virani et al., 2020).

Blood Pressure

The systolic blood pressure (SBP) rises with age; the diastolic blood pressure (DBP) remains the same or drops slightly over time. DPB tends to rise until the sixth decade of life and declines thereafter due to stiffer large arteries (Forman et al., 2019). Established HTN is a risk factor for CVD in older adults, with systolic elevations posing a greater risk than diastolic elevations. Overall, the risk of experiencing a cardiovascular event or death is two to three times higher in those with significant HTN than in those who are normotensive. Isolated systolic hypertension (ISH) is defined as an SBP greater than 160 mm Hg and a DBP of less than 90 mm Hg. Aggressive treatment of ISH has demonstrated a significant reduction in stroke, myocardial infarction (MI), and sudden cardiac death. Controlling HTN is important, but risk stratification should also be considered when treating the older person. The American College of Cardiology/American Heart Association (ACC/AHA) guidelines recommend an individualized cardiovascular risk assessment using the atherosclerotic CVD (ASCVD) risk calculator to direct treatment goals, the calculator is available on the Web at https://www.cvriskcalculator.com/ (Bakris et al., 2019). Control of HTN is the most potentially remediable risk factor, but control is challenging in those who are obese, continue to use tobacco, are physically inactive, and have poor glucose control.

Cholesterol

Serum cholesterol levels rise with age, up to age 60 years; thereafter, these levels begin to drop. The risk of the effects of an elevated cholesterol level persists from middle age to extreme old age. Aggressive efforts are often indicated to lower low-density lipoprotein (LDL) levels and raise high-density lipoprotein (HDL) levels for cardiac protection. Controversy exists about the role of statins in primary

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prevention of CVD in low-risk older adults, but a meta-analysis of the JUPITER and HOPE-3 trials demonstrated that in those 70 years of age and older, the use of statins offered a similar relative risk reduction of the incidence of CVD to those younger than the age of 70 (Grundy et al., 2019). The authors note, however, that the benefit needs to be weighed against the patient's life expectancy and the increased risk in this age-group of adverse events due to statin use.

Tobacco

Tobacco is an independent significant risk factor for CVD and the leading preventable cause of disease, disability, and death in the United States (Arnett et al., 2019). All tobacco cessation is strongly advised as both primary prevention and secondary prevention for those with known CVD, or in those who are at risk for developing CVD (Arnett et al., 2019).

Physical Inactivity, Impaired Glucose Control (Diabetes), and Obesity

Additional proven or postulated risk factors for CVD in older adults include lack of exercise, impaired glucose tolerance, and obesity. Older adults are most likely to have a combination of risk factors, which has a cumulative effect of increasing the risk of CVD. Evidence is compelling for improved exercise plans, control of blood glucose levels, and weight loss (Arnett et al., 2019).

Cardiac risk assessment tools, including the Global Framingham Risk Assessment, are available at https://www.nhlbi.nih.gov/health-pro/guidelines/in-develop/cardiovascular-risk-reduction/risk-assessment/. Assessment for metabolic syndrome and obesity, including body mass index (BMI) and waist circumference enhances risk assessment.

Age-Associated Changes in Cardiovascular Structure and Function

Aging is the main risk factor for CVD and the progression of CAD and cerebrovascular events. The progression of CAD and cerebrovascular disease is the leading cause of death for persons as they age. Vascular aging or arterial degeneration and hardening of the vasculature begins in the fifth and sixth decade of life and can accelerate incrementally depending on hereditary factors and cardiac risk factors (Hamczyk et al., 2020).

Aging is commonly seen as chronological years and a person's personal yearly milestone. Aging is more complex and is determined by the escalating toll of biological stresses. This includes oxidative stress and vascular inflammation that diminish one's capacity to overcome disease. Unless there is a break in the cycle of age-associated changes the renin-angiotensin-aldosterone signaling promotes a proinflammatory cycle that predisposes the person to CVD. Lifestyle health habits can either accelerate the disease process or slow it depending on one's willingness to adhere to healthy habits (Forman et al., 2019; Hamczyk et al., 2020). Aging causes structural and functional changes in the arterial system of the older adult. This occurs even if the person has no apparent CVD. With aging, the arterial wall media thickens due to smooth muscle cell hypertrophy, extracellular matrix accumulation, and calcium deposition. Intimal-medial thickness increases approximately threefold between the ages of 20 and 90 years in persons with normal SBP. This results in fraying of elastic fibers, reducing arterial flexibility, and an increase in vascular stiffness. Changes in vasodilating nitric oxide and vasoconstricting angiotensin II contribute to vascular aging (Forman et al., 2019). In the young, hearts are composed of approximately 25% cardiomyocytes and a complex structure of connective tissues. With aging, cardiomyocytes decrease due to apoptosis and hypertrophy occurs.

Left ventricular hypertrophy is usually due to increased cardiac demand caused by an increase in peripheral resistance. Peripherally, the vessels become atherosclerotic contributing to the increase in SBP with age. These structural and physiological changes in the aging cardiovascular system cause decreased capacity to endure stresses, decline in tolerance of physical activity, and limited functional reserve capacity. The left ventricle's (LV) diastolic performance is altered by aging, resulting in late LV filling facilitated by atrial contraction. The late filling is associated with modest left atrial size, thus increasing the risk for atrial arrhythmias. Fat deposits accumulate around the sinoatrial (SA) node, and the number of pacemaker cells usually decreases by age 75 years, contributing to chronotropic and arrythmia abnormalities. Baroreceptors become less sensitive with age, and the response to changes in BP and heart rate is often blunted.

These physiological changes have little functional impact on the aging heart at rest, but with exercise or stress, they render the aging heart less capable of increasing and sustaining an increase in cardiac output. Fast heart rates are commonly associated with diastolic filling abnormalities and higher LV diastolic pressure. This can result in higher pressures in the lungs, resulting in the development of heart failure with preserved ejection fraction (HF*p*EF). Maximal heart rate declines approximately 30% between ages 20 and 80 years. Cardiac dilation and increased stroke volume compensate somewhat for the diminished heart rate during exercise. (Forman et al., 2019).

Symptom Assessment

Using the Onset, Location, Duration, Characteristics, Aggravating factors, Relieving factors, Timing (OLDCART) mnemonic or Precipitating/Palliating factors, Quality, Radiation, Severity, Timing (PQRST) mnemonic, ask the patient about chest pain, shortness of breath, dizziness, palpitations, or edema. Establish the patient's usual baseline activities of daily living (ADLs) and activity level and ask how symptoms are affecting this. Some older adults experience palpitations as a nervous feeling, so include that in your questioning. Chest pain/pressure may present as heartburn or indigestion or as the patient's gastroesophageal reflux disease (GERD). Shortness of breath may be felt as anxiety but is a more common presentation of an acute coronary event than chest pain. Atypical presentation for MI includes vague symptoms such as nausea, decreased activities of daily living (ADL) status, and fatigue without chest pain/pressure, back pain. If the patient has known diabetes, the patient may present with a change in activity, general malaise, or with more heart failure symptoms, such as shortness of breath, dyspnea on exertion, paroxysmal nocturnal dyspnea, and orthopnea (Forman et al., 2019).

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CLINICAL EXAMINATION FEATURES

In the actual physical assessment of the older adult, the apical impulse is difficult to locate because the chest wall undergoes changes due to the intercostal muscles weakening, resulting in an increased anteroposterior diameter (Bickley, 2017).

Auscultation in the older adult frequently reveals changes in normal heart sounds, extra heart sounds, bruits, and murmurs. The S_1 is more easily heard, and splits of the first heart sound are more easily detected because of an ejection sound that occurs when the aortic valve cusp tissue fails to fold into the vessel wall during ejection. A change in the loudness of S_1, accompanied by a slow heart rate, may indicate heart block. The S_2 split on inspiration is narrower or absent because of decreased compliance of the pulmonary vasculature. An opening snap occurs when the mitral or tricuspid valve produces minor vibrations of increased intensity caused by more rapid cusp movement or a resistance to inflow caused by cusp fusion (Bickley, 2017). An audible opening snap is the best physical sign of mitral stenosis, but it becomes less obvious in the older adult whose valves are rigid and calcified.

Ventricular filling sounds, best heard with the stethoscope bell, are caused by the halting of the ventricle after ventricular filling. The physiological S_3, heard most clearly at the apex, disappears by the fourth decade as the ventricle stiffens and filling becomes less rapid. An S_3 in an individual more than 50 years old is usually pathological and reflects an increased filling rate, indicating heart failure (HF) or mitral regurgitation (Bickley, 2017). Early diastolic filling is reduced in healthy older adults resulting in an end-diastolic volume maintained by an increase in atrial contribution to left ventricular filling. This condition may cause an S_4, which in the absence of other findings, is considered normal in older adults.

The carotid arteries should be assessed routinely for the presence of bruit. Asymptomatic carotid bruit is a risk factor for stroke (Bickley, 2017). Studies demonstrate that a vessel is occluded more than 50% by the time a bruit can be heard. In older adults assess the top level of the internal jugular pulsation when evaluating jugular venous pressure. Do not use the external jugular veins because they may be sclerosed and appear to be falsely distended or may yield a falsely low pressure reading.

Prolonged extra heart sounds (murmurs), particularly systolic ones, are quite common in older adults. Systolic murmurs, which often indicate aortic valve disease, occur in more than 50% of individuals older than 70 years. The soft systolic ejection murmur is due to the dilation and the decrease in compliance of the aorta caused by stiffening of the aortic cusps without obstruction (aortic sclerosis). Loud murmurs, which usually indicate aortic stenosis, are often accompanied by a slow rising carotid pulse and left ventricular hypertrophy. An apical pansystolic or late systolic murmur also occurs frequently in older persons, resulting from floppy valves that become regurgitant over time. The two most common causes of mitral regurgitation are papillary muscle dysfunction (usually due to MI) and mitral annular calcification. Diastolic murmurs, which are always pathological, may be caused by heart block, aortic regurgitation, or mitral stenosis.

In the older adult, additional features of cardiac disease may be seen on physical examination of systems other than the heart. The eye examination may reveal the thick corneal arcus seen with lipid abnormalities or the funduscopic findings of atherosclerosis. The skin may demonstrate xanthomas or cholesterol nodules and changes in skin temperature, indicating a metabolic or peripheral vascular disease causing or contributing to cardiac disease. The presence of edema must be determined. The clinical cardiac examination features in the older adult include:

- Structural wall changes are common.
- S_1 is more easily heard.
- S_2 split is narrower.
- S_4 is common.
- Systolic murmurs are common.
- Bruits (carotid, abdominal) are common.

(Forman et al., 2019)

CARDIAC ARRHYTHMIAS

Signal Symptoms: No symptoms at times; feeling of heart "beating out of the chest."

Description: An arrhythmia is a disturbance of cardiac rhythm. Cardiac arrhythmias, which occur in either the presence or absence of underlying heart disease, may be life threatening or may be an incidental finding. Arrhythmias may be differentiated by type or mechanism (Khurshid et al., 2018; Prystowsky et al., 2020).

Atrial fibrillation (AF) is the most common sustained rhythm disorder. AF consists of numerous fibrillatory P waves that vary in shape, size, and timing. The ventricular response is often chaotic and rapid if the atrioventricular (AV) conduction is intact. AF can be clinically classified as follows:

- Paroxysmal: less than 7 days self-terminating or with intervention; episodes may occur with varied frequency
- Persistent: greater than 7 days and requires intervention to terminate
- Long-standing persistent: continuous AF more than 12 months
- Permanent: used when the patient and provider make a joint decision to stop further attempts to restore or maintain sinus rhythm
- Nonvalvular: in the absence of rheumatic mitral stenosis, a mechanical or bioprosthetic heart valve or mitral valve repair (Crawford et al., 2018)

Other prevalent forms of arrhythmias in the older adult population include:

Sick Sinus Syndrome: (1) Pathological bradyarrhythmia with an alternating supraventricular tachyarrhythmia (bradycardia-tachycardia syndrome); (2) There are three primary categories of supraventricular tachyarrhythmia: AF, atrial flutter, atrial tachycardia.

Arrhythmias Primarily of Atrial Origin. Atrial premature beats, ectopic atrial rhythms, multifocal atrial tachycardia, atrial flutter, and AF.

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Arrhythmias Arising Primarily Within the AV Node. AV nodal reentrant tachycardia, junctional premature beats, and nonparoxysmal junctional tachycardia.

Arrhythmias Partially Supraventricular in Origin. Pre-excitation syndromes.

Ventricular Arrhythmias. Ventricular ectopic beats are the most common variety.

Etiology: Most arrhythmias are thought to be caused by abnormalities either in impulse formation (disordered automaticity) or in impulse conduction (allowing reentry), or by a combination of the two. Increased automaticity is an accentuation of the inherent ability of many cardiac tissues to generate an independent rhythm. Reentry consists of a wave of excitation repeatedly circulating around a fixed anatomical obstacle. Triggered arrhythmias are caused by altered cellular depolarization (Prystowsky et al., 2020).

Occurrence: Studies show that asymptomatic older patients with no known structural heart disease have an incidence of up to 40% of sinus arrhythmia, supraventricular or ventricular premature beats, or supraventricular tachycardia (Khurshid et al., 2018).

Age: The prevalence of ventricular arrhythmia increases with age, occurring in 80% of healthy older adults ages 60 to 85 years. AF is diagnosed in 4.8% of women and 6.2% of men older than 65 years at baseline examination, and its prevalence is strongly associated with advanced age, particularly in women. Although no specific data are available, the incidence of junctional arrhythmias and tachycardias related to the accessory pathway may be lower in older adult individuals because of an age-related reduction in accessory pathway conduction.

Ethnicity: Not significant.

Contributing Factors: Pre-existing heart disease is a contributing factor to arrhythmias, with structural disease becoming more prevalent with age. The muscular response and contractility decrease as the patient ages. The patient experiences a reduction in cardiac function and contractility. This reduction is responsible for a decreased stroke volume and ejection fraction. The average older adult does not experience adverse symptoms with normal everyday activities. However, stressors (whether they are physical, psychological, environmental, or social) can increase the risk of illness in the patient. These illnesses are taxing to the patient's system, and the increased energy demands place an increased demand on the cardiac system. The aging process can also have an adverse effect on the cardiac valves. The valves tend to become thick and stiff secondary to arteriosclerosis and atherosclerotic plaques. Fibrosis or calcification in the vicinity of the AV node causes conduction disturbances. Atrial arrhythmias may be caused by a mechanical obstruction to atrial emptying with subsequent left atrial dilation, myocardial ischemia, and increased sympathetic activity.

An age-related factor associated with tachyarrhythmias is increased left atrial size. This enlargement may contribute to the increase in supraventricular ectopy. Increases in ventricular ectopic beats may be related to left ventricular enlargement. The overload of ionized calcium in the older myocardium may contribute to ectopy. Age-related factors associated with bradyarrhythmias include an age-related decline in the number of pacemaker cells and the presence of fat deposits around the SA node. His bundle cells are replaced with fibrous tissue, and adipose tissue and amyloid are deposited; this is also associated with conduction disturbance.

Systemic diseases (i.e., thyrotoxicosis, infection, hypoxemia, hypercapnea) can cause circulatory disturbances that may provoke an arrhythmia. Drugs that can cause an arrhythmia include digoxin and other antiarrhythmics, aminophylline, and alcohol. Electrolyte disturbances, particularly hyperkalemia, hypokalemia, hypercalcemia, and hypocalcemia, can precipitate ectopic beats. Family history of sudden cardiac death may indicate a predisposing factor for rhythm disorder, such as hypertrophic obstructive cardiomyopathy, congenital prolonged QT syndrome, or the presence of an aberrant conduction pathway (Khurshid et al., 2018).

Signs and Symptoms: The history, physical examination, and electrocardiogram (ECG) studies represent the cornerstone to evaluation of arrhythmias. Arrhythmias may cause symptoms due to a reduced blood flow or inadequate cardiac pump function. In the history, the patient may describe sensations that accompany abnormal cardiac rhythm such as pounding, racing, or skipped beats. Older adults are less likely to complain of palpitations and more likely to present with manifestations of heart failure (HF) or hypoperfusion (i.e., impaired mental function, dizziness, syncope). There appears to be a peak in syncopal episodes after age 65 years in both men and women. The Framingham study showed an increased incidence of syncope after age 70 years, from 5.7 events per 1,000 person-years in men ages 60 to 69 years, to 11.1 events in men ages 70 to 79 years (Grossman & Badireddy 2021). Along with the history of present illness, previous diagnosis and treatment for arrhythmia and cardiac disease should be elicited.

During physical examination, concentrate on the cardiac and peripheral vascular systems. Check the pulses for 1 full minute to determine rate and regularity (Prystowsky et al., 2020). Assess normal and extra heart sounds. S_1 intensity may provide information about the relation of atrial to ventricular contraction. The longer the PR interval, the softer the S_1. Note intermittent extra heart sounds (S_3 and S_4). The jugular vein must be assessed and in AV dissociation (when the atria and ventricles contract independently), giant A waves (cannon waves) may be observed. Provoking maneuvers should not be attempted by the advanced practice nurse but may be attempted by a cardiologist. These maneuvers include carotid massage (for atrial arrhythmias only), mild exercise, psychological stress, pharmacological stress, and electrical programmed stimulation (EPS).

Other indicators of hemodynamic response to an arrhythmia include level of consciousness and skin temperature and color. The history should guide the remainder of the episodic examination because it is also helpful in identifying the contributing factors that may precipitate or aggravate an arrhythmia.

Diagnostic Tests: Diagnostic testing includes a 12-lead ECG done with a rhythm strip, lasting at least 2 to 3 minutes. Include exercise testing for those with a clinical history suggesting exercise-induced arrhythmia. Ventricular arrhythmias can occur in individuals with or without cardiac disorders. The standard resting 12-lead ECG is indicated in all patients who are evaluated for ventricular arrhythmias (Prystowsky et al., 2020). An ambulatory 24-hour ECG (Holter monitoring) helps to quantify arrhythmias with reference to symptoms. Ambulatory ECG is indicated when there

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TEST	RESULTS INDICATING DISORDER
Rhythm strip	Rhythm disturbance may be present, or if transient, it may be absent
12-lead ECG	Acute MI or ischemia, prolonged QT intervals, and pre-excitation may be identified as precipitators of an arrhythmia
Ambulatory ECG monitoring	Quantifies arrhythmias with reference to symptoms
	Identifies patients at risk for sudden death by documenting ventricular arrhythmias and heart rate variability
Implantable loop recorder	In infrequent syncope this long-term device (14 months) may identify the precipitant
Echocardiogram	Identifies structural, functional, and hemodynamic abnormalities in the cardiovascular system
Cardiac electrophysiological study	Evaluates specific arrhythmias to distinguish these, determine location and characteristics, and guide therapy
Implantable cardioverter-defibrillator (ICD)	ICD firings may be due to recurrent arrhythmia
Electrolyte panel	Identify electrolyte disturbance (i.e., hypokalemia, hyperkalemia, hypomagnesemia, hypocalcemia) that may be causative or contributory
Coronary and LV angiography	Identifies CAD and LV function
Cardiac MRI	Especially useful in recognizing arrhythmogenic RV dysplasia, or infiltrative diseases

is a need to clarify the diagnosis by detecting arrhythmias, QT interval changes, T-wave alternans, or ST changes; to evaluate risk; or to judge therapy (Verrier & Ikeda, 2013). Event recorders are best suited for documenting less-frequent but more-prolonged bouts of arrhythmias, although not used with as much frequency. Patient-activated loop memory devices, which record the ECG before the symptomatic event, are most useful. His bundle electrograms involve the insertion of a transvenous electrode catheter into the right ventricle, to record depolarizations and the intervals. This method is most useful for distinguishing AV block from an ectopic focus.

Echocardiography is recommended in patients with ventricular arrhythmias who are suspected of having structural heart disease (Prystowsky et al., 2020). An echocardiogram is used more commonly than magnetic resonance imaging (MRI) or cardiac computed tomography (CT) scan because it is inexpensive in comparison. The echocardiogram is a useful tool in assessing for valvular disorders, left ventricular function and wall motion, and the ejection fraction. The electrophysiological (EP) testing is performed using intracardiac recordings, electrical stimulation, and drugs to assess and document ventricular tachycardia, guide ablations, and evaluate loss of consciousness in patients with arrhythmias as the suspected cause. EP testing is recommended for diagnostic evaluation of patients with remote myocardial infarction (MI) with symptoms suggestive of ventricular tachyarrhythmias, including palpitations, presyncope, and syncope. EP testing is recommended in patients with syncope of unknown cause with impaired left ventricular function or structural heart disease (Prystowsky et al., 2020).

In EPS, multipolar catheter electrodes are introduced into the venous or atrial circulation and advanced to various intracardiac positions to monitor the electrical activity or to induce an arrhythmia. EPS is most useful for determining sinus node dysfunction, AV block, intraventricular conduction disturbances, pre-excitation syndromes, supraventricular tachycardia, ventricular tachycardia, and unexplained syncope or palpitations. It is used also to monitor cardiac activity in survivors of sudden cardiac death.

Differential Diagnosis: Clarify the diagnosis with precision. Note reversible and precipitating causes of an arrhythmia and coexisting diseases.

Treatment: The incidence of asymptomatic arrhythmias of questionable clinical significance is high. Arrhythmias are never treated in isolation; some are benign, and some are lethal. Patients with hemodynamic compromise resulting from arrhythmia need to be hospitalized as soon as possible. Prehospital care for threatening hemodynamic instability secondary to tachyarrhythmia may include direct current cardioversion, and the nurse practitioner should be skilled in this intervention. After thorough investigation, the goals of arrhythmia treatment include the alleviation of bothersome symptoms, the prevention of complications from sustained arrhythmias, and the avoidance of sudden death associated with certain arrhythmias.

The risk of treatment is considerable. Aggressive therapeutic treatment is indicated when patients are symptomatic, and the urgency of therapy depends on the associated hemodynamic disturbance. A comprehensive treatment plan must address the three cornerstones of AF management: rate control, rhythm control, and prevention of thromboembolism. Goals of the therapy should be to obtain symptom control, stroke prevention, and a reduction in hospital recidivism (January et al., 2019; Khurshid et al., 2018). Three major factors determine how well a patient tolerates an arrhythmia: heart rate, duration of the arrhythmia, and presence and severity of associated underlying heart disease. Arrhythmias often cannot be controlled unless underlying cardiac problems are discovered and treated. No antiarrhythmic "wonder drug" exists, and the bothersome and potentially dangerous side effects necessitate determination of clear indications and use of the utmost caution. Pharmaceutical agent selection is based on the electrophysiology of the rhythm disturbance, the mechanism of action, and the side effects of the drug.

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Several new drugs are useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure, or advanced liver disease (Crawford et al., 2018; Prystowsky et al., 2020). Conditions common in older adults that can affect the choice, dosing, efficacy, and safety of antiarrhythmic therapy include decreased hepatic or renal function, decreased serum albumin levels, and electrolyte abnormalities.

The broad categories of arrhythmia treatment include medications, pacemakers, anti-tachycardia devices, implantable automatic cardioverter-defibrillators, catheter ablative procedure, and specific maneuvers. Defibrillation is the required intervention in ventricular fibrillation or pulseless ventricular tachycardia and is the most important determinant of survival in cardiac arrest. Patients defibrillated within 2 minutes have a 60% hospital discharge survival rate (Prystowsky et al., 2020). Vagal maneuvers (carotid massage or the Valsalva maneuver) may terminate or slow AV nodal reentry or AV reentry types. These maneuvers are associated with a high risk of emboli dislodgment. The carotid arteries should be assessed for bruit before administering massage. Because of the high mortality rate associated with antiarrhythmic surgery, it is not recommended in older adult individuals. The specifics of treatment are not detailed in this text because all assessment and management must be done in close collaboration with a physician specialist; much of the treatment is initiated by the specialist in the hospital setting.

Follow-Up: Because of their low therapeutic ratio, drug dosing and plasma concentrations of the antiarrhythmics are based on therapeutic monitoring. Side effects are significant and include the negative inotropic effect, which can precipitate HF or pro-arrhythmia in the presence of structural heart disease. Extracardiac side effects can also be significant, including anticholinergic effects, gastrointestinal effects, and neurological toxicity with some antiarrhythmic agents. Monitor patients after pacemaker insertion with regular follow-up appointments and ECG testing, specifically looking for pacemaker failure, infection, thromboembolism, perforation or dislodgment, and complicating arrhythmias.

Sequelae: Regardless of age, the nature and severity of underlying heart disease are of much greater prognostic significance than the arrhythmia alone. The following rhythm disturbances have been reported to carry a poor prognosis in patients with CAD: frequent ventricular premature contractions (VPCs) (greater than 10 per min), multiform VPCs, ventricular couplets, R-on-T phenomenon, and ventricular tachycardia.

Syncope can occur secondary to asystole. Syncope is an intermittent symptom that may be caused by an underlying arrhythmia with or without cardiac disease. Treatment goals are prevention of symptom recurrence, improvement of quality of life (QOL), and prolongation of survival. Permanent cardiac pacing may relieve the symptoms but may not affect the survival rate. Syncope recurs in approximately 20% of the patients (Grossman & Badireddy, 2021; Prystowsky et al., 2020). Bradycardia can contribute to complete heart block and to the development of HF in patients with associated ventricular dysfunction. Tachycardia can precipitate angina and circulatory arrest in patients with CAD. Bradyarrhythmias or tachyarrhythmias can cause systemic embolism and stroke. AF can result in HF and a low cardiac output state (Khurshid et al., 2018).

Prevention/Prophylaxis: All patients with AF should be considered for long-term anticoagulation with a direct-acting oral anticoagulant (DOAC) or warfarin. Aspirin, though less effective in preventing stroke, is an alternative for some patients in whom other anticoagulants are contraindicated. Electrolyte imbalances should be monitored, and metabolic disturbances treated. Patients receiving digoxin should be monitored for toxicity (Crawford et al., 2018).

Referral: All patients with treatable arrhythmias require collaborative management with a cardiologist. Clinically significant ventricular arrhythmias or any symptomatic arrhythmia is managed in the coronary critical care unit. A primary care provider may handle many atrial arrhythmias and low-grade ventricular arrhythmias; however, a cardiologist should be consulted for all clinically significant ventricular arrhythmias, arrhythmias resistant to routine therapy, or arrhythmias whose clinical significance is in doubt (Crawford et al., 2018; Khurshid et al., 2018).

Education: Carefully instruct all patients receiving antiarrhythmics about the therapeutic effects, side effects, and potentially adverse effects of these medications. Because patients with pacemakers are vulnerable to external electrical fields, they should be instructed to recognize this potential and avoid exposure. Patients with pacemakers must also be aware of signs and symptoms of pacemaker failure.

Clinical Recommendation	Evidence Rating	References
DOACs are useful as an alternative to warfarin for the prevention of stroke and systemic thromboembolism in patients with paroxysmal to permanent AF and risk factors for stroke or systemic embolization who do not have a prosthetic heart valve or hemodynamically significant valve disease, severe renal failure, or advanced liver disease. Based on shared decision making.	Warfarin—A Dabigatran—B Rivaroxaban—B Apixaban—B Edoxaban—B	January et al., 2019
A 2-minute delay in defibrillation is associated with a reduction in odds of survival of up to 17.1%.	C	Bircher et al., 2019
Permanent cardiac pacing may relieve the symptoms but may not affect the survival rate. Syncope recurs in approximately 20% of the patients.	C	Glaser et al., 2021

Continued

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Clinical Recommendation	Evidence Rating	References
EP testing is recommended in patients with syncope of unknown cause with impaired left ventricular function or structural heart disease.	C	Khurshid et al., 2018
EP testing is recommended for diagnostic evaluation of patients with remote MI with symptoms suggestive of ventricular tachyarrhythmias, including palpitations, presyncope, and syncope.	C	Khurshid et al., 2018
Echocardiography is recommended in patients with ventricular arrhythmias who are suspected of having structural heart disease.	B	Khurshid et al., 2018
Ambulatory ECG is indicated when there is a need to clarify the diagnosis by detecting arrhythmias, QT-interval changes, T-wave alternans, or ST changes, to evaluate risk.	C	Khurshid et al., 2018
The standard resting 12-lead ECG is indicated in all patients who are evaluated for ventricular arrhythmias.	B	Khurshid et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

HEART FAILURE

Signal Symptoms: Dyspnea on exertion, orthopnea, paroxysmal nocturnal dyspnea, progressive activity intolerance, weakness, peripheral edema.

Description: As a clinical syndrome, heart failure (HF) is a secondary process associated with multisystem pathophysiology involving neurochemical regulation, abnormal cardiac muscle structure, and/or wall function. The older term *congestive heart failure* does not represent symptom presentation in all HF patients; therefore, the preferred term is *heart failure.*

Etiology: Cardiovascular disease (CVD) and hypertension (HTN) are the most common etiologies of HF; other causes are listed in Table 10-1 (McDonagh et al., 2021).

Universal definitions of HF include heart failure with reduced left ventricular ejection fraction (HF*r*EF)—previously referred to as *systolic heart failure*—with an ejection fraction ≤40% and heart failure with preserved left ventricular ejection factor (LVEF) (HF*p*EF)—previously referred to as *diastolic heart failure*—with an EF ≥50% (Bozkurt et al., 2021). Two new definitions are heart failure with mildly reduced ejection fraction (HF*mr*EF), with an EF 41% to 49%, and heart failure with improved EF (HF*imp*EF) in which initial EF is ≤40%, a ≥10-point increase from initial EF occurs, and subsequent EF is >40% (Bozkurt et al., 2021).

TABLE 10-1 Common Causes of Heart Failure

Cardiovascular	Coronary, myocardial, valvular, dysrhythmias (atrial fibrillation is the most common), pericardial
Toxic	Alcohol, cocaine, chemotherapy
Inflammatory/ Infection	Myocarditis, HIV
Metabolic	Anemia, thiamine deficiency, thyroid disorders
Infiltrative	Amyloid, sarcoid, hemochromatosis
Genetic	Family history
Situational	Sepsis, peripartum, Takotsubo cardiomyopathy

Occurrence: Approximately 6.2 million people in the United States older than the age of 20 years are affected by HF with 960,000 new cases annually (Benjamin et al., 2019). The annual incidence of HF in patients older than 65 years is 21 per 1,000 population (Dumitru & Baker, 2022) with a 5-year mortality rate in patients hospitalized with all types of HF approximately 75% (Shah et al., 2017). Hospital readmissions within the first 30 days are correlated with increased mortality risk (Kehra et al., 2018). HF is more common in men in the general population, but rates are higher in women within the long-term care setting.

Age: More common in older adults.

Ethnicity: African Americans have higher rates of HF (Pfeffer et al., 2019)

Contributing Factors: Nonmodifiable risk factors include sex and ethnicity. Advanced age is an independent risk factor for HF. Modifiable risk factors for HF are tobacco use, systolic blood pressure (SBP) of more than 140 mm Hg, fasting glucose of more than 125 mg/dL, elevated cholesterol, obesity, diet, and physical inactivity. Use of NSAIDs, COX-2 inhibitors, glucocorticoids, and thiazolidinediones are common precipitating factors for HF in older adults (McDonagh et al., 2021).

HF is caused by myocardial structural or functional damage that impacts left ventricular function; difficulty with ejecting blood (HF*r*EF) or effective ventricular relaxation (HF*p*EF). To maintain cardiac output, stroke volume, and vital organ perfusion, the sympathetic nervous system and renin-angiotensin-aldosterone system (RAAS) are activated to release neurohormones. Angiotensin II, a potent vasoconstrictor, leads to increased systemic vascular resistance, enhances the release of catecholamines from noradrenergic nerve endings, and directly stimulates the adrenal cortex to

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increase secretion of aldosterone. Vasopressin (antidiuretic hormone) and aldosterone secretion cause sodium and fluid retention with subsequent increase in blood volume. Increased systemic vascular resistance, decreased arterial pressure, increased venous pressure, increased blood volume, and decreased venous compliance further increase ventricular wall stress and myocardial oxygen demand. Ultimately, these normal physiological responses become maladaptive and result in damage to the heart, cardiopulmonary, renal, and systemic vasculature, and cause progression of HF.

Signs and Symptoms: Left ventricular heart failure leads to pulmonary venous congestion, subsequent right ventricular dysfunction, and portal and systemic venous congestion. Clinical symptoms of dyspnea on exertion or at rest, orthopnea, dry cough (worse in recumbent position), bendopnea (breathless when bending over), and/or paroxysmal nocturnal dyspnea indicate increased pulmonary venous congestion. Progressive lower extremity edema (not due to venous insufficiency or hypoalbuminemia) and abdominal symptoms (pain, distention, nausea, and early satiety) related to hepatic enlargement are symptoms suggestive of right ventricular failure or systemic venous congestion.

Signs that suggest HF include weight gain, tachycardia, S_3 or S_4 heart sound, laterally displaced point of maximum impulse (PMI), neck vein distention, rales in bilateral lower lobes that are not due to atelectasis, positive hepatojugular reflux, and ascites. Diminished mental acuity and reduced exercise tolerance are common in older adults with HF (Stefil et al., 2020).

HF classification is based on risk, cardiac structural changes, symptom presentation, and functional impairment. The New York Heart Association (NYHA) classifies HF based on functional limitation (Yancy et al., 2013).

- Class I: No symptoms and no limitation in ordinary physical activity (e.g., shortness of breath when walking, climbing stairs)
- Class II: Mild symptoms (mild shortness of breath and/or angina) and slight limitation during ordinary activity
- Class III: Marked limitation in activity due to symptoms, even during less-than-ordinary activity (e.g., walking short distances (20 to 100 m). Comfortable only at rest.
- Class IV: Severe limitations. Experiences symptoms even while at rest. Mostly bedbound patients.

This system may be difficult to apply to older adults with HF who may have functional decline related to comorbid conditions. A unique aspect of the NYHA system is that it is dynamic. As patient's symptoms improve, they can be reclassified.

The ACC/AHA system classifies HF in four stages as the syndrome progresses along the natural trajectory and is used in conjunction with, not as a replacement for, the NYHA functional classification system (Yancy et al., 2017). The ACC/AHA rating system is based on risk factors, structural changes, and history of HF symptoms. Stages A and B refer to risk factors and present opportunities for primary and secondary prevention measures.

- Stage A: Risk factors are present for HF without structural changes, history of signs or symptoms, or functional limitations.
- Stage B: Risk factors and structural changes in the heart are present without signs or symptoms of HF.
- Stage C: Risk factors, structural changes in the heart, and past or current signs or symptoms of HF are present. At this stage, the patient is diagnosed with HF that does not regress back to former stages.
- Stage D: HF is refractory despite maximum medical management. Patients are symptomatic at rest or with minimal exertion.

Diagnostic Tests:

Two-Dimensional Transthoracic Echocardiography Combined with Doppler Flow Studies. Two-dimensional echocardiogram is considered the most useful diagnostic tool for evaluation of ventricular ejection fraction and structural abnormalities for prognostic and interventional purposes (Yancy et al., 2017). Two-dimensional echocardiograms are essential to accurate diagnosis and treatment plan development. Echocardiogram is essential for those with unknown history of HF and clinical presentation to evaluate ventricular function, size, wall thickness, wall motion, and valve function criteria. Diagnosis of HF*p*EF is supported by (1) evidence of clinical HF symptoms, (2) normal or mildly abnormal LV systolic function, and (3) evidence of abnormal LV relaxation, filling, diastolic distensibility, or diastolic wall function (Bozkurt et al., 2021).

Electrocardiography. ECGs may indicate left atrial enlargement, left ventricular hypertrophy, arrhythmias, or ST-T wave changes associated with myocardial infarction (MI) or ischemia.

Cardiac Angiography. Cardiac catheterization may benefit older adults who are candidates for revascularization and may reveal hemodynamic abnormalities, the presence and severity of valvular heart disease, or CAD.

Chest X-Ray. Chest x-ray may reveal cardiomegaly, increased pulmonary vascularity, interstitial or pulmonary edema, and assists in evaluating alternative etiologies that may contribute or cause heart failure-like symptoms.

Brain Natriuretic Peptide (BNP) or N-Terminal proBNP (NT-proBNP). BNP and NT-proBNP are helpful in narrowing differential diagnoses or establishing prognosis. BNP elevation occurs slowly; therefore, levels are not helpful in acute HF episodes and better to evaluate trends over time. BNP levels of less than 100 pg/mL indicate that HF is unlikely. Levels between 100 and 500 pg/mL are indeterminate. Levels of more than 500 pg/mL may suggest HF but are not appropriate as "stand-alone" tests. Many factors influence BNP levels, including sex, age, obesity, chronic kidney disease, pericardial disease, AF and pulmonary embolism (PE) (Bozkurt et al., 2021).

Blood Chemistries and Complete Blood Count (CBC). CBC, comprehensive metabolic profile (CMP), magnesium and thyroid-stimulating hormone (TSH) levels should be obtained initially and periodically to evaluate renal, liver, metabolic, and hemodynamic status.

Serial Cardiac Enzymes. Cardiac enzymes (CK-MB, troponin) may reveal myocardial ischemia or infarction. Cardiac enzymes require time-sensitive processing; therefore, they have limited value in the long-term care setting. If the presentation is uncertain, transport via emergency medical services to an acute care facility.

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Differential Diagnosis: Atypical symptom presentation in older adults necessitates a thorough health history that includes evaluation of risk factors with correlation to physical examination findings and diagnostic test results. Dyspnea on exertion, the most common heart failure symptom, may be caused by numerous diseases, including asthma, chronic obstructive pulmonary disease, anemia, renal failure, dysrhythmias, cardiomyopathies, valvular heart disease, primary pulmonary HTN, PE, abdominal masses, deconditioning, and anxiety neurosis. Differentiation between HF*p*EF and HF*r*EF is crucial and best determined by two-dimensional echocardiography (McDonagh et al., 2021; Yancy et al., 2017).

Treatment: Treatment options for HF are targeted at symptom management, treatment of the causative disease process(es), and the resulting multisystem pathophysiology. Fragility, multiple comorbid disease processes, polypharmacy, age-related changes in pharmacokinetics and pharmacodynamics, and prevalence of geriatric syndromes require individualized treatment plans.

Angiotensin-Converting Enzyme Inhibitors. Unless contraindicated, angiotensin-converting enzyme inhibitors (ACEIs) should be used in the treatment of asymptomatic HF*r*EF or in patients with recent or remote history of MI regardless of LVEF. ACEI contraindications include unilateral or bilateral renal artery stenosis, hypersensitivity to ACEIs, angioedema, pregnancy, serum potassium more than 5.5 mEq/L that cannot be reduced, and hypotension in patients at risk for cardiogenic shock. ACEI therapy should be discontinued as a last resort in HF patients due to cardioprotective properties. All ACEIs should be started at low doses and gradually titrated over several weeks to achieve target doses daily based on renal function, potassium levels, BP, and tolerance. Obtain baseline serum potassium, serum creatinine, and blood urea nitrogen (BUN) levels before initiation and with dosage adjustments. Dosage adjustments should be made accordingly for symptoms of dizziness, light-headedness, or unsteadiness. ACEI cough is a common side effect and is characterized as a dry nonproductive cough which may be worse at night and can occur at any point in treatment. ACEI cough is a class-wide side effect and is not dose dependent.

Angiotensin II Receptor Blockers. Angiotensin II receptor blockers (ARBs) are an appropriate substitute for ACEIs because they do not inhibit kininase and are associated with lower incidence of cough and angioedema (Yancy et al., 2013). Isosorbide dinitrate and hydralazine combination therapy is an appropriate alternative in patients who experience hypotension, hyperkalemia, angioedema, or renal insufficiency with ACEI or ARB therapy, and those who do not respond to treatment with ACEIs and beta blockers. These medications have also shown benefit in African Americans with NYHA class III–IV HF*r*EF receiving guideline-directed medical therapy (McDonagh et al., 2021).

Angiotensin Receptor/Neprilysin Inhibitors. Angiotensin receptor/neprilysin inhibitors (ARNIs) are ARBs combined with an inhibitor of neprilysin, an enzyme that degrades natriuretic peptides, bradykinin, adrenomedullin, and other vasoactive peptides (McDonagh et al., 2021). ARNIs are approved as first-line treatment as a substitute for ACEIs or ARBs in those with symptomatic HF*r*EF and should not be used concomitantly with these agents; a 3-day washout period is needed (McDonagh et al., 2021). Clinical trials of ARNIs have shown a 20% reduction in cardiovascular death or HF hospitalization (McDonagh, 2021; Yancy et al., 2017).

Beta-Adrenergic Blockers. Carvedilol, metoprolol succinate, and bisoprolol are the only beta blockers indicated for treatment of HF and with evidence to support morbidity and mortality reductions in HF patients. Unless otherwise contraindicated (heart block, bradycardia, hypotension, severe respiratory disease), beta blockers are recommended for patients with recent or remote history of MI regardless of LVEF. Use of carvedilol or metoprolol succinate has been shown to decrease morbidity and mortality in HF patients and is recommended in patients with stage C HF and/or a history of MI regardless of LVEF.

Beta blockers are strongly associated with reduced risk of mortality and reduced rehospitalization during 30-, 60-, and 90-day follow-up periods. Carvedilol is the best option in those with advanced HF. Beta blockers should be used in combination with ACEIs, ARB, or ARNI if possible, for synergistic effect. Monitor older patients closely for volume status, emotional side effects, and functional decline. Contraindications include bronchospastic lung disease (e.g., asthma), symptomatic bradycardia, or advanced heart block without a pacemaker. Beta blocker initiation should be started only in a euvolemic patient. Initial dosages should be low and titrated slowly based on response to treatment and tolerance. Carvedilol may have a greater hypotensive effect in the older adult because of the vasodilatory effect of alpha-1 receptor blockade properties. Metoprolol succinate may be better tolerated in those with lower baseline BP levels and for rate control in concurrent atrial fibrilation. Consider carvedilol or bisoprolol in patients who require crushed medications.

Diuretic Therapy. Loop diuretics are used to reduce symptoms of peripheral or pulmonary congestion. Loop diuretics inhibit the Na+/K+/Cl- symporter in the ascending loop of Henle, whereas thiazide-type diuretics affect the Na+/Cl- in the distal convoluted tubules. Use of diuretics in the treatment of HF without ACEIs, ARBs, or beta blockers activates the RAAS and may hasten progression of HF. Most HF patients are resistant to the effects of hydrochlorothiazide; therefore, loop diuretics are preferred. When used in equipotent dosages, loop diuretics appear to have comparable diuretic effects (1 mg bumetanide = 40 mg furosemide = 10 to 20 mg torsemide). Furosemide should be initiated at 20 mg daily oral dosage in the older adult patient with mild symptoms, with dosage titration based on effect and tolerance. Bumetanide is 40 times more potent than furosemide and is less ototoxic, but it is associated with myalgias in some patients.

Fluid overload refractory to loop diuretics results from downregulation in renal response and sodium retention (Trullàs et al., 2016). The addition of a thiazide diuretic to a loop diuretic may be an indicated and efficacious option to reduce acute HF symptoms if a sub-therapeutic response to loop diuretic dosage increase is noted (Trullàs et al., 2016). Metolazone (2.5 to 5 mg daily), a thiazide-like agent, is a long-acting diuretic that is effective in increasing the effects of loop diuretics if given 30 minutes before the loop diuretic dosage. Combination therapy with metolazone requires close

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monitoring of potassium and magnesium levels. Torsemide may be advantageous because absorption is unimpaired and the response is less variable than the other loop diuretics. Amiloride, triamterene, and ethacrynic acid should only be considered if there is a life-threatening allergy to sulfa due to side effects and inability to protect against damaging neurohormonal activity. Spironolactone, a mineralocorticoid receptor antagonist (MRA), is an effective therapy in conjunction with ACEIs or ARBs to more completely block the deleterious effects of the RAAS in patients with stages C and D class III–IV HF*r*EF and in patients with LVEF of 40% or less who have adequate renal function without hyperkalemia. Providers should consider ability to monitor for renal dysfunction and hyperkalemia before initiation of therapy.

Mineralocorticoid Receptor Antagonists (MRAs). Spironolactone and eplerenone are recommended at low dosages once daily and should not be initiated in men with serum creatinine levels of 2.5 or more; in women with serum creatinine levels of 2.0 or more; or potassium levels of more than 5.0.

Sodium-Glucose Cotransporter-2 Inhibitors (SGLT2is). These drugs, originally introduced as treatments for diabetes mellitus are now recommended in HF*r*EF to reduce risk of hospitalization or major cardiology event in patients with or without diabetes mellitus. Empagliflozin and dapagliflozin have a diuretic and natriuretic effect resulting in reduced preload and afterload (Maddox et al., 2021).

Digoxin. Digoxin may be considered in the treatment of patients with HF without bradycardia who have persistent symptoms despite optimal therapy with ARNIs, ACEs, ARBs, beta blockers, SGLT2is, and MRAs. Digoxin may be helpful to control ventricular response due to AF in men with HF with LVEF of less than 50% (Yancy et al., 2013, 2016). To reduce morbidity and mortality, lower therapeutic range (0.5 to 0.9 ng/mL) is advised (Yancy et al., 2013). Evidence from several trials supports the use of digoxin to improve functional status and decrease HF hospitalization without improvement in mortality. Dosages for older adults should not exceed 0.125 mg daily (American Geriatrics Society, 2019). In older adults with renal dysfunction, every-other-day dosage may be appropriate.

Follow-Up: Fatigue and weakness without vital sign changes may occur with titration of any medication but are transient and should resolve within several days following dosage titration. Ask the patient about the presence of symptoms of HF as noted previously. Asking specific questions specific to triad symptoms (nocturnal dyspnea, orthopnea requiring two or more pillows, and dyspnea with exertion) is considered an optimal approach to symptom recognition. Ask general questions related to the patient's quality of life (QOL) such as sleep patterns, sexual difficulties, symptoms of depression, and coping behaviors. HF is a chronic illness with acute exacerbations, so assess caregiver burden. Immediate follow-up post-hospitalization and frequent follow-up may reduce readmission rates (Boxes 10-1 and 10-2).

Sequelae: Complications of HF involve hepatic and renal end organ disease. Fifty percent of patients with HF die from sudden cardiac death. All patients with HF should have an advance care plan and documented goals of care, including the Medical Orders for Scope of Treatment (MOST).

BOX 10-1
R U Watching?

R - Reconcile medications post-hospital
U - Up-titrate medication to target dosages as tolerated (document failure attempts)

WATCHING

- Daily weight until stable × 4 weeks, then weekly
- Notification parameters (Call >3 # daily or >5 # weekly)

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BOX 10-2
ABCs of Transitions

A - ACEI/ARB or ARNI
B - Beta antagonist

Restart when stable on follow-up
C - Closely monitor labs
D - Diet (no added salt)

Teach families to read nutrition labels
E - Exacerbation plan
F - Follow-up visit within 7 days post-hospitalization; telephone follow-up within 3 days

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Prevention/Prophylaxis: Reducing cardiac risk factors is as effective in preventing coronary disease in older adults as it is in younger age-groups. Encourage risk factor reduction using age-specific guidelines to facilitate changes in lifestyle. Patients with HF are at risk for a vascular event, and there is no clear evidence regarding efficacy of prophylactic antithrombotic treatment (aspirin or warfarin) without other indications. Patients with HF should receive vaccination against influenza and pneumococcal disease.

Referral: Referral for interprofessional team and chronic care case management should be considered for all patients with HF. Warning signs for the need for hospitalization include increased dyspnea, weight gain that is resistant to diuresis, palpitations, persistent or recurrent dizziness, agitation or cognitive changes, inability to sleep because of paroxysmal-nocturnal dyspnea, abdominal pain, and a decline in activities of daily living (ADLs) and/or instrumental activities of daily living (IADLs).

Practice of best evidence involves shared decision making between an experienced, well-coordinated, primary care team in a patient-centered palliative care model. Referral to cardiology is indicated when the diagnosis is unclear, if the patient remains symptomatic despite appropriate therapy, and in those with significant cardiac disease. Hospice should

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be considered when a patient has stage D class IV HF, has an ejection fraction of 20% or less, is unable to tolerate optimal therapy due to hypotension or renal failure, or has symptoms that are not controlled with maximized medical management.

Education: Education and use of support groups are important for patients with HF, because adherence is a major cause of morbidity and unnecessary hospital admissions. Instruct patients and their families about the natural progressive trajectory of HF, necessary medications, dietary restrictions, HF symptoms that necessitate contact with provider, and prognosis. Discussions regarding advance directives should begin early in the trajectory. Explain typical symptoms of worsening HF and instruct patients to contact their health-care provider if these occur. Mild aerobic exercise increases functional capacity and improves the QOL for patients with HF but should be undertaken with provider supervision. Dietary sodium should be restricted to 2 or 3 g per day. Discourage alcohol use and tobacco use. Fluid restriction is not necessary unless there is hyponatremia, but patients with HF should avoid excessive fluid intake. Advise patients to contact the health-care provider if weight increases more than 2 pounds in a day or 5 pounds in a week.

Clinical Recommendation	Evidence Rating	References
Angiotensin-converting enzyme inhibitors (ACEIs) are recommended for all patients with HF*r*EF unless contraindicated.	A	Yancy et al., 2017 McDonagh et al., 2021
Angiotensin II receptor blockers (ARBs) are an appropriate option for those who have HF*r*EF and are intolerant to ACEIs.	A	Yancy et al., 2017 McDonagh et al., 2021
Angiotensin receptor-neprilysin inhibitors (ARNIs) are an appropriate substitute in those who have HF*r*EF and cannot tolerate ACEIs or ARBs.	A	Yancy et al., 2017 McDonagh et al., 2021
Beta blockers should be used in combination with ACEIs if possible, for synergistic effect.	A	Yancy et al., 2017 McDonagh et al., 2021
Beta blockers are recommended for patients with or without recent or remote history of myocardial infarction, regardless of left ventricular ejection fraction (LVEF).	A	Yancy et al., 2013
Aldosterone antagonist is recommended in HF*r*EF NYHA class II–IV given appropriate renal function (>30 mL/min/1.73m^2) and serum potassium is less than 5 mEq/L. Class II patients should have a history of prior hospitalization and elevated natriuretic peptides for consideration of therapy. Providers should consider ability to monitor for renal dysfunction and hyperkalemia before initiation of therapy. Renal function and electrolytes should be checked in 2 to 3 days and again in 7 days following initiation or dosage adjustment.	A	Yancy et al., 2017 Maddox et al., 2021
Use sodium-glucose cotransporter-2 inhibitors (dapagliflozin and empagliflozin) in addition to guideline directed medical therapy for patients with HF*r*EF to reduce hospitalizations and cardiovascular death following estimated GFR guidelines.	A	Maddox et al., 2021, McDonagh et al., 2021
Isosorbide dinitrate and hydralazine combination therapy is an appropriate alternative in patients who experience hypotension, hyperkalemia, angioedema, or renal insufficiency with ACEI or ARB therapy, in African Americans with NYHA class III–IV HF*r*EF receiving optimal therapy with ARNI, ACEI or ARB and beta blockers, unless contraindicated.	A	Yancy et al., 2017 McDonagh et al., 2021
Combined use of ACEI, ARB, and aldosterone antagonist is potentially harmful in those with HF*r*EF.	B	Yancy et al., 2017
Use of NSAIDs, COX-2 inhibitors, glucocorticoids, and thiazolidinediones are common precipitating factors for HF in older adults.	A	Yancy et al., 2013
Vaccination against influenza and pneumococcal disease is recommended unless contraindicated for HF patients.	A	Advisory Committee for Immunization Practices, 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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HYPERTENSION

Worldwide, hypertension (HTN) is one of the five leading risk factors for disease burden, including cardiovascular disease (CVD) and death (Virani et al., 2021). Nearly one in every two adults in the United States has HTN (Virani et al., 2021). This high prevalence combined with population growth and an increased life expectancy of adults older than 60 years equates to providers treating more patients with HTN.

Signal Symptoms: Often referred to as the "silent killer," HTN is usually asymptomatic, presenting without overt symptoms (Kalehoff & Oparil, 2020). Only a portion of patients with hypertensive crisis present with nonspecific symptoms (headache, dizziness, palpitations, epistaxis, vomiting), cardiopulmonary symptoms (angina, arrhythmias, syncope, dyspnea), or focal neurological deficits (Ipek et al., 2017).

Description: HTN is the most common condition diagnosed in outpatient office visits in the United States (U.S. Preventive Services Task Force [USPSTF] et al., 2021). According to the latest American College of Cardiology/American Heart Association (ACC/AHA) guidelines for the detection, evaluation, and management of HTN in adults, blood pressure (BP) is categorized as normal, elevated, or HTN (stages 1 or 2) (Whelton et al., 2018). Normal BP is defined as less than 120/less than 80 mm Hg. Elevated BP is defined as 120 to 129/less than 80 mm Hg. Stage 1 HTN is defined as SBP 130 to 139 mm Hg or diastolic blood pressure (DBP) 80 to 89 mm Hg. Stage 2 HTN is defined as systolic blood pressure (SBP) greater than or equal to 140 mm Hg or DBP greater than or equal to 90 mm Hg (see Table 10-2). Notably, the 2018 guidelines of the European Society of Hypertension and the European Society of Cardiology (Williams et al., 2018) and the 2020 guidelines of the International Society of Hypertension (Unger et al., 2020) defined HTN as SBP 140 mm Hg and above or DBP 90 mm Hg and above.

Over a lifetime SBP and pulse pressure rise with age (Nuotio et al., 2020). However, DBP rises until about age 50 years and then slowly decreases as one ages (Nuotio et al., 2020). This explains why the most common type of HTN in older adults is isolated systolic HTN, defined as SBP of 130 mm Hg or greater and DBP of less than 80 mm Hg (Whelton et al., 2018).

HTN is a key risk factor for CVD (Virani et al., 2021). For every 20 mm Hg higher SBP and 10 mm Hg higher DBP, risk of death doubles from stroke, heart disease, and other vascular disease (Whelton et al., 2018). Higher SBP and DBP is also associated with an increased risk of angina, myocardial infarction (MI), heart failure (HF), stroke, peripheral arterial disease, and abdominal aortic aneurysm in adults ranging from 30 to 80+ years of age (Whelton et al., 2018). However, multiple, robust, randomized clinical trials, including studies in older adults, document effective treatment and management of HTN improves survival rates with cardiovascular benefits (Kalehoff & Oparil, 2020). More than one-half of patients with HTN have cardiovascular risk factors, so it is also important to screen for diabetes, dyslipidemia, overweight/obesity, metabolic syndrome, and unhealthy lifestyles (physical inactivity, tobacco use, and high alcohol use) (Unger et al., 2020).

TABLE 10-2 Classification of Hypertension

SYSTOLIC BLOOD PRESSURE	DIASTOLIC BLOOD PRESSURE	CLASSIFICATION
<120 mm Hg	and <80 mm Hg	Normal blood pressure
120–129 mm Hg	and <80 mm Hg	Elevated blood pressure
130–139 mm Hg	or 80–89 mm Hg	Stage 1 hypertension
≥140 mm Hg	or ≥90 mm Hg	Stage 2 hypertension

Adapted from Whelton et al., 2018.

Etiology: HTN develops in response to an increase in cardiac output or an increase in peripheral resistance. The exact etiology of primary HTN remains unclear but is thought to be a result of genetic and environmental factors that affect cardiovascular and kidney structure and function. Secondary HTN, accounting for about 5% of hypertensive cases, is caused from common conditions such as kidney disease (including renal artery stenosis), sleep apnea, prescription and over-the-counter (OTC) medications, excessive alcohol use, and primary aldosteronism (Whelton et al., 2018). Less common causes of secondary HTN include Cushing's syndrome, hypothyroidism, hyperthyroidism, primary hyperparathyroidism, and acromegaly (Whelton et al., 2018).

Occurrence: Approximately 47% of adults in the United States have HTN (Virani et al., 2021). Prevalence increases with age, especially in those age 65 and older who have a prevalence rate of 77% (Virani et al., 2021). With an aging population, the absolute number of older adults with HTN is expected to grow (Unger et al., 2020).

Age: Until age 64 years, prevalence of HTN is higher in men than women, yet women have a higher prevalence than men in those 65 years of age and older (Virani et al., 2021).

Ethnicity: HTN is more common and develops at a younger age in Black people in the United States as compared to Whites and Hispanics (Virani et al., 2021).

Contributing Factors: Contributing factors in the development of HTN include genetics, obesity, stress, lifestyle factors, and loss of elasticity in blood vessels. Aging is also a major contributing factor to HTN. As one ages, pulse pressure increases as changes in the arterial vessel structure and function occur (Pont & Alhawassi, 2017). Vascular resistance increases as vascular walls become stiff and less compliant. Structural changes within arterial endothelial also occur contributing to arterial stiffness. Older adults are also more salt sensitive due to reduced sodium excretion. This increased salt sensitivity is caused by a decline in kidney function and reduced generation of natriuretic substances (such as prostaglandin E2 and dopamine), resulting in elevated blood pressure (Pont & Alhawassi, 2017). An increased prevalence of comorbid conditions (such as declining heart and kidney function, diabetes, and glucose intolerance) are also contributing factors to

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vascular dysfunction and corresponding BP elevation in older adults (Pont & Alhawassi, 2017). Progressive kidney dysfunction and autonomic nervous system sensitivity that occur with aging also influence response to treatment.

Diagnostic Tests: All adults 18 years and older without known HTN should be screened for elevated BP (USPSTF et al., 2021). To diagnose HTN the provider should use an average of two or more readings obtained on two or more occasions (USPSTF et al., 2021; Whelton et al., 2018;). Out of office BP measurements (ambulatory or home BP monitoring) are recommended to confirm the diagnosis of HTN before starting treatment (USPSTF, 2021; Whelton et al., 2018). As part of the evaluation and work-up for primary HTN, the following studies should be considered:

- Comprehensive metabolic profile (CMP) (sodium, potassium, serum creatinine, estimated glomerular filtration rate, and fasting glucose are the priority)
- Complete blood count (CBC)
- Lipid panel
- Thyroid-stimulating hormone (TSH) levels with reflex to T4 if abnormal
- Urinalysis (dipstick urine test as a backup) to evaluate urinary albumin to creatinine ratio
- 12-lead electrocardiogram (ECG) (for detection of atrial fibrillation, left ventricular hypertrophy, ischemic heart disease)
- Echocardiogram and uric acid level (Unger et al., 2020; Whelton et al., 2018)

Differential Diagnosis: Differential diagnoses to consider are secondary causes of HTN such as substance/drug-induced HTN, advanced kidney disease, obstructive sleep apnea, hyperaldosteronism, hypothyroidism or hyperthyroidism, hyperparathyroidism, and Cushing's syndrome (Whelton et al., 2018). Because secondary causes of HTN are rare and less common in older adults, testing for secondary causes is generally not warranted unless the patient has resistant HTN, an acute rise in BP from previously controlled BP, hypertensive urgency and emergency, or strong clinical findings that suggest a secondary cause (Unger et al., 2020). The most common secondary causes in adults 65 years and older are renal artery stenosis (secondary to atherosclerosis) and kidney failure (Charles et al., 2017).

Accurate measurement of BP is important to the identification of patients who would benefit from better BP control. Providers should use an automated BP device (versus taking BPs manually) because results more closely align with BPs on a daily basis (Muntner et al., 2019). Using the correct size BP cuff is important. The most common cause of measurement error is using the wrong size BP cuff (Muntner et al., 2019). A BP cuff that is too small may falsely elevate BP; whereas a cuff that is too large may result in a falsely low BP measurement (Muntner et al., 2019).

Obtaining BP readings outside of the clinical setting is important to assess for white-coat effect, masked HTN, orthostatic hypotension, or postprandial hypotension, which provides an opportunity to improve BP control without overtreating. White-coat HTN in older adults is defined as having an elevated BP only in the office with a nonelevated ambulatory or home BP (Unger et al., 2020; USPSTF et al., 2021). White-coat HTN indicates an intermediate cardiovascular risk, somewhere between patients who are normotensive and those with sustained HTN (Unger et al., 2020). If the total cardiovascular risk is low and there is no evidence of end organ damage, lifestyle modifications are generally the mainstay of treatment (pharmacological treatment is not usually indicated) (Unger et al., 2020).

Alternatively, masked HTN occurs when office BPs are nonelevated, yet out-of-the-office (ambulatory or home) BPs are elevated (Unger et al., 2020). Patients with masked HTN have approximately the same risk of cardiovascular events as those with sustained HTN (Unger et al., 2020). In this situation repeated out-of-the-office readings are needed to confirm the diagnosis of HTN and pharmacological therapy (in addition to lifestyle modifications) is usually indicated to normalize out-of-the-office readings (Unger et al., 2020).

Orthostatic hypotension is defined as a significant fall in BP when moving from a supine or sitting to a standing position and may occur in up to 40% of older adults with cardiovascular risk factors (Setters & Holmes, 2017). Orthostatic hypotension may result from reduced baroreflex sensitivity with age and loss of artery compliance, hypovolemia, or polypharmacy (Oliveros et al., 2019; Shaw et al., 2019). Because orthostatic hypotension is a significant risk factor for falls and fractures in older adults, screening for orthostatic hypotension is an important part of the provider's work-up for HTN, especially for those with dizziness, light-headedness, or unsteadiness when standing up (Shaw et al., 2019). Orthostatic testing involves measuring BPs in two different body positions (most commonly sitting then standing). Orthostatic hypotension is present with a decrease in systolic pressure of 20 mm Hg or a decrease in diastolic pressure of 10 mm Hg within 3 minutes of standing when compared with BP from a sitting or supine position (Shaw et al., 2019).

Postprandial hypotension, an often underrecognized cause of syncope in older adults, is another important consideration in the work-up for HTN (Oliveros et al., 2019). Postprandial hypotension, defined as a drop in SBP by 20 mm Hg within 2 hours of a meal, increases the risk for falls in older adults (Trahair et al., 2017). Approximately 25% of healthy older adults experience postprandial hypotension, which increases to about 40% in those who live in aged care facilities (Trahair et al., 2017). Ambulatory BP monitoring can help diagnosis postprandial hypotension (Oliveros et al., 2019). Prevention can be addressed by recommending increased water intake before meals and eating six smaller meals as opposed to three larger meals (Oliveros et al., 2019).

Although a single, accurately measured BP may be a predictor of future cardiovascular risk, the International Society of Hypertension (Unger et al., 2020) and the USPSTF et al. (2021) recommend obtaining out-of-the-office BP readings in addition to those taken in the clinical setting for diagnostic confirmation before starting pharmacological treatment. Ambulatory or home BP monitoring are a better predictor of cardiovascular risk and/or target organ damage as compared to using one-time office readings (Whelton et al., 2018). In addition, home BP monitoring, along with office monitoring, optimizes patient engagement with shared decision making and treatment adherence. However, the provider should assess the patient or caregiver's capability of doing home BP monitoring and provide adequate instructions.

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TABLE 10-3 2017 ACC/AHA Guidelines for the Treatment of Hypertension in Adults

Normal blood pressure	Evaluate yearly.
Elevated blood pressure or stage 1 hypertension with estimated cardiovascular risk less than 10%	Start treatment with nonpharmacological interventions and reevaluate in 3 to 6 months. Nonpharmacological interventions should include weight loss, heart healthy diet, sodium reduction, potassium supplement unless contraindicated due to chronic kidney disease or use of drugs that inhibit potassium excretion, increased activity, moderation in alcohol consumption, and smoking cessation. Goal of treatment <130/80 mm Hg.
Stage 1 hypertension with estimated cardiovascular risk 10% or greater	Initial treatment should include nonpharmacological interventions and antihypertensive drug therapy and reevaluate in 1 month. Goal of treatment <130/80 mm Hg.
Stage 2 hypertension	Initial treatment should include nonpharmacological interventions and antihypertensive drug therapy with two agents of different classes and reevaluate in 1 month. Goal of treatment <130/80 mm Hg.

Adapted from Whelton et al., 2018.

Treatment: The ACC/AHA guidelines incorporated new information regarding BP-related risk factors for cardiovascular disease and new BP thresholds for initiating antihypertensive drug therapy (Whelton et al., 2018). Based on these guidelines, BP targets for treatment should be SBP less than 130 mm Hg and DBP less than 80 mm Hg. These same targets are used for adults aged 65 or older who are noninstitutionalized, ambulatory, and community-dwelling (Whelton et al., 2018). However, for adults aged 65 years or older who have complex comorbid conditions and/or limited life expectancy (regardless of whether they are community-dwelling or residing in long-term care facilities) treatment should be based on clinical judgment, goals of care, and a team approach to determine risk/benefit for intensity of BP targets and choice of antihypertensive medications (Table 10-3) (Whelton et al., 2018).

The optimal BP target for older adults remains controversial in the literature, especially for those 70 years or older. Findings from a 2019 literature review of trials that tested various BP targets in adults aged 70 or older found benefits with a minimal SBP control of less than 150 mm Hg, with addition benefits being noted for those with SBP less than 120 mm Hg (Alsarah et al., 2019). Notably, the SPRINT study, which enrolled adults 70 years and older, found that intensive SBP control (<120 mm Hg) versus standard SBP control (<140 mm Hg) reduced cardiovascular disease by 33% and death by 32% without increasing the risk of falls, fractures, or kidney failure (Alsarah et al., 2019). A substudy of the SPRINT also found that intensive SBP reduction was associated with a significant reduction in the risk of mild cognitive impairment (Del Pinto et al., 2021). However, it is important to avoid hypotension (due to marked orthostasis or excessive BP variability) in older adults to prevent cerebral hypoperfusion resulting in negative cognitive effects (Del Pinto et al., 2021).

Guidelines from several American societies and the 2020 International Society of Hypertension guidelines (Unger et al., 2020) recommend that treatment goals in older adults be based on the patient's BP level and their overall cardiovascular risk. Because most older adults have a history of CVD or are determined to be high-risk based on risk calculators, a BP target of 130/80 mm Hg is reasonable. Regardless, management of HTN in older adults in the real world can be challenging and should be individualized.

Reaching and maintaining BP treatment goals in older patients also comes with challenges. Intensive BP lowering can result in dizziness or falls in older adults. Antihypertensive therapy in older adults may also result in polypharmacy, which increases the risk of side effects, adverse drug reactions (including drug-drug and drug-disease interactions), and cost (Reeve et al., 2020). Studies indicate that as the number of medications increase, patient adherence and quality of life (QOL) decrease, especially in older adults (Reeve et al., 2020). It is important to complete a medication reconciliation during each visit and specifically ask about how prescriptions are being filled and medications are being taken. Asking, "How do you take this medication?" will provide more information than asking, "Do you take this?" If possible, prescribing once-a-day treatments or single pill combinations to reduce the number of medications and the frequency of dosing supports medication adherence (Unger et al., 2020).

Hypertension in older adults is treated with the same medications as with younger patients, but the provider must consider age-related changes in metabolism and pharmacodynamics (Oliveros et al., 2019). Providers should first consider nonpharmacological interventions for BP reduction such as salt reduction, a healthy diet such as the DASH eating plan, weight loss (if overweight or obese), moderate consumption of alcohol, regular physical activity, smoking cessation, and reduction of stress (Unger et al., 2020).

When initiating antihypertensive drug therapy, first-line agents include thiazide diuretics, calcium channel blockers (CCBs), and angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin II receptor blockers (ARBs) (Unger et al., 2020; Whelton et al., 2018). Chlorthalidone is the preferred diuretic because of long half-life and proven reduction of CVD risk (Whelton et al., 2018). Loop diuretics and alpha blockers should be avoided because of their increased risk of falls with older patients (Oliveros et al., 2019). There is evidence that ACEIs and ARBs exert a protective effect on cognition for older adults (Del Pinto et al., 2021). However, simultaneous use of an ACEI and an ARB is contraindicated due to the increased risk of hyperkalemia or worsening kidney function (Whelton et al., 2018). Beta blockers are not considered first-line therapy for HTN because they do not have a strong antihypertensive effect. They may be considered in those with other comorbidities such as coronary artery disease (CAD) or HF. There is a risk that they may worsen cardiovascular outcomes in adults older than 60 years (Oliveros et al., 2019). The goal of the 2017 ACC/AHA guidelines is to facilitate evidence-based practice in the management of HTN in adults (Table 10-4).

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TABLE 10-4 Evidence-Based Dosing for Antihypertensive Agents

MEDICATION	STARTING DAILY DOSE	TARGETED DOSE IN RANDOMIZED CONTROLLED TRIALS
Thiazide Diuretics		
Hydrochlorothiazide	12.5–25 mg	25–50 mg
Chlorthalidone	12.5–25 mg	12.5–25 mg
Chlorothiazide	12.5 mg	12.5–25 mg
Indapamide	1.25 mg	1.25–2.5 mg
ARBs (examples)		
Lorsartan	50 mg	100 mg
Valsartan	40–80 mg	160–320 mg
ACEIs (examples)		
Enalapril	5 mg	40 mg
Lisinopril	10 mg	40 mg
CCBs (examples)		
Amlodipine	2.5 mg	10 mg
Diltiazem ER	120–180 mg	360 mg
Beta Blockers (examples)		
Metoprolol	50 mg	100–200 mg
Atenolol	25–50 mg	100 mg

Source: *Whelton et al., 2018.*

Medications should be started at the lowest dose and an assessment of orthostatic hypotension should be obtained as doses are gradually increased to meet the targeted BP goal. In addition, kidney function should be assessed at baseline and periodically to detect possible increases in creatinine or estimated glomerular filtration rate (GFR), especially if the patient becomes hypovolemic, increasing the likelihood of renal hypoperfusion (Oliveros et al, 2019). Most older adults will require more than one medication along with lifestyle changes to reach the desired BP goal (Unger et al., 2020). Specific comorbid illnesses may guide the initial and subsequent choice of drug therapy. For example, ACEIs or ARBs are recommended for patients with kidney disease and/or diabetes (Unger et al., 2020).

Follow-Up: Follow-up is important, as the majority of patients with HTN are not adequately controlled. Per ACC/AHA guidelines, after HTN treatment has been started, low-risk adults with elevated BP or stage 1 HTN with low cardiovascular risks should be reevaluated in 3 to 6 months (Whelton et al., 2018). Adults with stage 1 and stage 2 HTN with high cardiovascular risks should be reevaluated within 1 month (Whelton et al., 2018). Comorbid conditions such as diabetes, HF, and chronic kidney disease will influence the frequency of follow-up visits.

Sequelae: Uncontrolled HTN is associated with serious long-term complications, such as left ventricular hypertrophy, HF, stroke, and kidney disease (Unger et al., 2020).

Prevention/Prophylaxis: One of the primary preventive measures for HTN is lifestyle modification. Excess weight, excess sodium intake, inadequate physical activity, smoking, inadequate intake of fruits and vegetables, and excessive alcohol consumption are all modifiable factors that can contribute to the onset of HTN (Unger et al., 2020).

Referral: Providers should consider referring to a HTN specialist when the BP goal cannot be attained within 6 months, if a secondary cause of HTN is suspected, or in the management of complicated patients who may benefit from consultation (Whelton et al., 2018).

Education: Patient education is important in preventing HTN and/or adhering to treatment once diagnosed. Lifestyle modifications and medication adherence must be reinforced with every patient. There are many patient-education resources available for health-care professionals. The AHA has disease-specific pocket guides available for health-care professionals to give to their patients, or patients can be referred to their Web site. Several online subscription services for health-care professionals also include patient education materials for HTN.

Providers should refer to evidence-based guidelines, such as those provided by ACC/AHA, when assessing and treating older adults with HTN, but recommendations are not a substitute for clinical judgment for individual patients. Older adults often have comorbid conditions or lifestyle practices that may impact treatment outcomes. Balancing competing risk factors for HTN-related risk of stroke, MI, and HF with treatment-related risks, such as fall-related fractures and adverse reactions to medications, is challenging and requires a patient-centered approach to treatment in older adults.

Clinical Recommendation	Evidence Rating	References
In patients 18 years and older, BP screening should be done annually.	A	U.S. Preventive Services Task Force (USPSTF) et al., 2021
BP measurements from outside the clinical setting should be obtained for diagnostic confirmation before starting treatment.	A	USPSTF et al., 2021
In patients older than 50 years, SBP more than 140 mm Hg is a much more important risk factor for cardiovascular disease than DBP.	A	Campbell-Scherer et al., 2017
Self-monitoring of BP is a practical way to assess differences between out of office and office readings.	B	Campbell-Scherer et al., 2017

Continued

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Clinical Recommendation	Evidence Rating	References
Most patients with hypertension have primary hypertension, and more extensive testing for secondary hypertension is not necessary unless BP control is not achieved or if the patient has symptoms of catecholamine excess, bruits, or unprovoked hypokalemia.	B	Campbell-Scherer et al., 2017
Lifestyle modification (smoking cessation, sodium restriction, exercise, weight control, etc.) lowers BP and should be encouraged in all patients with all stages of hypertension.	A	Campbell-Scherer et al., 2017
Thiazide diuretics (e.g., chlorthalidone and hydrochlorothiazide) are the drugs of first choice for most patients given their enormous cost-effectiveness advantage and lack of evidence of superiority of any other medications.	A	Campbell-Scherer et al., 2017
While thiazide diuretics are the cornerstone for treating hypertension, patients with diabetes, chronic kidney disease, HF, and coronary artery disease should have tailored treatment.	B	Campbell-Scherer et al., 2017
Reducing the number of daily doses increases adherence to BP lowering medication.	A	Campbell-Scherer et al., 2017

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ISCHEMIC HEART DISEASE

Signal Symptoms: Angina pectoris and or anginal equivalent (shortness of breath/dyspnea, diaphoresis, extreme fatigue, or pain at site other than the chest) is the initial manifestation of ischemic heart disease (IHD). Typical angina is substernal chest discomfort associated with physical exertion or emotional stress and relieved with rest or nitroglycerin (Harber & Brenner, 2021). Women report epigastric discomfort; nausea; radiation of discomfort to the arms, neck, and interscapular areas; dyspnea; and fatigue (Antman & Loscalzo, 2018).

Description: IHD is also referred to as coronary artery disease (CAD) and occurs when there are one or more signs or symptoms of inadequate supply of blood to the myocardium. The most common problems resulting in IHD are related to obstruction of the epicardial coronary arteries due to atherosclerosis. Angina pectoris occurs when myocardial oxygen demand exceeds oxygen supply. Patients are considered stable when symptoms are manageable with either medical or revascularization therapy (Antman & Loscalzo, 2018). IHD is a chronic disorder that typically cycles through defined phases: asymptomatic, stable angina, accelerating angina, and acute coronary syndrome (ACS)/unstable angina/acute myocardial infarction (MI). The progression of the disease is not necessarily linear (Antman & Loscalzo, 2018).

Etiology: Atherosclerosis involving the coronary arteries is the common etiology of IHD. Evidence supports a multifactorial pathophysiology of coronary atherosclerosis that includes obstruction of the coronary arteries, reducing the quantity of oxygen-rich blood to the myocardium, and dysfunction of the coronary microvasculature and endothelium (Harber & Brunnell, 2021; Severino et al., 2020).

Occurrence: Cardiovascular disease (CVD) is the number one cause of death in both men and women. Among persons 55 to 85 years of age, approximately 21.5% of men and 15.3% of woman have IHD. Men have CVD at a younger age. Women lag behind men by 10 years. In those 40 to 59 years of age, men 6.3%, women 5.6%; in those 60 to 79 years of age, men 19.9%, women 9.7%; and in those 80 years of age and older, men 32.2%, women 18.8%. (Rodgers et al., 2019)

Deaths attributable to CVD steadily increased during the 1900s to the 1980s and declined into the 2010s, but they have increased over the last decade (Kahn et al., 2020; Virani et al., 2021). Recent studies (Arnett et al., 2019) state one in three deaths each year are caused by CVD. As of 2019, the annual incidence of new cases of MI and cerebrovascular accident (CVA) in the United States is 580,000 and 610,000, respectively (U.S. Preventative Services Task Force [USPSTF], 2019). Silent MIs are estimated to involve 160,000 additional persons (Gul & Markaryus, 2021). Mean predicted 10-year risk for CVD among adults aged 30 to 74 years has decreased from 7.2% during 1999 to 2000, to 6.5% during 2009 to 2010.

Age: The prevalence of CVD increases with age. The average age at first MI is 65.1 years for men and 72 years for women.

Ethnicity: In a meta-analysis involving 17 population-based cohorts worldwide, 60,211 participants without CVD at baseline were studied. The 10-year event rate for formation of carotid intima-media thickness was 6.7% in Asians, 7.8% in Hispanics, 8.1% in Whites, and 9.2% in Blacks. Ethnicity appears to significantly modify the association between risk factors and atherosclerotic disease (Willeit et al., 2020). The association between increase in age and atherosclerotic

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disease was weaker in Black and Hispanic populations. SBP elevations in Asians were strongly related to onset of disease. HDL cholesterol and smoking were associated less with disease onset in Black populations (Chi et al., 2020).

Contributing Factors: In the absence of an established model to predict outcome, consider the following risks:

1. Sociodemographic: Age is the single, strongest determinant of survival. Sex and ethnicity have fewer effects on risk. Lower socioeconomic status is associated with worse outcome.
2. Cardiovascular: Smoking, HTN, dyslipidemia, family history of premature CAD, obesity, and sedentary lifestyle have the greatest risk of complications.
3. Coexisting medical conditions: Diabetes, chronic kidney disease, chronic pulmonary disease, and malignancy influence the prognosis.
4. Cardiovascular comorbidities: Heart failure (HF), peripheral artery disease, and cerebrovascular disease are strong risk factors for mortality.
5. Psychosocial characteristics: Depression is strongly associated with worse survival rates. Poor social support, poverty, and stress are associated with poor outcome.
6. Health status: Patient's symptoms, functional capacity, and quality of life (QOL) are associated with poor survival and incidence of ACS.
7. Anginal frequency: The more frequent the angina, the stronger prediction of ACS and hospitalization.
8. Cardiac disease severity: The degree and distribution of stenosis are meaningful predictors of outcome (Nowbar et al., 2019).

Signs and Symptoms: A detailed assessment of chest pain includes the quality, location, severity, and duration of pain; radiation; associated symptoms; and provoking and alleviating factors. The quality of chest pain associated with IHD is most often described as squeezing, gripping, suffocating, or heavy. Women and older adults can present with atypical symptoms such as nausea, vomiting, mid-epigastric discomfort, or sharp pain. Anginal pain typically lasts minutes; is in the substernal area with pain that may radiate to the neck, jaw, epigastrium, or arms; often is aggravated by exertion or emotional stress; and relieved with rest or nitroglycerin. Patients with angina must be categorized as stable or unstable. Unstable angina is defined as new onset increasing in frequency, intensity, duration, or at rest.

Physical examination may be normal or nonspecific. The patient may present with HF, valvular disease, or cardiomyopathy. Bruits over vascular areas and/or diminished pulses might suggest vascular disease. Elevated blood pressure (BP) or xanthomas (lesions of the skin containing cholesterol and fat) may indicate risk factors for IHD (Antman & Loscalzo, 2018; Dababneh & Goldstein, 2021).

Diagnostic Tests: A resting electrocardiogram (ECG) is the initial test, followed by stress testing. See table below.

Differential Diagnosis: Aortic dissection, pericarditis, pulmonary embolism (PE), pneumothorax, pneumonia, pleuritic, esophagitis, spasm, reflux, biliary colic, cholecystitis, cholelithiasis, peptic ulcer, pancreatitis, costochondritis, fibrositis, rib fracture, herpes zoster, anxiety, panic disorder, affective disorders (anxiety/depression) (Antman & Loscalzo, 2018).

A resting ECG is recommended in patients when there is suspected cardiac cause of chest pain (Evidence Rating B). Those with evidence of prior MI, especially Q waves in multiple leads or an R wave in V1; persistent ST-T-wave inversions particularly in leads V1 to V3; left bundle-branch block or bifascicular block, second- or third-degree atrioventricular block, or ventricular tachycardias or hypertrophy have a worse prognosis than those with a normal ECG (Fihn et al., 2012).

When the evaluation is complete, the determination of the probability of IHD is sufficient to recommend further testing. The typical angina pain and the older age of the patient have a high likelihood of IHD. Diabetes has the greatest influence on increasing the probability of IHD (Antman & Loscalzo, 2018).

For those who have suspected IHD and a prior MI, Q waves or symptoms of HF, complex ventricular arrhythmias, or an undiagnosed heart murmur, an echocardiography to evaluate the left ventricular (LV) systolic and diastolic function and heart structures is recommended (Antman & Loscalzo, 2018).

TEST	RESULTS INDICATING DISORDER
ECG	ST-segment depression or elevation or T-wave inversion in the absence of left ventricular hypertrophy supports the diagnosis of ischemia
	Q waves may be evidence of an old MI
Exercise stress testing	Reproduces ischemic symptoms
	Defects in myocardial perfusion with exercise
	Cardiac risk identified in patients with a decrease in the BP, S_3, crackles, or prolonged down-sloping ST-segment depression after exercise
Myocardial perfusion imaging	Perfusion defects
	Left ventricular dysfunction
Echocardiogram	Assesses the severity of left ventricular dysfunction
Stress echocardiogram	Multiple reversible wall motion abnormalities
Cardiac catheterization	For patients who fail pharmacological therapy, have had an MI, or have unstable angina, to determine the severity of disease

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If there is a probability that IHD may be present, stress testing is the most common noninvasive test used to diagnose IHD. Stress testing is used to induce ischemia either by exercise or pharmacological stress agents. However, the production of ischemia is dependent on the stress imposed and submaximal exercise testing can fail to produce ischemia. Coronary artery stenosis under 70% may be undetectable. For those able to exercise, standard exercise ECG testing is recommended. The patient must have an interpretable ECG and a moderate physical ability to exercise. For those unable to exercise, pharmacological stress with nuclear myocardial perfusion imaging (MPI) or echocardiography is recommended.

Those patients who have survived sudden cardiac death, life-threatening ventricular arrhythmias, or HF should undergo coronary angiography (Antman & Loscalzo, 2018). Angiography is useful in patients with unacceptable ischemic symptoms despite guideline-directed medical therapy (Antman & Loscalzo, 2018). However, it should not be offered to those who are unwilling or are not candidates for revascularization.

Treatment: Details of treatment are noted in the following tables.

Follow-Up: See patient at regular intervals for chronic health management; instruct in emergency measures and lifestyle management.

Sequelae: IHD remains a major public health problem with more than 9 million people with angina worldwide. Survival rates of patient have been improving; however, it is still the number one cause of death in men and women. Patients

Medical Therapy to Prevent MI and Death

Clinical Recommendation	Evidence Rating	References
Cholesterol management		
Lifestyle modification including physical activity and weight management.	B	Fihn et al., 2012,2014 Braun et al., 2018
Dietary therapy inclusive of reduction of saturate fats of <7% of total calories, trans fatty acids to <1% of total calories, and cholesterol to <200 mg/day.	B	Fihn et al., 2012,2014 Braun et al., 2018
Moderate or high dose of a statin should be prescribed if not contraindicated.	A	Fihn et al., 2012, 2014 Braun et al., 2018
For those who do not tolerate statins, bile acid sequestrants, niacin, or both are reasonable.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Blood Pressure Management		
Lifestyle modification including weight control, physical activity, alcohol moderation, sodium reduction; increased consumption of fresh fruits, vegetables, and low-fat dairy products.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Antihypertensive drug therapy should be started for BP 140/90 mm Hg or higher.	A	Fihn et al., 2012, 2014 Braun et al., 2018
Diabetes Management		
For those with short duration of diabetes, a goal Hb A1c of 7% or less.	B	Fihn et al., 2012, 2014 Braun et al., 2018
An Hb A1c between 7% and 9% is reasonable for patients according to age, history of hypoglycemia, presence of microvascular or macrovascular complications, or presence of coexisting medical conditions.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Therapy with rosiglitazone should not be initiated.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Physical Activity		
30–60 minutes of moderate-intensity aerobic activity at least 5 days a week.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Physical activity history and an exercise test to guide prognosis and prescription.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Cardiac rehabilitation and physician-directed, home-based programs.	A	Fihn et al., 2012, 2014 Braun et al., 2018
Complementary resistance training at least 2 days per week.	C	Fihn et al., 2012, 2014 Braun et al., 2018

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Medical Therapy to Prevent MI and Death		
Clinical Recommendation	**Evidence Rating**	**References**
Weight Management		
Body mass index (BMI) and/or waist circumference should be assessed at every visit, and encouragement for weight maintenance or reduction to maintain or achieve BMI 18.5 to 24.9 and a waist circumference less than 40 inches in men and less than 35 inches in women.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Initial goal of weight loss should be to reduce body weight by approximately 5%–10% from baseline.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Smoking Cessation		
Smoking cessation and avoidance of exposure to secondhand smoke.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Management of Psychological Factors		
Screen for depression.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Alcohol Consumption		
Limit alcohol to 1 drink (4 ounces of wine, 12 ounces of beer, or 1 ounce of spirits) a day.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Antiplatelet Therapy		
Aspirin 75–162 mg daily in the absence of contraindication.	A	Fihn et al., 2012, 2014 Braun et al., 2018
Treatment with clopidogrel when ASA is contraindicated.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Dipyridamole is not recommended.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Beta Blocker		
Beta blocker therapy should be started and continued for 3 years in all patients with normal LV function after MI or ACS.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Beta blocker therapy should be used in all patients with LV systolic dysfunction (EF ≤40%) with HF or prior MI (carvedilol, metoprolol succinate, or bisoprolol have been shown to reduce risk of death).	A	Fihn et al., 2012, 2014 Braun et al., 2018
Beta blockers considered for chronic therapy for all other patients with coronary or other vascular disease.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Renin-Angiotensin-Aldosterone Blocker Therapy		
ACEIs for patients who have hypertension, diabetes, LVEF ≤40%, or chronic kidney disease.	A	Fihn et al., 2012, 2014 Braun et al., 2018
ARBS for patients with hypertension, diabetes, LV systolic dysfunction, or chronic kidney disease who are intolerant of ACEIs.	A	Fihn et al., 2012, 2014 Braun et al., 2018
Influenza vaccine is recommended.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Estrogen therapy; vitamins C and E and beta-carotene, folate, or vitamin B_6 and B_{12}, chelation therapy, garlic, coenzyme Q10, selenium or chromium.	No benefit	Fihn et al., 2012, 2014 Braun et al., 2018

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Medical Therapy for Symptom Relief

Clinical Recommendation	Evidence Rating	References
Anti-Ischemic Medications		
Beta blockers for initial therapy for symptom relief.	B	Fihn et al., 2012, 2014 Braun et al., 2018
CCBs or long-acting nitrates for symptom relief in those intolerant of beta blockers or contraindicated.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Sublingual nitroglycerin spray for immediate relief of angina.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Long-acting nondihydropyridine calcium channel blockers instead of beta blockers as initial therapy.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Ranolazine as a substitute for beta blockers if initial treatment with beta blockers leads to unacceptable side effects or is ineffective.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Ranolazine in combination with beta blockers if beta blockers alone are not successful.	A	Fihn et al., 2012, 2014 Braun et al., 2018

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Medical Therapy for Symptom Relief in Patients With Refractory Angina

Clinical Recommendation	Evidence Rating	References
Enhanced external counterpulsation (EECP)	B	Fihn et al., 2012, 2014
Spinal cord stimulation	C	Fihn et al., 2012
Transmyocardial revascularization	B	Fihn et al., 2012
Chelation therapy	B	Fihn et al., 2014

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Revascularization Decision to Improve Survival

Clinical Recommendation	Evidence Rating	References
Recommended in patients with unprotected left main or complex CAD.	C	Fihn et al., 2012, 2014 Braun et al., 2018
CABG to improve survival in patients with significant (≥50% diameter stenosis) left main.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Percutaneous coronary angioplasty and intervention (PCI) is an alternative to CABG in stable patients with significant unprotected left main who may have low risk of PCI complications or have a significantly increased risk of adverse surgical outcomes.	B	Fihn et al., 2012, 2014 Braun et al., 2018
CABG is beneficial in patients with significant (≥70) stenosis in two major coronary arteries with severe or extensive myocardial ischemia.	B	Fihn et al., 2012, 2014 Braun et al., 2018
CABG is reasonable in patients with mild to moderate LV systolic dysfunction (EF 35%–50%) and significant stenosis when viable myocardium is present.	B	Fihn et al., 2012, 2014 Braun et al., 2018
CABG is recommended over PCI to improve survival in patients with diabetes, multivessel CAD, particularly if a left internal mammary artery (LIMA) graft can be used on the left anterior descending artery (LAD).	B	Fihn et al., 2012, 2014 Braun et al., 2018

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with symptoms of angina have MIs at a rate of 3% to 3.5% per year (Benjamin et al., 2019; Nowbar et al., 2019). Many people with IHD do not return to work after coronary revascularization and 15% to 20% rate their health as fair or poor. IHD continues to be associated with considerable morbidity despite the decrease in mortality rate. The costs of caring for patients with IHD are estimated at $156 billion in the United States for both direct and indirect costs.

Prevention/Prophylaxis: Healthy, active lifestyle; smoking cessation, weight control and control of HTN, diabetes, and cholesterol.

Referral: Patients with IHD will be comanaged with cardiology. There are other medical conditions, such as HIV and connective tissue disease, which may result in increased IHD. These patients will be comanaged with infectious disease and rheumatology to provide optimum care of these disorders. Ongoing reassessment of the patient's adherence to the therapy, adverse events, treatment goals, effectiveness of interventions, and risk factor reduction should be done. For those who have not met their goals, especially in the management of diabetes, depression, smoking cessation, and chronic kidney disease, referral to an appropriate specialist may be considered. If angina becomes unstable, the patient should know to seek emergency medical care (Braun et al., 2018; Fihn et al., 2014).

Education:

Clinical Recommendation	Evidence Rating	References
Individualized Education Plan Including:		
Explanation of medication management and cardiovascular risk reduction strategies.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Comprehensive review of therapeutic options.	B	Fihn et al., 2012, 2014 Braun et al., 2018
Description of appropriate levels of exercise.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Information on recognition of worsening cardiovascular symptoms and appropriate actions.	C	Fihn et al., 2012, 2014 Braun et al., 2018
Adherence to diet that is low in saturated fat, cholesterol and transfat; high in fresh fruits, whole grains, and vegetables; reduction in sodium intake.	B	Fihn et al., 2014 Braun et al., 2018

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MYOCARDIAL INFARCTION

Signal Symptoms: Typical symptom is prolonged chest pain (more than 20 minutes' duration); atypical symptoms include shortness of breath, neurological symptoms (confusion, weakness), fatigue, gastrointestinal symptoms, and symptoms of or worsening heart failure (HF).

Description: Boyle (2017) defines myocardial infarction (MI) as a pathological clinical episode, triggered by myocardial ischemia, manifesting in myocardial injury or necrosis. MIs can be classified as acute ST elevation MI (STEMI) or non–ST elevation MI (NSTEMI). Essentials of diagnosis may include signal symptoms; chest "pressure" or "dull," "squeezing or aching" sensation; characteristic electrocardiographic changes; elevated biomarkers; troponins; and imaging that may show regional wall motion abnormality with normal wall thickness (Crawford et al., 2018). Thygensen and colleagues (2018) further expanded the definition of MI to include universal MI types (types 1 through 5). Each type has unique criteria, with types 4 and 5 being coronary procedure-related MI. Criteria to differentiate MI from myocardial injury was born out of the need to better define the occurrence of the myocardial event. The term *myocardial injury* should be used when there is evidence of elevated cardiac troponin values, and it is considered acute if it is at least one value above the 99th percentile upper reference limit (URL). The term *acute MI* (types 1, 2, and 3 MI) should be used when there is acute myocardial injury with clinical evidence of acute myocardial ischemia and detection of a rise and/or fall of the troponin values with at least one value above the 99th percentile URL and at least one of the following:

- Symptoms of myocardial ischemia
- New ischemic electrocardiogram (ECG) changes
- Development of pathological Q waves
- Imaging evidence of new loss of viable myocardium or regional wall motion abnormality
- Coronary thrombus found by angiography or on autopsy (autopsy does not apply to type 2 or 3 MIs)
  - Postmortem demonstrating acute atherothrombosis in the artery supplying the infarcted myocardium would meet type 1.

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- Evidence of imbalance of myocardial oxygen supply and demand not related to atherothrombosis meets type 2.
- Cardiac death in patients with symptoms suggestive of myocardial ischemia and presumed new ischemic ECG changes prior to troponin values are available or abnormal meets type 3 criteria.

Criteria for coronary procedure-related myocardial infarction (types 4 and 5) are as follows:

- MI related to percutaneous coronary intervention (4a)
  - MI related to stent thrombosis (4b) or restenosis (4c); both 4b and 4c meet the criteria for a type 1 MI
- MI related to coronary artery bypass grafting (CABG) is termed type 5 and is confirmed by elevation of troponin levels, new ECG changes, loss of viable myocardium, or angiographic flow limiting complications.

(Thygensen et al., 2018).

Etiology: The hallmark of acute coronary syndrome (ACS) is the sudden imbalance between myocardial oxygen consumption and demand, which is usually the result of coronary artery obstruction. This imbalance may also be caused by conditions such as excessive myocardial oxygen demand in the setting of a stable flow-limiting lesion and acute coronary insufficiency due to other causes (e.g., vasospastic angina, coronary embolism, and coronary arteritis). Noncoronary causes of myocardial oxygen supply-demand mismatch include hypotension, severe anemia, hypertension (HTN), tachycardia, hypertrophic cardiomyopathy, severe aortic stenosis, nonischemic myocardial injury, and multifactorial causes that are not mutually exclusive (Crawford et al., 2019; Thygensen et al., 2018).

Atherosclerotic plaque formation has been noted in persons younger than 20 years of age. Gradually, this atherogenic plaque builds up inside the intimal linings of the coronary artery(ies), resulting in both hardening of the arterial walls and narrowing of the coronary vessels. This atherosclerotic plaque contains lipid (cholesterol)–rich content, covered by a fibrous cap, which can ulcerate or fissure. Rupture of this vulnerable plaque can result in thrombosis, which partially or totally occludes the lumen of the affected artery(ies), either at the location where the thrombus formed or further downstream where a smaller artery could be blocked. The results are essentially the same—an abrupt decrease in coronary blood flow to the myocardium, termed *myocardial ischemia.* Prolonged myocardial ischemia can lead to tissue death and MI. Although there are other causes of MI due to reduced myocardial blood flow, including hypotension and prolonged coronary vasospasm, or severe hyperthyroidism (which can increase the heart's demand for oxygen), the most frequent cause of MI is due to atherosclerosis. Another factor that plays an important role in ACS is platelet activation and aggregation (Mechanic et al., 2021). Damaged blood vessels result in exposed collagen fiber in the basement membrane. Platelets subsequently adhere to this collagen fiber and become activated. On activation, platelets then release chemicals, including adenosine diphosphate and thromboxane (a vasoconstrictor), which causes additional platelet aggregation. A platelet plug (or clot) is formed, which decreases blood flow to the blood vessel (Maziar Zafari & Abdou, 2019).

Occurrence: When looking at all-cause mortality, coronary artery disease (CAD) is the most frequent cause of death in the United States. In persons aged 55 to 74 years in the United States, CAD occurs more frequently in men, with a median age of 64.9 years. Before menopause, due to estrogenic cardioprotective effect, women have a lower occurrence of MI than men; however, women of all ages have a greater risk of longer hospitalizations and complications. On average, women develop CAD 10 years later than men and suffer MIs and sudden death 20 years later than men. By age 75, postmenopausal women have an equal risk to men of CAD and MI (Rivera-Bou & Schrage, 2021).

In persons older than 75 years, CAD contributes to significant morbidities and mortality. In persons aged 75 years or older who present with MI, more than 60% have NSTEMI with associated in-hospital mortality, accounting for approximately 80% of all inpatient hospital deaths (Bradley et al., 2019). In addition, persons older than 65 years with MI are associated with higher post-discharge mortality, theoretically because of the higher incidence of diffuse CAD and existing poor myocardial perfusion. Data published by the Centers for Disease Control and Prevention (CDC, 2018, 2019) on coronary disease and MI found that males overall had a significantly higher MI rate than females; however, with successive age-groupings, the prevalence of MIs significantly increased. When identifying level of education with MI and CAD, persons who had less than a high school diploma experienced almost twice the occurrences of these conditions when compared with those who had college education.

Age: In 2010, the prevalence of cardiovascular disease (CVD) was greatest among persons aged 65 years and older (23.4%). Postmortem studies show that coronary atherosclerosis is widespread, even among asymptomatic adults. Aging itself may be a risk factor for MI in both men and women (CDC, 2019).

Ethnicity: The incidences and occurrences of patients having MIs and CVD by race and ethnicity have been reported by the CDC (2018, 2019). Specific groups were identified at increased risk, including those persons who are multiracial, Native Americans, and Alaskan natives, who have substantially higher prevalence of MI than non-Hispanic White or Black Americans (CDC, 2018, 2019). Overall, in patients with NSTEMI, Black patients (when compared to White patients) were younger, with comorbidities, including HTN, renal insufficiency, diabetes, and HF (CDC, 2018, 2019).

Contributing Factors: Risk factors for CAD and MI in older adults are essentially the same as in the younger population. Risk factors include HTN, hyperlipidemia, diabetes, insulin resistance, physical inactivity and sedentary lifestyle, overweight or obesity, family history of heart disease, poor diet, sleep apnea, alcohol, and stress. Cigarette smoking is associated with new coronary events for older adults. The risks of MI drop rapidly after smoking cessation and, at 5 years, the risk for new coronary events is similar to that of a nonsmoker (Virani et al., 2021).

Aging alters the cardiovascular system in ways that reduce cardiac reserve and efficiency, thus compromising the ability to respond to stress or illness. The cardiovascular system becomes less compliant as diastolic filling of the ventricles declines and afterload increases secondary to increased

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stiffness in the ascending aorta. The result is moderate left ventricular hypertrophy, which creates a more precarious balance between myocardial oxygen supply and demand. Other changes in the cardiovascular systems of older adults include decreased responsiveness to beta-adrenergic stimulation, decreased baroreceptor sensitivity, and an increased dependence on a higher end-diastolic volume to maintain cardiac output (Acharya et al., 2019; Walter et al., 2021).

Signs and Symptoms: With advancing age, the presentation of acute MI will be less likely to include the classic symptoms of crushing substernal chest pain, nausea, vomiting, and diaphoresis. Rather, atypical symptoms such as a vague ache or discomfort may be present. Older adults may not recognize that throat, shoulder, arm, jaw, or abdominal pain may be referred cardiac pain or angina equivalent. Dyspnea is the second most common symptom of MI in both younger and older populations. For patients 85 years and older, syncope, acute confusion, or stroke may be the only presenting symptom. Some older adults may present only with faintness, weakness, or restlessness (Acharya et al., 2019).

On physical examination, the patient may be anxious and weak and may appear cyanotic. Arrhythmias may be noted on the ECG. The skin may be diaphoretic, cold, and clammy. Thrills, heaves, and an abnormal point of maximal impulse (PMI) may be palpated. Peripheral pulses may be irregular, slow, fast, or thready. Auscultation may reveal an S_3 or S_4, pericardial friction rub, murmurs, or crackles. The physical examination must focus on ruling out diagnoses other than MI (Johnson & Ghassemzadeh, 2021).

Diagnostic Tests: Along with a chest x-ray examination, complete blood count (CBC), clotting profile, electrolytes, and cardiac biomarkers including troponin, evaluation for acute MI includes serial 12-lead ECGs (Boyle, 2017). Changes on the ECG indicative of STEMI include ST-segment elevation in leads facing the infarction. ST-segment depression is sometimes present. With the increased incidence of NSTEMI, the presence of a single normal ECG does not rule out MI; therefore, serial ECGs are necessary. However, ECG findings may be nondiagnostic or difficult to interpret in older adults because of possible abnormalities, such as left bundle branch block, left ventricular hypertrophy, and previously unrecognized MIs.

In older adults, the cardiac enzyme profile may be atypical. Creatine kinase (CK), an enzyme found in myocardial cells, is released into the bloodstream when cells are damaged, approximately 6 to 8 hours after the onset of pain. Because the baseline CK in older adults may be significantly lower than normal, even those with MI may not develop CK levels high enough to be interpreted as abnormal, owing to decreased muscle mass. CK-MB, an isoenzyme of CK, is released on the death of myocardial cells and not during ischemia. The presence of CK-MB is also found in skeletal muscle, which can result in false-positive results from noncardiac conditions such as renal failure, head or chest trauma, pulmonary embolism (PE), acute and chronic muscular disorders, hypothyroidism, or hyperventilation. Therefore, CK-MB measurements do not provide additional information to the algorithms of STEMI and are not preferred over cardiac troponins (Lan et al., 2019). Cardiac troponin T (cTnT) is a cardiac-specific marker for MI, with rises in concentration levels soon after chest symptoms begin (Lan et al., 2019). Although elevations may not occur for 6 to 12 hours after onset of symptoms, in approximately 80% of patients use of cTnT alone can result in a definitive diagnosis of STEMI. Lactate dehydrogenase levels are occasionally useful in patients with delayed presentation because this enzyme remains elevated for several days. Other tests for MI may include echocardiography or stress thallium scans (Gulati et al., 2021)

Differential Diagnosis: The pain from MI can be like that of acute pericarditis, PE, acute aortic dissection, or costochondritis. Many conditions can present as cardiac disease in older adults, including cor pulmonale, pneumonia, esophageal spasm, gastroesphageal reflux disease (GERD), hiatal hernia, gallbladder disease, osteoarthritis of the spine, inflammation at the chondrocostal junction, muscle injury, and panic disorder (Johnson & Ghassemzadeh, 2021; Kumar et al., 2020).

Treatment: The American College of Cardiology (ACC) and American Heart Association (AHA) have examined pharmacological and interventional treatments for acute MI and established guidelines for care. Nitrates, the cornerstone of therapy for ischemic pain, reduce preload and improve coronary perfusion. Chest pain should be treated with sublingual nitroglycerin, repeated three times, 5 minutes apart, unless the patient is hypotensive, has right ventricular infarction, or has aortic stenosis (Gulati et al., 2021). IV nitrates have been shown to limit infarct size and reduce pain, complications, and mortality. IV nitroglycerin is started at 5 mcg/min on an infusion pump and titrated to desired effect. Frequent monitoring is required because harmful effects can be seen if the systolic blood pressure (SBP) drops below 90 mm Hg. Morphine sulfate, 2 to 4 mg IV, repeated at 5- to 15-minute intervals, is also effective for pain relief and can be given with anxiolytics (Gulati et al., 2021). Supplemental oxygen (2 to 6 L/min nasal cannula) should be given if oxygen saturation is less than 94% or arterial oxygen saturations are low.

Thrombolytics. Reperfusion in patients who present to hospitals with percutaneous coronary angioplasty and intervention (PCI) capability has become the standard of care (Gulati et al., 2021). In hospitals without PCI capability and where patients cannot be transferred to a hospital with PCI capability within 90 minutes, treatment with fibrinolytic (thrombolytic) therapy initiated within 30 minutes of presentation should be performed unless contraindicated. The use of thrombolytics in STEMI patients has been shown to decrease mortality by up to 30% (Gulati et al., 2021; Ko et al., 2018). Thrombolytic agents include tissue-type plasminogen (tPA) and streptokinase (SK). Indications for thrombolysis are based on the existence of chest pain and specific ECG changes. Studies show that this therapy is frequently omitted for older adults. Reasons for this include frequent delay in seeking medical care, atypical presentation of MI, and a higher prevalence of NSTEMIs. Fear of hemorrhage following use of thrombolytics must be weighed against the proven gains in survival for all age-groups, especially for those presenting early with MI. A variety of studies suggest that SK may be as beneficial as tPA in treating the older MI patient, which is considerably less expensive (Rivera-Bou & Schrage, 2021).

Aspirin. Aspirin therapy in post-PCI STEMI patients without demonstrated aspirin resistance should be initiated at 162 to 325 mg daily and, depending on the type of stent implanted,

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the recommended maintenance dose to be used with ticagrelor is 81 mg (Gulati et al., 2021). In patients at risk for increased bleeding after stent implantation, lower-dose aspirin is reasonable. Aspirin (non–enteric-coated) should be given as soon as possible if there is no obvious contraindication. Patients taking nonselective NSAIDs (excluding aspirin) and cyclooxygenase-2 inhibitors should have these agents discontinued at the time of presentation with STEMI and not readministered during the course of hospitalization due to increased risk of mortality, reinfarction, myocardial rupture, HF, shock, or HTN (Boyle, 2017).

Thienopyridines. Concurrent use of dual antiplatelet therapy (aspirin and thienopyridines) in MI patients (STEMI or NSTEMI) following PCI with stent implantation is the gold standard for secondary prevention of subsequent cardiovascular events. Use of thienopyridines, including clopidogrel or prasugrel, is important to decrease the risk of death and stroke and to prevent reinfarction or in-stent thrombosis (Johnson & Ghassemzadeh, 2021). Thienopyridines should be initiated as a loading dose early, either before or at the time of primary or nonprimary PCI, and continued for a minimum of 12 months after bare metal stent placement in patients who are not at high risk for bleeding (Howard & Khot, 2021). In patients for whom nonemergent coronary artery bypass is planned, thienopyridine therapy should be discontinued for a minimum of 5 days for those patients receiving clopidogrel and 7 days for those patients receiving prasugrel (Howard & Khot, 2021).

Parenteral anticoagulants are recommended in all patients with ACS or in myocardial patients regardless of whether or not reperfusion therapy was received. Low molecular weight heparin (LMWH), unfractionated heparin, bivalirudin, enoxaparin, or fondaparinux is recommended in patients undergoing PCI (Howard & Khot, 2021). If a CABG is planned, anticoagulants should be withheld for 5 to 7 days before the procedure due to risks of excessive bleeding.

For patients not receiving thrombolytics, low-dose subcutaneous heparin or LMWH is indicated for prophylaxis of deep venous thrombosis. Older adult patients with large anterior MIs and HF, as well as those with documented left ventricular thrombus, should receive full heparin anticoagulation.

Angiotensin-Converting Enzyme Inhibitors (ACEIs). ACEIs reduce mortality in post-MI patients. ACEIs are recommended and should be continued indefinitely for every patient recovering from STEMI and for those with MI with a left ventricular ejection fraction (LVEF) less than 40% and no obvious contraindications to their use. For patients with preserved LVEF with HTN, chronic kidney diseases, or diabetes, ACEIs are recommended unless contraindicated (Bahit et al., 2018).

Angiotensin Receptor Blockers (ARBs). ARBs are recommended in those patients who are intolerant of ACEIs, who have HF with LVEF of 40% or less, or who have HTN.

Aldosterone Blockade. Aldosterone blockade is recommended for post-MI patients without severe renal dysfunction or hyperkalemia, with HF, with LVEF of 40% or less, or with diabetes who are already on a therapeutic dose of ACEI and beta blockade (Bahit et al., 2014).

Beta Blockers. Beta blockers have been shown to limit infarct size, decrease chest pain, improve prognosis, and reverse cardiovascular remodeling. They are generally well tolerated in patients ages 65 to 75 years. However, their use in this population "should be tailored based on other concomitant cardiovascular conditions and completeness of revascularization" (Motivala et al., 2016, p. 1647). Conditions that contraindicate the use of beta blockers in older adults include bronchospastic lung disease, marked bradycardia, hypotension, depression, acute heart failure, and diabetes. Beta blockers "have consistently been shown to improve outcomes in a variety of cardiovascular settings and therefore remain widely used" (Kumar et al., 2020; Motivala et al., 2016, p. 1647).

In acute MI, metoprolol or atenolol is given 2.5 to 5 mg IV every 5 minutes, for a total of 15 mg and 10 mg, respectively. Beta blockers should be initiated in the emergency department before PCI and within 24 hours in patients presenting with STEMI, MI, ACS, or left ventricular dysfunction with or without HF, unless contraindicated. Beta blocker use in this population has increased over time (Ko et al., 2018). Contraindications to beta blocker therapy include HF, evidence for a low cardiac output state, or risk for cardiogenic shock (Mechanic et al., 2021).

Statins and Lipid-Lowering Therapy. A lipid profile that includes total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL), and triglycerides should be performed and assessed on all patients with ACS or MI within 24 hours of admission. Lipid-lowering therapy is recommended before discharge, with the LDL goal to be less than 100 mg/dL, preferably with further LDL reduction to less than 70 mg/dL (Wang et al., 2018). Dietary therapy is recommended for all patients, including consumption of omega-3 fatty acids, weight management, and physical activity.

Calcium channel blockers (CCBs) have limited use in STEMI and NSTEMI patients. Hypotension-induced tachycardia has been associated with the use of short-acting CCBs. Long-acting CCBs should be used sparingly, if needed, with additional precautions in those patients already taking digoxin or beta blockers (Zafari & Yang, 2019).

In terms of interventional management of older adults with MI, guidelines by both the AHA and ACC have established "door to needle" time of less than 30 minutes and "door to balloon" time within 90 minutes of initial presentation to the hospital for the best possible outcomes (Acharya et al., 2019). Percutaneous transluminal coronary angioplasty (PTCA) with PCI may be a valuable alternative in those for whom thrombolytics are contraindicated. CABG is preferred for patients with left main stenosis and those with moderately severe left ventricular depression. Emergency PTCA or CABG in older adult patients presenting with cardiogenic shock or HF is associated with high morbidity and mortality.

Glucose Control. Hyperglycemia (defined as blood sugar greater than 180 mg/dL) in patients with STEMI has been associated with adverse outcomes, including increased morbidity and mortality, as well as prolonged hospitalizations. Maintaining glucose control may decrease the inflammatory response and improve LVEF (Virani et al., 2021).

Follow-Up: Risk stratification for future cardiac events following stabilization from MI is necessary. Tests to evaluate for ischemia or myocardium at risk include low-level exercise test, nuclear perfusion scanning, and dobutamine echocardiography. Left ventricular function can be determined by

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echocardiography or radionuclide ventriculogram. Routine coronary angiography is not recommended for all patients with MI, but should be performed on patients with demonstrable ischemia. Patients at high risk for sudden death from arrhythmias should undergo electrophysiological (EP) evaluation.

Sequelae: Increasing age is associated with more complications after MI, including HF, arrhythmias, PE, cardiogenic shock, cardiac rupture, and death.

Prevention/Prophylaxis: Secondary prevention in the older adult patient includes use of aspirin, beta blockers, and ACEIs, unless there are absolute contraindications to these agents. Lipid-lowering therapy is also beneficial. Reduction of risk factors is necessary. Cardiac rehabilitation can be as beneficial in older MI patients as in younger ones. Emotional support remains important.

Referral: Suspicion of acute MI should prompt transfer of the patient to an environment equipped with cardiac monitoring and the ability to administer advanced cardiac life support. As hospitalization continues, consultation with a variety of disciplines, such as surgery, social work, and physical therapy, may be necessary.

Education: Individualized teaching following MI should be provided to the patient and family using age-specific teaching methods. Teach the basic definitions of CAD, angina, and MI. Patients need information on the healing process following MI, when to return to work or resume normal daily activities, and when to resume sexual relations. Give an exercise prescription. Involve patients and families in a discussion of the psychological adjustment following MI. Encourage risk factor reduction. Health-care practitioners should work with patients to set goals and design plans. Give patients information on community resources, such as the AHA or support groups in their area. Smoking cessation should be strongly encouraged, and pharmacological and nonpharmacological therapies should be discussed. Medication teaching and review are very important. Health-care providers should be aware of all medications prescribed for the patient and any over-the-counter (OTC) medications, including vitamins, minerals, and supplements. Patients should bring in all of their medications at each visit. Teach patients about the desired effects and common side effects of their medications. Emphasize the importance of taking aspirin and anticoagulants as directed to prevent in-stent thrombosis. Review what to do if medication cannot be taken or obtained. Discuss the use of nitrates for any chest pain, but avoid using nitrates in patients taking medications such as sildenafil, tadalafil, or vardenafil because of sudden drops in blood pressure (BP), resulting in hypotension.

Teach older adult patients about altered pain perception that can occur with age and with diseases such as diabetes. Teach patients and their families about warning signs such as chest pain or pressure, shortness of breath, indigestion, choking, sweating, dizziness, palpitations, severe weakness, and loss of consciousness. Establish a clear plan for obtaining prompt medical attention.

Clinical Recommendation	Evidence Rating (COR/LOE)	References
Oxygen		
Administer supplemental oxygen only if $SpaO_2$ is <90%, respiratory distress, or other high-risk features for hypoxia	C	Amsterdam et al., 2014
Nitrates		
Administer sublingual nitroglycerin (NTG) every 5 minutes × 3 for continuing ischemic pain and then assess need for IV NTG.	C	Amsterdam et al., 2014
Administer IV NTG for persistent ischemia, HF, or HTN	B	
Nitrates are contraindicated with recent use of a phosphodiesterase inhibitor.	B	
Analgesic Therapy		
IV morphine sulfate may be reasonable for ongoing ischemic chest pain.	B	Amsterdam et al., 2014
NSAIDs (except ASA) should not be started and should be stopped during hospitalization for non-ST elevation (NSTE)-ACS due to increased risk of MUSE	B	
Beta-Adrenergic Blockers (Beta Blockers [BBS])		
Oral BBs should be started within the first 24 hours if no HF is present or no low-output state, risk for cardiogenic shock, or other contraindications to BB.	A	Amsterdam et al., 2014
Use of long-acting metoprolol succinate, carvedilol, or bisoprolol is recommended for BB therapy with concomitant NSTE-ACS, stabilized HF, and reduced left ventricular (LV) function.	C	
Reevaluate to determine subsequent eligibility in patients with initial contraindication to BBs.	C	
It is reasonable to continue BBs in patients with normal LV function with NSTE-ACS.	C	

Continued

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Clinical Recommendation	Evidence Rating (COR/LOE)	References
Calcium Channel Blockers (CCBS)		
Administer initial therapy with nondihydropyridine CCBs with recurrent ischemia and contraindications to BBs in the absence of LV dysfunction, increased risk for cardiogenic shock, PR interval >0.24 sec, or second- or third-degree AV block without a cardiac pacemaker	B	Amsterdam et al., 2014
Administer oral nondihydropyridine calcium antagonists with recurrent ischemia after use of BBs and nitrates in the absence of contraindications.	C	
CCBs are recommended for ischemic symptoms when BBs are not successful, are contraindicated, or cause unacceptable side effects.	C	
Cholesterol Management		
Initiate or continue high-intensity statin therapy in patient with no contraindications.	A	Amsterdam et al., 2014
Obtain a fasting lipid profile within 24 hr.	C	
Aspirin		
Give non–enteric-coated aspirin to all patients promptly after presentation (162–325 mg).	A	Amsterdam et al., 2014
Aspirin maintenance dose is continued indefinitely (81 mg/day–325 mg/day).	A	
$P2Y_{12}$ Inhibitors		
Give a clopidogrel loading dose followed by daily maintenance dose in patients unable to take aspirin (75 mg/day).	B	Amsterdam et al., 2014
Prescribe clopidigrel or tricagrelor, in addition to aspirin, for up to 12 months for patients treated initially with either an early invasive or initial ischemia-guided strategy.	B	
Continue P2Y (clopidogrel or ticagrelor) for at least 12 months in post PCI with stents.	B	
Ticagrelor is preferred over clopidogrel for patients with early invasive or ischemia guided strategy.	B	
Cardiac Isoenzyme		
Troponin measurement should be done early (within 6 hours of arrival) ideally at presentation and at 3–6 hours after symptoms onset. Troponin T and I should be the only cardiac Isoenzyme to be measured.	A	Amsterdam et al., 2014 Jneid et al., 2017 American Society for Clinical Pathology, 2014–2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. COR = Class (Strength) of Recommendation. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html. For more information about the ACC/AHA rating system, go to www.ahajournals.org

Adapted from Amsterdam E.A., Wenger, N. K., Brindis, R. G., Casey, D. E. Jr., Ganiats, T. G., Holmes, D. R. Jr., Jaffe, A. S., Jneid, H., Kelly, R. F., Kontos, M. C., Levine, G. N. Liebson, P. R., Mukherjee, D. Peterson, E. D., Sabatine, M. S. Smalling, R.W., &. Zieman, S. J. (2014). 2014 AHA/ACC guideline for management of patients with non-ST-elevation acute coronary syndromes. *Journal of the American College of Cardiology, 64*(24), e139–e228; Jneid, J., Addison, D., Bhatt, D. L., Gonarow, G. C., Gokak, S., Grady, K. L., Green, L. A., Heidenreich, P. A., Ho, P. M., Jurgens, C. Y., King, M. L., Kumbhani, D. J., & Pancholy, S. (2017). 2017 AHA/ACC Clinical Performance and quality measures for adults with ST-elevation and non-ST-elevation myocardial infarction: A report of the American College of Cardiology/American Heart Association Task Force on performance measures. *Journal of the American College of Cardiology, 70*(16), 2048–2090.

VALVULAR HEART DISEASE

Signal Symptoms: Asymptomatic in early stage; fatigue and dyspnea are common, progressive valvular heart disease may present with accompanying chest pain, syncope, and heart failure (HF).

Description: Valvular heart disease (VHD) is damage to a valve or valves of the heart, causing cardiac dysfunction. Progressive, symptomatic VHD requires either a surgical or interventional procedure and is not able to be reversed via medical intervention. The most prevalent types of VHD in older adults result from calcific and degenerative valve disease. Valvular abnormalities can also occur secondary to dilated, restrictive, and infiltrative disease, which is often challenging to diagnosis (Falk & Hershberger, 2019). The most prevalent VHD disorders are aortic stenosis (AS), one of the most common valvular abnormalities seen in the aging heart, and mitral regurgitation (MR). Other types of VHD

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include aortic regurgitation (AR), mitral stenosis (MS), and (to a much lesser degree), tricuspid regurgitation (TR). AR can often be present with AS, complicating treatment options (Dewaswalal & Chait, 2021; Wang & O'Brien, 2018).

With the projection of the United States octogenarian population to triple to 32.4 million by 2050, the prevalence and the need for monitoring and treatment of VHD will increase (Kodali et al., 2018). Causes of VHD vary. Congenital conditions at birth can predispose someone to VHD as well as rheumatic heart disease due to strep infection, but incidence has decreased with rapid identification and treatment with antibiotics. Endocarditis can affect the valve leaflets causing VHD. Although IV drug abuse is not common in the older adult, screening for any history of IV drug use at any age is important in the face of VHD. HF, atherosclerosis, aortic aneurysm, hypertension (HTN), and myocardial infarction (MI) are all risk factors for developing VHD. Other causes for VHD include autoimmune disease, lupus, connective tissue disease, Marfan's syndrome, and restrictive heart disease. Amyloidosis must also be considered (Centers for Disease Control and Prevention [CDC], 2018; Falk & Hershberger, 2019).

Considerations for the Older Adult and Valvular Heart Disease

Management of VHD in the older adult requires careful and thoughtful decision making. VHD is complex and the decision to intervene and the choice of intervention should be through a shared decision between the patient and providers involved, including an integrated heart valve team. All risks, benefits, and alternatives as well as the patient's life expectancy and quality of life (QOL) need to be considered against the natural course of untreated disease when interventions for VHD are presented. It is important to evaluate whether they have a minimum of one-year good life expectancy and whether the perioperative risk of postoperative complications is low. A risk and frailty score should be calculated to assess for potential success of VHD intervention (Searle et al., 2008). The EuroSCORE and Society of Thoracic Surgeons (STS) score (http://riskcalc.sts.org/stswebriskcalc/#/) is used to calculate risk estimates of hospital mortality and postoperative complications (Kumar et al., 2018; Walter et al., 2021) Frailty score/index along with STS and other clinical variables such as major organ system dysfunction, and procedure-specific barriers, assist in deciding if the patient is low, intermediate, high, or prohibitive of surgical/procedural risk.

Surgical and/or transcutaneous approaches may be considered depending on specific parameters of left ventricular (LV) dimensions and ejection fraction (EF). In general, older patients have an increased risk of postoperative complications, often requiring longer lengths of hospital stay and convalescence (Pulok et al., 2020; Theou et al., 2021; Walter et al., 2021).

Aortic Stenosis: General Principles

In AS, there is a supravalvular or subvalvular obstruction of the left ventricular outflow tract. AS is graded using the valve hemodynamics that correlates with the A through D classification. In clinical practice, AS can generally be described as mild, moderate, severe, or critical but those descriptors are dependent on maximum aortic valve velocity, calculated aortic valve area as defined by aortic gradient and calculated aortic valve index (Table 10-5). It is more accurate to describe AS as the following: At risk, Progressive, Asymptomatic severe, Asymptomatic severe with LV systolic dysfunction, Symptomatic severe high-gradient AS, Symptomatic severe low-flow, low-gradient AS with reduced LVEF, Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS (Otto et al., 2021).

Etiology: AS diagnosed before age 60 years is usually caused by a congenital bicuspid valve, whereas AS after age 60 years

TABLE 10-5 Stages of Valvular Heart Disease

AORTIC STENOSIS STAGE AND DEFINITION	VALVE HEMODYNAMICS
A: at risk	• Aortic V_{max} <2 m/s with normal leaflet motion
B: Progressive AS	• Mild AS: aortic V_{max} 2.0–2.9 m/s or mean ΔP <20 mm Hg • Moderate AS: aortic V_{max} 3.0–3.9 m/s or mean ΔP 20–30 mm Hg
C: Asymptomatic severe AS	
C1 Asymptomatic severe AS	Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg AVA typically is ≤1.0 cm^2 Very Severe AS is an aortic V_{max} ≥5 m/s or mean P ≥60 mm Hg
C2 Asymptomatic severe AS with LV systolic dysfunction	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically ≤1.0 cm^2
D: Symptomatic severe AS	
D1 Symptomatic severe high-gradient AS	• Aortic V_{max} ≥4 m/s or mean ΔP ≥40 mm Hg • AVA typically ≤1.0 cm^2 but may be larger with mixed AS/AR
D2 Symptomatic severe low-flow, low-gradient AS with reduced LVEF	• AVA ≤1.0 cm^2 with resting aortic V_{max} <4 m/s or mean ΔP <40 mm Hg • Dobutamine stress echocardiography shows AVA <1.0 cm^2 with V_{max} ≥4 m/s at any flow rate
D3 Symptomatic severe low-gradient AS with normal LVEF or paradoxical low-flow severe AS	• AVA ≤1.0 cm^2 with an aortic V_{max} <4 m/s or mean ΔP <40 mm Hg AND • Stroke volume index <35 m>/m^2 • Measured when patient is normotensive (systolic blood pressure <140 mm Hg)

AR, Aortic regurgitation; AS, Aortic stenosis; AVA, aortic valve area circulation; ΔP, pressure gradient between the LV and aorta; HF, Heart Failure; LV, Left Ventricular, LVEF, left ventricular ejection fraction; V_{max} maximum velocity.

Adapted from Otto, C. M., Nishimura, R. A., Bonow, R. O., Carabello, B. A., Erwin, J. P. III, Gentile, F., Jneid, H., Kriege, E. V., Mack, M., McLeod, C., O'Gara, P. T., Rigolin, V. H., Sundt, T. M. III, Thompson, A., & Toly, C. (2021). 2020 ACC/AHA guideline for the management of patients with valvular heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. Circulation, 143(5), e35–e71.

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is usually caused by calcific degeneration of the valve. Occasionally, a patient after 60 years of age may present with a calcific bicuspid or rare, unicuspid aortic valve (Lewin & Otto, 2005). Other less common causes of AS include rheumatic fever, endocarditis, systemic lupus erythematous, and Fabry's disease (Otto et al., 2021; Slostad et al., 2019).

Occurrence: AS is the most common VHD in developed countries. It affects approximately 12.4% of the population older than 75 years of age with a predominance of 80% male in symptomatic AS (Akin & Nienaber, 2017). In the absence of a congenitally malformed valve, occurrence increases with age due to focal thickening or calcification of the valve. In terms of surgical prevalence, 40% of patients older than 70 years will be noted to have a bicuspid valve at time of intervention, but prevalence is much higher in those younger than 70 years. More than 50% of valve surgeries were performed in patients older than 70 years of age, with approximately 60% of these patients having trileaflet valve surgery and 40% having bicuspid aortic valve surgery (Otto & Bonow, 2014).

Age: Congenital valvular heart disease is present at birth; acquired valvular heart disease is found as chronological age progresses.

Ethnicity: Not significant.

Contributing Factors: Factors associated with degenerative aortic valve stenosis include age, male sex, current tobacco use, dyslipidemia, HTN, diabetes, and chronic obstructive pulmonary artery disease (Yan et al., 2017).

Prevention/Prophylaxis: There are no effective strategies to prevent VHD, particularly AS. Clinical trials looking at high-dose HMG-CoA reductase inhibitor (statin) therapy failed to prove any decreased progression nor regression of AS (Akin & Nienaber, 2017). However, angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) have been found to be beneficial with patients who have mild, moderate AS and symptomatic severe AS. Patients who have HF, LV dysfunction, and low blood pressure were prone to hypotension with the use of ACEI/ARBs; they should be used with caution and monitoring in these patients. The PARTNER 2 trial and registries looking at clinical implications of treatment with both ACEI and ARBs with severe symptomatic AS independently showed a decreased 2-year risk of all-cause and cardiovascular mortality when used pre- and post-transcatheter aortic valve replacement (TAVR). Caution is necessary so as not to give vasodilators in the presence of significant AS because they can potentiate significant hypotension and increase outflow obstruction from AS, worsening outcomes (Chen et al., 2020)

Signs and Symptoms: Many of these patients are asymptomatic. Prognosis is poor for patients who exhibit symptoms. Symptoms that may be associated with worsening prognosis are syncope, chest pain/angina, dizziness, and dyspnea. The survival rate decreases to 2 to 3 years for the patients who exhibit symptoms and do not have appropriate intervention (Walter et al., 2021). Angina is an early and more common symptom and can occur in the presence or absence of coronary artery disease (CAD). Presyncope followed by effort syncope occurs in about one-third of the patients with symptoms and is related to a fixed cardiac output due to the obstruction of the left ventricle created by AS. Exertional dyspnea indicates left ventricular dysfunction and HF.

Physical Examination Findings. The classic crescendo-decrescendo systolic murmur is heard at the second right intercostal space and radiates to the carotids. The murmur in older adults may radiate to the apex (Walter et al., 2021). This murmur, which peaks in intensity in mid to late systole, may also be associated with a thrill if greater than grade IV. The murmur intensity does not correlate with the severity of AS; often in the setting of HF the AS murmur may become softer as the cardiac output falls. S_1 is often soft, and can be inaudible in severe or critical AS. The S_2 may also be paradoxically split due to the late closure of the aortic valve (A_2). An S_4 is common, representing forceful atrial contraction in the setting of left ventricular hypertrophy. Other findings may include delayed carotid upstroke, a carotid and apical pulse lag time, systemic HTN, prominent "A" waves in the jugular venous pulse, and a sustained and forceful apical impulse. Isometric handgrip increases systemic vascular resistance, decreasing the intensity of the murmur. Standing and the Valsalva maneuver decreases ventricular filling, reducing the intensity of the murmur; squatting increases ventricular filling, reducing the intensity of the murmur (Walter et al., 2021).

Diagnostic Tests: In AS, the electrocardiogram (ECG) may be abnormal, demonstrating QRS or T-wave changes consistent with left ventricular hypertrophy. Chest x-ray examination is not recommended in routine screening of asymptomatic patients, but may provide information on valve calcification, cardiac chamber sizes, enlarged cardiac silhouette, and pulmonary vasculature.

Echocardiography is the standard test for assessing aortic valve stenosis and may demonstrate thickening and calcification of the aortic valve with decreased mobility of the leaflets. Doppler measurement of intracardiac blood velocity can help determine hemodynamic severity. The echocardiogram is useful for providing detail on the valve morphology. The following questions which can be answered include, but are not limited to: Is there congenital absence of valve cusp, degree of valve calcification, valve cusp mobility, aortic valve area, aortic valve pressure gradient, size of aortic root, left ventricular size, ejection fraction, posterior and septal left ventricular wall thickness, and concomitant valvular dysfunction and estimation of pulmonary artery pressures?

The frequency of echocardiogram assessment of AS is dependent on the degree of severity and symptoms (Table 10-6) (Otto et al., 2021). Exercise testing has limited utility in the evaluation of patients with AS. Pharmacological echocardiogram may be done in patients with low-gradient AS and can help to risk stratify patients in this category. Cardiac catheterization measurement of the systolic pressure gradient across the aortic valve is the definitive method for assessing AS in patients being considered for surgery or when there is a discordance between the clinical findings and the diagnostic tests. In patients with congenital AS there may also be abnormalities noted in the coronary arteries, which can be evaluated with the left heart catheterization. Right heart catheterization will provide information on hemodynamics. Cardiac MRI may be used to stratify patients with AS and assess the effect of chronic left ventricle pressure overload, volume, and overall function.

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TABLE 10-6 Frequency of Echocardiograms in Asymptomatic Patients with VHD and Normal LV Function

	TYPE OF VALVE LESION			
Stage	Aortic Stenosis*	Aortic Regurgitation	Mitral Stenosis	Mitral Regurgitation
Progressive (Stage B)	Every 3–5 yr (mild severity V_{max} 2.0–2.9 m/s) Every 1–2 yr (moderate severity; V_{max} 3.0–3.9 m/s)	Every 3–5 yr (mild severity) Every 1–2 yr (moderate severity)	Every 3–5 yr (MV area >1.5 cm^2)	Every 3–5 yr (mild severity) Every 1–2 yr Moderate severity
Severe asymptomatic Stage C1	Every 6–12 mo (V_{max} >4 m/s)	Every 6–12 mo Dilating LV: More frequently	Every 1–2 yr (MV area 1.0–1.5 cm^2) Every year (MV area <1.0 cm^2)	Every 6–12 mo Dilating LV: More frequently

Patients with mixed valve disease may require serial evaluations at intervals earlier than recommended for single-valve lesions. These intervals apply to most patients with each valve lesion and do not take into consideration the etiology of the valve disease.

**With normal stroke volume.*

LV: Left ventricular; MV, mitral valve; VHD: valvular heart disease; V_{max} Maximum Velocity

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Treatment: No medical therapies are available to delay the progression of AS. The patient with asymptomatic AS will need frequent monitoring for the development of symptoms and progression of disease. Symptoms of AS are associated with substantial valvular obstruction and a risk of sudden death; surgical/transcutaneous management must be considered. Aortic valve replacement is associated with a higher mortality rate in older adults than in younger individuals. Factors associated with greater operative risk include emergency surgery, left ventricular dysfunction, right-sided heart failure, female sex, significant coronary disease, cachexia, additional valve replacement, kidney disease, or concomitant coronary artery bypass graft (CABG). The proper selection of the type of valve replacement is important in older adult patients. The bioprosthetic valves have fewer structural failures and are advantageous in that their use obviates the need for long-term anticoagulation (which is associated with substantial morbidity and mortality in older adults). The disadvantage of this valve type is that the tissue degrades, and many patients may require reoperation in 10 years. Mechanical valves are more durable and have better hemodynamic profiles, but they require lifelong anticoagulation therapy with vitamin K antagonists such as warfarin.

Balloon aortic valvuloplasty (BAV) was developed more than 30 years ago as an alternative to conventional surgical aortic valve replacement in older and frail patients. BAV remains a consideration as a bridge to surgical aortic valve replacement (SAVR) or TAVR or transcutaneous aortic valve implantation (TAVI) in patients with severe symptomatic AS (Dawkins & Makkar, 2017). Common bridge indications for BAV found in the literature include cardiogenic shock, poor LV function, patients at extreme-risk, and patients undergoing concomitant coronary interventions (Alkhouli et al., 2017). BAV is an alternative method of treatment; however, because it is associated with rapid restenosis and significant residual outflow obstruction, it is reserved as a palliative procedure for the symptomatic patient who is not a surgical candidate or as a bridge to surgery.

In the past, patients with advanced age and symptomatic severe AS who were not able to undergo surgery were often referred for palliation. The first successful percutaneous aortic valve replacement performed on an inoperable patient was in 2002. The first approval for the indication of severe AS came in 2011. The U.S. Food and Drug Administration (FDA) approved the TAVR procedure for high-risk surgical patients in 2012, and an indication for "valve-in-valve" procedure for failed surgical bioprosthetic valves was approved in 2015. In 2016, the FDA approved TAVR valves for patients with severe AS at intermediate risk. Following the results of the PARTNER-3 trial in 2019, the FDA further approved the indication for TAVR in low-risk patients. With the advent of new procedures, more options are available to patients with severe symptomatic AS, including high-risk, frail, older adults (Mahmaljy et al., 2021). Trials regarding the types of TAVR devices to use for specific patient types are ongoing.

Recent results of the CHOICE Trial (Randomized Comparison of Transcatheter Heart Valves in High Risk patients with Severe Aortic Stenosis: Medtronic CoreValve Versus Edwards SAPIENT XT) that spanned over a 5-year period and compared self-expanding versus balloon-expanding heart valves found no statistical significant difference between balloon-expandable (BE) valves and self-expanding (SE) valves in death from any cause, death by cardiovascular cause, stroke, or repeat hospitalization due to HF. Ongoing randomized clinical trials need to take place to ensure TAVR is appropriate for those patients with a longer life expectancy (Abdel-Wahab et al., 2020).

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Contraindications for TAVR/TAVI include:

- Life expectancy less than 12 months secondary to a non-cardiac cause
- MI within 30 days
- Congenital unicuspid, bicuspid, noncalcified valve
- Hypertrophic cardiomyopathy
- Short distance between annulus and coronary ostium
- Emergency need for surgery
- LVEF greater than 20%
- Severe pulmonary HTN with right ventricular dysfunction
- Echocardiographic evidence of intracardiac mass
- Thrombus or vegetation
- Native aortic annulus smaller than 18 or larger than 25 mm
- Severe MR
- Magnetic resonance imaging (MRI)-confirmed cerebrovascular accident (CVA) or transient ischemic attack (TIA) within 6 months
- End-stage renal disease
- Mixed aortic valve disease (AS and AR)
- Significant aortic disease

(Mahmaljy et al., 2021)

Indication for Aortic Replacement (Surgical or Transcatheter) for Aortic Stenosis

Aortic Stenosis (AS)	Class Indication	Level of Evidence
	I	Level B
Asymptomatic patients with severe AS and LVEF <50	I	Level B
Asymptomatic, severe AS and low surgical risk	IIa	Level B
Symptomatic with low-flow/low-gradient severe AS	IIa	Level B
Moderate AS and undergoing other cardiac surgery	IIa	Level C
TAVR is approved for the following: ■ Low to prohibitive surgical risk patients with severe AS ■ Valve-in-valve procedures for failed prior bioprosthetic valves		

Adapted from: Mahmaljy, H., Tawney, A., & Young. M. (2021) Transcather aortic valve replacement. In *StatPearls* [Internet].

The AHA and ACC 2020 guideline recommendation for AS intervention can be found at https://doi.org/10.1161/CIR.0000000000000932

Mitral Regurgitation

Description: Mitral regurgitation (MR) is retrograde blood flow during systole from the left ventricle into the left atrium through an incompetent mitral valve. The mitral valve apparatus consists of mitral valve annulus, chordae tendineae, and papillary. Distortion of any of these structures may lead to an incompetent mitral valve and thus mitral regurgitation. MR is categorized by grades A to D. Grade A is patients at risk for MR, grade B is progressive MR, grade C is asymptomatic severe MR, and grade D is symptomatic severe MR. The progression of untreated disease may lead to pulmonary HTN and a failing left ventricle.

Etiology: Some of the common causes of MR are rheumatic heart disease, mitral valve prolapse, and ischemic heart disease (Crawford, 2017). In the older adult population, the most common causes of significant MR are myxomatous degeneration and ischemic heart disease. Congenital MR is rare but may be seen with cleft mitral valve in persons with Down's syndrome. MR may be further delineated as acute or chronic. Common causes of acute MR include chordal rupture, papillary muscle rupture, leaflet perforation, and trauma. Common causes of chronic MR include rheumatic fever, mitral leaflet prolapse, CAD, papillary muscle dysfunction, congenital heart disease, left ventricular dilation, myxomatous degeneration, and HTN.

Signs and Symptoms: The symptoms associated with MR can be quite variable from a state of asymptomatic to symptoms of left ventricular dysfunction, shortness of breath, paroxysmal nocturnal dyspnea, fatigue, as well as concomitant right-sided heart failure.

Physical Examination Findings. The murmur of MR is a holosystolic murmur heard best at the apex and may radiate to the axillae or back and may be associated with an S_3 gallop. In more acute mitral regurgitation, often from acute MI, an S_4 may be present secondary to a chordal rupture. Patients often will present in pulmonary edema if the acute MR is due to an acute MI. Chronic MR can cause dilation of the left atrium and may led to AF. Other examination findings may include edema, displaced apical impulse, and crackles on lung examination (Crawford, 2017).

Diagnostic Tests: In MR, the ECG shows left atrial enlargement or AF and the chest x-ray examination shows left ventricular dilation; in nonrheumatic forms of MG these are less distinctive. Echocardiography delineates overall ventricular function and Doppler studies show the jet and severity of the regurgitation, as well as the mechanism. Transesophageal echocardiography is a more precise way of visualizing the regurgitant jet.

Treatment: Medical management of MR includes use of ACEIs, digoxin, diuretics, and vasodilators to reduce the

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symptoms of HF and reduce the regurgitant volume. Anticoagulation may be needed if the patient has AF. Mitral valve surgery is considered in asymptomatic and symptomatic patients with progressive disease before signs of irreversible left ventricular dysfunction are present. The mortality rate associated with mitral valve replacement could be as high as 14% in the older adult. Mitral valve repair is associated with a lower operative mortality than mitral valve replacement and is preferred, as preservation of the existing valve architecture allows synchrony of left ventricular contraction. When mitral annular calcification is the cause, medical therapy is prudent because the operative risk is substantially higher in patients with this disease process. Acute MR from papillary muscle rupture or chordal rupture requires patient stabilization followed by surgery, which still carries a high mortality rate. Other therapeutic options for repair of the mitral valve may include mitral transcatheter edge to edge repair or MitralClip (Otto et al., 2021).

The American Heart Association (AHA) and American College of Cardiology (ACC) 2020 guideline (Otto et al., 2021) recommendations for MR intervention include:

Clinical Recommendation	Recommendation	References
MV surgery is recommended for symptomatic patients with severe primary MR (stage D) and ejection fraction greater than 30%.	B	Otto et al., 2021
Medical therapy is recommended for symptomatic or asymptomatic patients with severe primary MR and left ventricular dysfunction (stages C2 and D) in whom surgery is not possible or must be delayed and guideline-directed medical therapy should be initiated	A	Otto et al., 2021
MV repair is recommended when procedure is limited to posterior leaflet in the setting of chronic severe primary MR.	B	Otto et al., 2021
MV repair is recommended over MV replacement in patients with chronic MR involving anterior or posterior leaflets.	B	Otto et al., 2021
If patient undergoing other cardiac surgery and has chronic primary MR, they should also have MV repair or replacement surgery at the same setting.	B	Otto et al., 2021

Adapted from: Otto, C. M., Nishimura, R.A., Bonow, R. O., Carabello, B. A., Erwin 3rd, J. P., Gentile, F., Jneid, H., Kriege, E.V., Mack, M., McLeod, C., O'Gara, P.T., Rigolin, V. H., 3rd Sundt, T. M., Thompson, A., & Toly, C. (2021). 2020 ACC/AHA guideline for the management of patients with valvular heart disease: Executive summary: A report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation, 143*(5), e35–e71.

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

VALVULAR HEART DISORDER	MURMUR	OTHER CARDIAC FINDINGS
Aortic stenosis	Systolic murmur heard at second right intercostal space and may radiate to carotids	Decreased cardiac upstroke. Best heard with patient sitting up and exhaling.
Aortic regurgitation	Diastolic blowing murmur at left sternal border	Rapidly collapsing pulse (Corrigan's pulse), preservation of A2 component of second heart sound, widened pulse pressure.
Mitral stenosis	Diastolic rumble	May be associated with signs of right heart failure including edema, ascites, elevated jugular venous pressure.
Mitral regurgitation	Holosystolic murmur heard at apex and may radiate to axilla	AF, ventricular gallop (S_3), displaced apical impulse laterally, crackles on lung examination.
Mitral valve prolapse	Mid-systolic click heard at apex	May be associated with mitral regurgitation.
Tricuspid stenosis	Mid-diastolic rumble heard at left sternal border; may increase with inspiration	Very rare finding but may be associated with right atrial myxomas or carcinoid syndrome.
Tricuspid regurgitation	Holosystolic murmur heard at right sternal border and increase with inspiration	May be associated with signs of right heart failure including edema, ascites, elevated jugular venous pressure.
Pulmonic stenosis	Harsh mid-systolic murmur heard at the 2nd left interspace and may radiate to the left carotid	May be associated with a palpable thrill. The second heart sound is widely split.
Pulmonic regurgitation	High-pitched diastolic murmur	Accentuated P2 of the second heart sound. May be louder in setting of pulmonary hypertension.

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General Principles

Diagnosis: Often the first indication of VHD may be the auscultation of a cardiac murmur. It is important for advanced practice nurses to have good cardiovascular assessment skills. Auscultatory and other associated findings are listed in the table that follows and can be a useful guide in approaching the cardiovascular examination of all patients (Otto et al., 2021).

Follow-Up: For patients treated medically for valvular disease, close follow-up to monitor the effectiveness of treatment, adverse effects of medication, and progressiveness of the disease process is indicated. Medication therapy, particularly the use of anticoagulation therapy, requires meticulous attention. Surgically treated patients are monitored for valve function, fluid balance, and anticoagulation. Periodic echocardiographic (see Table 10-6), electrocardiographic, and chest x-ray monitoring may be indicated.

Sequelae: Untreated VHD may lead to progressive HF, dysrhythmias, and death. Valve replacement risks include thrombus formation, infection, or rupture at the attachment points to the valve ring. Infective endocarditis, which may occur with artificial valves, has a high risk of mortality, and requires reoperation. There is a high prevalence of gallstones in patients with prosthetic valves, thought to be due to low-grade intravascular hemolysis. In patients who are not surgical candidates, the symptoms of HF are progressive and disabling. Even in surgical patients, the symptoms of HF may recur or persist.

Prevention/Prophylaxis: In patients with prosthetic valves, the risk of thromboembolism decreases with an individualized antithrombotic regimen. The specific therapy is determined based on the comorbid state and the patient's overall status. Consider prophylactic antibiotic therapy (endocarditis prophylaxis) before any surgical or dental procedures in all patients with valvular disease, especially patients with valve replacement, rheumatic heart disease, aortic regurgitation, or mitral valve prolapse with significant MR murmurs.

Referral: All patients with symptoms of progressive valvular disease must be managed collaboratively with a cardiologist. Many require further collaboration with a cardiac surgeon. The Practice Guidelines for Cardiothoracic Surgery Concerning Valvular Heart Disease include the indications for surgery. In general, these include symptoms that cannot be controlled with medical therapy or indications of a threat to survival (i.e., angina, dyspnea, effort syncope or progressive impairment of ventricular contractility, and infective endocarditis).

Education: Older adults constitute 40% to 60% of all cases of endocarditis. Instruct all at-risk patients in the importance of good oral hygiene and antibiotic prophylaxis. Patients should be taught to monitor and report febrile illness.

Teach all patients with valve disease requiring medication therapy to report lack of therapeutic effect or any adverse effects of the drugs. Teach patients to be aware of drug-food interactions (e.g., green leafy vegetables and warfarin). Teach patients to have prothrombin time/INR checked on a regular basis if they are taking warfarin. Teach the patient with disabling HF about energy-conservation measures. Patients with hemodynamically significant valvular heart disease may need to limit vigorous physical activity. Deterioration may be rapid and symptoms insidious, so patients should be taught to report any changes in condition, even those they may feel are subtle.

CASE STUDY

Your 76-year-old patient has returned today for a focused visit. Her chief complaint is increasing fatigue and palpitations. She was discharged from the hospital 5 weeks ago after being treated for decompensated heart failure due to development of atrial fibrillation/flutter. She received an ablation and converted to normal sinus rhythm. When you saw her in follow-up within 1 week of discharge, she was euvolemic, remained in normal sinus rhythm, and reported feeling the best she had felt in 5 years. Her HF*r*EF was class C/II. She was able to walk in her neighborhood with minimal discomfort and manage her activities or daily living independently. Now she reports that starting about 4 days ago she noticed increasing fatigue. She was unable to do her daily walk without great distress so has discontinued those completely. She also reports feeling her heart in her throat several times a day.

PM: HF*r*EF 40%, obesity BMI 40, CKD stage 4, history of atrial fibrillation/flutter, s/p ablation 5 weeks ago, prediabetic diet managed.

Medications: Metformin XL 100 mg daily, lisinopril 10 mg daily, Bumex 4 mg daily, metolazone 2.5 mg every other day, spironolactone 25 mg daily, Eliquis 5 mg twice a day.

Vital signs Temp 36.8C BP 148/72 Pulse 110 R 18 Pulse Ox 98% on room air

1. What is your working diagnosis at this point?
2. Is there additional history you will need to obtain?
3. What physical examination elements will be most important?
4. What laboratory tests would be helpful?
5. What other tests will be necessary to refute or support your working diagnosis?
6. How would you classify her heart failure based on her current concerns?
7. What options would you consider for your next steps?

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CHAPTER 11

Respiratory Disorders

Evelyn Duffy

ASSESSMENT

This chapter addresses problems of the lower respiratory tract, which includes the bronchi, bronchioles, alveolar ducts, and alveoli. Problems of the upper respiratory tract, nose, mouth, pharynx, larynx, and trachea are addressed in Chapter 9. Some problems of the upper respiratory tract can contribute to concerns that present as symptoms in the lower respiratory tract (e.g., postnasal drip), and should not be excluded from the broad initial differential diagnosis. Special considerations for assessing an older adult include changes in tissue and in the musculoskeletal and respiratory systems that are a result of the aging process.

Changes with Aging

The aging process is characterized by a loss of elasticity and flexibility in collagen and elastin that are components in lung tissue and can impede the normal expiratory recoil of the lung. The concurrent decrease in body water composition dries mucous membranes and interferes with the protective functions of the upper airway in expelling foreign material. Loss of elastin also affects the alveoli and the basement membrane of the capillary wall, where gas exchange occurs. A thickening occurs in both areas, limiting the amount of diffusion (Teall et al., 2021). Musculoskeletal changes, including calcification of costal cartilage and weakening of inspiratory muscles, result in a relaxation of the skeletal contours and an increased anteroposterior diameter, causing a barrel chest, although not as pronounced as that found in patients with chronic obstructive pulmonary disease (COPD). An exaggeration of the thoracic curvature may also occur, with some tracheal displacement. Expiratory muscles must work harder because expiration is no longer a passive act, resulting in use of accessory muscles (Teall et al., 2021). The residual capacity of the lungs is increased and inspiratory reserve capacity lessened. Air tends to fill the apices and not the bases. Because of decreased muscular strength, the cough reflex is not as forceful or as effective. All these changes occur gradually and are hardly noticeable unless a physiological challenge or stress arises. Even in such an event, exertional dyspnea may be the only observed change in the healthy older adult. Older adults who live an active lifestyle may not present with typical age-related changes. Healthy older adults or those with stable, chronic problems may first seek care when there is a change in functional capabilities. When presenting with a change in function, problems related to the respiratory system should be considered. Signs could include decreased exercise tolerance, shortness of breath with exertion, poor sleep quality, or easy fatigability.

Past Medical History

History questions should address each symptom using the OLDCART or PQRST symptom analysis. If there has been a history of respiratory issues, details regarding the extent of the problem need to be documented. Current or past tobacco use has been identified as the cause of many diseases of the respiratory system. To determine whether the patient should be screened for lung cancer requires documentation of how much the patient smoked, for how long, if they have quit smoking, and when that occurred (Wood et al., 2018). Exposure to vapors, gas, dust, and fumes in the workplace setting contributes to lung diseases including asthma, COPD, interstitial lung disease, sarcoidosis, pneumoconiosis (silicosis and asbestosis), and respiratory infections (Blanc et al., 2019). To further understand the patient's risk requires details about present or past occupational exposure. Medications should always be evaluated for those that might be contributing to symptoms. In addition to the well-known effect of dry cough associated with angiotensin-converting enzyme (ACE) inhibitors, cancer drugs, rheumatology drugs, amiodarone, and antibiotics all have been shown to contribute to the development of interstitial lung disease (Skeoch et al., 2018). If the patient is using inhalers, it is important to ask *how* they use them and have them demonstrate their use if possible. With the multiple inhalers on the market today and the constantly changing formularies of Medicare plan providers, it is also important to be sure the patient has not confused which inhaler is for rescue and which is for maintenance therapy. Inquire about a history of allergies, including seasonal, environmental, and food allergies. Include a review of immunizations for influenza, pneumococcal pneumonia, and pertussis. Family history of chronic lung diseases, tuberculosis (TB), or lung cancer may be elicited by asking if anyone in the family has had lung problems (Teall et al., 2021).

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Review of Systems

Key symptoms of lung disease should be assessed in the review of systems, including cough, dyspnea, and chest pain. If the concern is a cough, ask about onset and duration, timing, sputum production, or hemoptysis. If the patient describes coughing up blood, clarification of the amount and timing limits the differential. Coughing up sputum first thing in the morning that includes a few streaks of blood is more consistent with upper, rather than lower, respiratory concerns. Details regarding the cough should include whether there has been fever, chills, or night sweats (which may be present with TB). Cough that has been present for 3 to 8 weeks is considered subacute, and 8 weeks or more is considered chronic (Teall et al., 2021). This timing helps to define the list of possible differential diagnoses. Further details regarding associated symptoms are also important. Ask about the quality of the cough: Is it a deep cough, or does the patient hear themselves wheezing, barking, or whooping?

If there is dyspnea, ask if it is related to activity, or does it occur at rest or when lying down? Specific questions about changes in endurance, stair-climbing, or activities of daily living (ADLs) can quantify the extent that the dyspnea affects function. Knowing how many pillows are required to sleep comfortably at night defines orthopnea. If the patient reports waking up from sleep short of breath, they are describing paroxysmal nocturnal dyspnea (PND). If dyspnea interferes with eating, establishing if it occurs while eating or after the meal can help refine the diagnosis.

To assess any complaint of pain the initial questions need to address the possibility of life-threatening situations. Chest pain includes a broad list of possible causes including cardiac, gastrointestinal, musculoskeletal, and dermatological. Pain from pulmonary issues is usually a result of inflammation of the parietal pleura that occurs when the pleurae rub together. This can result from a number of conditions, including pneumonia, COPD, lung cancer, sarcoidosis, and pulmonary hypertension (Teall et al., 2021).

Physical Examination

Physical examination of the respiratory system begins with general observation of the patient: rate and ease of respirations at rest, conversational ability (limited by breathing problems), use of accessory muscles, posture, color, pursed lips, circumoral or nailbed cyanosis, and capillary refill. The chest and upper back should be exposed for full inspection and examination. Are both sides symmetrical, with equal respiratory effort and diaphragmatic movement? Is there any evidence of kyphosis, lordosis, or scoliosis? What is the anterior/posterior to lateral diameter?

Palpation of the posterior chest to confirm equal chest expansion is done by placing the thumbs on the chest wall near the vertebrae at T9 and T10 and spreading the hands. A small fold of skin should be between the thumbs. When the patient takes a deep breath per your instruction, the thumbs should move apart symmetrically. If pneumonia or consolidation is suspected, palpating for tactile fremitus may be helpful. Using the ball of the hand (metacarpophalangeal area of the palm) or the ulnar side of the hand, feel the vibrations in a side-to-side pattern while the patient says "ninety-nine." The vibrations should feel the same on both sides and should be stronger in the upper areas of the chest. Increased fremitus occurs with marked consolidation, such as lobar pneumonia.

Percussion of the posterior chest for resonance and symmetry is the next step, again using a side-to-side approach. Dullness is indicative of increased density, as found with pneumonia, tumor growth, or pleural effusion. Hyperresonance is found with air trapping in emphysema or with pneumothorax. Correlation should be made with the findings from the result of tactile fremitus.

Auscultation of posterior breath sounds for symmetry, presence or absence of adventitious sounds, and air movement is done with the patient seated and the arms resting on the knees or folded across the chest to retract the scapulae. Have the patient take a deep breath through the mouth, with the mouth open, inhaling and exhaling. The open mouth helps to amplify the breath sounds. Decreased breath sounds are common with a large body habitus or present in disease such as COPD, pleurisy, or pleural effusion. Wheezing is commonly heard with asthma or acute bronchitis, although it may also be part of the background of chronic bronchitis or COPD. Wheezing on inspiration is more indicative of large airway obstruction while wheezing on expiration occurs with obstruction of the small airways. If wheezing is heard on inspiration, have the patient cough, and wheezing that clears with cough is not pathological. Crackles are heard with heart failure, pulmonary edema, or pneumonia; basilar crackles that clear with coughing or deep breathing, as with wheezing that clears, are not pathological. Older patients may become lightheaded with deep breathing and may need this part of the examination to be spaced out over time. If pneumonia is suspected, vocal fremitus techniques such as bronchophony, egophony, or whispered pectoriloquy may be indicated. Examination of the lateral areas of the chest should be included with the posterior examination. The right middle lobe is best assessed on the right lateral area. Pneumonia is more common on the right because the right main bronchus is shorter, wider, and more vertical (Teall et al., 2021). The anterior examination is approached in the same way as the posterolateral examination.

After completion of the history and physical examination further assessment using laboratory studies and imaging may be considered. Pulse oximetry may have been done in the initial admission. Results can help to inform the need for more extensive testing such as pulmonary function tests (PFTs) or blood gasses. For older adults, PFTs may be difficult to complete. The patient's cooperation along with good coaching on the part of the technician improves reliability. When ordering a chest x-ray, consider whether the patient is able to stand for a posterior to anterior view (PA) or require an anterior to posterior view (AP). The AP view is less preferred because heart magnification is increased. (Teall et al., 2021). X-rays should be used judiciously and not in patients for whom the physical examination was without abnormal findings. Additional testing is described in detail in each of the disease sections in this chapter.

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ASTHMA

Signal Symptoms: Wheezing, shortness of breath, cough (especially at night), chest tightness.

Description: The Global Initiative for Asthma (GINA) 2021 describes asthma as a heterogenous disease, usually characterized by chronic airway inflammation. It is defined by a history of respiratory symptoms such as wheezing, shortness of breath, chest tightness, and cough that vary overtime and in intensity, together with variable expiratory airflow limitation. Asthma is further classified by the several different phenotypes and categorized as intermittent, mild, moderate, or severe. The symptoms of asthma are often episodic, and a patient may be completely asymptomatic between attacks/exacerbations.

Etiology: Asthma represents a wide range of heterogeneous phenotypes. Each of these are different in the pathophysiology, etiology, and presentation. Risk factors include genetic, environmental, and host factors. Asthma is most prevalent in English-speaking countries.

The increase in asthma supports the theory that environmental changes are responsible. Genetics most likely play an important role in allergies in general and specifically in asthma. Multiple genes contribute to the development of asthma in different ethnic groups; research into genetic phenotypes is ongoing (GINA, 2021). Prenatal exposure to tobacco smoke is associated with asthma risk, which is increased when combined with postnatal exposure. Diet and stress in the prenatal period may affect the risk of atopic disease. Social determinants of health include family structure, socioeconomic status, and exposure to animals. When asthma is present in adults it may represent persistent childhood asthma, relapse of childhood asthma, or may be a true adult-onset asthma. Adult-onset asthma may be related to occupational exposure, but it is more often due to irritants, such as gastroesophageal reflux, or secondary to certain drug treatments.

Occurrence: Asthma affects 8% of adults older than 18 years. In the United States, it is responsible for 5.9% of clinic visits, and it has a mortality rate of 1.1/100,000 in the U.S. population (Centers for Disease Control and Prevention [CDC], 2021). Women are affected by asthma more often than men (CDC, 2021)

Age: Depends on the phenotype; allergic asthma is the most common form and most prevalent overall, but most often affects children. Late-onset asthma, also known as adult-onset, affects adults, as its name suggests. It is more difficult to differentiate late-onset asthma from other chronic lung conditions, such as chronic obstructive lung disease COPD or asthma-COPD overlap syndrome. Differentiation is important because it affects treatment choice and risk stratification (Enilari & Sinha, 2019)

Ethnicity: Moraes et al. (2018) acknowledge the challenge of identifying ethnic differences. They note the challenge of separating genes and environment and the increasing complexity of how we define ethnicity across studies. They found that Puerto Ricans had the highest prevalence of asthma with African Americans in second place.

Contributing Factors: Exposure to allergens, respiratory infections, family history/genetic predisposition, atopy, occupational irritants, tobacco smoke (smoking and passive smoke exposure), high levels of indoor and outdoor pollution, and obesity; rhinitis is a specific factor in older adults (GINA, 2021).

Signs and Symptoms: Patients may experience recurrent wheezing, cough (especially at night), chest tightness, breathing difficulty, and rhinorrhea/postnasal drip. Symptoms may occur in conjunction with a respiratory infection, weather changes, exposure to environmental allergens, strong emotional reactions, animal dander, mold, smoke, exercise, or other triggers. Medications, including aspirin, NSAIDs, and beta blockers can exacerbate symptoms. Older adults are less likely to sense dyspnea related to airway obstruction, even in the presence of cough, chest tightness, or wheezing (Seggev, 2019).

Differential Diagnosis:

- COPD
- Asthma-COPD overlap syndrome
- Heart failure
- Pneumonia
- Upper respiratory infection
- Cystic fibrosis/bronchiectasis
- Pulmonary embolism
- Obstructive sleep apnea
- Anxiety disorder
- Vocal cord dysfunction
- Cough secondary to drugs, most commonly ACE inhibitors
- Gastroesophageal reflux disease (GERD)
- Allergic bronchopulmonary aspergillosis

Diagnostic Tests: Spirometry is the gold standard for establishing a diagnosis of asthma. Ideally, this should be done prior to starting controller medications to best evaluate the severity of disease. Asthma is an obstructive lung disease, so the spirometry would show obstruction (reduced FEV_1/FVC ratio). Spirometry is generally repeated after the administration of a short-acting bronchodilator. On this post-bronchodilator study, an improvement of 12% and 200 mL in either the forced expiratory volume in 1 second (FEV_1) or forced vital capacity (FVC) indicates a reversible component. This may be helpful in differentiating asthma from COPD. If spirometry is normal, bronchoprovocation such as a methacholine challenge test may help to differentiate asthma from other conditions with a similar presentation (Urbankowski & Przybyłowsk, 2021); however, this test is extremely intensive and may be contraindicated in certain populations. Referral to pulmonology for further evaluation is recommended prior to ordering methacholine testing. Older adults tend to have increased hyperresponsiveness to bronchoprovocation even

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when adjusting for the baseline amount of airway obstruction, atopy, or smoking status, so the testing procedure itself may need to be adjusted.

The American Thoracic Society has endorsed the use of fractional nitrous oxide, measurement in exhaled breath, as a biomarker for eosinophilic inflammation and a complimentary tool to assess airway disease, including asthma (Duong-Quy, 2019). A history of atopy or allergen testing may establish an allergic component. In a patient with dyspnea, measurement of brain natriuretic peptide (BNP) and chest x-ray may be needed to rule out other conditions.

Laboratory testing, including absolute eosinophil count and immunoglobulin E (IgE) may be helpful in distinguishing allergic asthma from other types, especially when considering some of the newer biologic treatment options.

Despite the many available options diagnostic for testing, a thorough history and physical are an essential part of the work-up and should not be underemphasized. Ultimately the nurse practitioner needs to focus on the patient and their unique presentation.

Treatment: Long-term goals of asthma management include controlling symptoms to allow normal activity levels and minimize the risk of asthma-related morbidity and mortality. A partnership between provider and patient is an indispensable element of asthma management, which empowers the patient and allows for education, ongoing assessment, and early intervention. Asthma care paths that facilitate open communication and incorporate the patient's beliefs, goals, and values will improve health outcomes.

Identifying and avoiding potential triggers and treating modifiable risk factors are the first steps in managing asthma. It is critical to encourage patients to adhere to prescribed medication regimens, and all patients who can read and comprehend should have an asthma action plan that is updated whenever changes in treatment are made. A printable asthma action plan, including information on controlling environmental triggers is available at: www.nhlbi.nih.gov/health/public/lung/asthma/asthma_actplan.pdf. The plan may need to be adapted to older adults who cannot or will not perform peak expiratory flow rate (PEFR) monitoring. It is recommended that patients with moderate to severe asthma use a diary every day to record the PEFR and their symptoms (Dobra & Equi, 2018).

Beta-2-agonists, both long-acting (LABA) and short-acting (SABA), inhaled corticosteroids (ICSs), leukotriene antagonists (LTRAs), and long-acting muscarinic antagonists (LAMAs) are all medications used in the treatment of asthma, mainly in a stepwise approach. These steps are fluid, moving up or down along with the patient's symptoms.

When GINA updated recommendations for treatment of asthma in 2019 (Boulet et al., 2019) the primary change was a suggestion of the use of a combination ICS/LABA inhaler as a reliever medication instead of a SABA alone to reduce the risk of an exacerbation. Formoterol was the LABA chosen because the onset of action is more rapid than others in the same category.

The 2021 GINA updated guidelines now have two tracks, each with a 1 to 5 stepwise approach for the management of asthma for adults and adolescents (Fig. 11-1) The current guidelines no longer distinguish between mild intermittent and persistent asthma, noting that the distinction was arbitrary and both groups would benefit from an ICS to prevent exacerbations.

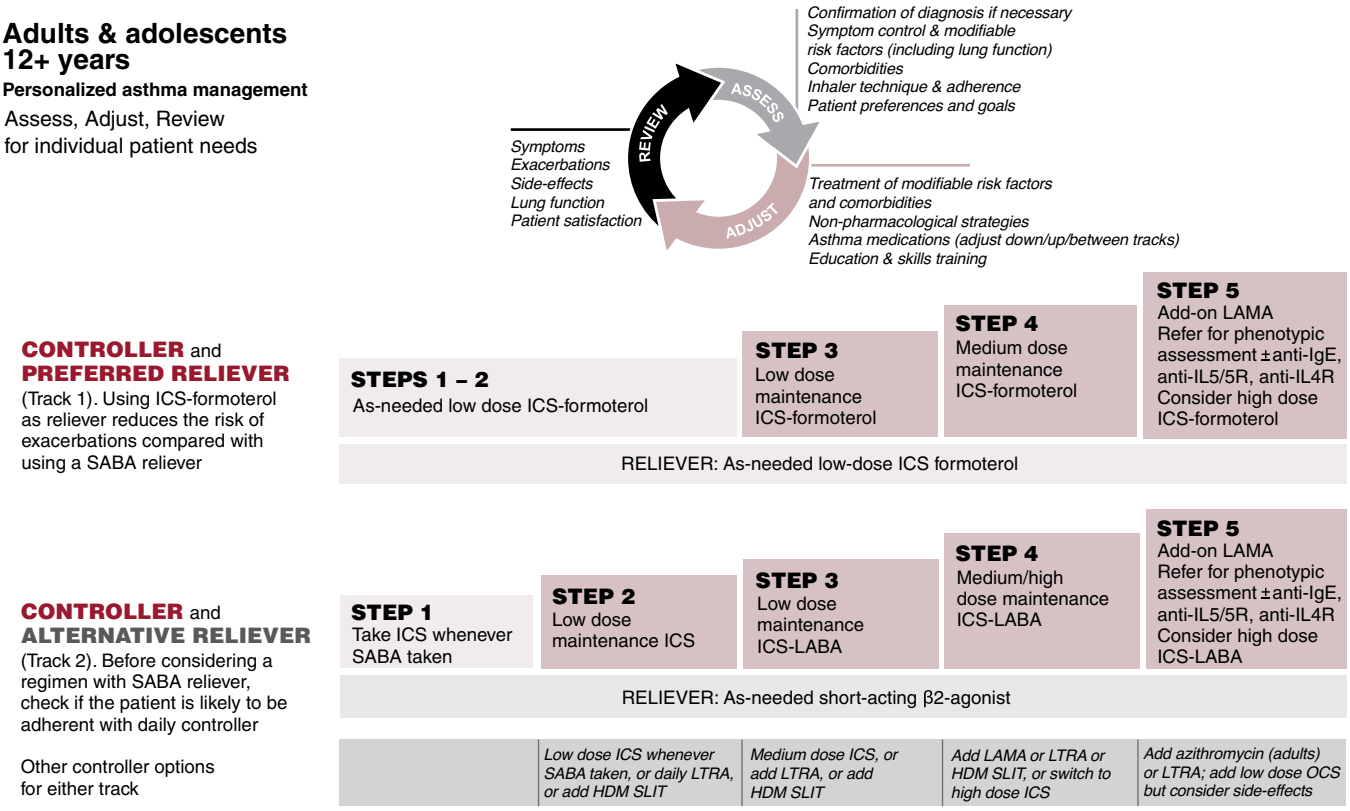

FIGURE 11-1. Global Initiative for Asthma stepwise approach for the management of asthma.

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Track one uses a combination ICS/formoterol as a reliever medication.

- Steps 1–2: Patients who have symptoms fewer than 4 to 5 days in the week can use a low dose ICS/formoterol inhaler as needed. Due to its more rapid onset, only formoterol is acceptable as the LABA in this approach.
- Step 3: Patients who have symptoms most days, or who wake with asthma symptoms once a week or more should be on a maintenance low dose ICS/formoterol inhaler with prn SABA.
- Step 4: Patients who have daily symptoms or wake with symptoms once a week or more and have low lung function should use medium dose ICS/formoterol inhaler with prn SABA.
- Step 5: Consider high dose ICS/formoterol inhaler, consider adding on LAMA, consider assessing for allergic contribution, consider assessing for/adding biologic.

Track two uses SABA for reliever, but the patient is either on an ICS controller or uses the ICS every time they use the SABA.

- Step 1: Symptoms less than twice monthly: take a dose of ICS whenever they use the SABA.
- Step 2: Symptoms twice monthly or more but less than 4 to 5 days per week: low dose maintenance ICS inhaler with prn SABA.
- Step 3: Symptoms most days or waking with asthma once a week or more: low dose maintenance ICS/LABA inhaler with prn SABA.
- Step 4: Symptoms daily, or waking with asthma once weekly or more and low lung function should be on medium to high dose ICS/LABA with prn SABA.
- Step 5: Symptoms still not controlled consider adding LAMA, consider assessing for allergic contribution, consider assessing for/adding biologic.

For steps 2 to 4 of either track, consider adding an LTRA, such as montelukast, either alone (step 2) or in combination with ICS (steps 3 to 4). A 2014 Cochrane review (Chauhan & Ducharme, 2014) found that LTRAs were safe but not as effective as monotherapy ICS for asthma. Because the response to LTRAs is both difficult to predict, with some patients dramatically improved and others minimally, a therapeutic trial is indicated with close monitoring for response. The use of theophylline is discouraged, especially in older adults, because of toxicity, drug interactions, and adverse effects.

Therapy may need to be customized in older adults or patients with comorbidities. For example, increasing the dose of an ICS and avoiding a LABA is prudent in a patient with heart disease, and in a patient with glaucoma or osteopenia, adding a LABA or LTRA instead of increasing the dose of ICS may be preferable. In short, guidelines are not meant to be absolute and do not preclude the use of clinical judgment.

Stepping down therapy is a gradual process compared to stepping up treatment. If a patient has been stable and well controlled for 3 months or more, it is generally safe to decrease the dose of ICS by 25% to 50% (GINA, 2021).

Patients experiencing an acute asthma exacerbation that is not responding to reliever medication should seek immediate emergency medical care. Aggressive treatment with nebulized SABAs and systemic (IV or oral) glucocorticoids for exacerbations remains the standard of care in the acute care setting. Patients who do not respond well within 4 to 6 hours should be hospitalized.

The long-term goals of treating asthma include assessing frequently, making adjustments to optimize symptom control to allow normal activity levels, minimizing side effects, and decreasing risks associated with exacerbations, including airway remodeling/fixed obstruction and death.

Prevention/Prophylaxis: There is no known strategy to prevent asthma. Patients with asthma should be given an influenza vaccine annually, pneumococcal pneumonia vaccine per schedule, and a COVID vaccine unless patient-specific contraindications exist. Partnership with the patient/family in education to recognize triggers, identify changes in status, and seek prompt medical assistance to avoid complications is key to success. Avoidance of environmental factors is also critical.

Education: Patient/family education is an important component of asthma management. In addition to educating patients on the disease and the need for frequent monitoring and immediate reporting of increased symptoms, a written asthma action plan should be initiated, detailing how to identify and deal with environmental triggers, medications dosage and frequency, and when to seek emergent care. Instruction in use and care of inhalers and spacers, if used, is also important. If the patient is on an ICS, instruct on the need for daily use and oral hygiene to prevent a fungal infection. Clarification of the action and role of quick relief inhaler versus daily controller therapy is important for medication adherence. The role of patient as partner in asthma management should be emphasized.

Gearing education to the health literacy level of the patient is crucial to gaining patient understanding and partnership. Patients who are still smoking should receive brief motivational counseling at each visit and referral to a Quitline or community-based smoking cessation program when ready to quit.

Referral: Consultation with an asthma specialist in pulmonology is advised at step 4, with a suggestion to consider a consultation at step 3. Older adults who have multiple comorbidities, have been treated in the emergency department (ED), or have been hospitalized due to an asthma exacerbation within the past year should also be managed in collaboration with an asthma specialist. Patients who require ongoing oral corticosteroids or more than two courses of oral corticosteroids in a year should be referred to an asthma specialist. Biologics such as an anti-IgE agent (omalizumab), IL-5/5R and IL-4 blockers (mepolizumab, benralizumab, dupilumab) may be a consideration for patients with poorly controlled allergic asthma, but they should be prescribed either by or in collaboration with an asthma specialist. Patients having any complications that affect asthma or those who require further testing should also be referred (GINA, 2021). Patients with characteristics of both asthma and COPD fall into this category. Patients and their families may also be referred to a community-based asthma education program, although many of these initiatives are more focused on childhood asthma. Referral to case management through local Area Agency on Aging services can be helpful if the patient has unmet care needs or financial problems with obtaining medications.

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Follow-Up: Regular monitoring should be done 1 to 3 months after initiation of treatment, and then every 3 to 12 months, depending on the level of control and severity. Patients should be seen within 1 week after an asthma exacerbation, and within 2 to 6 weeks when changes are made in stepwise management (GINA, 2021). Treatment step-down can be considered if the patient has had good control for 3 months; follow-up should be scheduled every 1 to 3 months after treatment step-down has been initiated (GINA, 2021).

Sequelae: Older adults with asthma may have increased bronchial hyperresponsiveness and a more rapid decline in lung function than in older adults without asthma. Older adults also may have increased treatment-related adverse events. Comorbidities such as COPD, cardiovascular disease, osteoporosis, glaucoma, diabetes mellitus, and other health problems complicate management and may limit treatment options. Older adults have the highest rate of asthma-associated mortality.

Clinical Recommendation	Evidence Rating	References
Inhaled corticosteroids (ICSs) are the preferred controller medication for all asthma.	A	GINA, 2021
Long-acting beta agonists (LABAs) are the preferred add-on agent due to lack of control, but they should never be used as monotherapy without ICSs.	A	GINA, 2021
It is important to educate patients on the proper technique for inhaled medications and trigger avoidance.	A	Maricoto et al., 2019
In severe or life-threatening exacerbation, the initial treatment should include oxygen, short-acting beta agonists, and systemic corticosteroids for most patients while arranging for transfer to an acute facility with monitoring.	A	GINA, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Signal Symptoms: Dyspnea, chronic cough with or without sputum production, decreased activity tolerance, wheezing.

Description: Chronic obstructive pulmonary disease (COPD) is defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) as "a common, preventable and treatable disease that is characterized by persistent respiratory symptoms and airflow limitation that is due to airway and/or alveolar abnormalities usually caused by significant exposure to noxious particles or gases and influenced by host factors including abnormal lung development" (GOLD, 2022, p. 4). Airflow limitation in COPD results from parenchymal destruction (such as emphysema) and small airway disease that vary among individuals and evolve at different intervals over time (GOLD, 2022). Chronic inflammation is responsible for structural changes, narrowed passages of the small airways, and lung parenchyma destruction, leading to loss of alveolar attachments to the small airways and a reduction in lung elastic recoil (GOLD, 2022). As a result of the structural changes, the ability of the airways to remain open is diminished during expiration as a result. Characteristics of COPD are airflow limitation and mucociliary dysfunction, both of which are likely attributed to loss of small airways (GOLD, 2022). Emphysema is a pathological diagnosis, not a clinical one, although it is possible to see evidence of emphysema on chest imaging.

Patients with symptoms and/or exposure to risk factors for COPD should be considered for further assessment (GOLD, 2022). The most widely available test of airway obstruction is spirometry; however, it is possible for people to have evidence of structural lung disease (such as emphysema) without showing airflow limitation on spirometry. Both structural lung disease and airway obstruction in varying combinations can be seen in COPD (GOLD, 2022).

Etiology: The most significant etiological factor in the development of COPD and the progression of the disease is cigarette smoking (GOLD, 2022). However, individuals who are non-tobacco users may also develop airflow limitations and COPD (GOLD, 2022). Long-term asthma, especially if poorly controlled, has been attributed to some cases of COPD, and advancing age is a factor with symptoms presenting often after the ages of 40 to 50 years old (World Health Organization [WHO], 2017). Long-term cumulative exposure to noxious particles and gases, in combination with various other host factors such as airway hyperresponsiveness, inadequate lung growth and development during childhood, genetics, occupational/industrial gases or fumes, and indoor/outdoor air pollution are all contributing risk factors for COPD (GOLD, 2022; WHO, 2017).

Occurrence: COPD is a chronic disease with substantial morbidity and mortality worldwide, lending to social and economic burdens, long-term disability, and premature death (GOLD, 2022). Chronic lower respiratory disease, the predominant one being COPD, was the fourth leading cause of death in the United States in 2018 (Centers for Disease Control and Prevention [CDC], 2021). Globally, it is estimated that there are over 3 million deaths attributed to COPD (CDC, 2021; GOLD, 2022). An approximate 15.7 million Americans or 6.4% have been diagnosed with COPD (CDC, 2021). Over one-half of adults with abnormally low PFTs were unaware they had COPD and as a result the prevalence

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of COPD may be underrepresented (CDC, 2021). Low socioeconomic status is associated with an increased risk of developing COPD (Grahn et al., 2021).

The prevalence of COPD has been increasing more rapidly in women than in men (Grabicki M., et al., 2018). Some studies have suggested women are more susceptible to the detrimental effects of smoking than men, leading to greater severity of disease and burden of small airway disease despite a similar history of tobacco exposure (GOLD, 2022; Jenkins, 2017). Women who have COPD and have fewer pack-years of smoking than men, experience earlier onset, greater dyspnea, and progress to severe COPD more rapidly than men. Additionally, women with comparable smoking history have shown more loss of lung function, airflow obstruction, and exercise intolerance than men (GOLD, 2022; Jenkins, 2017). Grabicki et al. (2018) conclude that different gender phenotypes exist, which may indicate a need for more targeted assessment and management.

Age: Individuals aged 65 and older have the highest incidence of COPD (CDC, 2021). COPD development occurs gradually over time and most commonly becomes apparent after 40 to 50 years of age (WHO, 2017). Advancing age is a risk factor for COPD, although the evidence is unclear if it is the normal aging of the lungs that lead to COPD or if it is a result of cumulative exposures throughout life (GOLD, 2022).

Ethnicity: Incidence of COPD is lower in Black and south Asian people than in Whites (Gilkes et al., 2017).

Contributing Factors: Cigarette smoking is the most important risk factor for COPD (CDC, 2021; GOLD, 2022). Inhaling other pollutants and exposure to particles (e.g., second-hand smoke, pipe, water pipe, or cigar use), environmental and occupational exposures (e.g., biomass fuel exposure, chemicals, dust, fumes), and genetic determinants (e.g., alpha-1 antitrypsin deficiency) are other causative factors in COPD (GOLD, 2022; WHO, 2017). Chronic bronchitis and frequent respiratory infections have been associated with a greater risk of COPD (GOLD, 2022).

Signs and Symptoms: COPD is a complex, chronic disease that requires a comprehensive symptom assessment. A thorough history to include pattern of symptom development, past medical history, family history, exposure to risk factors, history of exacerbations, and/or hospitalizations for respiratory conditions aid in establishing the diagnosis of COPD (GOLD, 2022).

The most common symptom is chronic and worsening dyspnea. Other symptoms vary among individuals and depend on the severity of the airflow obstruction. In mild COPD, there may be dyspnea, cough (either productive or non-productive), wheezing, and chest tightness. As the disease progresses, dyspnea and cough will likely worsen, and other symptoms may emerge, including nocturnal waking with cough and or dyspnea. These patients may also experience more frequent episodes of temporary, sometimes severe, exacerbations and have increased oxygen requirements. In its more severe stages, symptoms will worsen, exacerbation rates may increase, and patients may feel increasing fatigue. They are also more likely to experience a decreased quality of life including anxiety and depression (GOLD 2022). In most people, symptoms vary from day to day and season to season. (GOLD, 2022).

Physical examination is not typically diagnostic in early COPD and may be normal (GOLD, 2022). In the early to middle stages, chest auscultation may reveal longer expirations with wheezing on forced expiration. Wheezes can sometimes be heard (most frequently with chronic bronchitis); the presence of crackles suggests possible pneumonia, pulmonary edema, or interstitial lung disease.

As the severity of the disease progresses, signs of airway limitations are more apparent on physical examination (GOLD, 2022). In advanced COPD, the examination may reveal decreased breath sounds, hyperinflation with resonance to percussion, use of accessory muscles of respiration, wheezes, crackles in the lung bases, pursed-lip breathing, and/or distant heart sounds (Bickley, 2017; Han et al., 2013). Hyperinflation restricts diaphragmatic movement, and the chest takes on a barrel-like appearance (Bickley, 2017). As the cardiovascular system attempts to compensate, tachycardia or a gallop rhythm commonly occurs. Right-sided heart failure and cor pulmonale seen in the later stages may present as jugular venous distension, hepatomegaly, or peripheral edema (Bickley, 2017). Patients frequently present for treatment due to health-related issues, such as upper or lower respiratory infections. In these instances, the clinician should assess for COPD as the underlying cause.

The impact of activity limitation, socioeconomic loss (e.g., missed workdays), and comorbid conditions (cardiovascular disease, heart failure, or osteoporosis) can help establish the diagnosis of COPD. The severity of symptoms and airflow limitation associated with COPD affect both quality of life and activities of daily living (ADLs). Functional limitation to activities, such as socializing, doing chores, sleeping, and work performance may vary daily (GOLD 2022).

Diagnostic Tests: Spirometry is the gold standard for measuring airflow limitation (GOLD, 2022; Guirguis-Blake et al., 2016). Airflow limitation that is not fully reversible is evident if post-bronchodilator first second of forced expiration/forced vital capacity (FEV_1/FVC) is <0.70 and FEV_1 is less than 80% predicted (Table 11-1) (GOLD, 2022). The U.S. Preventive Services Task Force (USPSTF) recommends spirometry only in symptomatic patients because there was no direct evidence to support screening asymptomatic individuals (Guirguis-Blake et al., 2016). Symptoms for considering a diagnosis and performing spirometry include dyspnea, cough, chronic sputum production, and recurrent lower respiratory tract infections, especially in the presence of risk factors, including

TABLE 11-1 Global Initiative for Chronic Obstructive Lung Disease: Post-Bronchodilator FEV_1 Classification of Severity of Airflow Limitation

PATIENT CRITERIA: FEV_1/FVC <0.70	
FEV_1 ≥80% predicted	GOLD 1: Mild
50% ≤FEV_1 <80% predicted	GOLD 2: Moderate
30% ≤FEV_1 <50% predicted	GOLD 3: Severe
FEV_1 <30% predicted	GOLD 4:Very Severe

Adapted from GOLD Pocket guide to COPD diagnosis, management, and prevention: A guide for health care professionals, *2022.*

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family history of COPD and/or childhood factors (GOLD, 2022). Because airflow usually decreases with age, spirometry predicted values are age adjusted. Spirometry has good sensitivity, but a peak expiratory flow measurement alone is unreliable when used as the only diagnostic tool because of weak specificity (GOLD, 2022). Because there is a weak correlation between FEV_1, symptoms, and impairment impacting an individual's health status, a more formal assessment of symptoms is indicated.

The 2017 GOLD guidelines added important multidimensional recommendations regarding COPD assessment, management, and treatment. In addition to results of spirometry, assessing the impact of COPD, the burden of disease, the risk of disease progression, and COPD exacerbation risk are integral components. The most comprehensive disease-specific questionnaires with reliability and validity focused on health status include the Chronic Respiratory Questionnaire (CRQ) and the St. George's Respiratory Questionnaire (SGRQ) (GOLD, 2022). Although comprehensive, these questionnaires are lengthy, and have very complex scoring, making them impractical for clinical use (GOLD, 2022). The brief and simple COPD Assessment Test (CAT) and COPD Control Questionnaire (CCQ) are both valid and reliable assessment tools and are the best for use in clinical practice (GOLD, 2022). The CAT is the more widely used clinically, and it is applicable worldwide because it is available in multiple languages (GOLD, 2022). The modified Medical Research Council (mMRC) questionnaire measures dyspnea on a scale from 0 to 4; this is also very useful clinically (GOLD 2022).

The most accurate staging of COPD now includes both spirometry and symptom burden. First introduced in the 2011 GOLD guidelines, the ABCD assessment tool considers the number and severity of exacerbations in addition to patient self-assessment using mMRC or CAT. High symptom burden and rate/severity of exacerbations combined with severity of airflow limitation allows for a more accurate assessment and therefore customized treatment plan.

Radiographic imaging with a chest x-ray alone is not diagnostic of COPD but can provide value in excluding differential diagnoses, detecting the presence of concomitant pulmonary disease (bronchiectasis, pleural diseases, pulmonary fibrosis), pneumonia, or cardiac diseases (e.g., cardiomegaly) (GOLD, 2022). Chest radiography in early COPD appears normal (Martini & Frauenfelder, 2018). Radiographic abnormalities associated with COPD such as lung hyperinflation, hyperlucency of the lungs, or tapering of vascular markings may be seen (GOLD, 2022; Martini & Frauenfelder, 2018). Structural lung disease (e.g., emphysema, gas trapping, or airway wall thickening) consistent with COPD findings may also be shown. Radiographic signs of advanced COPD with emphysema include hyperinflation, bullae/blebs, and a flattened hemidiaphragm. A chest x-ray is not recommended for screening of lung cancer, instead, the USPSTF (2017) recommends annual screening with low-dose computed tomography (CT) in adults aged 55 to 80 years with a 30 pack-year smoking history and who currently smoke or have smoked in the past 15 years.

Pulse oximetry is a noninvasive way to assess a patient's arterial oxygen saturation and need for supplementation oxygen therapy. If pulse oximetry is less than 92%, arterial or capillary blood gases are recommended (GOLD, 2022).

Laboratory tests are not routinely used in the assessment of COPD, but because it is common for those patients to have other chronic diseases, such tests can be useful to assess the overall health of the patient. Some consideration could be given to a complete blood count (CBC) with differential to rule out anemia, polycythemia which can occur in advanced COPD with hypoxemia, infection (elevated white blood cell count), or concomitant allergy/asthma (eosinophilia). Serum alpha-1-antitrypsin levels are not recommended for routine screening but should be considered for individuals presenting with COPD at early ages (less than 45 years of age), in non-tobacco users with clinical emphysema, and individuals with a family history of COPD or alpha-1-antitrypsin deficiency at a young onset (Carreto et al., 2020).

To evaluate for the comorbidity of coronary artery disease, an electrocardiogram (ECG) is recommended because patients with COPD and older adults often have atrial arrythmias. Peaked P waves in leads II, III, and aVF may be apparent in patients with pulmonary disease. If cardiac involvement is severe, an ECG in advanced COPD may demonstrate evidence of right-axis deviation, sinus tachycardia, and pulmonary hypertension with the presence of ongoing S waves in the lateral precordial leads.

Differential Diagnosis: Aside from asthma, COPD is fairly easy to distinguish from other potential differential diagnoses when appropriate testing, history taking, and examination are completed (GOLD 2022). Other differential diagnoses may include interstitial lung disease, heart failure, pneumonia, bronchiectasis, tuberculosis (TB), obliterative bronchiolitis, and diffuse panbronchiolitis.

Treatment: Individualize treatment goals according to the stage of disease, symptom assessment, patient goals, comorbidities, and risk of a COPD exacerbation. Treatment is targeted toward improvement of health/functional status and quality of life, prevention of disease progression, avoidance of exacerbations or complications, prevention of treatment side effects, and management of exacerbations (GOLD, 2022). The GOLD Report identifies four segments of a COPD management program: (1) diagnosis and assessment, (2) prevention and maintenance therapy, (3) management of stable COPD, and (4) management of COPD exacerbations.

Prevention and Prophylaxis:

- COPD is almost 100% preventable by avoidance of smoking. Early detection of COPD may alter the course and progression (CDC, 2020).
- All COPD patients should have annual influenza vaccine, and both the pneumococcal polysaccharide vaccine (PPSV23) and the Previnar 13 (PCV 13) are recommended for all patients at age 65 years (CDC, 2021). Prior to age 65, adults 19 to 64 years of age at high risk (e.g., cigarette smoking, chronic conditions, COPD) are recommended to have the PPSV23 and for individuals who receive a PPSV23 prior to age 65 years, revaccination is recommended with PPSV23 at age 65 years (CDC, 2022).

Risk Factor Reduction:

- Identification and reduction of exposure to risk factors is key in the prevention and treatment of COPD (GOLD, 2022).

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- Smoking cessation is the most effective and cost-effective intervention and should be promoted at every visit (CDC, 2021; GOLD, 2022). Counseling (brief or intensive), educational, and community resources are helpful. Pharmacotherapy (e.g., nicotine replacement therapy, bupropion, varenicline, or combination therapy) should be offered as a component of a supportive intervention program but not alone (CDC, 2021; GOLD, 2022).
- Identify and reduce personal exposure to occupational or environmental risk factors (fumes, gases, dust, indoor/outdoor air pollutants).
- Vaccination for influenza and pneumococcal pneumonia (PCV13 and PPSV23) are recommended unless contraindicated.
- Adequate hydration and nutrition are important.

Management of Stable COPD:

- Individualize assessment and treatment to reduce current symptoms and risk of exacerbations.
- Establish an active care-partnership with patients using shared decision making. Educate patients on the disease process, reasonable functional goals, pharmacological therapies, and risk factors for progression. Education must include recognition of instability and when to seek medical assistance. Adherence to treatment regimen should be included in education provided.
- Discussion of healthy living, nutrition, and physical activity is essential.
- Pulmonary rehabilitation is recommended in patients with high symptom burden to reduce symptomatology and risk of exacerbations (GOLD, 2022). Pulmonary rehabilitation has been shown to be a highly effective therapeutic intervention to improve dyspnea, health status, and exercise intolerance (GOLD, 2022).
- Long-term supplemental oxygen therapy in patients with severe resting hypoxia has been shown to improve survival (GOLD, 2022). Additional benefits include reduction in nocturnal hypoxemia, arrhythmias, polycythemia, and dyspnea. Increased exercise tolerance and improved cognition have also been observed. Criteria for oxygen therapy include resting PaO_2 ≤55 mm Hg or SaO_2 ≤88% with or without hypercapnia. Qualification criteria may be broader if there is evidence of pulmonary hypertension, polycythemia, or peripheral edema suggesting heart failure (GOLD, 2022).
- Anxiety and depression are comorbidities associated with COPD and attributed to poor health outcomes (Paine et al., 2019). Assess for symptoms and provide psychological interventions as indicated.

Pharmacological management is the cornerstone of COPD treatment and is directed at symptom improvement, exacerbation severity and risk reduction, and exercise tolerance and health status improvement (GOLD, 2022). The GOLD report recommends initiation therapy along with subsequent escalation and/or de-escalation of pharmacological management.

In select patients, surgical options such as lung volume reduction surgery (LVRS), bullectomy, and lung transplant may be considered. Bronchoscopic endobronchial valve placement, a less invasive alternative to LVRS, is now more broadly available (GOLD, 2022).

Open communication between the patient and provider is a vital part of comprehensive care. When COPD progresses, discussion of philosophy of care, including resuscitation and mechanical ventilation, becomes increasingly important, allowing patients to make their own decisions. Ideally, goals of care discussions should take place during periods of disease stability. In advanced or end-stage COPD, palliative care may be useful, and hospice is a reasonable consideration.

Management of COPD Exacerbations: COPD exacerbations are defined as "an acute worsening of respiratory symptoms that result in additional therapy." They are most often precipitated by respiratory tract infections (GOLD, 2022). Exacerbations are attributed to progression of disease, worsening health status, and increased mortality. COPD exacerbations are classified as mild, moderate, or severe (GOLD, 2022). Interventions aligned with severity include short-acting bronchodilators (SABDs) for mild exacerbations and SABDs and/or or oral corticosteroids for moderate exacerbations. For severe exacerbations, patients should seek care in an ED because hospitalization may be required (GOLD, 2022). Severe exacerbations may be associated with acute respiratory failure, which can be life-threatening (GOLD, 2022). When hospitalization for a COPD exacerbation is required, it is associated with a poor long-term prognosis.

Treatments for exacerbations include SABAs with or without anticholinergics, long-acting bronchodilators, systemic corticosteroids, antibiotics, oxygen therapy, noninvasive mechanical ventilation, and/or invasive mechanical ventilation (GOLD, 2022). Individualized action plans for management of COPD exacerbations, along with patient education, have been found to significantly reduce the risk of hospitalization (Schrijver et al., 2021). Goals for treatment include minimizing the negative impact of the current exacerbation and preventing future events (GOLD, 2022).

Pharmacological Management for Stable COPD: Pharmacological therapy for COPD has a significant role in reducing symptoms and minimizing exacerbations. It can also lead to improved exercise tolerance, health status, and quality of life (GOLD, 2022). Individualized treatment regimens should be based on severity of symptoms, degree of airflow limitation, and exacerbation history. A stepwise approach to therapy is utilized in the treatment of COPD. No current drug therapy has been proved to influence the long-term, progressive decline in lung function (GOLD, 2022). Classes of medications in the treatment of COPD are shown in Table 11-2.

Follow-Up: A newly diagnosed patient should be seen frequently until an optimal treatment plan is in place and disease education has been completed. For stable patients, routine reassessment every 3 to 6 months is advisable, with instructions to the patient or caregiver to schedule an interim visit if there is a change in status, increased symptoms, or an infectious process. For stable patients with other significant comorbidities, visits every 3 months are advisable. A team model for chronic care is optimal for COPD management. Periodic reassessment of pulmonary function and assessment of patient report of breathing status can guide therapy. Patients who are unstable or have had an acute exacerbation will need more frequent follow-up visits initially. Collaborative management with these patients is strongly advised. During the immediate

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TABLE 11-2 Medications for Chronic Obstructive Pulmonary Disease

Inhaled $Beta_2$-Agonist Bronchodilators	*Short-acting (SABAs)* • Albuterol, levalbuterol • Reverse bronchoconstriction by relaxing smooth muscles in the airways • Rapid onset (about 15–30 minutes) • Duration of action: 4–6 hours • Are not recommended as scheduled monotherapy in patients with ongoing or frequent symptoms; stepping up therapy would be indicated in those instances *Long-acting (LABAs):* • Formoterol and salmeterol (12-hour duration) • Olodaterol, vilanterol, and indicaterol (24-hour duration) • Used for maintenance therapy to prevent acute bronchospasms • Not for relief of acute symptoms
Inhaled Anticholinergic/ Antimuscarinic Bronchodilators	• Block the bronchoconstricting effects of acetylcholine on muscarinic cholinergic receptors in the smooth muscle of the airways • Have anticholinergic properties and should be used cautiously in patients with narrow-angle glaucoma, significant prostatic hypertrophy, or bladder neck obstruction, and are contraindicated in patients who are allergic to atropine *Short-acting* • Ipratropium • 6- to 8-hour duration • Used in long-term and acute COPD management *Long-acting* • Tiotropium • Used for maintenance treatment • 24-hour duration • Shown to decrease symptoms of dyspnea and reduce the frequency of COPD exacerbations and hospitalizations
Glucocorticoids	• Have anti-inflammatory effects on COPD-associated inflammation *Inhaled corticosteroids:* • Monotherapy with ICSs is not recommended unless they are used in combination with inhaled bronchodilators. • Instruct the patient to rinse the mouth after using any ICS to reduce the risk of oral thrush. *Systemic corticosteroids:* • Have nonspecific anti-inflammatory properties and are used for short-term treatment in the management of an acute COPD exacerbation. • Are associated with numerous side effects and, therefore, have no role in long-term management of COPD.
Combination Bronchodilator Therapy	• Bronchodilators with different mechanisms of action may improve the degree of bronchodilation with a lower risk than that associated with increasing the dose of a monotherapy agent. • Combination inhaled therapy with LABAs, ICSs, or LAMAs are used for stable COPD patients with symptoms and may be more effective than the individual agents. • ICS/LABA combinations have been shown to be more effective than either component alone in terms of symptom improvement and exacerbation reduction. • Fluticasone/salmeterol and budesonide/formoterol are examples of combination ICS/LABAs. • In patients with stable, moderate to very severe COPD, a maintenance combination of an ICS/LABA or ICS/LAMA should be considered. • For patients with severe or very-severe COPD and persistent symptoms, triple therapy is recommended with a combination ICS/LABA/LAMA. • There are now single inhalers which offer this triple combination. • It is challenging to keep up with all the options available in inhaled format. The use of charts that include pictures can be useful in communicating with patients about what it is they are using for inhaled therapy.
Methylxanthines	*Theophylline* • A nonspecific phosphodiesterase inhibitor/oral bronchodilator • The most common methylxanthine, but use has decreased significantly • Has been found to be modestly effective with a narrow therapeutic index, potential for toxicity, many drug-to-drug interactions, and wide range of toxic adverse effects
Phosphodiesterase-4 (PDE4) Inhibitors	• Inhibit the breakdown of cyclic AMP, thus reducing inflammation. *Roflumilast:* • Once daily oral PDE4 inhibitor indicated in patients with severe or worse disease and frequent exacerbations • Has a high rate of side effects, including nausea, diarrhea, weight loss, headaches, and sleep disturbances • Using lower doses to start may be helpful • Avoid use in underweight patients or those with depression

Sources: *Anzueto & Miravitlles, 2020; Brightling & Greening, 2019; GOLD, 2022*

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post-acute period, a pulmonary specialist should manage the patient. Pulmonary rehabilitation is helpful in moderate to severe disease (GOLD, 2022).

Sequelae: COPD is a multisystem disease and can lead to respiratory infections, cor pulmonale, pulmonary hypertension, malnutrition, acute or chronic respiratory failure, steroid-induced myopathy, or Cushing's syndrome, bullous lung disease, polycythemia, and sleep-related hypoxemia. Depression is frequently associated with COPD (Paine et al., 2019).

Prevention/Prophylaxis: Avoidance of tobacco, smoking cessation, and avoidance of second-hand smoke are encouraged.

Referral: Collaborative management is advised in all patients. Refer patients to a pulmonary specialist during instability, for hospital and post-acute care, to evaluate for the appropriateness of surgical options, and for oxygen therapy evaluation. Refer patients to pulmonary rehabilitation for reconditioning and education on breathing techniques and energy-conserving measures. Consult with a dietary health professional when applicable. Post-acute COPD patients in the community should be referred for home care. Refer all patients to community resources and support groups. Palliative care and hospice options are considerations.

Education: Teach the patient, family, and/or caregivers about the disease process and its management, the association of risk factors such as smoking and importance of cessation, pharmacological therapy, oxygen therapy and precautions, and the importance of seeking early care for symptoms of exacerbation or infectious processes (GOLD, 2022). Self-management education and coaching are integral components of a chronic care model approach (GOLD, 2022). Self-management skills include monitoring and managing signs and symptoms of COPD, treatment adherence, and maintaining regular follow-up with health-care providers.

Clinical Recommendation	Evidence Rating	References
Smoking cessation is the most effective and cost-effective intervention and should be promoted at every visit.	A	GOLD, 2022 CDC, 2021
In patients with respiratory symptoms, particularly dyspnea, spirometry should be performed to diagnose airflow obstruction. Spirometry should not be used to screen for airflow obstruction in asymptomatic individuals.	B	GOLD, 2022
Pulmonary rehabilitation consisting of exercise training, muscle strengthening, nutritional counseling, energy conservation, ADLs, breathing modifications, medication education (including use of inhaler devices), and oxygen use is beneficial, particularly in moderate-to-severe COPD.	A	GOLD, 2022
Supplemental oxygen therapy in patients with resting hypoxia improves survival.	A	GOLD, 2022
Bronchodilators are the foundation of symptomatic management	A	GOLD, 2022
ACP, ACCP, ATS, and ERS recommend that clinicians prescribe either long-acting inhaled anticholinergics or long-acting inhaled beta agonists for symptomatic patients with COPD and FEV_1 <60% predicted. Clinicians should base the choice on patient preference, cost, and adverse effect profile.	A	GOLD, 2022
Chronic oral corticosteroids are not recommended in COPD.	A	GOLD, 2022
Regular treatment with ICSs improves symptoms, lung function, and quality of life and reduces exacerbations in COPD patients with an FEV_1 <60% predicted.	A	GOLD, 2022
Education improves patient response to exacerbations.	B	GOLD, 2022
Prospective end-of-life discussions can lead to effective end-of-life decisions through improved understanding.	B	GOLD, 2022

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

INFLUENZA

Signal Symptoms: Acute onset of fever, headache, myalgia, and malaise. These symptoms usually coexist with other respiratory complaints such as cough, dyspnea, sore throat, coryza, and rhinorrhea. Fevers generally range between 37.8°C to 40.0°C (100°F to 104°F). Older adults may present with more subtle symptoms such as confusion, appetite loss, fatigue or malaise, weakness, and dizziness along with exacerbations of other chronic conditions such as COPD or heart failure (Dolin, 2020a; Talbot, 2017).

Description: Seasonal influenza is an acute viral infection that affects the entire respiratory tract (nose, mouth, throat, and lungs). Several modes of influenza transmission have been identified, including inhalation of airborne particles or

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respiratory droplets (exhalation or talking within six feet, coughing and/or sneezing), fomites, and contact with contaminated surfaces. Seasonal outbreaks generally occur during colder months in temperate climates (U.S. Department of Health and Human Services [HHS], 2021a; Dolin, 2020a; Gaitonde et al., 2019).

The incubation period for influenza is between 1 and 4 days. The infectious period occurs 1 or 2 days before symptom onset and lasts 5 days on average but up to 10 days in some cases. Viral shedding may be even more prolonged in patients who are immunocompromised. Magnitude of shedding is variable and associated with disease severity (Dolin, 2020a; Gaitonde et al., 2019).

Etiology: Influenza infection is caused by a strain of A, B, or C viruses of the Orthomyxoviridae family. Influenza A infects both humans and animals and can rapidly mutate, resulting in novel virus variations. Lack of immunity to new viral strains resulting from these antigenic shifts has triggered numerous seasonal pandemics and epidemics over the last century. Influenza B viruses have two separate lineages and a lower propensity for mutation. Influenza B only infects humans and carries lower risk of causing seasonal epidemics than type A. Influenza C only infects humans and results in mild illness. Influenza C outbreaks tend to be sporadic and localized. Different strains of the virus may cocirculate during the influenza season (HHS, 2021a; Dolin, 2020b; Keilman, 2019).

Influenza A viruses carry greater transmissibility and disease burden than B or C type viruses. Subtypes of the influenza A virus vary in their degree of transmissibility and severity of disease burden. This group of viruses are responsible for the pandemics in 2018 (H1N1), 2009 (H1N1), 1957 (H2N2), and 1968 (H3N2). Although risk of human infection from Avian Influenza A (H5N1) is low, this strain has a much higher mortality rate compared to H1N1—50% and less than 15%, respectively (HHS, 2021a; Park & Ryu, 2018).

Occurrence: Pneumonia and influenza together are the eighth leading causes of death in the United States. The World Health Organization (WHO) (2017) reports lower respiratory infections as the fourth leading cause of death worldwide and the leading cause of death due to infectious disease. The 2019–2020 seasonal influenza caused approximately 35 million cases of symptomatic illness and more than 300,000 hospitalizations in the United States alone. The CDC also estimates flu burden of 16 million medical visits and 20,000 deaths during the 2019–2020 season. Visit rates to the ED for patients with influenza are 4.4 per 1,000 persons (HHS2021b; Herron, 2021; Reid & Fingar, 2020; WHO, 2021).

Older adults (65 years and older) carry the greatest risk of severe influenza disease. Hospitalization rates for older adults with influenza are estimated at 316.4 per 100,000 persons, compared to 191 per 100,000 adults aged 18 to 64. Influenza related mortality among older adults is more than twice that of adults under age 65. It is estimated that this vulnerable population accounts for up to 70% of influenza-related hospitalizations and more than 70% of flu-related deaths (HHS, 2021b). The number of deaths due to pneumonia and influenza is greater for women compared to men (Herron, 2021).

Age: Older adult patients are at increased risk for severe influenza and related complications (HHS, 2021c).

Ethnicity: Cause of death due to pneumonia and influenza is highest among Americans of Asian and Pacific Islander descent and lowest among non-Hispanic Black and White persons. Non-Hispanic Black, Hispanic or Latino, and American Indian or Alaskan Native persons are at increased risk for hospitalization from influenza (HHS, 2021b; Herron, 2021).

Contributing Factors: Modifiable risk factors related to flu-related complications include tobacco and alcohol use. Main factors associated with influenza morbidity and mortality in older adults are advanced age, presence of any medical comorbidity, immune-compromised states, and genetic predisposition. Older adults are much more likely to require hospitalization and develop serious complications secondary to influenza infection (HHS, 2021c; Keilman, 2019; Paules & Subbarao, 2017).

Chronic comorbidities commonly associated with severe flu-related illness and secondary complications include asthma, chronic lung disease, heart failure, diabetes mellitus, morbid obesity, renal disease, liver disorders, and those with history of stroke. Patients who are immunocompromised, such as those with cancer undergoing chemotherapy or those who require chronic use of corticosteroids and immune-suppressing drugs, are at increased vulnerability (Keilman, 2019; Walker et al., 2020; Zachary, 2021).

Immune senescence, genes, and genetic polymorphisms can influence susceptibility to influenza A infection by modulating risk for severe disease and mortality. Certain alleles operate along protective pathways by inhibiting viral replication and/or cellular entry by influenza viruses. Alternatively, other alleles, or lack thereof, result in defective complement system and impaired immune response (Clohisey & Baillie, 2019; Paules & Subbarao, 2017).

Residents of long-term care (LTC) facilities are particularly vulnerable, with influenza being a leading cause of communicable disease outbreaks. The prevention and control of seasonal influenza outbreaks in LTC has proven to be challenging. Older adults' atypical presentation of influenza often leads to delayed recognition and treatment, contributing to mortality rates as high as 55% due to outbreaks in LTC facilities (Richards & Stuart, 2020; Talbot, 2017).

Signs and Symptoms: Textbook clinical presentation includes subjective complaints of sudden onset fever, chills, cough, myalgia, arthralgia, and headache. Patients may also have complaints of fatigue, malaise, sore throat, nasal congestion, dyspnea and/or pleuritic chest pain. Older adults typically do not present with classic symptomatology. Fever is often absent, especially in patients who have received seasonal influenza vaccines. Gastrointestinal complaints such as nausea, vomiting, and diarrhea are not common. Older adults may present with anorexia, delirium, fatigue and/or low-grade fever (temperature greater than 37.3°C or 99.0°F). Older adults often present with signs of chronic illness exacerbations such as COPD or heart failure. (Dolin, 2020a; Keilman, 2019; Talbot, 2017).

Physical examination in uncomplicated influenza is often unremarkable, but when present, findings most commonly include skin flushing or oropharyngeal hyperemia. Ocular

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findings including conjunctivitis or excessive lacrimation may be present but are uncommon. Cervical lymphadenopathy generally is not present in the older adult presentation. Chest examination is often unremarkable, but diffuse rhonchi or rales are present in approximately 25% of cases (Dolin, 2020a; Paules & Subbarao, 2017).

Diagnostic Tests: Selection of diagnostic test for seasonal influenza should be determined by test availability and how quickly results are needed.

Molecular Assays: These tests preferred over antigen detection tests because they have the highest sensitivity, but they may not always be readily available. Molecular assays remain the gold standard for influenza testing of outpatient and hospitalized patients (Dolin, 2021; Uyeki et al., 2019). Rapid molecular assays, or nucleic acid amplification tests, are recommended for use in outpatient setting because of their high sensitivity and specificity and can be used at point of care, taking less than 20 minutes to result. These tests are also able to differentiate between type A and B influenza. They are not able to distinguish between variant influenza subtypes (Dolin, 2021; Uyeki et al., 2019).

Reverse-Transcription Polymerase Chain Reaction (RT-PCR) Tests: These tests are preferred for patients who are hospitalized and have high sensitivity. RT-PCR can differentiate between influenza types and subtypes. Multiplex RT-PCR tests should be used for hospitalized patients who are immunocompromised or mechanically ventilated, or cases in which such testing may alter treatment course. Multiplex assays can identify multiple etiologies of acute respiratory infections. The U.S. Food and Drug Administration (FDA) has approved several multiplex assays that can distinguish between strains of influenza A or B, and SARS-CoV-2. These assays are particularly useful during peak periods of influenza activity where these three viruses cocirculate (Dolin, 2021; Uyeki et al., 2019; Uyeki et al., 2020).

Antigen Detection Assays: These tests have poor sensitivity and are only recommended for use in hospitalized patients when molecular assays are not available. These tests should not be considered diagnostic and follow up testing with a molecular assay is needed to confirm or rule out diagnosis of influenza. Digital immunoassays are a newer option showing promise with sensitivity near that of molecular assays, but further experience with these tests is needed. They are not currently recommended because stronger evidence supporting test validity is needed (Dolin, 2021; Uyeki et al., 2019).

Viral Culture and Serological Testing: Viral cultures, formerly the gold standard for diagnosis, are no longer recommended for primary influenza diagnosis. These tests are still used in public health surveillance and institutional outbreaks to confirm negative rapid influenza diagnostic tests and antigen detection assays. Viral cultures typically take 48 to 72 hours or longer to be processed (Dolin, 2021; Uyeki et al., 2019).

Serological testing is not recommended for influenza diagnosis. Clinically, this test's only utility is in retrospective influenza diagnosis and is therefore generally reserved for research purposes only (Dolin, 2021; Uyeki et al., 2019).

Diagnostic Imaging: Chest x-ray or CT scan are appropriate if primary influenza pneumonia and/or secondary bacterial pneumonia are suspected. Chest x-ray findings in primary influenza pneumonia typically include bilateral opacities without consolidation. CT scan may demonstrate multifocal consolidation and/or ground glass opacities. Patients with concomitant viral and bacterial influenza pneumonia often have evidence of frank consolidation and bilateral pulmonary infiltrates on chest radiograph (Dolin, 2020a; File, 2020).

Outpatient Testing: Although uncomplicated influenza generally does not require hospitalization, high-risk populations benefit from prompt diagnosis and treatment to reduce risk of deterioration in condition. Accurate detection of influenza provides clinicians an opportunity to prescribe the appropriate treatment course, promoting antibiotic stewardship and reduces number of unnecessary tests to rule out alternate symptom etiologies (Uyeki et al., 2019).

The Infectious Disease Society of America (IDSA) recommends diagnostic testing during peak influenza activity periods for high-risk populations or for cases in which testing will alter the patient's treatment course. Testing is warranted if it will influence decision making regarding antibiotic versus antiviral medication, appropriate treatment setting, or reduce need for additional diagnostic testing (Uyeki et al., 2019).

Nasopharyngeal specimens collected within 4 days of symptom onset are preferred for diagnostic testing of influenza in the outpatient setting. Collection of nasal and throat swab specimens combined is acceptable when nasopharyngeal specimens are unavailable. Collection of nasal or throat swab specimens alone is not recommended. Flocked-swab specimen collection is preferred over non-flocked swab specimens (Uyeki et al., 2019).

During periods of low influenza activity, testing is not routinely recommended, except in patients presenting with acute onset of respiratory symptoms, with or without fever. Clinicians should also consider testing patients who present with non-specific respiratory illness, especially those who are immunocompromised or at high-risk of influenza-related complications (Uyeki et al., 2019).

Hospitalized Patients: During peak periods of influenza activity, the IDSA recommends diagnostic testing of patients with an acute respiratory illness or acute exacerbation of COPD, asthma, heart failure, or coronary artery disease upon hospital admission. During periods of low influenza activity, the IDSA recommends testing patients with known exposure to influenza or recent travel to an area of known outbreak who present with acute respiratory illness. Testing should be considered for hospitalized patients who are immunocompromised or at high risk of complications secondary to influenza (Uyeki et al., 2019).

Nasopharyngeal specimen collection is preferred for hospitalized patients without severe lower respiratory tract disease. Testing should be completed upon hospital admission or as soon as able. Endotracheal aspirate or bronchoalveolar lavage fluid specimens should be collected from all mechanically ventilated patients, even if upper respiratory tract specimens tested negative for influenza (Chow et al., 2019; Uyeki et al., 2019).

Differential Diagnosis:

- Common cold
- Allergic or seasonal rhinitis
- Coronavirus disease 2019 (COVID-19)
- Acute bronchitis

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- Asthma exacerbation
- Respiratory syncytial virus
- Rhinovirus
- Bacterial pharyngitis or tonsillitis
- Acute bacterial rhinosinusitis
- Pertussis
- COPD exacerbation
- Heart failure

Treatment: The IDSA recommends initiation of antiviral therapy for the following patients with suspected or confirmed influenza, regardless of immunization status or illness duration:

- All hospitalized patients with influenza
- All outpatients with severe or progressive illness
- All outpatients who are at high risk of influenza-related complications

Antiviral therapy should be considered for the following patients with suspected or confirmed influenza, who are not considered high risk for influenza-related complications, regardless of immunization status or illness duration:

- Outpatients presenting with symptom onset within the past 48 hours
- Symptomatic outpatients with household contacts who are immunocompromised or considered high risk of influenza-related complications
- Symptomatic health-care providers who regularly care for patients who are immunocompromised or considered high risk of influenza-related complications

Treatment with antiviral therapy should be initiated as early as possible, ideally within 48 hours of symptom onset, which is associated with reduction in illness severity and duration. It is recommended to initiate antiviral treatment while awaiting results of diagnostic tests. Patients with negative rapid antigen tests should still be treated with antiviral therapy if clinical presentation is highly suspicious for influenza because of the low sensitivity of these tests. Administration of antiviral therapy to hospitalized patients within 48 hours of symptom onset is also associated with shorter hospital length of stay (Dou et al., 2020; Gaitonde et al., 2019; Uyeki et al., 2019; Zachary, 2021).

Medication Management: IDSA recommends treatment of confirmed or suspected influenza with a single neuraminidase inhibitor (NAI) or cap-dependent endonuclease inhibitor. Oseltamivir is the preferred choice for uncomplicated and severe influenza; however, treatment selection should be individually based on patient needs and characteristics. Other acceptable antiviral treatment options include zanamivir, peramivir, or baloxavir marboxil. Treatment with combination NAI therapy is not recommended (Uyeki et al., 2019; Zachary, 2021).

Treatment with oseltamivir or peramivir is recommended for severely ill patients with influenza. Both drugs are subject to renal dose adjustments in older adults. The dose of antiviral medication should not be increased for treatment of patients with severe influenza. Initiation of antiviral treatment within 48 hours of symptom onset is associated with decreased length of hospital stays. No significant reduction in mortality rates, complications, or illness duration has been identified in patients treated with antiviral medication doses that exceed standard of care (Chow et al., 2019; Dou et al., 2020; Uyeki et al., 2019; Zachary, 2021).

Duration of treatment of uncomplicated influenza with oral oseltamivir or inhaled zanamivir is 5 days, while peramivir or baloxavir marboxil can be administered in a single dose. Clinicians should consider an extended course of antiviral treatment for patients who are immunocompromised, have influenza pneumonia, or acute respiratory distress syndrome (ARDS). Refer to Table 11-3 for comparison of antiviral medication options (Uyeki et al., 2019; Zachary, 2021).

Adjunct Therapies: Treatment of influenza with adamantanes (amantadine and rimantadine) is not recommended. These drugs are only effective against influenza A viruses and the rate of viral resistance to these medications is high. Adjunct therapy with corticosteroids is not recommended for adults with confirmed or suspected influenza unless there are other medical indications. Treatment with intravenous immunoglobulin therapy is not recommended for adults with confirmed or suspected influenza (Uyeki et al., 2019; Zachary, 2021).

Various herbal and homeopathic treatments are marketed for influenza treatment, none of which have strong evidence to support their use. These treatments pose additional risks for older adults. There is positive correlation between number of medications used, risk of adverse medication reactions, and drug-related hospitalizations. Older adults should be instructed to avoid over-the-counter (OTC) treatments for influenza without consulting their primary care provider (Halli-Tierney et al., 2019).

Symptom Management: Acetaminophen is the drug of choice for relief of fever, headache, myalgias, and arthralgias in older adults. NSAIDs should be used with extreme caution in the older adult population because of the increased risk of acute kidney injury, bleeding, and cardiovascular side effects. Symptom management with NSAIDs should be reserved for use in older adult patients when acetaminophen is contraindicated. NSAID therapy should be prescribed for the shortest duration possible and at the lowest effective dose. (American Geriatrics Society Beers Criteria® Update Expert Panel, 2019; Zachary, 2021).

Oral suspension guaifenesin or menthol lozenges are reasonable options for older adult patients who find cough associated with influenza particularly bothersome. Older adult patients should be cautioned to avoid OTC antihistamines and decongestants for symptom management. Patients should be instructed to maintain adequate fluid intake to avoid dehydration. Physical activity should be encouraged as tolerated to minimize deconditioning (Zachary, 2021).

Follow-Up: Follow-up is dependent on individual patient characteristics, comorbidities, and treatment response. Patients diagnosed with influenza in the outpatient setting should be counseled that recovery can take 1 to 2 weeks without antiviral treatment. Older adults who are at high risk of complications should schedule a follow-up office visit within a few days after completion of antiviral treatment. Patients should be instructed to call if symptoms worsen, if no response occurs after 3 to 5 days of treatment, or if symptoms recur. Patients hospitalized with influenza should follow up with their primary care provider within 1 week of hospital discharge.

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TABLE 11-3 Comparison of Antiviral Medications for Seasonal Influenza Treatment in Adults

ANTIVIRAL AGENT	INDICATION	ROUTE/ FORMULA	DOSING WITH RENAL ADJUSTMENTS				SPECIAL CONSIDERATIONS
			CrCl >60	*CrCl 30 to 60*	*CrCl 10 to 30*	*CrCl <10*	
oseltamivir (Tamiflu)	Uncomplicated and severe influenza	Oral capsules	75 mg PO twice daily ×5 days	30 mg PO twice daily ×5 days	30 mg PO daily ×5 days	Avoid use	Preferred as first-line therapy over other neuraminidase inhibitors
zanamivir (Relenza)	Uncomplicated influenza	Inhalation	Two 5-mg inhalation (10 mg) twice daily ×5 days				N/A
			CrCl >50	*CrCl 30–49*	*CrCl 10–29*	*CrCl <10*	
peramivir (Rapivab)	Uncomplicated and severe influenza	IV infusion	600 mg IV ×1 dose over 15–30 minutes	200 mg IV ×1 dose	100 mg IV ×1 dose	Avoid use	Do not use if resistance to oseltamivir suspected.
			CrCl >50	*CrCl <50*			
baloxavir marboxil (Xofluza)	Uncomplicated influenza	Oral tablets	<80 kg: 40 mg PO ×1 dose; >80 kg: 80 mg PO ×1 dose	Undefined/not studied in this population.			Avoid administration with dairy products, calcium-fortified beverages, antacids, or other oral supplements.

CrCl = creatinine clearance

Sources: *Gaitonde et al., 2019; Hibberd, 2022; Uyeki et al., 2019*

Sequelae: The most common influenza-related complication is pneumonia, and older adults are disproportionately affected. Secondary bacterial pneumonia is most common, but primary influenza pneumonia is most severe. Patients predisposed to primary influenza pneumonia include those with valvular heart disease, chronic inflammatory lung disease, and pulmonary hypertension.

Secondary bacterial pneumonia should be considered in patients who have not improved following 3 to 5 days of antiviral therapy. Patients with deterioration in condition, respiratory failure, hypotension and/or fever should also be evaluated for presence of more extensive disease (Chow et al., 2019; Gaitonde et al., 2019; Uyeki et al., 2019).

The most common organisms associated with secondary bacterial pneumonia are *Streptococcus pneumoniae*, *Staphylococcus aureus*, and *Streptococcus pyogenes*. Sputum cultures should be obtained if able to aid decision making regarding antibiotic therapy. Empiric treatment should include a third generation cephalosporin such as ceftriaxone or respiratory fluoroquinolone such as levofloxacin or moxifloxacin. Treatment with vancomycin or linezolid should be considered in critically ill patients or those who do not improve with empiric treatment regimens, as these cases are suspicious for infection with multi-drug resistant organisms (MDRO) (File, 2020b; Khorramdelazad et al., 2021; Zachary, 2021).

Cases of H1N1 influenza A are associated with increased risk of clinical deterioration leading to rapidly progressive pneumonia, acute respiratory distress syndrome (ARDS), respiratory failure and multisystem organ failure. Combination of viral and bacterial pneumonia secondary to influenza infection is also common (Dolin, 2020a; Khorramdelazad et al., 2021; Malosh et al., 2018).

Older adults are at increased risk for secondary cardiac complications including acute myocardial infarction (MI), arrhythmia, myocarditis, and pericarditis. Other serious but less common complications include rhabdomyolysis, myositis, and toxic shock syndrome. Central nervous system complications are also rare but may include encephalopathy, encephalitis, transverse myelitis, aseptic meningitis, and Guillain-Barré syndrome (Dolin, 2020a; Khorramdelazad et al., 2021).

Older adults hospitalized with influenza are susceptible to complications that may be hospital- and/or geriatric-associated, including nosocomial infection, delirium, falls, medication-related problems, or exacerbation of chronic illness. These problems share multiple risk factors common to older adults, including functional impairment, cognitive impairment, gait instability, and frailty. These complications frequently occur together, prolonging hospitalization. Length of inpatient stay correlates with increased risk of morbidity and mortality during hospitalization and after discharge (Keilich et al., 2019; Mudge et al., 2019; Romero-Ortuno et al., 2017).

Functional decline resulting in slowed or a potentially incomplete recovery following influenza infection is common among older adults. Approximately 67% of older adults with influenza find themselves temporarily homebound, and 25% become temporarily bedbound, resulting in a tremendous impact on patients, families, and caregivers (Andrew et al., 2021; Talbot, 2017).

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Older adults hospitalized for influenza are particularly vulnerable to experiencing permanent decline in function. Approximately one-third of hospitalized adults aged 70 years and older will experience the loss of one basic activity of daily living (ADL). Only 30% of these older adults will fully recover this loss within 1 year of discharge. Skilled nursing care following hospital discharge is required for approximately 70% of adults aged 65 years and older. Risk of functional loss is associated with the number of pre-existing comorbidities, frailty, and disability prior to hospitalization (Andrew et al., 2021; Mattison, 2021).

Prevention/Prophylaxis: The most effective strategy for influenza prevention is vaccination, and herd immunity is an essential component for protection of older adults from seasonal influenza. All household contacts, caregivers and health-care professionals caring for older adults should be administered seasonal influenza vaccination every year. Immune senescence in older adults increases their risk for severe illness and mortality. This risk multiplies among institutionalized older adults with pre-existing functional impairments, frailty, and comorbidities, making presence of herd immunity imperative where institutional outbreaks are common and potentially devastating (Keilich et al., 2019).

All adults should be administered seasonal influenza vaccine each year. Older adults who become infected with seasonal influenza despite vaccination experience milder symptoms, shorter illness duration and are less likely to require hospitalization. Risk of influenza-related complications and mortality is also decreased among vaccinated older adults with influenza compared to those who are not (Andrew et al., 2019; Arriola et al., 2017). The American College on Immunization Practices (ACIP) and CDC recommend administration of influenza vaccine to all adults annually. Ideally, vaccination should occur before the end of October each year, but administration can be completed at any point during the influenza season (CDC, 2021; Hibberd, 2022).

The unique ability of the influenza virus to periodically mutate poses challenges to development of immunizations for upcoming influenza seasons. Quadrivalent influenza vaccines containing four strain antigens, two influenza A strains and both influenza B lineages, have shown greater efficacy in disease prevention than past trivalent formulas. These vaccines have also proven beneficial in reducing illness severity and hospital admissions due to influenza. Despite chance of mismatch between vaccine strains and seasonal circulating strains, vaccination is still the most efficacious strategy to reduce serious influenza outcomes (Andrew et al., 2019; Hibberd, 2022). Table 11-4 compares FDA-approved influenza vaccines.

Vaccine Contraindications and Precautions: Patients with history of anaphylaxis, angioedema, respiratory distress, lightheadedness, or recurrent vomiting secondary to egg exposure should not receive egg-based vaccine formulations. These individuals should be offered an alternative licensed formulation such as RIV4 or cell-cultured IIV4. Egg allergy should not be considered a contraindication to vaccination if the patient only experiences urticaria following exposure (Grohskopf et al., 2021). Egg-based formulations are contraindicated for all patients with history of anaphylaxis following any influenza vaccine. Administration of alternative formulations should be supervised by a healthcare provider capable of managing a severe allergic response in an in- or outpatient medical setting (Grohskopf et al., 2021).

Caution should be taken with patients who have a history of Guillain-Barré syndrome within 6 weeks following influenza vaccination. If the patient is considered low risk of secondary influenza complications, it is reasonable not to vaccinate. In adults or those who are at increased risk of influenza-related complications, a discussion of risk versus benefit of vaccination is essential. Antiviral chemoprophylaxis should be considered for any adult who has not received seasonal influenza vaccine (Grohskopf et al., 2021). Treatment with oral anticoagulants is not a contraindication for influenza vaccination, however a small gauge needle (23 gauge or smaller) should be used to reduce risk of hematoma (Hibberd, 2021).

Co-administration with Other Vaccines: Inactivated influenza vaccines can be administered at the same time as other inactivated or live virus vaccines, including the COVID-19 vaccine. When multiple injections are being given in a single visit, vaccines should not be administered in the same site. Deltoid muscle is the recommended site of administration for influenza vaccine (Hibberd, 2022).

Vaccination of Acutely Ill Patients: Influenza vaccination may be administered to patients with mild respiratory illness, with or without fever. Vaccination should be delayed for older adult patients with moderate or severe acute illness, with or without fever. The influenza vaccine should be administered as soon as possible, once patient symptoms have resolved (Hibberd, 2022).

Antiviral Chemoprophylaxis: IDSA recommends antiviral preexposure and postexposure chemoprophylaxis with oral oseltamivir or inhaled zanamivir in certain situations.

For outpatient exposures, IDSA recommends antiviral chemoprophylaxis for older adults in whom vaccination is contraindicated or unavailable and considered high risk of developing influenza-related complications for the duration of influenza season. Antiviral chemoprophylaxis of severely immunocompromised older adults regardless of vaccination status is recommended for the duration of influenza season. Antiviral chemoprophylaxis should be initiated as soon as possible after the first influenza case has been detected in the community (Uyeki et al., 2019).

IDSA recommends short-term antiviral chemoprophylaxis for unvaccinated adults who are at high risk of influenza-related complications and confirmed influenza outbreak in the community. These individuals should also be vaccinated as soon as possible. During peak periods of influenza activity, short-term antiviral chemoprophylaxis is recommended for health-care providers and close household contacts of older adults at high risk of secondary influenza complications in whom influenza vaccine is contraindicated or unavailable (Uyeki et al., 2019).

For institutional outbreaks, IDSA recommends outbreak control measures (active surveillance and antiviral chemoprophylaxis) be initiated when two cases of laboratory confirmed influenza are identified within 72 hours of one another in patients of the same ward or hospital unit. When results of molecular assays are not available on the same day of specimen collection, initiation of outbreak control measures should be considered if one or more patients are suspected to have healthcare-associated influenza. Active surveillance

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TABLE 11-4 Comparison of FDA-approved Influenza Vaccine Formulations

TRADE NAME (MANUFACTURER)	FORMULATION	INDICATIONS (AGES)	DOSE/ MANUFACTURING	ADMINISTRATION ROUTE
Standard-dose, egg-based vaccines				
Fluarix (GlaxoSmithKline) Fluzone	Inactivated quadrivalent influenza vaccine (IIV4)	Healthy individuals ≥6 months	0.5 mL PFS or SDV	Intramuscular injection
FluLaval (GlaxoSmithKline)	Inactivated quadrivalent influenza vaccine (IIV4)	Healthy individuals 6 months to 64 years	0.5 mL PFS	Intramuscular injection
Afluria (Seqirus)	Inactivated quadrivalent influenza vaccine (IIV4)	Healthy adults 18–64 years	0.5 mL PFS or 5 mL MDV	Intramuscular injection or intramuscular jet injector device ("needle free")
Fluzone (Sanofi Pasteur)	Inactivated quadrivalent influenza vaccine (IIV4)	Adults ≥65 years	0.5 mL PFS or 5 mL MDV	Intramuscular injection
High-dose, egg-based vaccine				
Fluzone High-Dose (Sanofi Pasteur)	High-dose inactivated quadrivalent vaccine (HD-IIV4)	Adults ≥65 years	0.7 mL PFS	Intramuscular injection
Standard-dose, cell culture-based vaccine				
Flucelvax Quadrivalent (Seqirus)	Inactivated quadrivalent influenza vaccine (ccIIV4) non-egg based	Individuals ≥6 months	0.5 mL PFS or 5 mL MDV	Intramuscular injection
Standard-dose, egg-based adjuvanted vaccine				
Fluad (Seqirus)	Inactivated quadrivalent vaccine with MF59 adjuvant (aIIV4)	Adults ≥65 years	0.5 mL PFS	Intramuscular injection
Recombinant hemagglutinin vaccine				
Flublok (Sanofi Pasteur)	Recombinant quadrivalent HA vaccine (RIV4)	Adults ≥18 years	0.5 mL PFS	Intramuscular injection
Live attenuated egg-based vaccine				
FluMist (AstraZeneca)	Live attenuated quadrivalent vaccine (LAIV)	Healthy, non-pregnant individuals 2–49 years	0.2 mL prefilled single-use sprayer	Intranasal spray

HD-IIV4: high-dose influenza vaccine, quadrivalent; ccIIV4: inactivated adjuvanted influenza vaccine, quadrivalent; RIV4: recombinant hemagglutinin vaccine, quadrivalent; HA: hemagglutinin; PFS: pre-filled syringe; SDV: single dose vaccine; MDV: multidose vial.

Source: *Hibberd, 2022*

should begin immediately when one laboratory-confirmed case of hospital-associated influenza is confirmed (Uyeki et al., 2019).

In institutional settings with confirmed influenza outbreak, any patient presenting with acute onset of any respiratory symptom, with or without fever, or behavior change should be tested for influenza. Empiric antiviral treatment should be initiated as soon as possible for any patient suspected to have healthcare-associated influenza regardless of incomplete or pending diagnostic test results. All exposed patients should receive antiviral chemoprophylaxis as soon as possible, regardless of vaccination status or laboratory confirmed diagnosis (Uyeki et al., 2019). Also, antiviral chemoprophylaxis should be considered during the institutional outbreak for unvaccinated caregivers and staff and those who were administered an inactivated influenza vaccine during the institutional outbreak and for 14 days post-vaccination for the outbreak's duration (Uyeki et al., 2019).

Referral: Physical therapy for deconditioning due to influenza may be initiated during the acute recovery period and continued upon discharge with home health or skilled nursing services. Referral to an allergist should be considered for patients with history of allergic response to influenza vaccine.

Education: Patient education regarding appropriate prescribing of antibiotics is helpful in decreasing drug-resistant organisms. Teach groups of older adults (especially adults with comorbidities) about preventive measures, including care after discharge, follow-up, and possible vaccination. Educate patient and caregivers about the importance of nutrition, hydration, deep breathing exercises, and smoking cessation (Zachary, 2021).

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Vaccination	Evidence Rating	References
Annual influenza vaccination is recommended for all people aged 6 months and older.	A	CDC, 2021 Uyeki et al., 2019 Gaitonde et al., 2019
Influenza vaccination should be administered before the end of October each year but can be given at any point during influenza season.	A	CDC, 2021 Hibberd, 2022
Older adults (≥ 65 years) should be administered quadrivalent inactivated influenza vaccine (IIV4) annually.	A	CDC, 2021 Hibberd, 2022
High-dose quadrivalent inactivated influenza vaccine (HD-IIV4) is preferred for adults ≥65 years when available.	B	Hibberd, 2022
Egg-based vaccine formulations are contraindicated in patients with history of anaphylaxis or other severe allergic response following egg exposure.	A	Grohskopf et al., 2021
Egg-based vaccine formulations are not contraindicated in patients who only experience urticaria secondary to egg exposure.	A	Grohskopf et al., 2021
Consider risk versus benefit of vaccination for older adults considered high risk of influenza-related complications who have history of Guillain-Barré syndrome within 6 months of previous influenza vaccination.	B	Grohskopf et al., 2021
Vaccination of otherwise healthy patients with history of Guillain-Barré syndrome within 6 months of previous influenza vaccination is generally not recommended.	B	Grohskopf et al., 2021
Diagnostic Testing		
Rapid molecular assays should be used to test outpatients for influenza.	B	Uyeki et al., 2019
Reverse-transcription polymerase chain reaction (RT-PCR) or molecular assays should be used to test hospitalized patients for influenza.	B	Uyeki et al., 2019
During Periods of Peak Influenza Activity		
Test all hospitalized patients with acute respiratory illness, with or without fever, or exacerbation of other chronic health condition upon hospital admission.	A	Uyeki et al., 2019
Test all patients who develop acute onset of respiratory symptoms, with or without fever, while hospitalized.	A	Uyeki et al., 2019
During Periods of Low Influenza Activity		
Test all hospitalized patients with acute onset of respiratory symptoms and recent known influenza exposure upon admission.	A	Uyeki et al., 2019
Treatment (Confirmed or Suspected Influenza)		
All hospitalized patients with influenza should receive antiviral therapy regardless of illness severity or duration.	B	Uyeki et al., 2019
Outpatients at low risk of influenza-related complications who present within 48 hours of symptom onset should be prescribed antiviral therapy.	B	Uyeki et al., 2019; Gaitonde et al., 2019
Outpatients with severe illness, or those considered high risk of influenza-related complications, should be prescribed antiviral therapy regardless of illness severity or duration.	B	Uyeki et al., 2019; Gaitonde et al., 2019
Older adults (≥65 years) should be prescribed antiviral therapy regardless of illness severity or duration.	B	Uyeki et al., 2019
Treatment with a single NAI (oral oseltamivir, inhaled zanamivir, or intravenous peramivir) is recommended. More than one is not recommended	A	Uyeki et al., 2019
Treat uncomplicated influenza in otherwise healthy outpatients for 5 days with oral oseltamivir; or 5 days with inhaled zanamivir; or single-dose intravenous peramivir.	A	Uyeki et al., 2019
Pre-Exposure Chemoprophylaxis		
Oral oseltamivir or inhaled zanamivir should be prescribed for pre-exposure influenza chemoprophylaxis.	B	Uyeki et al., 2019

Continued

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Vaccination	Evidence Rating	References
Administer antiviral chemoprophylaxis for the duration of influenza season to unvaccinated older adults considered high risk of influenza-related complications as soon as influenza has been detected in the community.	B	Uyeki et al., 2019
Patients receiving antiviral chemoprophylaxis who become symptomatic should be transitioned to another antiviral drug with different resistance profile at the recommended treatment dose.	B	Uyeki et al., 2019
Institutional Outbreaks		
Implement outbreak control measures (antiviral chemoprophylaxis and active surveillance) when two cases of healthcare-associated influenza have been detected within 72 hours of each other among patients in the same ward or unit.	B	Uyeki et al., 2019
Complete influenza testing for any patient with acute onset of respiratory symptoms, with or without fever, or behavior change.	B	Uyeki et al., 2019
Initiate empiric antiviral treatment to any patient with suspected influenza during institutional outbreak, regardless of incomplete or pending test result status.	B	Uyeki et al., 2019
Initiate antiviral chemoprophylaxis as soon as possible to all patients in setting of confirmed institutional outbreak regardless of vaccination status.	B	Uyeki et al., 2019
Administer antiviral chemoprophylaxis to institutionalized patients for a minimum of 14 days, continuing for at least 7 days after symptom onset of last identified case.	B	Uyeki et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

LUNG CANCER

Signal Symptoms: Cough, dyspnea, weight loss, anorexia, hemoptysis.

Description: Lung cancer is a malignant neoplasm originating in the parenchyma of the lung or airways. Approximately 95% of all lung cancer is classified as non-small cell lung cancer (NSCLC) or small cell lung cancer (SCLC) (National Cancer Institute [NCI], 2020). NSCLC comprises 85% of cancer diagnoses and includes adenocarcinoma, squamous cell cancer, and large cell cancer (NCI, 2020).

Etiology: Research has shown conclusively that smoking is the number one risk factor for lung cancer (Centers for Disease Control and Prevention [CDC], 2020). Lung cancer can also be seen in patients who are never-smokers. The causative factors are not fully understood but are thought to be due to environmental factors, including exposure to second-hand smoke and chemicals such as radon, asbestos, arsenic, and diesel exhaust (CDC, 2020). Prior radiation therapy to the chest can increase the risk of a second primary lung cancer (CDC, 2020). Patients with pre-existing diseases that involve the lungs, such as chronic obstructive pulmonary disease (COPD), prior lung cancers, sarcoidosis, and scleroderma, are at increased risk for developing lung cancer. Studies have shown that patients with pulmonary fibrosis have an 8- to 14-fold increased risk for developing lung cancer (Mannino, 2021). Carriers of an alpha-1 antitrypsin deficiency have a twofold increased risk for lung cancer (Mannino, 2021). Genetic predisposition to carcinoma of the lung continues to be studied, but there is growing evidence that genetics can affect the risk of developing lung cancer and the prognosis (Mannino, 2021).

Occurrence: Lung cancer is the most common cause of cancer-associated deaths in the United States. It is the third most common cancer among men and women. Annually, more than 200,000 new cases of lung cancer are diagnosed and the disease accounts for 21.7% of all cancer deaths (NCI, 2021). More men (60.1 per 100,000 persons) have lung cancer than do women (47.9 per 100,000 persons) (NCI, 2021).

Age: Lung cancer can occur at any age, but there is a dramatic increase in new diagnosis after age 55 years. Most recent statistics show 34.4% diagnosed between 65 and 74 years, 26.6% between 75 and 84 years, and 9.7% among those more than 84 years old (NCI, 2021). More men (60.1 per 100,000 persons) have lung cancer than do women (47.9 per 100,000 persons) (NCI, 2021).

Ethnicity: Black men in the United States have a higher incidence of lung cancer than White men (55.4/100,000 persons vs. 47.1/100,000 persons [NCI, 2021]). No significant difference exists between Black and White women.

Contributing Factors: The cumulative dose or pack-years for cigarette smoking is related directly to the risk of developing lung cancer. The more cigarettes smoked per day and the longer the individual has smoked, the higher the risk of developing lung cancer. The risk of lung cancer is 10 to 30 times higher in smokers than in nonsmokers (Mannino, 2021).

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Cigar and pipe smokers and passive smokers have double the risk. The risks of developing NSCLC steadily decline for people who quit smoking and approach that of a nonsmoker after 15 years of abstinence. Individuals who have smoked for more than 20 years probably always will have a slightly increased risk of developing the disease, even after 15 years as a nonsmoker. Asbestos exposure alone increases the risk of developing pulmonary carcinoma, but when combined with interstitial lung disease, the risk increases. Other inhaled agents implicated in the development of the disease are radon, arsenic, nickel, chromates, halo ethers, alkylating compounds, and polycyclic aromatic hydrocarbons. Radon is a risk factor; air pollution also is thought to contribute to the development of lung cancer. Sarcoidosis carries a threefold increased risk; scleroderma increases risk of bronchoalveolar cancer.

Signs and Symptoms: Signs and symptoms of lung cancer are usually present only after the disease has progressed beyond the early stages. Routine screening for the disease with chest x-ray and/or sputum cytology is not recommended. The U.S. Preventive Services Task Force (USPSTF) (2021) updated lung cancer screening guidelines recommend annual low-dose computed tomography (CT) in adults aged 50 to 80 years with a 20 pack a year smoking history who currently smoke or have quit in the past 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or ability to have curative lung surgery. Symptoms suggestive of lung cancer include a new or changing cough, hoarseness, hemoptysis, anorexia, cachexia, unexplained weight loss, dyspnea, hypoxia, wheezing, unresolving pneumonia, and chest wall pain (National Comprehensive Cancer Network [NCCN], 2021a). Patients initially may present with symptoms related to extra thoracic disease, including tracheal obstruction, esophageal obstruction with dysphagia, laryngeal nerve paralysis, phrenic nerve paralysis with elevated hemidiaphragm, sympathetic nerve paralysis or Horner's syndrome, pleural effusion owing to lymphatic obstruction, Pancoast's syndrome involving the eighth cervical and first and second thoracic nerves, or superior vena cava syndrome from vascular obstruction (NCCN, 2021a).

Patients with pericardial and cardiac extension of tumor may have symptoms of arrhythmia, tamponade, or failure. The presenting illness in patients with lung cancer may be paraneoplastic syndromes, including hypercalcemia, hypophosphatemia, hyponatremia with syndrome of inappropriate antidiuretic hormone, and hypercoagulable states.

Diagnostic Tests: After a history and physical examination suggestive of disease, the following tests are recommended (note that tissue biopsy results are required for diagnosis):

Noninvasive Testing:

- Chest x-ray: This may show nonspecific abnormalities, hilar masses, atelectasis, pleural effusions or masses, and infiltrates.
- CT scan, preferably with contrast: CT scan can assist in defining the characteristics, size, and location of the primary tumor, lymphadenopathy if present, and any abnormalities of the liver and adrenal glands (NCCN, 2021a,b).
- Fluorodeoxyglucose positron emission tomography (FDG-PET): This is a test that measures the metabolic uptake of glucose by cells; lung cancer cells have a higher cellular glucose uptake than normal cells. It is helpful in diagnosing metastatic disease (NCCN, 2021a,b).
- Magnetic resonance imaging (MRI) of the brain, with contrast: An MRI can assist in identification of brain metastases (NCCN, 2021a,b).

Invasive Testing:

- Transthoracic needle aspiration is usually reserved for specific circumstances.
- Fiberoptic bronchoscopy with biopsies has a very high sensitivity rating for diagnosis.
- Bronchoscopy with CT-guided transbronchial needle aspiration has an important role in diagnosis and staging of lung cancer.
- Endoscopic ultrasound, endobronchial ultrasound, and mediastinoscopy also contribute to staging; mediastinoscopy is considered the gold standard for identifying mediastinal involvement (NCCN, 2021a).
- If abnormalities suggest more extensive cancer, further testing will be conducted looking for extrathoracic, metastatic disease.

Staging: NSCLC staging was revised in 2017 and follows the tumor, node, metastasis (TNM) classification (Detterbeck et al., 2017). Correct staging is essential at diagnosis to identify treatment options, prognosis, and potential for recurrence.

SCLC staging also follows the TNM staging system, but delineates limited stage SCLC as any T, any N, M0, with the exception of T3–4. Extensive stage refers to any T, any N, M1a/b and T3-4 due to involvement of multiple lung nodules (Detterbeck et al., 2017).

Differential Diagnosis: TB, infectious granuloma, pneumonia, empyema, bronchiectasis, abscess, sarcoidosis, pneumonitis, and asbestosis all can mimic lung cancer.

Treatment: Surgical resection, radiation therapy, and chemotherapy are indicated for NSCLC; the stage of the disease, patient's functional status, and histology of the tumor determine the treatments. Recent advances in genotyping and targeting of altered signal mechanisms in lung cancer have allowed targeted treatment with immunotherapy, monoclonal antibodies, anti–vascular endothelial growth factor (anti-VEGF) agents, and other modalities (NCCN, 2021a). Multimodal chemotherapy and radiation are the treatment of choice for limited stage SCLC; cisplatin and etoposide are the preferred agents (NCCN, 2021b). Prophylactic cranial irradiation is done in select patients. In some patients with very limited disease, surgical resection may be done (NCCN, 2021b). Treatment of extensive stage SCLC is chemotherapy combined with immunotherapy for up to 6 cycles and then maintenance immunotherapy until intolerable toxicity or disease progression (NCCN, 2021b). Treatment after relapse is dependent on response to initial chemotherapy. If there is a positive response, the treatment is repeated. If nonresponsive to initial chemotherapy, "salvage chemotherapy" with a nonplatinum, single agent such as topotecan, gemcitabine, or taxane is attempted (NCCN, 2021b). Treatment for older adults should be individualized. A comprehensive geriatric assessment is

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often conducted and used in determining treatment options and the Karnofsky Performance Scale is also used by some specialists (McNair et al., 2022).

Follow-Up: Follow-up is individualized; generally, patients should be seen for follow-up every 3 to 4 months after treatment for lung cancer. During years 3 to 5, follow-up should be every 6 months. Yearly examinations are advised thereafter.

Sequelae: Disability and death are the chief sequelae of lung cancer.

Prevention/Prophylaxis: Prevention of lung cancer should focus on smoking cessation. Ask about and record the tobacco use status of every patient, advise patients who smoke to quit, and offer smoking cessation treatment at every office visit. Screening for lung cancer in asymptomatic patients is not advised. Screening in high-risk patients has not demonstrated any decrease in mortality; newer methodologies studying biomarkers have not been proved to date. The NCCN (2021a) and the USPSTF (2021) have issued guidelines endorsing screening with low-dose helical CT scan in high-risk patients. There is currently no recommended chemoprevention for lung cancer.

Referral: On suspecting lung cancer, refer the patient to a pulmonary specialist. At a later stage, referral to palliative care or hospice may be indicated. Give the patient information on the American Lung Association Information Line (1-800-LUNGUSA). Referral to a mental health specialist is indicated in severe depression unresponsive to treatment.

Education: Many smoking cessation programs are available. Examples include the National Cancer Institute Tobacco Quitline, the American Academy of Family Physicians Stop Smoking Kit, various pamphlets from the American Cancer Society, and A Healthy Beginning Counseling Kit from the American Lung Association; the Web site www.smokefree.gov is another resource. The primary health-care provider can assess the smoker's motivation to quit and offer brief motivational interventions at each visit. Provide information about support groups and community programs available to help with smoking cessation.

When a patient is diagnosed with lung cancer, education about type of cancer, treatment options, and prognosis is very important. This is typically done by the oncology team, but primary care providers can monitor for patient questions and communicate this to the specialty team.

Clinical Recommendation	Evidence Rating	References
Low-dose computed tomography should be used to screen high-risk individuals for lung cancer.	B	USPSTF, 2021 NCCN, 2021a NCCN, 2021b
Surgery is the treatment of choice for patients with local or only locally advanced non-small cell carcinoma (stage I through stage IIIA).	B	NCCN, 2021a
Treatment for unresectable non-small cell carcinoma may involve radiotherapy and chemotherapy.	B	NCCN, 2021a
Chemotherapy, combined with radiotherapy in limited disease, is the mainstay of treatment for small cell carcinoma.	B	NCCN, 2021b
Both radiotherapy and chemotherapy are used in treatment of superior vena cava syndrome because of non-small cell or small cell lung cancer.	B	NCCN, 2021a NCCN, 2021b
Early palliative care results in improved quality of life and a decreased incidence of depression in patients with newly diagnosed non–small cell lung cancer.	B	NCCN, 2021a NCCN, 2021b

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PNEUMONIA

Signal Symptoms: Chills or hyperthermia, fever, sweating, chest discomfort or dyspnea, a new or worsening chronic cough with or without sputum. Nonspecific symptoms include fatigue, weakness, abdominal pain, nausea, appetite loss, headache, myalgia, and exacerbation of other chronic illnesses. In older adults, atypical presentations with confusion, increased falls, functional decline, or other nonrespiratory symptoms are more common, often leading to delayed treatment and increased mortality (Grief & Loza, 2018; Henig & Kaye, 2017; Lanks et al., 2019).

Description: Community-acquired pneumonia (CAP) is an acute lower respiratory tract infection of the lung parenchyma in which consolidation occurs as exudate fills the alveoli. CAP can be bacterial or viral. It begins outside of the hospital or is diagnosed within 48 hours of admission without recent (14 day) residence in a long-term care (LTC) facility. Hospital-acquired pneumonia (HAP) is defined as infection occurring 48 hours or more after hospital admission (Lanks et al., 2019).

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Ventilator-associated pneumonia (VAP), the most frequently acquired intensive care unit (ICU) infection, develops after 48 hours of endotracheal intubation. Cumulative risk increase corresponds with number of mechanical ventilation days, but identification of VAP most commonly occurs between days 5 and 9. Multiple factors contribute to VAP, including microaspiration, pathogenic colonization of the endotracheal tube and surrounding structures (oropharynx, sinuses, and stomach), secretions around the cuff, and impairment of secretion clearance within the airway (Modi & Kovacs, 2020b; Papazian et al., 2020).

Etiology:

Community-Acquired Pneumonia: The most common organism associated with CAP infection is *Streptococcus pneumoniae*. It is responsible for more than 25% of cases worldwide. Other common pathogens include *Mycoplasma pneumoniae, Chlamydophila pneumonia*, *Haemophilus influenzae, Legionella* species, and *Staphylococcus aureus.* Multi-drug resistant organisms (MDRO) such as methicillin-resistant *S. aureus* (MRSA) and *Pseudomonas aeruginosa* have also been identified as causative pathogens but are less common in patients with CAP. *S. aureus, S. pneumoniae,* and *H. influenza* are most commonly reported as causative organisms in LTC residents. Infection with MDROs is closely associated with disease severity and risk for hospitalization (Henig & Kaye, 2017; Lanks et al., 2019).

Hospital-Acquired and Ventilator-Associated Pneumonia: HAP in older patients can also be caused by *S. pneumonia and S. aureus;* however, other gram-negative bacilli, including *P. aeruginosa, Klebsiella pneumonia, Enterococcus coli,* and *Enterobacter species* account for a large number of cases. It is common to have a mixture of multiple organisms, including viruses such as influenza or SARS-CoV-2. The most common pathogens found in VAP are similar to those in HAP. Variations in microorganisms responsible for VAP are more likely related to ICU characteristics, the patient's underlying clinical condition, and length of mechanical ventilation (Lanks et al., 2019; Luyt et al., 2018).

Occurrence: Pneumonia and influenza together are the eighth leading causes of death in the United States. The World Health Organization (WHO) (2020) reports lower respiratory infections as the fourth leading cause of death worldwide and the leading cause of death due to infectious disease. Annual occurrence rates of CAP in adults younger than 65 years old in the United States are 24.8 cases per 10,000 persons. The incidence sharply increases with age to 63 cases per 10,000 persons aged 65 to 79 and 164 cases per 10,000 persons aged 80 and older (Herron, 2021; WHO, 2020).

Approximately 1 million adults seek hospital care each year due to pneumonia. Aside from childbirth, pneumonia is the leading cause of hospitalization for adults and causes 50,000 deaths each year. The emergency department (ED) visit rates for patients with pneumonia are 7.9 per 1,000 persons, and 12.2 per 1,000 persons for patients with both influenza and pneumonia. The ED visit rates also increase with age, from 7.1 per 1,000 adults aged 18 to 44 to 45.6 per 1,000 adults aged 85 and older (Arnold et al., 2020; Herron, 2021).

Approximately 30% of adults diagnosed with pneumonia require hospitalization on average. Hospitalization rates for older adults with pneumonia are 2 to 4 times higher than those of younger people. The mortality rate for intensive care unit (ICU) patients due to pneumonia is approximately 23%. Mortality risk increases with age and disease severity (Henig & Kaye, 2017; Herron, 2021; WHO, 2020). The number of deaths due to pneumonia and influenza is greater for women compared to men (Herron, 2021).

Age: Pneumonia is the most common cause of death from infectious disease in older adult patients (Herron, 2021).

Ethnicity: Cause of death due to pneumonia and influenza is highest among Americans of Asian and Pacific Islander descent and lowest among non-Hispanic Black and White persons (Herron, 2021).

Contributing Factors: Modifiable risk factors for acquiring pneumonia include tobacco use, alcohol use, protein-calorie malnutrition, and poor dental hygiene. Other contributing factors include age and comorbidities such as influenza, chronic obstructive pulmonary disease (COPD), structural lung disease, renal impairment, and cardiovascular disease. Other comorbidities that increase patient aspiration risk, such as dementia, stroke, and epilepsy, should also be considered (Lanks et al., 2019). Colonization of the oropharynx by gram-negative bacteria, an institutional setting, decline in immune function, hospitalization, use of sedating medications and proton-pump inhibitors, recent surgery or trauma, and diminished cough reflex also contribute to development of pneumonia. Presence of multiple risk factors are additive in weighing patient overall risk (Mandell & Niedermann, 2019; Modi & Kovacs, 2020b).

The greatest risk factor for HAP is mechanical ventilation. Other significant risk factors for include:

- Older age
- Reintubation or prolonged intubation
- Depressed consciousness
- Aspiration
- Trauma
- Chest or upper abdominal surgery
- Comorbidities
- Recent or current use of antibiotic therapy, especially broad-spectrum coverage
- Genetic polymorphisms
- Presence of an intracranial pressure monitor or nasogastric tube
- Agents that increase gastric pH (H_2 blockers, antacids, proton pump inhibitors)
- Paralysis
- Total opioid exposure
- Multiple surgeries and/or central venous catheter placements
- Frequent ventilator circuit changes
- Paralysis
- Underlying illness such as protein-calorie malnutrition, anemia, or chronic renal insufficiency
- Charlson Comorbidity Index (CCI) ≥ 3 (Klompas, 2022a).

The most significant risk factor associated with VAP is length of mechanical ventilation. Ten percent of patients ventilated for over 2 days will be diagnosed with VAP. Other risk factors include site-specific issues (poor compliance with VAP prevention bundle), immune system compromise, comorbidities, adult respiratory distress, patient positioning,

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and medications. Risk factors for VAP due to MDR pathogens include:

- Intravenous antibiotics treatment (within past 90 days)
- Septic shock
- Acute respiratory distress syndrome preceding VAP
- Acute renal replacement therapy preceding VAP
- Hospitalization of greater than or equal to 5 days before VAP diagnosis (Jean et al., 2020; Klompas, 2022b; Metersky & Kalil, 2018; Papazian et al., 2020).

Factors most associated with pneumonia-related deaths are age, disease severity, and number of chronic comorbidities. Chronic obstructive pulmonary disease, diabetes mellitus, cancer and dementia diagnoses are associated with pneumonia 1-year mortality risk. Rehospitalization within 30 days of discharge is another contributing factor (File, 2020a; Klompas, 2022a).

The CURB-65 score is used to stratify risk in patients with CAP. The five indicators that comprise the CURB score include the following:

- Confusion
- Blood urea nitrogen level greater than 19 mg/dL
- Systolic blood pressure <90 mm Hg or diastolic blood pressure ≤0 mm Hg
- Respiratory rate ≥30 per minute
- Age ≥65 years (Yealy & Fine, 2021)

There is a 21-fold increase in mortality among patients with two or more symptoms, specifically elevated BUN, decreased diastolic blood pressure, and/or tachypnea. A nine-fold increase in mortality is associated with presence of all three of these symptoms. The CURB-65 tool was designed to help guide provider decision making regarding need for hospitalization. With a score ≤1 the patient is considered low risk and can be treated at home, with a score of ≤2 it is recommended that the patient have a short inpatient hospitalization or be closely supervised in outpatient treatment. Providers should consider hospitalization and ICU care for a CURB score ≥3 (File, 2020a; Yealy & Fine, 2021). An interactive version of the score is available on the Web at https://www.mdcalc.com/curb-65-score-pneumonia-severity.

The pneumonia severity index (PSI) was designed to predict the 30-day mortality rate of patients with CAP and aid provider decision making related to need for home health support or inpatient hospitalization. The PSI score is calculated based upon patient demographic factors, comorbidities, physical examination findings, laboratory, and imaging studies with higher scores indicative of greater disease severity (Yealy & Fine, 2021). The PSI is most useful in the acute care setting where rapid laboratory results can be attained. An interactive PSI resource is available on the Web at https://www.mdcalc.com/psi-port-score-pneumonia-severity-index-cap.

Additional factors associated with pneumonia-related mortality include delirium, hypotension, hypothermia, multilobar disease, and laboratory abnormalities such as leukopenia, thrombocytopenia, thrombocytosis, and hyperglycemia. Increased mortality risk has been found with *S. aureus,* and gram-negative organisms including *P. aeruginosa* and *Klebsiella* species. Mortality risk is also increased for patients infected with drug resistant organisms and pneumonia due to multiple organisms (i.e., viral and bacterial disease) (File, 2020a).

Signs and Symptoms: The typical patient may present with subjective complaints of fever, chills, cough (with or without sputum), fatigue, malaise, dyspnea, decreased appetite and/or pleuritic chest pain. These symptoms however are commonly absent in individuals who are frail and in older adults, leading to a lag time before diagnosis. In the older patient, altered mental status (delirium), new onset or increased frequency of falls, increased respiratory rate, hypotension, anorexia, a marked functional decline, and new onset of urinary incontinence are typical symptoms. (Henig & Kaye, 2017; Ramirez, 2021).

Physical examination findings may include tachypnea, tachycardia, hypoxemia, accessory muscle use, tactile fremitus, dullness on percussion, and egophony. Adventitious lung sounds such as a wheeze and/or crackles that do not clear with cough or deep breathing are typical. Patients may also present with signs of dehydration and appear anxious, restless, or withdrawn (Henig & Kaye, 2017; Ramirez, 2021).

The most current guidelines for HAP/VAP diagnosis and management were released by the IDSA and American Thoracic Society (ATS) in 2016. These guidelines specify that diagnoses should be made based on clinical criteria alone and must include all the following:

- New or worsening pulmonary infiltrate on chest imaging
- Fever
- Increased oxygen requirement
- Productive cough

Fever and increased purulent secretions are common in HAP/VAP, and patients usually have diffuse rhonchi with an inability to mobilize secretions and may have either leukocytosis or leukopenia. Crackles, diminished breath sounds, tachypnea, wheezing, and hemoptysis, are common findings (Fernando et al., 2020; Metlay et al., 2019).

Diagnostic Tests: The diagnosis of CAP may be difficult in patients with underlying chronic comorbidities, especially those with pulmonary fibrosis, lung cancer or other chronic lung diseases, and heart failure. Recommendations for diagnostic testing continue to be controversial; however, the chest x-ray is considered the gold standard for the diagnosis of CAP. Other routine testing for patients treated on an outpatient basis is not recommended (Metlay et al., 2019; Modi & Kovacs, 2020a; Ramirez, 2021).

Laboratory Testing: Routine blood tests, including CBC with differential and basic metabolic panel, are helpful to determine disease severity and need for hospitalization. Leukocytosis with left shift is the most common abnormal finding. Measurement of C-reactive protein and/or procalcitonin can be helpful in distinguishing between bacterial or viral pneumonia. These tests should not be used to diagnose but can be helpful to prescribe appropriate treatment course and setting. (Klompas, 2022c; Modi & Kovacs, 2020a).

Diagnostic Imaging: CT scans of the chest are often ordered and are more accurate than chest x-ray, especially in the ED setting. CT scan should be considered for patients with negative chest x-ray and clinical presentation highly suspicious for pneumonia in addition to immunocompromised patients or those with structural lung disease (Ramirez, 2021). Studies have shown that ultrasound of the chest has better sensitivity and specificity than a chest x-ray and is comparable to that of a CT scan (Huggins & Mayo, 2021).

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Pulmonary infiltrate, lobular consolidation, or opacities found on chest x-ray, CT scan, or ultrasound confirm the diagnosis of pneumonia; however, chest x-rays have lower sensitivity and positive predictive rates compared to CT scan and thoracic ultrasonography. Validity of chest x-ray results are affected by interrater variability and patient-specific characteristics. (Klompas, 2022c; Modi & Kovacs, 2020a).

Microbiological Testing: Microbiological tests should be reserved for patients admitted to the hospital. Noninvasive respiratory cultures are preferred over invasive techniques and are recommended for patients with VAP, HAP (non-VAP), or severe CAP. Noninvasive cultures are more cost-effective, have faster turnaround, and offer a nonempiric approach to treatment. Treatment course for VAP, HAP, and hospitalized patients with CAP should be based upon clinical criteria and noninvasively obtained respiratory specimens or endotracheal aspirate (Kalil et al., 2016; Metlay et al., 2019).

Blood cultures are recommended for hospitalized adults with VAP, HAP, or severe CAP at time of diagnosis. Bacteremic pneumonia is indicative of disease severity and occurs in approximately 25% of cases. Urinary antigen test to detect pneumococcal disease is appropriate, and specificity for these assays exceeds 98% in adults. Urine antigen assay to identify *Legionella* pneumonia should be reserved for those patients with known exposure or recent travel (Doern, 2021; Metlay et al., 2019; Musher & Tuomanen, 2021).

Differential Diagnosis: The differential diagnoses of CAP are dependent on the results of the chest x-ray. Differentials for those with a positive chest x-ray include:

- Aspiration or chemical pneumonitis
- Pulmonary embolism
- Heart failure with pulmonary edema
- Exacerbation of pulmonary fibrosis or bronchiectasis
- Acute eosinophilic pneumonia
- Interstitial lung diseases
- Atelectasis
- Lung cancer
- Drug reactions
- Lung injury associated with e-cigarette, vaping products (EVALI) or cocaine use

For those without an abnormal chest x-ray the differentials are:

- COPD, asthma, or bronchiectasis exacerbations
- COVID-19
- Influenza
- Pertussis
- Acute bronchitis
- Upper respiratory tract infection (Klompas, 2022c; Ramirez, 2021).

Early stage VAP occurs within 48 hours of intubation, whereas later stage VAP emerges after the fourth day of intubation and is more likely to be associated with MDR bacteria. Differential diagnosis for VAP includes ventilator-associated respiratory infection and ventilator-associated tracheobronchitis (Jean, 2020).

Treatment: A crucial element in treatment is determining the severity of the illness and the setting, but other factors including oral intake, adherence, substance abuse, mental illness, cognitive impairment, patient function, and living situation. For community-dwelling older patients, the presence of a responsible caregiver and a supportive home environment is necessary. Temporary measures to increase support and monitor status of response may be introduced by ordering home health services. If the patient fails to recover or deteriorates despite these interventions, hospitalization should be contemplated. IDSA/ATS guidelines advocate the use of the PSI as a guide for determining outpatient treatment versus hospitalization (Metlay et al., 2019; Yealy & Fine, 2021).

Use of any prediction rule or tool should be tempered by clinical judgment. Objective criteria for hospital admission include (Ramirez, 2021; Yealy & Fine, 2021):

- Support at home
- Inability to take oral medications or fluids
- Delirium
- Severe acute metabolic, hematological, or electrolyte abnormalities
- Acute concomitant medical condition (e.g., malignancy, hepatic disease, renal insufficiency, cardiac disease)
- Hypoxemia on room air (PaO_2 less than 60 mm Hg)
- Multilobular involvement on chest x-ray
- Secondary suppurative infection
- Severe vital sign abnormality (systolic blood pressure less than 90 mm Hg, pulse greater than 125/min, respirations greater than 30/min)

CAP: The latest consensus guidelines from the IDSA/ATS for CAP (Metlay et al., 2019) support the following recommendations:

- Outpatient treatment for previously healthy adults with no risk factors for drug-resistant pathogens should consist of amoxicillin, a macrolide or doxycycline.
- Outpatient treatment for healthy adults who have been on an antibiotic in the previous 3 months should consist of a macrolide or respiratory fluoroquinolone (levofloxacin or moxifloxacin).
- Outpatient treatment for those with comorbidities, including diabetes mellitus, malignancies, alcoholism, chronic heart, lung, liver and or renal disease; recent hospitalization and receipt of oral antibiotics within the past 90 days; or history of MRSA or *P. aeruginosa,* monotherapy treatment should consist of a respiratory fluoroquinolone. Alternatively, combination therapy with a beta-lactam or cephalosporin and either macrolide or doxycycline may be considered based on patient characteristics.
- Outpatient treatment for those in an area with more than 25% macrolide-resistant *S. pneumoniae,* consider combination therapy with a beta-lactam or cephalosporin plus either macrolide or doxycycline or monotherapy with respiratory fluoroquinolone.
- Inpatient treatment of CAP (non-severe) should include a respiratory fluoroquinolone monotherapy or combination therapy with beta-lactam and macrolide; cefotaxime, ceftriaxone, ceftaroline, and ampicillin plus sulbactam are preferred.
- Inpatient treatment of severe CAP (requiring ICU management) with monotherapy is not recommended. Combination therapy should consist of beta-lactam antibiotic and either macrolide or respiratory fluoroquinolone.

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- Inpatient treatment of CAP with *Pseudomonas* risk factors should include a beta-lactam antibiotic (piperacillin/tazobactam, cefepime, ceftazidime, imipenem, meropenem, aztreonam) plus fluoroquinolone (levofloxacin or ciprofloxacin).
- Inpatient treatment of CAP with MRSA risk factors should include additional coverage with either vancomycin or linezolid.
- Doxycycline is an accepted substitution only when the patient has contraindications for both macrolide and fluoroquinolone treatment.
- Treatment should be instituted as soon as possible, and transition from IV to oral therapy should occur as soon as the patient is hemodynamically stable, shows clinical improvement, can ingest oral medications, and has no gastrointestinal tract problems. Duration of therapy is 5 to 7 days for those with mild infection and 7 to 10 days for those with severe infection or chronic comorbidities. Treatment should not be discontinued until the patient has been afebrile and clinically stable for a minimum of 48 hours (Metlay et al., 2019; Ramirez, 2021).

HAP and VAP: The most current guidelines for management of adults with HAP and VAP were published by the IDSA/ATS in 2016 (Kalil et al., 2016). After the potential for HAP/VAP is identified and specimens have been obtained, rapid empirical treatment with local antibiogram-driven choice of antimicrobial should be started. Knowledge of local resistance patterns, extent of MRSA, and other regional factors is essential. Treatment should be tailored to optimize antibiotic therapy and prevent resistance using pharmacokinetic and pharmacodynamic data (blood levels). The current guidelines recommend treatment for 7 days. Patients on IV antimicrobial therapy should be switched to oral therapy as soon as possible. Patients who are clinically stable and improving should be transitioned to oral antibiotics assuming they can tolerate oral medication (Kalil et al., 2016; Klompas, 2022b; Metersky & Kalil, 2018).

Routine treatment with adjunctive glucocorticoids is not recommended. The use of glucocorticoids in the treatment of HAP/VAP has had varying results and should be reserved for patients who may benefit from their anti-inflammatory effects. Glucocorticoid use is only recommended for critically ill ICU patients, defined by:

- Septic shock or respiratory failure with FiO_2 requirement of >50% plus or more of the following:
- Metabolic acidosis with arterial pH <7.3, lactate >4 mmol/L, or C-reactive protein >150 mg/L (File, 2021; Kalil et al., 2016).

Follow-Up: Follow-up depends on comorbidities and response to the prescribed treatment regimen. All patients diagnosed with CAP should schedule a follow-up office visit within a few days after the initial diagnosis and after completion of treatment, with future follow-up as needed. Patients should be instructed to call if symptoms worsen, if no response occurs after 3 to 5 days of treatment, or if symptoms recur. In most cases, follow-up chest x-ray is not necessary. In patients with comorbidities, smokers, and those older than 40 years old repeat chest x-ray after 7 to 12 weeks may be indicated (File, 2021).

Sequelae: The older patient with comorbidities is especially prone to complications and has a higher long-term mortality rate than those without comorbidities (Arnold et al., 2020; Henig & Kaye, 2017; Ramirez, 2021). Serious complications can occur with pneumonia, including respiratory failure and sepsis. Cardiovascular complications may occur and commonly include acute myocardial infarction (MI), heart failure, arrhythmias, pulmonary embolism, and stroke. Increased mortality is largely attributed to comorbidities and underlying illness, especially cardiovascular disease, COPD, diabetes, and renal disease (Arnold et al., 2020; Klompas, 2022a; Ramirez, 2021).

Prevention/Prophylaxis: Strategies for CAP prevention include smoking cessation and annual influenza vaccination and pneumococcal vaccination for at risk populations. Most current guidelines recommend that PPSV23 be administered to all patients 65 years and older. Those who have already received one dose of PPSV23 before age 65 should receive a booster 5 years after the first administered dose (Centers for Disease Control and Prevention [CDC], 2022; Ramirez, 2021).

In 2019, ACIP updated their recommendations regarding administration of PCV13 to all adults aged 65 and older. The current recommendation is to administer PCV13 to adults aged 65 and older with an immunocompromising condition, cerebrospinal fluid leak, or cochlear implant. Administration of PCV13 should be done first and at least one year apart from PPSV23. For immunocompetent adults, vaccination with both PCV13 and PPSV23 should be based on patient-provider shared clinical decision-making discussion. Healthy community-dwelling adults aged 65 or older are at low risk of exposure to pathogens covered by PCV13. This is due to the routine administration of this vaccine to children since 2010, reducing pneumococci transmission (Matanock et al., 2019).

Nursing home residents and adults residing in communities with low childhood vaccine uptake are at increased risk for pneumococcal disease. Adults with history of chronic heart, lung or liver disease, diabetes, alcoholism, and smoking are also at increased risk if they are exposed. PCV13 vaccine recommendation would be reasonable for these populations therefore, and a discussion regarding risk versus benefit of immunization should be prioritized. Patients hospitalized for pneumonia may be immunized before discharge (CDC, 2022; Matanock et al., 2019).

Best practices for VAP prevention include (Klompas, 2022a):

- Using noninvasive positive pressure ventilation
- Avoiding patient sedation whenever possible
- Instituting daily sedation vacations
- Assessing daily assessment extubation readiness
- Facilitating early mobility
- Changing ventilator circuits only if visibly soiled or malfunctioning
- Elevating the head of bed 30 to 45 degrees
- Using endotracheal tubes with subglottic secretion drainage ports (for patients expected to require mechanical ventilation 48 hours or longer)
- Using selective oral or digestive decontamination
- Performing routine oral care with chlorhexidine

Referral: Physical therapy measures for strengthening and ambulation may be initiated during the acute recovery period

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and continued during convalescence or replaced by restorative nursing measures. For those with chronic comorbidities, follow-up or referral to the appropriate specialist is indicated.

Education: Provider education regarding appropriate prescribing of antibiotics is helpful in decreasing drug-resistant organisms. Teach groups of older adults (especially adults with comorbidities) about preventive measures including care after discharge, follow-up, and possible vaccination. Educate patient and caregivers about the importance of nutrition, hydration, deep breathing exercises, and smoking cessation (Klompas, 2022a).

Clinical Recommendation	Evidence Rating	References
Consider pneumonia in patients with cough, dyspnea, or sputum production, especially if accompanied by fever, altered breath sounds, or crackles.	C	Klompas, 2022c
Presence of infiltrates on chest x-ray are the preferred method to confirm pneumonia diagnosis. Computed tomography and ultrasound are more accurate and should be considered for those with negative chest radiograph but high clinical suspicion for pneumonia.	C	Klompas, 2022c Ramirez, 2021 Huggins & Mayo, 2021 Modi & Kovacs, 2020a
The Pneumonia Severity Index and CURB-65 are validated tools for determining severity of illness and appropriate site of care of patients with CAP.	A	Ramirez, 2021 Metlay et al., 2019
Delayed treatment with antimicrobial therapy is associated with greater risk for clinical deterioration and poor prognoses. Initiate empiric treatment as soon as able and adjust accordingly based on culture and sensitivity results.	C	Klompas, 2022b Kalil et al., 2016
Treat previously healthy outpatients with amoxicillin, macrolide, or doxycycline.	C	Metlay et al., 2019
Treat outpatients with comorbidities or recent antibiotic use with respiratory fluoroquinolone or beta lactam plus macrolide.	B	Metlay et al., 2019
Treat inpatients empirically until pathogen is identified with a second- or third generation beta lactam plus macrolide, or respiratory fluoroquinolone.	A	Metlay et al., 2019
Vap Management/Prevention Evidence		
Strategies to prevent aspiration include elevation of head of bed 30–45 degrees, minimization of sedation and nonessential suctioning, maintenance of cuff pressure 20–30 cm H_2O, and application of positive end-expiratory pressure ≥5 cm H_2O.	A	Klompas, 2022a Modi & Kovacs, 2020b Agency for Healthcare Research and Quality, 2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PULMONARY EMBOLISM

Signal Symptoms: Subjective: Acute onset chest discomfort, palpitations, dyspnea, dizziness, anxiety. Objective: often nonspecific findings, such as tachypnea, tachycardia, S_3, tricuspid regurgitation murmur, chest wall, back, or flank tenderness. Pulmonary embolism (PE) is difficult to diagnose due to variability in presentation (Rivera-Lebron et al., 2019). Some pulmonary emboli are asymptomatic and might be found incidentally on imaging. Clinical symptoms alone should not be used to confirm or exclude PE, instead probability scores and diagnostic algorithms should be utilized (Doherty, 2017; Kearon et al., 2016).

Description: PE is a life-threatening condition. It is the occlusion of the pulmonary artery or one of its branches by a thrombus originating from elsewhere in the body. A blood clot is the most common embolism, although fat, air, bone marrow, tumor cells, and foreign material also can occlude the pulmonary vasculature. A blood clot PE is one component of venous thromboembolism (VTE), which also encompasses deep venous thromboembolisms (Robertson & Jones, 2017).

Etiology: PE usually is caused by a dislodged thrombus from one of the veins of the legs or pelvis (deep vein thrombosis [DVT]). Most emboli are believed to arise from areas of decreased blood flow in the lower extremity proximal veins (iliac, femoral, popliteal). More than 50% of patients with proximal vein DVT also present with PE (Robertson & Jones, 2017).

Occurrence: The estimated incidence of PE is one to two per 1,000 (about 900,000 per year) in the United States. Both PE and DVT are VTE, and they often occur concurrently.

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PE is the third leading cause of vascular death after myocardial infarction (MI) and stroke, and 10% to 30% of patients will die of VTE within 1 month of diagnosis (Centers for Disease Control and Prevention [CDC], 2015).

Age: Risk of VTE increases with age, and more so in men than in women. However, many risk factors increase relative risk separate from age, such as oral contraceptive use or lifestyle choices such as smoking (Phillippe, 2017).

Ethnicity: Incidence varies by race; highest incidence is in those of African American descent, with Europeans in North America and Europe almost as prevalent. There is lower incidence in Hispanic, Asian, and Native American populations (Zakai & McClure, 2011).

Contributing Factors: PE may occur unprovoked or secondary to an environmental risk factor. Persistent risk factors include cancer, heart failure, obesity, and varicose veins. Transient risk factors include immobility such as bedrest of more than 3 days, presence of a central venous catheter, insertion of a pacemaker, or use of estrogen. Virchow triad of stasis or prolonged immobility, hypercoagulation, and venous trauma (endothelial injury with inflammation of the vessel lining) is a leading cause (Phillippe, 2017). Unprovoked PE is associated with nonenvironmental risk factors, such as age, male sex, and hereditary thrombophilias (e.g., deficiencies of natural coagulation inhibitors such as antithrombin, protein C and S, factor V Leiden, and prothrombin (Factor II) G20210A. Pregnancy, especially in the postpartum period, oral contraceptives, and hormone replacement therapy increase PE risk as well (Phillippe, 2017).

Signs and Symptoms: Signs and symptoms of PE tend to be nonspecific. Less than 20% of patients present with classic symptoms of chest pain, dyspnea, or hemoptysis. The Prospective Investigation of Pulmonary Embolism Diagnosis (PIOPED II) study showed that 97% of patients had more than one of the symptoms of dyspnea, pleuritic chest pain, and tachypnea; however, the great variability in presentation and multitude of potential causes for those symptoms make it difficult to diagnose PE without laboratory tests or imaging (Rivera-Lebron et al., 2019). A thorough history and review of system should reveal any subjective experiences such as acute onset chest discomfort, palpitations, dyspnea, dizziness, anxiety. This should be complemented by physical examination, which in case of PE may reveal tachypnea, tachycardia, S_3, tricuspid regurgitation murmur, chest wall, back, or flank tenderness. Auscultation of the lungs may be normal or may show localized wheezing, consolidation, or friction rub. Jugular venous distention and atrial arrhythmia may be present. Examination of the legs, especially of the iliofemoral and popliteal areas, may reveal signs of DVT. The arms, abdomen, and pelvic areas also should be examined for pain, erythema, or palpable vein cords. In the case of a massive PE, hypotension, circulatory instability, and cyanosis may be present (Rivera-Lebron et al., 2019). Some pulmonary emboli are asymptomatic and might be found incidentally on imaging. Clinical symptoms alone should not be used to confirm or exclude PE, instead probability scores and diagnostic algorithms should be utilized (Doherty, 2017; Kearon et al., 2016).

Diagnostic Tests: Clinical judgment in conjunction with clinical prediction scoring tools and diagnostic studies is recommended. The Wells Clinical Prediction Scoring Tool for Pulmonary Embolism considers clinical symptoms, tachycardia, recent immobility or surgery, hemoptysis, malignancy, and prior DVT/PE to help assign a pretest probability of PE (Table 11-5). A high Wells score does not require a d-dimer; instead, it should prompt imaging (Doherty, 2017).

TABLE 11-5 Wells Criteria

Clinical symptoms of DVT (minimum of leg swelling, pain with palpation of the deep veins)	3.0
An alternative diagnosis less likely than pulmonary embolism	3.0
Heart rate >100	1.5
Immobilization or surgery in the previous four weeks	1.5
Previous DVT/PE	1.5
Hemoptysis	1.0
Malignancy (on treatment, treated in the last six months or palliative)	1.0
Simplified clinical probability assessment	
PE likely	>4.0
PE unlikely	≤4.0

DVT: deep vein thrombosis.

From Wells, P. S., et al. (2000). Derivation of a simple clinical model to categorize patients probability of pulmonary embolism: Increasing the models utility with the SimpliRED D-dimer. Thromb Haemost; 83: 416-20. © Georg Thieme Verlag KG.

The chest x-ray is often abnormal, but usually nonspecific. It is used primarily to rule out other causes of symptoms such as pneumonia or heart failure. Electrocardiogram (ECG) changes that show signs of right ventricular strain, T-wave inversion in leads V1 to V4, QR pattern in V1, new-onset right bundle branch block, or S1Q3T3 complex can sometimes be seen in severe cases of PE. Mild PE cases may only reveal sinus tachycardia or atrial arrhythmias such as atrial fibrillation. PE patients may also have normal ECGs, which is why they are not normally considered diagnostic. In a patient deemed to be at low or intermediate risk of PE, a negative enzyme-linked immunosorbent assay (ELISA) d-dimer test can rule out the possibility of PE. The ELISA or ELISA-derived d-dimer assays have a sensitivity of 95% and can exclude PE in patients with a low to intermediate pretest probability (Doherty, 2017; Kearon et al., 2016; Konstantinides et al., 2019; Rivera-Lebron et al., 2019). The sensitivity of d-dimer testing varies; it increases with the extent of PE, and it decreases with age to only 10% in patients older than 80 years. D-dimer is nonspecific; it can also be elevated in the patient with cancer, during hospitalization, and in pregnant patients. Some studies suggest age-adjusted cutoffs to improve d-dimer testing in older adults (Konstantinides et al., 2019). Along with a high Wells score it may be found diagnostic, but in patients with low Wells scores, imaging should be pursued (Doherty, 2017).

Multidetector CTA (MDCTA) is widely available, and when used with IV contrast, the MDCTA can outline thrombi in the pulmonary arteries. MDCTA has almost replaced lung scanning and angiography as the standard for PE diagnosis (Doherty, 2017). Limitations for using MDCTA include patients

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with renal dysfunction, allergy to contrast media, possible pregnancy, critical illness, requiring ventilator support, or recent MI. In these cases, a ventilation/perfusion (V/Q) scan may be done. Additionally, if there is a high suspicion of PE but a negative MDCTA, a V/Q scan may be ordered. However, most clinicians feel more comfortable with MDCTA as a diagnostic tool because of its ability to provide anatomical demonstration of presence of a clot versus relying on the V/Q scans to assess the probability of embolism based on V/Q mismatch. V/Q scanning is done in the nuclear medicine department and may not be as readily available as MDCTA in many cases (Konstantinides et al., 2019; Rivera-Lebron et al., 2019).

Echocardiography is not recommended to diagnose PE, but it can help determine risk of mortality or adverse outcome. An echocardiogram can evaluate right ventricular function and detect a free-floating thrombus in the right heart, which can be associated with PE and increased mortality. In addition, if a massive PE is diagnosed, transesophageal echocardiography should be done to assess right ventricular function (Kearon et al., 2016; Konstantinides et al., 2019; Rivera-Lebron et al., 2019)

The myocardial markers, including cardiac troponin levels and BNP or NT-proBNP have no role in the diagnosis of PE but may serve to rule out other processes, reflect severity of PE, and have been associated with increased mortality (Rivera-Lebron et al., 2019).

Differential Diagnosis:

- Pneumonia
- MI
- Pericarditis
- Heart failure
- Pleural effusion
- Panic attacks
- Hyperventilation syndrome
- Pneumothorax
- Esophageal rupture
- Gastritis
- Gastric or duodenal ulcer
- Gastroesophageal reflux disease (GERD)
- Asthma
- Musculoskeletal pain
- Mediastinitis

Treatment: Treatment recommendation varies by PE severity, which is classified by hemodynamically stable or unstable patient status, by time of onset, and by location. Anticoagulation is the cornerstone of treatment. Goal of anticoagulation is to prevent early death, recurrence, or fatal VTE/PE. If no contraindications, anticoagulation should be initiated immediately in patients with high or moderate suspicion of PE while awaiting diagnostic test results. For acute PE, low molecular weight heparin (LWMH) is preferred over unfractionated heparin to reduce complications, but there is no difference in mortality (Robertson & Jones, 2017).

Severity of PE presentation may be determined by hemodynamic stability. In patients with a massive PE, acute right ventricular failure and low systemic output is the leading cause of death. Treatment should be individualized and supportive and may include the use of vasopressors. Oxygen administration and/or mechanical ventilation may be needed to reverse hypoxia (Konstantinides et al., 2019). If the patient is hemodynamically unstable (systolic blood pressure <90, heart rate <40) or is presenting with worsening respiratory insufficiency, severe right ventricular dysfunction, or major myocardial necrosis but has a low risk of bleeding complications, the patient should be treated in the inpatient setting with heparin and alteplase (Kearon et al., 2016). Catheter embolectomy or surgical embolectomy may be considered if absolute or severe contraindications to systemic thrombolysis or after failed thrombolysis (Rivera-Lebron et al., 2019).

Oral anticoagulation should be initiated simultaneously with or shortly after parenteral anticoagulation. Warfarin (Coumadin) has been the gold standard vitamin K antagonist (VKA) for more than 50 years and is monitored by measuring the international normalized ratio (INR). With warfarin therapy, an INR of 2.0 to 3.0 should be maintained. Long-term anticoagulation recommendations depend on existence of comorbidities such as cancer. If no cancer is present, direct oral anticoagulants (DOACs) and VKAs are preferred over LWMH; if cancer is present, LWMH is preferred. For anticoagulated patients, no IVC filter or compression stockings are recommended (Doherty, 2017; Robertson & Jones, 2017).

Follow-Up: Follow-up visits are on an individualized basis. Anticoagulation usually is continued for a minimum of 3 to 6 months after PE. Experts differ on optimal length of therapy and dosing adjustments in specific situations. CHEST 2016 guidelines recommend at least 3 months of anticoagulant therapy for provoked or unprovoked PE. The risk-benefit ratio should be evaluated after 3 months of therapy for the unprovoked PE. For the unprovoked first-time VTE with low to moderate bleeding risk, CHEST guidelines recommend extended anticoagulant therapy (no scheduled stop date). If bleeding risk is high, 3 months of anticoagulant therapy is recommended. In any case of extended anticoagulant therapy, risk–benefit for continued treatment should be reassessed at periodic intervals (i.e., annually). Extended therapy is recommended for the patient with active cancer and PE regardless of bleeding risk, keeping in mind the need to reassess risk–benefit periodically (Kearon et al., 2016).

Sequelae: Unrecognized PE can be fatal and is associated with overall mortality of up to 30% within the first month. Most deaths occur rapidly, and PE may only be diagnosed after death (CDC, 2015; Rivera-Lebron et al., 2019). Cardiac right ventricular function may become permanently affected leading to heart failure. Other complications include alveolar collapse, atelectasis, and pulmonary infarction. Complications from anticoagulation include uncontrolled bleeding and hematoma (Rivera-Lebron et al., 2019).

Prevention/Prophylaxis: PE is one of the most common preventable causes of hospital deaths in the United States. Patients should avoid controllable risk factors for PE such as sedentary lifestyle, obesity, and smoking. Encourage frequent ambulation, safety precautions to avoid injury to lower extremities, evaluation of possible hypercoagulation pathology, and prophylactic anticoagulation after orthopedic surgery of hip or knee. Prolonged sitting should be avoided. Consideration of prophylactic anticoagulation in any immobilized hospitalized patient and use of sequential compression devices may be helpful. Compression stockings and IVC filter

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are no longer recommended because of potential secondary complications (Doherty, 2017; Robertson & Jones, 2017).

Referral: Refer patients to internal medicine or emergency medicine for emergent evaluation and initial treatment plan when PE is suspected. When stable, patients can be managed on warfarin or DOAC therapy and therapy may be de-escalated after 3 to 6 months depending on risk factors. Warfarin requires regular monitoring of INR to maintain a therapeutic range. Although no regular monitoring of DOAC therapy is required for dosing, compliance is of utmost importance in order to achieve adequate therapeutic anticoagulant benefits (Doherty, 2017; Robertson & Jones, 2017).

Education: Provider education about awareness of PE in differential for chest pain or dyspnea is needed. Teach the patient, family, or caregiver about risk factors and preventive measures, disease pathology, monitoring for signs of recurrence, and need for compliance with anticoagulation therapy. Instruct the patient to use a soft toothbrush and an electric razor and to report bleeding gums, hemoptysis, and any blood in stool or urine. Advise patients to avoid aspirin, to consult with their health-care provider before taking any over-the-counter (OTC) medications, and to take precautions to avoid bumping or bruising.

Clinical Recommendation	Evidence Rating	References
Prevention of VTE should be considered according to the patient's baseline risk. Cancer, COVID-19, and other issues may contribute to needing prophylaxis. Acutely or critically ill patients with COVID-19 should receive anticoagulant thromboprophylaxis with low-molecular-weight heparin (LMWH) or fondaparinux over anticoagulant thromboprophylaxis with unfractionated heparin (UFH). Anticoagulant thromboprophylaxis with LMWH, fondaparinux, or UFH is recommended over anticoagulant thromboprophylaxis with a direct oral anticoagulant (DOAC).	A B A	Rivera-Lebron et al., 2019 Moores et al., 2020 Doherty, 2017
Clinical decision making: Estimate probability of PE based on a validated clinical decision tool such as Wells score and Pulmonary Embolism Rule-out Criteria (PERC), then use a validated diagnostic algorithm integrating findings from d-dimer and CTA (CT pulmonary angiography If CTA contraindicated may use ventilation/perfusion (V/Q) scan, or echocardiogram. After PE diagnosis is established: risk stratification is recommended using a composite of clinical appearance, systolic blood pressure, heart rate, respiratory rate, oxygen requirement, Pulmonary Embolism Severity Index (PESI) or sPESI, imaging for rigth ventricular dysfunction (CTA or echocardiography) and/or biomarkers (troponin, BNP or NT-pro-BNP).	A A A A	Doherty, 2017 Kearon et al., 2016 Rivera-Lebron et al., 2019 Konstantinides et al., 2019
Occurrence: 900,000 people could be affected (1 to 2 per 1,000) each year in the United States. 10%–30% of people will die within one month of diagnosis. Sudden death is the first symptom in about one-quarter (25%) of people who have a PE. 60% of all VTE events occur in those 70 years of age and older: The overall incidence of VTE is 1 to 2 per 1,000 person-years in the general population, which rises to 8 per 1,000 person-years in people older than 85 years. There are ethnic differences: highest incidence is in those of African American descent, with Europeans in North America and Europe almost as prevalent.	A A A	CDC, 2015 Phillippe, 2017 Zakai & McClure, 2011
Long-term anticoagulation recommendations depend on existence of comorbidities such as cancer. If no cancer is present, DOACs and vitamin K antagonists are preferred over LWMH, if cancer is present LWMH is preferred. With warfarin therapy an International Normalized Ratio of 2–3 should be maintained. For anticoagulated patients, no IVC filter or compression stockings are recommended.	A	Doherty, 2017 Robertson & Jones, 2017
Immediate anticoagulation is recommended for acute PE. LWMH is preferred over unfractionated heparin to reduce complications, but there is no change in mortality	A	Robertson & Jones, 2017
Thrombolysis: If hemodynamically unstable (systolic blood pressure <90, heart rate <40) or worsening respiratory insufficiency, severe right ventricular dysfunction, or major myocardial necrosis, and low risk of bleeding complications, treatment should be in the inpatient setting with heparin and alteplase. Catheter embolectomy or surgical embolectomy mostly only if contraindications to systemic thrombolysis (ST), after failed ST or catheter-directed thrombolysis (CDL).	A A	Kearon et al., 2016 Rivera-Lebron et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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PULMONARY TUBERCULOSIS

Signal Symptoms: Productive, prolonged cough; fatigue; low-grade fever; night sweats; poor appetite; weight loss.

Description: Pulmonary tuberculosis (TB) is a chronic necrotizing infection caused by a slow-growing acid-fast bacillus (AFB), *Mycobacterium tuberculosis* (Mtb). Airborne Mtb particles are called droplet nuclei which are 1 to 5 microns (use if symbol is fine) in diameter. These droplet nuclei remain suspended in the air for several hours when a person with active Mtb coughs, sneezes, or speaks (Churchyard, et al., 2017). The droplet nuclei multiply causing primary lesions in the lungs. Not all individuals exposed to Mtb become infected. The primary site for most cases of Mtb is the lungs. Extrapulmonary Mtb can affect any organ or tissue, such as the kidneys, spine, or brain. Most extrapulmonary disease is not contagious, except for laryngeal Mtb.

Etiology: The Mtb infection spreads by inhalation of airborne particles or droplets produced by persons with active pulmonary or laryngeal Mtb during coughing, sneezing, singing, and other expiratory efforts. The development of infection after exposure depends on the exposed person's ability to mount an effective immune response on the cellular level. In the initial 2 to 4 weeks before cellular immunity response occurs, direct pulmonary infection may develop, or lymphohematogenous circulation may lead to miliary, meningeal, or Mtb adenitis. When T cells recognize the specific antigen, they become sensitized, engaging the macrophages in destroying or containing the tubercle bacilli. This leads to healing, with no residual or calcified lymph nodes in the pulmonary or tracheobronchial areas. This latent stage is typical of 90% to 95% of infected persons, leaving them at lifelong risk for reactivation. Tuberculin skin testing documents exposure at 2 to 10 weeks after exposure.

Occurrence: In 2016, "a WHO endorsed estimate updated the global prevalence of LTBI to 23% corresponding to 1.7 billion people infected worldwide" (Cohen et al., 2019). Men have double the incidence of Mtb worldwide, but disparity may be explained partly by underreporting in women. Mtb was one of the top 10 causes of death worldwide in 2019, known as the disease of poverty. It is the leading cause of death in people with HIV and a major cause of death secondary to antimicrobial resistance. In 2019, of the 10 million people who fell ill with Mtb, 5.6 million were men, 3.2 million were woman and 1.2 million were children, and of all the combined TB cases, 8.2% have HIV (WHO, 2020). Eight countries accounted for two-thirds of the worldwide total: India, Indonesia, China, the Philippines, Pakistan, Nigeria, Bangladesh, and South Africa (WHO, 2020). In 2019, 1.4 million people died from Mtb. Worldwide the Mtb incidence rate fell by 9% between 2015 to 2019 (from 142 to 130 new cases per 100,000 population), including a reduction of 2.3% between 2018 and 2019 (WHO, 2020). Treating Mtb saved 63 million lives worldwide between 2000 and 2019 (WHO, 2020).

The WHO's 2021 *Global Tuberculosis Report* announced Mtb deaths rose for the first time in more than a decade due to the COVID-19 pandemic. In 2020, more people died from Mtb, with far fewer people being diagnosed and treated or provided with Mtb preventive treatment compared with 2019, and overall spending on essential Mtb services falling. The increase in the number of Mtb deaths occurred mainly in the 30 countries with the highest burden of Mtb. The WHO's modeling projections indicate the number of people developing Mtb and dying from the disease could increase in 2021 and 2022.

Age: Children and adolescents are more likely to have primary disease; adults and older adults are more likely to have recrudescent disease. Mtb disease in children under 15 years of age (also called pediatric Mtb) is a public health problem of special significance because it is a marker for recent transmission of Mtb. Also of special significance, infants and young children are more likely than older children and adults to develop life-threatening forms of Mtb disease (e.g., disseminated Mtb, Mtb meningitis). Among children, the greatest numbers of Mtb cases are seen in children younger than 5 years of age and in adolescents older than 10 years of age.

Ethnicity: As reported by the Centers for Disease Control and Prevention (CDC) (2020):

- Native Americans or Alaskan Natives: 3.2 Mtb cases per 100,000 persons
- Asians: 13.3 Mtb cases per 100,000 persons
- Blacks/African Americans: 3.4 Mtb cases per 100,000 persons
- Native Hawaiians and other Pacific Islanders: 18.7 Mtb cases per 100,000 persons
- Hispanics or Latinos: 3.5 Mtb cases per 100,000 persons
- White: 0.4 Mtb cases per 100,000 persons

Risk Factors: Overall, about 5% to 10% of infected persons who do not receive treatment for latent Mtb infection will develop Mtb disease at some time in their lives. For persons whose immune systems are weak, especially those with HIV infection, the risk of developing Mtb disease is much higher than for persons with normal immune systems. Persons who are at increased risk include those with:

- HIV infection
- Substance abuse issues (especially IV drug use)
- Recent infection with *M. tuberculosis* (less than 2 years ago)
- Chest x-ray findings suspicious of previous Mtb with no treatment or ineffective treatment
- Diabetes mellitus
- Silicosis
- Prolonged corticosteroid therapy
- Other immunosuppressive therapy
- Cancer of the head and neck
- Hematological and reticuloendothelial diseases
- End-stage renal disease
- Intestinal bypass or gastrectomy
- Chronic malabsorption syndromes
- Low body weight (less than 10% ideal body weight)

Other factors associated with increased risk include homelessness, residence in a congregate setting (e.g., nursing home, boarding home, prison, mental health facilities), low socioeconomic status, and health-care work in a high-risk area.

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Signs and Symptoms: Typical presentation includes cough, hemoptysis, weight loss, anorexia, adenopathy, fever, night sweats, decreased activity level, and pleuritic pain. In the average population, the onset is gradual and may go undetected for some time. In the older patient, these findings are not usually present, or they are so subtle and intermingled with other chronic illness symptoms as to be undistinguishable. Weight loss, dyspnea, or anorexia may be the only symptoms. Typical presentations include pneumonia, bronchitis, or heart failure with pleural effusion. Extrapulmonary Mtb may manifest with symptoms typical to the site involved (e.g., urinary incontinence or frequency and urgency for bladder Mtb).

Diagnostic Tests:

Tuberculin Skin Test (TST): The TST is used to determine whether a person is infected with Mtb. If a person is infected, a delayed-type hypersensitivity reaction is detectable 2 to 8 weeks after infection. The skin test is administered intradermally using the Mantoux technique by injecting 0.1 mL of 5 TU purified protein derivative (PPD) solution. The reading and interpretation of TST reactions should be conducted within 48 to 72 hours of administration.

TST Interpretation (CDC, 2020): Induration of 5 mm and more is considered positive in:

- Immunosuppressed individuals
- HIV infected individuals
- Recent contact with active TB patients
- Prior tuberculosis signs on chest radiograph such as fibrotic changes
- Organ transplant patients

An induration of 10 mm or more is considered positive in:

- Immigrants from endemic/high prevalence countries in the last 5 years
- High-risk area employees and residents
- Injection drug abusers
- Mycobacteriology laboratory professional
- Chronic medical conditions that increase the risk of tuberculosis include diabetes, kidney failure, malignancy

An induration of 15 mm or more is considered positive in:

- In any person, including healthy individuals without any risk factors for TB
- Patients who do not meet any of the above criteria

TST Conversion:

- According to the CDC (2020), the repeat TST is considered positive if there is ≥10 mm induration and the induration is increased by ≥6 mm compared to the previous test. This test interpretation is less sensitive but more specific. For more information about tuberculin skin testing, visit the CDC Web site.

The CDC in 2019 revised its guidelines that anyone working or volunteering in health-care settings should receive a TB risk assessment, TB symptoms screen, and a TST upon hire (Dobler et al., 2018; Sosa et al., 2019). A recent retrospective cohort study by Dobler et al. (2018) of about 40,000 health-care workers at a tertiary U.S. medical center in a low TB-incidence state found an extremely low rate of TST conversion (0.3%) during 1998 to 2014, with only a limited amount attributed to occupational exposure. Annual skin testing is not required unless there is a known exposure. It is recommended that you refer to your state and local TB screening and testing regulations which may be different that the current CDC guidelines.

Key Points:

- Training is essential for health-care providers to be proficient in the administration and interpretation of the TST.
- The TST should not be performed on a person who has written documentation of either a previous positive TST result or treatment for TB disease.
- Interpretation of the TST result is the same for persons who have had bacille Calmette-Guérin (BCG) vaccination because a majority of BCG cross-reactivity wanes over time.
- A TST that was not measured and recorded in millimeters (mm) of induration must be repeated.
- A TST cannot differentiate between a latent tuberculosis infection (LTBI) and active Mtb infection.

Interferon–Gamma Release Assays (IGRAs): IGRAs are used to determine whether a person is infected with Mtb by measuring the immune response to Mtb proteins in whole blood. Specimens are mixed with peptides that simulate antigens derived from Mtb and controls. In a person infected with Mtb, the white blood cells recognize the simulated antigens and release interferon-gamma (IFN-γ); results are based on the amount of IFN-γ released (CDC, 2011). As noted earlier, there are two U.S. Food and Drug Administration (FDA) approved IGRAs commercially available in the United States:

- QuantiFERON®-TB Gold-in-Tube test (QFT-GIT)
- T-SPOT® TB test

Key Points:

- Advantages of IGRAs include:
  - Requires a single patient visit to conduct the test.
  - Results can be available within 24 hours.
  - Does not boost responses measured by subsequent tests.
  - Prior BCG vaccination does not cause a false-positive IGRA test result.
- Limitations of IGRAs include:
  - Blood samples must be processed within 8 to 30 hours after collection.
  - Errors in collecting or transporting blood specimens or in running and interpreting the assay can decrease the accuracy of IGRAs.
  - Limited data on the use of IGRAs to predict who will progress to TB disease in the future.
  - Limited data on the use of IGRAs for:
    - Children younger than 5 years of age
    - Persons recently exposed to *M. tuberculosis*, persons who are immunocompromised, and serial testing.
  - Tests may be expensive.

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For more information, see *Latent Tuberculosis Infection: A Guide for Primary Health Care Providers* at https://www.cdc.gov/tb/publications/ltbi/.

Differential Diagnosis: Pneumonia, lymphoma, fungal infections, heart failure, pleural effusion, and lung cancer can mimic Mtb.

Treatment: Mtb treatment focuses on cure and reducing the transmission of Mtb to other people while ensuring safety and efficacy of treatment in the shortest time frame. Patients who are diagnosed with Mtb should be referred to a provider who specializes in treating Mtb (infectious disease, or pulmonary specialist). Before treatment, baseline laboratory tests, including liver function, bilirubin, complete blood count (CBC), blood urea nitrogen (BUN), creatinine, and serum uric acid, diabetes screen, HIV screen (if positive, CD4 lymphocyte count and HIV RNA load), and hepatitis B and C; chest x-ray; sputum smear and culture; drug susceptibility; visual assessment; color discrimination; weight; and symptom review are recommended. Once treatment begins, monthly liver function, bilirubin, CBC, BUN, creatinine, and serum uric acid, visual assessment, color discrimination, weight, and symptom review are recommended. Follow-up cultures should be done monthly, until two consecutive negative specimens are obtained, to determine response to treatment. If the culture is not negative after 3 months, suspect drug resistance or noncompliance and reevaluate. After culture is negative, obtain one additional culture at treatment completion.

- *Active Mtb:* In a patient who is not suspected of having drug-resistant Mtb treatment the preferred regimen consists of an intensive phase of 2 months of isoniazid (INH), rifampin (RIF), pyrazinamide (PZA), and ethambutol (EMB) followed by a continuation phase of 4 months of INH and RIF (Sterling et al., 2020). If Mtb is susceptible to INH and RIF, EMB is not necessary, and the intensive phase consists of INH, RIF, and PZA only. Pyridoxine is given with INH to those at risk for neuropathy (e.g., persons infected with HIV; patients with diabetes, alcoholism, malnutrition, or chronic renal failure; or those of advanced age) (Sterling et al., 2020). It is preferred to have individuals take medication daily. Directly observed therapy (DOT) 5 days a week is considered the standard in most TB programs in the United States and Europe (Karumbi & Garner, 2015). DOT can be administered in the office, clinic, or any other place that is mutually agreed upon by trained personnel. This method is helpful in compliance and decreasing risk of developing resistant Mtb. There have been no large clinical trials that have compared 5-day administration versus 7-day administration, but experts agree that this is an acceptable alternative to meeting the definition of daily dosing (Karumbi & Garner, 2015; Sterling et al., 2020). *Note:* HIV-positive individuals require specific modifications in therapy. Refer to the CDC 2022 guidelines (https://www.cdc.gov/tb/publications/guidelines/hiv_aids.htm)
- *Latent Tuberculosis Bacillus Infection (LTBI):* The LTBI treatment guidelines were updated in 2020, comprising of three preferred rifamycin-based regimens and two alternative monotherapy regimens with daily INH. These treatments are for treating individuals who are infected with MtB that is presumed to be susceptible to INH or rifampin. (Sterling, 2020). These guidelines do not apply when the Mtb strain is resistant to INH and rifampin. There are specific guidelines that were published in 2019 for treating contacts who have been exposed to multidrug resistant MtB (Nahid et al., 2019).

The three preferred rifamycin-based regimens are:

- **3 months of once-weekly isoniazid plus rifapentine (3HP)**
  - Preferred regimen recommended for adults and children aged >2 years, including HIV-positive persons.
  - Administered through DOT.
  - Treatment completion rates were higher with the 3-month regimen (Nahid et al., 2019).
  - Possible disadvantages of this regimen include cost of medications that are greater than alternative treatments.
  - Systemic drug reaction or influenza-like syndrome that can include syncope and hypotension may occur (Nahid et al., 2019).
- **4 months of daily rifampin (4R)**
  - Preferred treatment of 4 months of daily rifampin is strongly recommended for HIV-negative adults and children of all ages.
  - Toxicity is less than 9 months of daily INH regimens.
  - Lower rates of discontinuation due to less adverse effects, lower hepatoxicity and a higher treatment completion rate.
  - The potential disadvantages of the rifamycin-based regimens are the many drug interactions, including warfarin, oral contraceptives, azole antifungals, and HIV antiretroviral therapy (Sterling et al., 2020).
  - Rifabutin may be used in place of rifampin when rifampin is contraindicated due to drug-drug interactions and INH cannot be used (Sterling et al., 2020).
- **3 months of daily isoniazid plus rifampin (3HR).**
  - Preferred treatment of 3 months of daily INH plus rifampin is conditionally recommended for adults and children of all ages and for HIV-positive persons as drug interactions allow.
  - Less hepatotoxicity occurs among those receiving the shorter course of therapy, although discontinuation of therapy because of adverse effects was more frequent (Sterling et al., 2020).
  - There is a higher risk of hepatotoxicity with the two drugs given together than with either drug given alone (Sterling et al., 2020).

Prescribing providers or pharmacists who are unfamiliar with rifampin and rifapentine might confuse the two drugs. They are not interchangeable. Careful attention should be taken to ensure that patients receive the correct medication. Preference for these rifamycin-based regimens is based on effectiveness, safety, and high treatment completion rates. Refer to the CDC for further information on treatment (https://www.cdc.gov/tb/topic/treatment/ltbi.htm).

- *Antibiotic resistant Mtb:* For drug-resistant Mtb, different culture guidelines apply. Several treatment options are available. Refer to the CDC for further information on treatment (https://www.cdc.gov/tb/publications/guidelines/mdr_tb.htm).

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Follow-Up: Monitor the patient closely during treatment for potential adverse events such as hepatotoxicity. (Refer to the section Treatment.) For the frail, older adult in a long-term care facility, more frequent monitoring for adverse effects of treatment, including anorexia, polyneuropathy, or development of medication-induced hepatitis, is warranted. DOT is normally used in these settings, so compliance is less of a concern. Refer community-dwelling older adults to the local or state health department for follow-up, monitoring of medication compliance and side effects, patient, and family education, and testing of close contacts.

Many agencies charged with monitoring and control have outreach services, such as home visits. Emphasize to patients that compliance is crucial to successful control. If no follow-up visitation is available through the monitoring agency, see the patient for monthly follow-up visits in the office.

Sequelae: Post-treatment complications include relapse, aspergilloma, bronchiectasis, carcinoma, chronic respiratory failure, cor pulmonale, chronic pulmonary inflammation. Development of drug-resistant organisms, particularly if a patient is noncompliant with the prescribed treatment.

Prevention/Prophylaxis: Individuals admitted to long-term care facilities must have a two-step PPD test unless there is documented proof of a positive test. PPD testing is also required if TB exposure is suspected. Any patient with a positive PPD must have a chest x-ray to evaluate for active or latent disease. When targeted testing reveals a positive tuberculin skin reaction but no evidence of active Mtb, it is referred to as latent Mtb. For those with a positive PPD test, it is recommended to screen annually for the presence of Mtb symptoms. The decision to institute chemoprophylaxis is a clinical judgment, based on a comparison of individual factors with the risk of developing Mtb (see Contributing Factors) versus the risk of toxicity. Refer to Treatment section for latent Mtb treatment.

Referral: Mtb is a mandated reportable disease. When a positive test is received, it is to be reported to your state or local jurisdiction. Refer to a TB clinic, infectious disease specialist, or pulmonary specialist for evaluation and management of Mtb treatment.

Education: Teach the patient, caregivers, close contacts, and paraprofessional providers about the nature of the disease, its mode of transmission, screening and control measures, and follow-up. Teach the patient or caregiver about medications, drug actions and possible side effects, length of treatment, and compliance in drug treatment regimens.

Clinical Recommendation	Evidence Rating	References
For individuals with latent tuberculosis infection, it is recommended and preferred to use rifamycin-based regimens if they are susceptible to isoniazid and/or rifampin.	A	Sterling et al., 2020
Individuals working in or volunteering in health care should receive a tuberculin skin test upon hire along with tuberculosis risk and symptom assessment.	A	Dobler et al., 2018 Sosa et al., 2019
Annual skin testing is not recommended in individuals working in or volunteering in health care unless there is a known exposure.	A	Dobler et al., 2018 Sosa et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

RESTRICTIVE LUNG DISEASE

Signal Symptoms: Rapid, shallow respirations; dyspnea; decreased activity tolerance; easy fatigability; nonproductive, irritating cough provoked by deep breathing or exertion.

Description: *Restrictive lung disease* refers to a heterogeneous group of disorders that share a common abnormal ventilatory function: a decrease in lung volumes, both in total lung capacity and vital capacity (Lutfi, 2017). This reduced capacity may be due to stiffness in the lungs themselves or stiffness of the chest wall, weak muscles of respiration, or obesity. Restricted breathing is characterized by small tidal volume and rapid respiratory rate. Unlike obstructive lung diseases the issue is not exhaling, it is inhaling that is the problem.

Etiology: Restrictive lung diseases, which have a variety of etiologies, are most easily divided into two subgroups: pulmonary parenchymal diseases (intrinsic causes) and extrapulmonary diseases (extrinsic causes).

Pulmonary parenchymal disease (intrinsic) includes (but not limited to):

- Idiopathic pulmonary fibrosis (IPF)
- Non-specific interstitial pneumonitis (NSIP)
- Cryptogenic organizing pneumonia (COP)
- Sarcoidosis
- Occupational exposures (silica, asbestos, talc, beryllium, coal)
- Organic dust exposures (farmer's lung, bird fancier's lung)
- Hypersensitivity pneumonitis
- Drug/radiation induced interstitial lung disease

Extrapulmonary (extrinsic causes)

- Kyphoscoliosis
- Pleural conditions (e.g., pleural effusion)
- Obesity

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- Neuromuscular disorders (amyotrophic lateral sclerosis, polio, muscular dystrophy)
- Diaphragm paralysis
- Cervical spine injuries
- Guillain-Barré syndrome

Occurrence: The overall incidence of restrictive lung disease is undeterminable because several distinct entities are involved; however, there are some statistics available for specific diseases. The prevalence of IPF was estimated in a systematic review as 2.8 to 9.3 per 100,000 in North America and Europe (Barratt et al., 2018). Occupational lung diseases are common in farmers and in people who work with silica, asbestos, beryllium, organic solvents, or cotton. The prevalence of sarcoidosis in the United States is 8 to 11 cases per 100,000 persons (Arkema & Cozier, 2020).

Age: Occupationally induced disease and IPF are seen predominantly in the older population; other restrictive lung diseases may occur at any age.

Ethnicity: The highest incidence and prevalence in the United States is in non-Hispanic Blacks, with Black women having the highest rate (Arkema & Cozier, 2020).

Contributing Factors: Risk factors vary with etiology, including smoking history, exposure to occupational dusts, abnormalities in skeletal structure, genetics, chemotherapy, certain antibiotics, amiodarone, neuromuscular, and autoimmune disorders (Kalchiem-Dekel et al., 2018).

Signs and Symptoms: Patients often present with complaints of dyspnea. The pattern and severity vary greatly according to the etiology. A nonproductive cough may be present. A careful, detailed history is essential, including prior systemic diseases, occupational or environmental exposures, family history, social history, and history of drug use (Kalchiem-Dekel, et al., 2018). Medications including amiodarone, nitrofurantoin, hydralazine, gold, chemotherapeutic agents, and procainamide can cause drug-induced pulmonary parenchymal disease (Kalchiem-Dekel et al., 2018). Prior radiation can result in fibrosis. Use of tobacco should also be ascertained; it is common for patients to have a mixed pattern of obstructive and restrictive disease. The initial presentation of breathing problems often occurs after an acute respiratory viral infection.

Physical findings may reveal skeletal abnormalities, such as kyphoscoliosis, limiting lung expansion. Physical assessment of the lung initially may be unremarkable. In intrinsic disease, with progression of the disease, inspiratory crackles ("Velcro") typically are heard at the bases. Cyanosis and clubbing of fingers and toes may occur in IPF. In the end stages, signs of right-sided heart failure, including cor pulmonale, appear.

Diagnostic Tests: Because of the diverse nature of the conditions leading to restrictive lung disease, it is challenging to address diagnostic testing and results. Many results are specific to the causative condition. Routine testing includes complete blood count (CBC), chemistry profile, and liver function tests. If more common lung diseases are ruled out the patient should be referred to a pulmonologist for further assessment.

Test	Results Indicating Disorder
Pulmonary function test	Normal FEV_1/FVC ratio but decreased FVC and FEV_1; decreased total lung capacity, residual volume, and functional residual capacity. Residual volume–to–total lung capacity ratio is normal to low. Most have a gas exchange problem with marked decrease in single breath diffusing lung capacity for carbon monoxide. Diagnosis of restriction and extent of restriction is based on total lung capacity.
Chest x-ray	Increased interstitial markings, especially in lower fields. Hilar and mediastinal lymphadenopathy in sarcoidosis, some lymphomas, and silicosis. Pleural effusion and thickening with collagen-vascular disease, lymphoma, and asbestosis. A scattered reticulonodular pattern and ground glass opacities are common.
High-resolution computed tomography scan	In idiopathic pulmonary fibrosis, patchy, peripheral bibasilar reticular abnormalities in the subpleural area; with advanced disease, subpleural fibrosis and honeycomb pattern are present.

Source: Kalchiem-Dekel et al., 2018

In the late stages, arterial blood gases help to identify the degree of hypoxemia and carbon dioxide retention. In select cases, bronchoscopy and biopsy may be indicated (Kalchiem-Dekel et al., 2018).

Differential Diagnosis:

- Infectious or neoplastic diseases
- Chronic obstructive pulmonary disease (COPD)
- Heart failure
- Wegener's granulomatosis
- Goodpasture's syndrome
- Bechet's disease
- Sjögren's syndrome
- Systemic sclerosis
- Pneumoconiosis
- Tuberous sclerosis
- Eosinophilic pneumonia

Treatment: Therapy depends on the specific diagnosis obtained from clinical evaluation, imaging, and lung biopsy, and the disease progression. If occupational exposure is suspected, the causative agent should be avoided. Any patient with suspected intrinsic/parenchymal restrictive lung disease should be referred to a pulmonologist for a formal evaluation and treatment planning. Therapy with corticosteroids and cytotoxic agents (e.g., azathioprine and cyclophosphamide) is the primary treatment for many interstitial diseases, although objective data to support their use are lacking (Kalchiem-Dekel, et al., 2018)

The American Thoracic Society (ATS) and other global organizations' official statement on the evidence-based treatment of IPF was issued in 2011 and updated in 2018 (Raghu et al., 2018), citing the weakness of the evidence for current

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treatments, including corticosteroids, cytotoxics, immunosuppressants, and other miscellaneous drugs, and encouraging individual patient and specialist discussion before implementing any drug therapy. The ATS statement recommends against treatment of IPF with corticosteroids alone or in combination with cytotoxics or immunosuppressants (Raghu et al., 2018). Pirfenidone and nintedanib are approved for IPF and have been shown to slow functional decline and disease progression, although they are not curative and have a side-effect profile that may preclude continued use (Spagnolo et al., 2021). Lung transplantation is the only treatment to prolong survival in IPF (Kalchiem-Dekel et al., 2018); post-transplant the patient will be on immunosuppression for life. In the end stage of restrictive lung diseases, administer supplemental oxygen for supportive care; consider palliative care and hospice.

Follow-Up: Follow-up visits are scheduled as indicated by symptoms and comorbidities. Periodic chest x-rays or pulmonary function tests (PFTs) may help to chart diseases course and evaluate response to treatment. For many of the restrictive lung diseases the patient will be comanaged with a pulmonologist.

Sequelae: Use of corticosteroids or immunosuppressives may result in increased risk of infection and should be started and managed by a pulmonologist. Pulmonary hypertension and right-sided heart failure may occur. Restrictive lung diseases are chronic and there is no known cure.

Prevention/Prophylaxis: Give patients the pneumococcal pneumonia and influenza vaccines. Advise patients to avoid known exposures, tobacco use, and persons with acute, infectious upper respiratory illness.

Referral: Any patient with interstitial lung disease should be referred to a pulmonologist who should manage their pulmonary disease.

Education: Teach the patient and family about chronic disease management, regular self-care habits, and early intervention in acute illness. Discuss prognosis and preferred choices for end-stage disease.

Clinical Recommendation	Evidence Rating	References
Interstitial lung disease diagnosis can be made with a chest x-ray, pulmonary function tests consistent with restrictive lung disease, and typical findings on high-resolution computed tomography. Lung biopsy is necessary in atypical cases.	C	Oliveira et al., 2018
No treatment has been shown to have consistent benefit in idiopathic pulmonary fibrosis (IPF).	C	Kalchiem-Dekel et al., 2018 Spagnolo et al., 2021
Corticosteroids, supplementary oxygen, and pulmonary rehabilitation may provide symptomatic relief.	C	Kalchiem-Dekel et al., 2018
At present, there is no evidence for an effect of corticosteroid treatment in patients with IPF. On the other hand, other fibrotic lung diseases, such as nonspecific interstitial pneumonia, are reported to show a better response to corticosteroids. Making a clear distinction between IPF and other entities grouped under the umbrella term interstitial lung disease is, therefore, essential, because this may have therapeutic and prognostic implications.	C	Kalchiem-Dekel et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

UPPER RESPIRATORY TRACT INFECTIONS (RHINITIS, RHINOSINUSITIS)

Signal Symptoms: Nasal congestion, rhinorrhea, purulent nasal discharge, sneezing, sore throat, cough, headache, facial pain, myalgias, malaise, low-grade fever.

Description:

Rhinitis: Can be either allergic, non-allergic, mixed, atrophic, or acute and chronic rhinosinusitis in origin. Allergic rhinitis (AR) is intermittent or persistent with symptoms of sneezing, rhinorrhea, nasal congestion, postnasal drainage, and nasal/ocular pruritis with immunoglobulin E (IgE)-dependent events. It can be either seasonal or perennial with different allergen triggers. Non-allergic rhinitis (NAR) has symptoms of sneezing, rhinorrhea, and conjunctivitis (Bozek, 2017) along with postnasal drainage without specific IgE-dependent events (Baptist & Nyenhuis, 2016). NAR can be intermittent, persistent, seasonal, and/or completely caused by triggers (Baptist & Nyenhuis, 2016). Mixed rhinitis symptoms can be variable with a mixture of symptoms from AR and NAR. Presence of symptoms are not explained completely by the IgE specific reaction (Baptist & Nyenhuis, 2016) and therefore may show IgE elevated levels in the serum at times, whereas other times these levels will not be elevated in the same person (Bozek, 2017). Symptom triggers help to determine whether the person has mixed rhinitis or not. Atrophic rhinitis manifests with symptoms of congestion, nasal crusting, and strong foul odor but can have symptoms of both AR and NAR (Baptist & Nyenhuis, 2016).

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Rhinosinusitis: Chronic rhinosinusitis (CRS) is the chronic inflammation of the nose and paranasal sinuses along with having two of the following symptoms for more than 12 weeks: nasal discharge, nasal congestion or obstructions, facial pain or pressure, purulent rhinorrhea, and reduction or loss of smell. Acute rhinosinusitis (ARS) can be viral or bacterial in nature and lasts less than 4 weeks (London & Ramanathan, 2018).

Etiology: Viruses that cause upper respiratory tract infections (URIs) are adenovirus, coronavirus, rhinovirus, human metapneumovirus, enterovirus, influenza, parainfluenza, and respiratory syncytial virus (Pelzman & Tung, 2021). Certain bacteria and other pathogens are also causes. Bacterial infections may occur after viral infections because of the immune system being activated so much that normal tissue is left open with little to no defense.

Differential Diagnosis: In the older adult, other causes of the rhinitis should be considered, including granulomatous diseases such as Wegener's granulomatosis and sarcoidosis along with nasal polyposis, hypothyroidism, cerebrospinal fluid leak and malignancy (Baptist & Nyenhuis, 2016). Medications that can cause drug-induced rhinitis in the older adult are antihypertensives, psychotropics, alpha-adrenergic antagonists, and phosphodiesterase-5 inhibitors (Baptist & Nyenhuis, 2016). There can also be an overlap of AR and NAR in atrophic rhinitis, which means there can be different triggers for the symptoms of someone with all three conditions (Baptist & Neynhuis, 2016).

Prevalence: Upper respiratory tract symptoms are in the top 10 reasons year-round that adult patients seek medical help (Pelzman & Tung, 2021). Rhinitis occurs in about 32% of adults aged 54 to 89 years of age, with AR occurring in about one out of every six Americans. Rhinosinusitis occurs in as many as one in every eight adults (London & Ramanathan, 2018), with CR occurring in 10% of adults (Baptist & Neynhuis, 2016).

Age: AR has an increasing occurrence in those older than 60 years of age (Bozek, 2017).

Ethnicity: No Specific data found.

Contributing Factors: The older adults have changes that occur with aging that increase their risk or symptomatology to viral and bacterial infections. Exposure to allergens can activate worsen the symptoms (Baptist & Nyenhuis, 2016).

Signs and Symptoms: See signal symptoms.

Diagnostic Tests: Diagnosing URIs and differentiating between the different types of URIs is done from signs, symptoms, and physical examination (Baptist & Nyenhuis, 2016; Pelzman & Tung, 2021). There are some tests that can be performed to help with diagnosis, and those are serum IgE, skin prick test, streptococcus A test (rapid or culture), imaging, complete blood count (CBC), and procalcitonin (Baptist & Nyenhuis, 2016; Pelzman & Tung, 2021). The severity of the symptoms and signs can help determine which diagnosis is most likely. Some types of URIs have the same symptoms, but the severity of the symptoms will help to determine which type is the most likely diagnosis (Pelzman & Tung, 2021).

Treatment: Many URIs are viral. Symptom management is the best treatment (Pelzman & Tung, 2021). Viral URIs will generally resolve within 2 weeks even without treatment (London & Ramanathan, 2018; Pelzman & Tung, 2021). One mainstream treatment for rhinitis and any URI is avoidance of triggers or exposures that will cause worsening of symptoms (Baptist & Nyenhuis, 2016; Valdes & Tewfik, 2018). Second generation antihistamines and topical antihistamines are preferred over first generation antihistamines because of their central nervous system effects and increased interaction with other medications. These medications help with ocular and nasal pruritis, rhinorrhea, and sneezing (Baptist & Nyenhuis, 2016). Intranasal corticosteroids help reduce nasal congestion, rhinorrhea, and nasal pruritis, but they can cause epistaxis, nasal dryness, and mucosal crusting. Decongestants and nasal saline irrigation can help with congestion and other symptoms (Baptist & Nyenhuis, 2016). Analgesics and antipyretics are used for headaches, myalgias, and malaise that may arise with URIs (Pelzman & Tung, 2021). The combination of a topical antihistamine and a topical steroid has shown to help control symptoms of NAR better than taking either as monotherapy (Baptist & Nyenhuis, 2016).

Antibiotics, such as amoxicillin with or without clavulanate, should be prescribed for uncomplicated bacterial rhinosinusitis for 5 to 10 days (London & Ramanathan, 2018). ARS can become bacterial when it lasts more than 7 to 10 days or when symptoms improve followed by a period of worsening symptoms (Franck & Zehtabchi, 2019; London & Ramanathan, 2018). It is recommended not to use antibiotics in those with CRS (Franck & Zehtabchi, 2019). Bacterial otitis media and pharyngitis can also be treated with amoxicillin with or without clavulanate (Pelzman & Tung, 2021).

Follow-Up: No specific time frame for follow-up has been established, but generally patients can be advised to return if symptoms worsen or do not resolve in an allotted amount of time (such as 2 weeks for ARS).

Sequelae: Symptoms of URI may get better followed by a period of worsening symptoms. At that time, this may indicate the URI has become bacterial in nature and treatment with the appropriate antibiotic is recommended (Franck & Zehtabchi, 2019; London & Ramanathan, 2018).

Referral: Referral to an ear, nose, and throat specialist might be needed with recurrent epistaxis to help determine the cause and when someone with CRS has not responded to empiric treatment. Refer to an allergist for those who appear to have an allergic component that fails to respond to empiric treatment and in cases where the diagnosis is uncertain (London & Ramanathan, 2018).

Prevention/Prophylaxis: Advise patients to avoid exposure allergens and triggers, touching their face, and contact with other people who are sick/infected. Advise patients to use good hygiene by washing their hands regularly.

Education: Provider Education: Providers should remember that most URIs are generally viral in nature and therefore symptom management is recommended. Only after the course of sickness has improved then becomes worse or has lasted more than 7 to 10 days should antibiotic treatment be considered (Franck & Zehtabchi, 2019; London & Ramanathan, 2018). Purulent nasal discharge does not necessarily indicate a bacterial infection (Valdes & Tewfik, 2018).

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Patient Education: Explain the diagnosis and nature of the diagnosis to the patients. Explanation as to why antibiotics are not being prescribed may be necessary. Make sure that patients follow the plan of care and inform them of what to do if they do not respond to treatment or, if during treatment, they become worse. If antibiotics are indicated and prescribed, explain the importance of the patient completing this course of treatment and not to stop taking the medication because symptoms have improved or resolved.

Clinical Recommendation	Evidence Rating	References
Purulent nasal discharge is not indicative of a bacterial cause of upper respiratory tract infection (URI).	A	Valdes & Tewfik, 2018
Diagnosis is determined from clinical signs and symptoms. Acute infections are generally viral in nature.	A B A C B	Baptist & Nyenhuis, 2016 Bozek, 2017 Valdes & Tewfik, 2018 London & Ramanathan, 2018 Pelzman & Tung, 2021
Antibiotics are used for the bacterial state of acute rhinosinusitis. Use symptom management for viral URIs.	B B C C	Bozek, 2017 Pelzman & Tung, 2021 London & Ramanathan, 2018 Franck & Zehtabchi, 2019
Treat of viral and noninfections URIs with topical antihistamines, topical steroids, first and second generation antihistamines, oral decongestants, nasal saline irrigation, and immunotherapy.	A C A B	Baptist & Nyenhuis, 2016 London & Ramanathan, 2018 Valdes & Tewfik, 2018 Pelzman & Tung, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

A 70-year-old patient comes to the clinic for their annual Medicare Wellness visit. The patient reports that over the past year they have noticed increased dyspnea with exertion and a cough productive of sputum that varies in color from thick white to thicker and more yellow. They have no history of an acute illness and no fever, chills, or GI symptoms. The patient does have a history of seasonal allergies with occasional wheezing and bronchitis. The patient uses an inhaler during those periods of exacerbation. The patient states that the albuterol inhaler has not helped the current symptoms. They continue to work on cutting back on smoking but currently smoke about a pack in 3 days. Medications include lisinopril for hypertension, metformin for diabetes, famotidine at bedtime for GERD, fluticasone 1 spray in each nostril twice a day, and cetirizine at bedtime as needed for seasonal allergies. Other findings include:

- Vitals: BP 140/70, P 80, R 18, T 37°C, pulse ox 95% on room air.
- PE: HEENT moist mucous membranes, TMs intact
- Chest AP:LAT diameter 1:1, lungs resonant to percussion, tactile fremitus symmetrical, breath sounds distant, but no crackles, rhonchi, or wheezes heard.
- Heart: RRR no murmurs or gallops
- Extremities: Nonpitting edema bilaterally
- Dermatological: Skin warm, intact, no lesions.

1. From the patient's chief concern, how would you classify the cough—acute, subacute, or chronic?
2. What differentials would you include based on that classification?
3. What can you rule out based on the history and physical examination?
4. What follow-up investigation, laboratory studies, or other tests would be helpful in confirming your presumptive diagnosis?
5. What is the #1 recommendation you can provide the patient today regardless of their final diagnosis?
6. Will you prescribe any additional medication or treatment? If so, what will you prescribe?
7. When would you have the patient return in follow-up?

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CHAPTER 12

Peripheral Vascular Disorders

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ASSESSMENT

A comprehensive vascular assessment may be integrated into the general history and physical examination for the patient with vascular disease. A systematic head-to-toe examination, done consistently for each patient, will minimize the chance of missing subtle signs related to vascular deficits.

The clinician should begin with auscultation of the carotid arteries bilaterally. Cardiac murmurs will usually radiate into the carotid arteries, and an underlying bruit may not be discerned. The subclavian arteries should then be auscultated over the upper anteromedial chest area. During this phase of the examination, the jugular veins should be inspected for jugular vein distention. This can best be assessed when the patient is lying down with the head of the bed elevated 15 degrees.

The clinician should proceed to the palpation of the brachial, radial, and ulnar arteries. Such palpation should be scored on a scale of 0 to 4 (4 = pulsatile, bounding; 3 = easily palpable with full triphasic pulse; 2 = biphasic pulse that may be a bit harder to locate initially; 1 = monophasic pulse that may come and go depending on position of fingertips; and 0 = absent pulse by palpation, which may be detected by Doppler ultrasound). All palpable pulses should be graded in the assessment and documented.

The clinician should evaluate any pain, coolness, paresthesia, motor weakness, discoloration, or tissue loss in the hands. Careful inspection of the distal fingers and the nailbeds may reveal signs of tissue malperfusion. The finger joints should be inspected for cyanosis and/or petechiae. The fingernails should be checked for clubbing, which suggests chronic hypoxemia. For any patient confirmed or suspected to have vascular disease, blood pressure should be checked in both arms.

The heart should then be auscultated to detect rhythm regularity, S_1, S_2, and any extrasystolic sounds such as S_3, S_4, or pericardial rub. Murmurs should be noted and classified as per the cardiac assessment guidelines. The abdomen should be auscultated for celiac artery, superior mesenteric artery, and renal artery bruits, which are best heard 4 to 8 cm above the umbilicus and 1 to 2 cm to the right and left of midline abdomen. The clinician should listen to the femoral artery in each groin for the presence of bruits. Following this, the abdomen should be lightly palpated just to the left of midline, approximately 4 cm above the umbilicus, to evaluate for a pulsatile abdominal aorta. In slender individuals, the abdominal aorta is often fairly easy to palpate. A bounding, pulsatile abdominal aorta in an individual may suggest aneurysmal formation. The clinician should note and document any tenderness or guarding associated with the abdominal palpation. There are many other causes for abdominal tenderness that the clinician should be aware of, in addition to arterial and venous disease, including pancreatitis, liver contusions, cholecystitis, appendicitis, splenic infarction, pyelonephritis, cystitis, gastroenteritis, peptic ulcer, and small bowel obstruction.

Once the abdominal examination is complete, the clinician should progress to the vascular assessment of the lower extremities. The femoral arteries should be palpated over the groin area and documented on the scale of 0 to 4. Any pulse deficits should be followed up with a Doppler examination. The popliteal fossa should be inspected and palpated bilaterally in order to locate the popliteal artery and assess for the possibility of popliteal artery aneurysms. The clinician should inspect the calves and feet for edema, skin turgor, and skin pigmentation. Thick, hyperpigmented skin in the lower calves and feet may be an indication of chronic venous insufficiency, whereas thin, shiny, pale skin is more consistent with peripheral arterial insufficiency. The dorsalis pedis and posterior tibial pulses should be palpated. If those pulses are not palpable, Doppler ultrasound should be used. Any Doppler signals should be located and identified with an indelible marker pen. At this time, the heel, the medial and lateral malleoli, and the toes of each foot should be inspected for breakdown. As in the hands, any pedal pain, coolness, paresthesia, motor weakness, discoloration, or tissue loss should be documented. Dorsal and plantar flexion of the feet should be assessed and recorded with muscular strength graded on a scale of 1 to 5.

The vascular examination then turns to a careful evaluation of the cranial nerves (CNs), usually focusing on CN II to CN XII. Evaluation of pupillary light and accommodation

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response (CNs II and III); following the eyes in a lateral, medial, superior, and inferior gaze (CNs III, IV, and VI); and evaluation of facial smile, scowl, and opening eyes against pressure (CNs V and VII) should be completed. Gross hearing assessment, with follow-up by Weber and Rinne testing, may ascertain any CN VIII deficits. Evaluating the tongue protrusion, uvula rise, cough reflex, gag reflex, and shoulder shrug will provide information on the integrity of CNs IX, X, XI, and XII. Document the conformation of the uvula, which may be bifid or singular (some connective tissue disorders have associated bifid uvula).

Completion of the CN examination provides the healthcare team with an excellent neurological baseline before interventions for carotid artery disease. Assessment findings related to vertebrobasilar insufficiency may include balance problems, dizziness, and coordination deficits. Focal neurological deficits such as arm, leg, and/or facial weakness on one side of the body; loss of speech; difficulty speaking or swallowing; and unilateral or partial vision loss signify transient cerebral ischemia that may be related to severe carotid artery stenosis (Rasmussen et al., 2019).

Following the neurological examination, the clinician should ascertain any specific end organ perfusion deficits, as shown by the following signs and symptoms:

- Pain in the feet, calves, thighs, and or buttocks, either at rest or with ambulation (peripheral arterial disease [PAD])
- Any open wounds or blisters on the distal aspects of feet and/or hands (PAD)
- Abdominal pain, nausea, vomiting, and/or diarrhea after a meal (mesenteric ischemia)
- Persistent abdominal/back pain (abdominal aortic aneurysm or dissection)
- Unilateral CN deficits (carotid artery disease)
- Balance/coordination deficits (possible vertebrobasilar malperfusion)
- Chest and/or back pain (ruling out myocardial ischemia, pneumothorax, and pulmonary embolus)

Once the focused vascular assessment and history are completed, the clinician will have achieved a baseline to guide future interventions to delineate and treat vascular lesions.

ABDOMINAL AORTIC ANEURYSM

Symptoms: Persistent or intermittent pain in the middle or lower abdomen, often radiating to the lower back, which is characteristic of a rapidly expanding, leaking, or ruptured abdominal aortic aneurysm (AAA). Most AAAs are asymptomatic.

Description: The abdominal aorta is the large artery that provides blood to the digestive organs, liver, kidneys, spleen, spinal cord, and lower extremities. It extends inferiorly from the descending aorta to the iliac arteries. An AAA is a dilation of the abdominal aorta that is one and one-half to two times greater than the size of the nondilated proximal or distal aorta. The AAA involves all three layers of the arterial wall.

Etiology: Most AAAs are atherosclerotic in nature; other causes include trauma, infection, and inflammation. Connective tissue disorders, such as Ehlers-Danlos' syndrome and Marfan's syndrome, predispose the patient to AAA formation (DelloStritto et al., 2017) Most AAAs are infrarenal (65%), occurring below the renal arteries. Patients with AAAs are more likely to have arterial aneurysms in other locations such as the thoracic aorta, the common iliac arteries, the common femoral arteries, and the popliteal arteries.

Occurrence: Ruptured AAA is ranked as the 13th leading cause of mortality in the United States, which is approximately 15,000 deaths per year (Kohlman-Trigoboff et al., 2020) Mortality rates for ruptured aneurysms are 70% to 90%, compared with 5% operative mortality for elective open surgical repair and 2% to 3% for endovascular stent AAA exclusion.

Age: More frequent in adults older than 50 years old; prevalence rate is 2% to 4%.

Ethnicity: Occur more frequently among Whites than any other race, and there is a familial history associated with AAA development particularly among first-degree relatives.

Contributing Factors: Risk factors for developing AAA include arteriosclerotic heart disease and arteriosclerotic changes of other vessels, smoking history, hypertension, hyperlipidemia, chronic obstructive pulmonary disease, obesity, family history of AAA, diabetes mellitus, cystic medial necrosis, Marfan's syndrome, and previous spinal cord injury. Individuals with an aneurysm of other large blood vessels in the extremities and carotid arteries also have an increased risk for AAA (Ullery et al., 2018). Onset occurs around age 50 years for men and 60 years for women. Incidence steadily increases with age and peaks at age 80 years. AAA is five times more likely in men than in women. Aortic dissection involves a splitting apart of the aortic wall layers, such that two or more blood flow channels are created within the aorta. Acute aortic dissection may produce intimal flaps that occlude major take-off vessels, leading to end organ ischemia. Progressive dissection may lead to weakening of the entire aortic wall, resulting in aneurysm formation and possible rupture. Isolated celiac and/or superior mesenteric artery dissection may occur, although this is much less likely than the initial aortic dissection (Duraikannu et al., 2020).

Signs and Symptoms: Most patients with AAAs are asymptomatic (66% to 75%), except in the presence of dissection, rupture, or impending rupture. A pulsatile abdominal mass at or slightly above the umbilicus in the epigastrium palpated, on the abdomen, is consistent with but not conclusive for an AAA. Palpation is easier in thin individuals. If noted in an obese individual, they are usually quite large. AAA should be

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suspected in individuals with a femoral or popliteal aneurysm because 30% of individuals with a peripheral aneurysm also have an AAA. In patients with symptomatic AAAs, the complaints include mild-to-severe abdominal, flank, or lower back pain. Other symptoms may include nausea and vomiting, gastrointestinal bleeding, and lower extremity ischemia. Rupture is the most lethal clinical presentation, with symptoms including sudden onset of severe abdominal and back pain, hypotension, and the presence of a pulsatile, expanding mass. There is a high mortality rate associated with ruptured AAAs. The possibility of ruptured AAA should be considered in any adult with acute abdominal or flank pain (Ullery et al., 2018).

Diagnostic Tests: The best initial screening test is an ultrasound of the abdominal aorta. In cases where surgery is planned, angiography and computed tomography (CT) scan with IV contrast are indicated to size the aneurysm and diagnose any tears or perforations.

Differential Diagnosis: It is important to evaluate for and treat hypertension and heart disease, because early steps in AAA management include blood pressure control and recognition or enhancement of cardiac function. An ectatic abdominal aorta (aortic diameter of 2.5 to 2.9 cm) without aneurysm may be palpated and confused with AAA. Other acute causes of abdominal and back pain may mimic a ruptured AAA and must be ruled out. Major imaging modalities for a patient with suspected or known AAA include abdominal ultrasound, CT scan, magnetic resonance angiogram (MRA), and angiogram.

Treatment: The rate of AAA growth for an individual is unpredictable. Some aneurysms may remain stable for long periods, whereas others may enlarge quickly. Medical management of an asymptomatic, small AAA should include blood pressure control, regulation of heart rate, and smoking cessation. Beta blockers have been shown to slow the long-term growth of aortic aneurysms. Angiotensin receptor blockers (ARBs), such as losartan, may also have a major role in critical blood pressure and heart rate control for patients with aortic aneurysms or dissections.

Initial treatment for symptomatic AAA, whether ruptured or not, involves aggressive blood pressure control. Mean arterial pressure should be maintained between 60 and 70 mm Hg, and systolic blood pressure should be kept between 100 and 120 mm Hg. Arterial pressure monitoring is recommended, and parenteral antihypertensive agents, such as esmolol, nicardipine, nitroprusside, labetalol, or nitroglycerin, should be used to quickly and consistently maintain blood pressure in these ranges. Cardiology should be consulted, and a transthoracic echocardiogram should be done to assess heart function. If the patient is to be medically managed, transition to oral antihypertensive agents should begin, using beta blockers, calcium channel blockers, clonidine, ARBs, and labetalol to maintain blood pressure control.

The two invasive options for excluding an AAA when it becomes symptomatic or becomes greater than 5 cm in diameter in women or greater than 5.5 cm diameter in men include open surgical repair and endovascular repair (EVAR) (Krishna et al., 2020). Elective EVAR is associated with lower rates of perioperative (30-day) morbidity and mortality compared with elective open repair (<2% versus 5%); long-term outcomes are similar to open AAA repair (Chaikof et al., 2018).

Thirty to fifty percent of individuals with ruptured AAA die before reaching a hospital and 30% to 40% of those with ruptured AAA die after reaching the hospital (Kohlman-Trigoboff et al., 2020). Average postoperative length of stay for an elective AAA surgical repair is 5 days. The major cause of death after AAA repair is myocardial infarction. Other complications include renal failure, limb ischemia, ischemic colitis, hemorrhage, and pneumonia with prolonged ventilator dependence, and paraplegia (Chaikof et al., 2018).

EVARs are less invasive procedures used for AAA repair. Stent-graft selection is dependent upon physician preference and patient anatomic characteristics as determined by preprocedure imaging results. The graft is deployed through the femoral or the iliac artery. Not all AAAs are anatomically appropriate for stenting. Current success rates are higher than 90%, with a mortality rate of less than 2%. Most patients are discharged from the hospital in 1 to 2 days (Kohlman-Trigoboff et al., 2020). Complications after endovascular treatment may include arterial injury at access site, arterial embolization, endoleak (blood flow outside the lumen of the graft but within the original aneurysmal sac), postimplant syndrome (back pain and fever without elevated white blood cell count or other signs of infection), and graft limb distal thrombosis (Kohlman-Trigoboff et al., 2020).

Follow-Up: Surveillance of patients with an AAA, including imaging at 12-month intervals for patients with an AAA of 4.0 to 4.9 cm in diameter. Rescreening intervals to check for AAA expansion shorten as the AAA enlarges (Chaikof et al., 2018). When anatomically feasible, EVAR is recommended over open repair for ruptured AAA (Chaikof et al., 2018).

Sequelae: The most common complication of AAA is rupture. Infrequent complications are thrombi to the lower extremities and preexisting infection of the aneurysm (mycotic aneurysm), with *Salmonella* and *Staphylococcus aureus* being the most commonly identified organisms. Fungal infections of the aorta pose significant challenges and require long-term IV antimycotics, such as fluconazole after 6 weeks of an IV course of antifungal agents, until surgical repair is done.

Prevention/Prophylaxis: Because most AAAs are atherosclerotic in nature, the same long-term preventive measures for reducing coronary artery disease, cerebrovascular disease, hypertension, and hypercholesterolemia should be applied. Diabetes mellitus has been shown to be protective against AAA. These include lifestyle modifications with control of hypertension, prescribing statin therapy, and daily aspirin (Ullery et al., 2018). The Society for Vascular Surgery (SVS) recommends AAA screening in men and women aged 55 years with a family history of AAA. Patients with diabetes have a lower incidence of AAA, a lower growth rate, and a reduced risk of rupture, which could be from the excess of vascular matrix deposition and increased collagen synthesis (aortic wall stiffness) characteristically seen in diabetic arteriopathy (Sprynger et al., 2019). The prevalence of AAA in the first-degree relatives of affected families is reported to be associated with a two- to fivefold increase in the risk of AAA. Several inheritance patterns for AAA development have been proposed. Although genetic disorders associated with aneurysm formation, such as Marfan's syndrome, Ehlers-Danlos'

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syndrome, and Loeys-Dietz's syndrome, are more commonly associated with aneurysms of the ascending and thoracoabdominal aorta (Ullery et al., 2018).

Referral: Referral to a vascular surgeon is essential for all patients with symptomatic AAAs. Furthermore, any patient with a known AAA, even if not symptomatic, should be screened with serial ultrasound imaging at least once a year.

Education: Patients and their families should be taught the importance of follow-up; ways to manage hypertension, hypercholesterolemia, smoking, and other risk factors; and the signs and symptoms of rupture that should be reported to the physician immediately (sudden onset of abdominal or back pain, dizziness). The risks of operative versus nonoperative treatment should be explained thoroughly to the patient and family.

CHRONIC LYMPHEDEMA

Signal Symptoms: Swelling of the affected body part, usually the limb, because of impaired flow of lymph fluid.

Description: Lymphedema is a progressive condition of abnormal lymph accumulation in the interstitial tissues due to a disruption of lymph flow. The lymph system is a low-pressure system that includes capillaries and depends on muscle movement to advance the fluid to the vascular system. Most of the lymph drains into the thoracic duct on the left side of the body and into the brachiocephalic vein.

Etiology: Lymphedema is swelling caused by impaired lymph transport, which results in an accumulation or pooling of protein-rich fluid in the interstitial space. Lymphedema is most commonly caused by surgery, radiation, or infection that damages the lymphatic system.

Occurrence: Lymphedema affects about 250 million patients worldwide. Secondary causes of lymphedema vary according to geographic distribution. In developing countries, it is often a part of parasitic infections, with filariasis being the most common cause in the world. In developed countries, secondary lymphedema mainly occurs after cancer therapy (Schulze et al., 2018). Primary (vascular anomalies) lymphedema is rare, with an estimated prevalence of 1 in 100,000 individuals, and it usually occurs during childhood, but may present at any age. Approximately 99% of individuals with lymphedema have a secondary disease (such as systemic disease, trauma, or surgery) (Grada & Phillips, 2017).

Age: Not confirmed as a risk factor for lymphedema.

Ethnicity: Not significant.

Contributing Factors: The types of cancer associated with secondary lymphedema include breast cancer, gynecological cancer, lymphoma, melanoma, and urological cancers. Surgery, radiation, trauma, infection, malignancy, or scar tissue can cause secondary lymphedema by obstructing the lymphatic system. For example, patients with a history of breast cancer with axillary node dissection or radiation, groin node dissection or radiation, and a postoperative infection have an increased risk for developing lymphedema. With primary or congenital lymphedema, females are affected twice as often as males. With secondary lymphedema in the United States, females may be affected more often, but that is because a common cause of secondary lymphedema is breast cancer, which is primarily a woman's disease. Morbid obesity (body mass index >25) can also increase the rate of secondary lymphedema (Torgbenu et al., 2020).

Signs and Symptoms: Swelling or edema is the characteristic symptom of lymphedema. Additional symptoms may include heaviness or tightness, aching and fatigue in the affected limb, restricted range of motion, recurring cellulitis in the affected extremity, and hardening and thickening of the skin. The Stemmer sign (or Kaposi-Stemmer sign) is another clinical indication of lymphedema in which one is unable to pinch a fold of skin at the base of the second toe on the dorsal aspect of the foot or between the second and third finger. Skin that does not fold up into a pinch is considered a positive sign of lymphedema. False-positive Stemmer signs may be seen in individuals with obesity or spinal muscle atrophy. Because the test exhibits moderate specificity, lymphoscintigraphy may be considered for patients with a high suspicion of lymphedema that have a negative Stemmer sign (Goss & Greene, 2019).

Diagnostic Tests: Diagnosis of lymphedema is typically made through clinical presentation and medical history, such as a cancer diagnosis. Lymphoscintigraphy is a well-established radiological examination to evaluate and confirm the diagnosis, as well as to measure lymphatic function and effect of complex decongestive therapy (CDT) (Forte et al., 2019). Bioimpedance spectroscopy (BIS) measures the composition of tissues (e.g., fluid such as lymph) and may be used for early diagnosis as well as determining the effectiveness of therapy (Forte et al., 2019).

Differential Diagnosis: Knowing if the patient had a prior history of comorbid conditions that can cause swelling of the extremities, such as cardiac disease, venous ulcer disease, renal disease, hepatic disease, trauma, and infection, is also important. Patients with rheumatoid arthritis, obesity, lipedema (painful fat syndrome), and venous ulcer disease are at greater risk for lymphedema because these conditions add additional stress to the impaired lymphatics. Lymph nodes are located around most joints, so patients undergoing such surgical procedures as total knee replacements may be at greater risk for developing lymphedema because lymph nodes can become injured during the surgery. Procedures such as vein-stripping can exacerbate mild lymphedema (Grada & Phillips, 2017).

Treatment: Complete decongestive physiotherapy (CDP) is the gold standard for lymphedema management. CDP is a specialized massage technique designed to stimulate the lymph vessels, break up subcutaneous fibrous tissue, and redirect the lymph fluid to areas where lymph flow is normal.

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It involves four steps: manual lymph drainage (MLD), compression bandaging, exercises, and skin care.

Conservative Treatment: The use of multilayer compression bandages and/or compression stockings is an important component for all patients with lymphedema to prevent the reaccumulation of lymph fluid in the limb.

Pharmacological Treatment: Diuretics are not beneficial with lymphedema because they draw off excess water in the interstitial spaces but not the protein. Lymphedema is a high-protein edema, and the high osmotic pressure from the increased protein in the interstitial space causes rapid reaccumulation of edema. In addition, the higher concentration of protein in the edema fluid causes increased fibrosis and induration of the skin. Diuretics are not contraindicated for the treatment of other conditions in lymphedema patients, but they should not be used as primary treatment for lymphedema.

Surgical Treatment: Surgical intervention is indicated for those with persistent lymphedema with a positive lymphoscintigram who do not respond to more conservative methods such as CDP. These procedures can be broadly categorized as physiological, including lymphovenous bypass and using a vascularized lymph node transplant; or de bulking, by suction-assisted lipectomy or direct excisional procedures (Schaverien & Coroneos, 2019).

Follow-Up: Patients with lymphedema need regular follow-up by health-care providers to make sure that the CDP is effective and adequate and, if not, appropriate modifications can then be made to the care plan.

Sequelae: Lymphangitis and cellulitis are complications seen with lymphedema. Once patients develop these infections, they are at greater risk for developing them again.

Prevention/Prophylaxis: Lifelong CDP is essential to prevent worsening of the lymphedema and to avoid complications.

Referral: Patients with lymphedema should be referred to a lymphedema specialist or clinic.

Education: It is important to teach patients with lymphedema about the disease process, its lifelong treatment with compression bandaging, the importance of avoiding complications such as lymphangitis, and resources, such as the National Lymphedema Network, that are available to them.

PERIPHERAL VASCULAR DISEASE

Signal Symptoms: Pain, intermittent claudication of the feet, tissue loss in affected leg/arm.

Description: Peripheral vascular disease (PVD) refers to a disease or process that alters blood flow to or from the extremities and vital organs other than the heart. These processes may involve the arterial, venous, or lymphatic systems, but most often are due to enlarging atherosclerotic plaques in the distal aorta or in major bifurcations or areas of angulation in the iliac, femoral, and popliteal arteries. Peripheral arterial disease (PAD) is characterized by impaired circulation to the lower extremities. In its most severe stage, known as critical limb ischemia (CLI), patients are at an increased risk of cardiovascular events, amputation, and death.

Etiology: Atherosclerotic plaques may be fatty streaks, fibrous plaques, or complicated calcified lesions. Fatty streaks are early lesions that occur in the intima of arteries. Fibrous plaques and areas of intimal thickening are the most frequently occurring type of lesion. Complicated (heterogeneous) plaques, as well as calcified fibrous plaques with potential for necrosis and thrombosis, are associated most often with symptoms in PAD patients (Duff et al., 2019).

Occurrence: CLI prevalence in the United States is estimated to be approximately 2 million and is likely to increase with age, in individuals with diabetes, and in those who smoke. Prevalence estimates in studies of the U.S. Medicare population range from 0.3% to 2.0% (Duff et al., 2019). Symptomatic PAD is two to five times more prevalent in men than in women; particularly for more severe or symptomatic disease.

Age: The prevalence of PAD increases with age, affecting over 10% of individuals in their seventh and eighth decades of life and over 20% of those older than age 80 years (Krawisz et al., 2021).

Ethnicity: Black individuals have the highest rates of PAD (Krawisz et al., 2021).

Contributing Factors: Risk factors for PAD include type 2 diabetes mellitus, smoking, obesity, hypertension, dyslipidemia, family history of PAD, cerebrovascular disease, and stroke. The presence of three or more of these risk factors increases the risk of PAD ten times. The most significant risk factor for the development of PAD is smoking (Krawisz et al., 2021).

Signs and Symptoms: Intermittent claudication is the early symptom of PAD. It is described as a painful cramping of the muscles of the leg during walking. It goes away when the patient stops walking and resumes after the patient starts walking again. It also may be described as a sensation of tiredness or fatigue. Intermittent claudication is present in only 10% to 20% of PAD patients. Walking limitations in PAD patients are multifactorial (reduced limb perfusion, systemic inflammation, vascular dysfunction, impaired angiogenesis, reduced microcirculatory flow, and skeletal muscle dysfunction) reflected in the self-restriction of activity to reduce leg pain (Hamburg & Creager, 2017). Ischemic rest pain is described as a burning sensation and localizes to the metatarsal heads or to an ischemic ulcer. Pain is often worse at night when the leg is elevated. Relief may occur with dependency of the foot. Ischemic rest pain requires immediate attention. Ulceration or gangrene develops at an area of external pressure or at the site of a minor injury, with gangrene representing CLI. Acute arterial ischemia results from arterial thrombosis, embolism, or trauma, with symptoms that are sudden in onset. It often causes the five Ps: pain, pallor, pulselessness, paresthesia, and paralysis. Other symptoms may include decreased sensation and mottling of the extremity. Acute arterial ischemia may be due to thrombus from the left atrium, sudden onset of atrial fibrillation, dislodging of

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calcium plaque in the aorta, and/or intrinsic hypercoagulopathy. A thorough patient history and physical examination are essential to determine the stage and type of vascular disease. (Hamburg & Creager, 2017).

Diagnostic Tests: Ankle-brachial index and systolic arterial pressure measurement with continuous-wave Doppler are first-line tests. In cases where surgical intervention is being considered, angiography is indicated. Assessment of distal arterial system patency can be done by Doppler ultrasound, which can also detect and pinpoint occluded areas (Kieback et al., 2019).

Differential Diagnosis: Buerger's disease and Raynaud's phenomenon also should be considered when diagnosing PAD. Buerger's disease may occur in individuals less than 35 years old who are smokers, and it may affect the upper as well as the lower extremities. This rare disease causes inflammation of the blood vessels, which can result in clot formation. Raynaud's phenomenon affects the fingertips, the tips of the ears and nose, and the feet. Patients with Raynaud's phenomenon have symptom exacerbation with any cold temperatures. Other diagnoses that mimic the symptoms of PAD include gout, arthritis, diabetic neuropathy, sciatica, and severe venous insufficiency (Dua & Lee, 2016).

The hallmark signs and symptoms of venous ulcers include distal lower extremity edema; warmth of the foot; large, irregular, copiously draining ulcers in the distal calf or foot dorsum; and hyperpigmentation of the surrounding skin. Arterial insufficiency ulcers usually are found over the medial or lateral malleolus, heel, or distal aspect of the toes. Wounds associated with arterial ischemia are small and drain minimally but are extremely painful.

Treatment: The main goal of PAD treatment is to slow the progression of the disease. Treatment may be conservative, pharmacological, operative, or endovascular. Risk factor recognition and lifestyle modification are the central tenets for managing patients with long-term PAD.

Conservative Treatment: Conservative treatment involves modification of risk factors, including smoking, blood pressure control, and diet. Smoking is the number one modifiable risk factor, and there are numerous methods available to help individuals stop smoking (Ding et al., 2019). In addition, managing diabetes and hyperlipidemia are key measures. Exercise is an essential element of PAD management because collateral vessels are strengthened and stimulated to grow with the onset of an exercise program such as walking. Formalized vascular rehabilitation programs are becoming more common with better reimbursement by insurers. Home exercise programs should focus on exercising three or more times per week for at least 30 minutes per day. Patients should be instructed to walk until pain develops, walk a few steps more through the pain, rest until pain goes away, then resume walking. Over time, the patient should be able to walk farther with fewer rest breaks. Meticulous foot care is important to prevent complications of ulceration and gangrene. Patients should be instructed about wearing properly fitted footwear, daily inspection of feet and legs, avoidance of walking barefoot, application of lotion on feet and legs, and meticulous toenail trimming. Podiatrist consultation is recommended for patients with fungal overgrowth and/or ingrown toenails.

Pharmacological Treatment: Pharmacological treatment is provided with conservative treatment. Currently, aspirin (81to 325 mg daily) is one of the mainstays for such treatment. Aspirin has been shown to prevent progression of disease in patients with claudication. Cilostazol (Pletal) may be effective in relieving symptoms of claudication by improving walking distance through the promotion of vasodilation and antiplatelet activity. Vasodilators and anticoagulants have not proved effective in relieving pain symptoms. Clopidogrel (Plavix) 75 mg daily is an antiplatelet medication that helps reduce the risk of stroke, heart attack, and other atherosclerotic problems. Clopidogrel is frequently used for at least 3 months after peripheral arterial stents have been placed. Medications for the management of hypertension, diabetes, and hyperlipidemia should be used with the goals of euglycemia, normotension, and attainment of a healthy lipid profile (Rasmussen et al., 2019).

Surgical Treatment: Surgical treatment of PAD involves revascularization of the affected extremity. Surgical options should be considered when pain limits the patient's lifestyle or when ulceration or gangrene is present. Surgical options involve using vein graft or synthetic graft material. Long-term patency rate is dependent on smoking cessation, exercise, antiplatelet therapy, and diabetic control, as well as the location, length, and diameter of the graft (Rasmussen et al., 2019).

Endovascular Treatment: Endovascular options for the treatment of PAD include balloon angioplasty and endoluminal stents, which are minimally invasive for the patient. Angioplasty involves inflating a balloon across a stenotic lesion. Stents are devices that are deployed in a stenotic lesion to keep the vessel open. Other interventions include thrombolysis with fibrin-degrading infusions, mechanical thrombectomy, atherectomy, and subintimal recanalization (Rasmussen et al., 2019).

Follow-Up: Follow-up should include evaluating the patient's response to pharmacological intervention and the progression of risk factor modification. Ankle Brachial Indexes (ABIs) with pulse volume recordings (PVRs) should be done at least yearly to assess lower extremity perfusion (Rasmussen et al., 2019).

Sequelae: Patients with PAD have a 30% to 50% incidence of coronary artery disease and a 15% to 25% rate of carotid artery stenosis. The yearly cardiovascular rate including myocardial infarction, stroke, or death is approximately 5% to 7% in patients with PAD. Only 20% to 30% of patients with PAD die of noncardiovascular-related issues (Dua & Lee, 2016).

Prevention/Prophylaxis: Prevention of PAD focuses on slowing the progression of disease in patients with symptoms. This can be accomplished through risk factor modification, as discussed earlier. Good foot care, in conjunction with exercise, smoking cessation, glucose management if diabetic, and lipid management can prevent the development of tissue loss or gangrene.

Referral: Referral for surgical or endovascular treatment should occur when claudication becomes disabling to the patient, when ischemic rest pain or gangrene is present, or when nonhealing ulceration is present.

Education: Education needs to focus on proper follow-up and the modification of risk factors as discussed earlier; patients also need to be taught to report any new onset of symptoms, including nonhealing ulcers. There is a need for more research on the differences between the treatment for PAD in men and in women (Dua & Lee, 2016).

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VENOUS DISEASE (CHRONIC VENOUS INSUFFICIENCY)

Signal Symptoms: May be asymptomatic but could also present with swelling that subsides with elevation of lower extremities, eczematous skin changes, dull ache in lower extremities, and presence of varicosities.

Description: Venous leg ulcers (also known as chronic venous insufficiency ulcers, venous stasis ulcers, lower extremity venous ulcers, or varicose ulcers) are the most common leg ulceration. They typically occur over the medial malleolus, but they can also occur over the lateral malleolus. The ulcers are irregular and shallow with granulation tissue and fibrin present in the wound bed. Exudate is moderate to heavy, but if there is an arterial component, the amount of exudate may be decreased. These wounds often have a foul odor as well. The area around the wound often presents with dermatitis from the increased permeability of the venous capillaries causing protein to leak into the interstitial space, becoming irritating to the epidermis and dermis. The loss of protein and red blood cells into the subcutaneous tissue results in a brownish discoloration of the skin referred to as hemosiderin staining. Over time, the induration and hyperpigmentation is associated with fibrosis of the adipose tissue of the leg, which is called lipodermatosclerosis.

Etiology: Venous hypertension as a result of venous reflux (incompetence) or obstruction is thought to be the primary underlying mechanism for venous ulcer formation. Normally, blood flows from the superficial veins to the deep veins. Unidirectional valves and contraction of the calf muscles assist in blood flowing from the superficial to the deep veins. If there are any abnormalities (i.e., valvular incompetence, deep vein thrombosis, and/or failure of calf muscle pump), the deep and superficial veins become distended, increasing venous pressures.

Occurrence: Approximately 7 million individuals worldwide have venous disease, 2 million of which have venous leg ulcer. Venous leg ulcers account for 80% to 90% of all leg ulcers (Kelechi et al., 2020).

Age: As one ages (>50 years of age), the incidence of venous ulcers increases (Kelechi et al., 2020).

Ethnicity: There are no data to support an ethnic predisposition to venous disease.

Contributing Factors: Risk factors for venous leg ulcers include advanced age, obesity, pregnancy, thrombophilia, systemic inflammation, anticardiolipin antibody, venous thromboembolism (VTE)/phlebitis, varicose veins, pulmonary embolus, sedentary lifestyle or occupation, reduced mobility, simultaneous insufficiency of two out of three venous systems, trauma/surgeries/leg fractures, impaired calf muscle pump, restricted range of motion of the ankle, family history of venous disease, injection drug user, and previous leg wound (Kelechi et al., 2020). The presence of comorbid conditions such as cardiovascular disease, hypertension, lymphedema, and orthopedic procedures can also increase the risk of venous leg ulcers (Kelechi et al., 2020). Women are affected more than men, with multiple pregnancies or pregnancies close together increasing the risk.

Signs and Symptoms: Edema that worsens with standing and decreases with leg elevation is the classic sign of venous leg ulcers. The edema may be pitting or nonpitting. Other signs include hemosiderosis (hemosiderin staining), venous dermatitis (manifested as erythematous, scaly, pruritic skin), ankle flaring (cluster of spider veins), varicose veins, scarring from previous ulcers, and lipodermatosclerosis.

Diagnostic Tests: In many cases of venous ulcers, diagnosis may be made by clinical assessment alone, which includes skin changes in the leg, extent and location of edema, capillary refill less than 2 seconds, and palpation of pedal pulses. Duplex ultrasonography imaging with or without color has become the standard diagnostic tool for assessing venous disease. Duplex imaging produces images of blood flow and its direction through vessels, pinpointing the anatomical site of reflux or obstruction; thickened, abnormal vein walls; and the presence and age of a thrombus. Duplex scanning can be used to calculate the superficial venous pressures and allows for quantification of venous reflux and valve closure times. An ankle-brachial pressure index is also recommended to rule out significant arterial disease, especially before application of compression therapy.

Differential Diagnosis: Lower leg edema, which is one of the classic signs of venous disease, is also seen with other diseases as well. Deep vein thrombosis usually presents with pain and the presence of a thrombus on ultrasound. Patients with heart failure usually present with dyspnea, orthopnea, and a decreased ejection fraction. Patients with cirrhosis will have abnormal liver function studies, and those in renal failure will have proteinuria. The diagnosis of venous disease can be narrowed by categorizing the edema according to its duration (acute or chronic), distribution (unilateral or bilateral), and accompanying symptoms (e.g., pain, itching, skin changes).

Treatment: Treatment for venous ulcers includes management with compression therapy, leg elevation, medications, and surgery.

Conservative Treatment: Compression therapy is the gold standard for venous ulcers and is used by those with chronic venous disease to manage the edema and increase venous return. Compression has been shown to improve healing of venous ulcers when compared to no compression (Wound, Ostomy, and Continence Nurses Society, 2019) and reduce venous ulcer recurrence (Wound, Ostomy, and Continence Nurses Society, 2019). Compression is also effective in the improvement of symptoms of chronic venous disease, reduction of edema and pain, and improvement of quality of life (Kelechi et al., 2020).

Compression can be achieved with the use of a single layer wrap (bandage) or the use of multiple layer wraps (bandages) (Wound, Ostomy, and Continence Nurses Society, 2019). There are also compression garments, such as reusable Velcro wraps (e.g., CircAid®), sleeves (for example, the tube-shaped Tubigrip™), compression stockings, and intermittent pneumatic compression pumps (Wound, Ostomy, and Continence Nurses Society, 2019).

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Another feature of compression products is based on the type of material in the wrap (bandage). Elastic (which adapts to changes in limb size) should be prescribed for those who are sedentary. Inelastic (which will not change with limb size), should be prescribed for those who frequently ambulate. For patients with mixed venous and arterial disease (ankle-brachial index of greater than 0.5 to 0.8), a trial of supervised modified light compression up to 30 mm Hg may help decrease edema and promote ulcer healing (Wound, Ostomy, and Continence Nurses Society, 2019). Leg elevation above the heart for 30 minutes three or four times per day when used with compression can also help reduce edema (Wound, Ostomy, and Continence Nurses Society, 2019).

Pharmacological Treatment: Horse chestnut seed extract (HCSE) in a dose of 300 mg twice daily may reduce edema and pain in venous leg ulcers (Wound, Ostomy, and Continence Nurses Society, 2019). People with bleeding disorders, kidney disease, or liver disease should not take HSCE. There may also be interactions with certain medications, such as lithium, diabetic drugs, and anticoagulants, which might result in low blood sugars and slower blood clotting (Wound, Ostomy, and Continence Nurses Society, 2019). Pentoxifylline (Trental) 400 mg three times per day has been used to treat venous ulcers. It has been shown effective when used with compression and may be beneficial as monotherapy in those patients who cannot tolerate compression (Wound, Ostomy, and Continence Nurses Society, 2019). Topical steroids may provide short-term improvement of venous dermatitis. Oral antibiotics are only warranted in cases of suspected cellulitis (Wound, Ostomy, and Continence Nurses Society, 2019).

Surgical Treatment: Surgery should be considered when topical therapy and compression are not able to heal the venous ulcer. Surgical options to treat venous disease include interruption of the perforating veins with subfascial endoscopic perforator surgery (SEPS), laser ablation, radiofrequency ablation (RFA), and sclerotherapy (Wound, Ostomy, and Continence Nurses Society, 2019). Surgical procedures available for valvular incompetence include artificial valve insertion, direct valvuloplasty, and autogenous vein valve transplantation (Wound, Ostomy, and Continence Nurses Society, 2019). Skin grafts and bioengineered human skin equivalents may be used for those with large or refractory venous ulcers, but they must be used in conjunction with compression therapy to improve healing (Wound, Ostomy, and Continence Nurses Society, 2019).

Follow-Up: The goals of care are to reduce edema, promote ulcer healing, and prevent reoccurrence of the ulcer.

Sequelae: Compliance with compression, ulcer size, and duration of the ulcer affect ulcer healing. Ulcers larger than 5 cm^2 and present for more than 6 months are predictive for nonhealing, so early assessment and treatment with compression therapy is important to reduce complications such as infection from nonhealing ulcers (Wound, Ostomy, and Continence Nurses Society, 2019).

Prevention/Prophylaxis: The daily use of compression therapy for the rest of one's life is recommended to promote healing and reduce the chance of reoccurrence.

Referral: Patients with venous leg ulcer disease with impaired calf muscle pump function may benefit from physical therapy that includes flexion and extension exercises, as well as walking programs to improve calf muscle pump function (Wound, Ostomy, and Continence Nurses Society, 2019).

Education: Patients with venous ulcer disease should be instructed to use compression stockings every day for the rest of their lives and replace these compression stockings at least every 6 months. They should elevate the affected leg or legs above the heart several times a day. Physical activity is recommended to increase venous return and should be performed based on the patient's medical condition, but may include ankle flexion exercises, brisk walking, and sitting in a rocking chair and using the feet to push down to plantar flex the ankles.

Clinical Recommendation	Evidence Rating	References
Smoking cessation, dietary management, exercise, and diabetic management are key treatments to slow the progression of peripheral arterial disease.	A	Ullery et al., 2018 Dua & Lee, 2016
Hypertension treatment is an essential treatment for patients with known abdominal aortic aneurysms.	A	Ullery et al., 2018
Patients with known abdominal aortic aneurysms should receive periodic ultrasound, magnetic resonance imaging, or CT-guided images at least once a year.	A	Sprynger et al., 2019
Endovascular grafts for complex aortic aneurysms permit a lower perioperative risk profile than does the open surgical procedure for such patients. After the procedure, nursing proficiency with aortic endograft is key to the patient's safe postoperative progression.	A	Sprynger et al., 2019 Chaikof et al., 2018 Kohlman-Trigoboff et al., 2020
Compression improves healing of venous leg ulcers compared to no compression.	A	Kelechi et al., 2020 Wound, Ostomy, and Continence Nurses Society, 2019

Continued

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Clinical Recommendation	Evidence Rating	References
Compression stockings reduce the chance of venous ulcer recurrence when compared with no compression.	A	Kelechi et al., 2020 Wound, Ostomy, and Continence Nurses Society, 2019
Manual lymph drainage may offer an additional benefit to compression bandaging for swelling reduction in lymphedema.	A	Grada & Phillips, 2017
Clinicians should prescribe one or more of the following medications for patients with peripheral arterial disease: aspirin, statin and Cilostazol (Pletal).	A	Rasmussen et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

M. J. is a 76-year-old woman who lives on the side of a very steep mountain. The home health nurse has visited her once a week for the last year. She has running water, electricity, and a coal stove with backup oil heat for very cold winter nights. She uses the telephone for communication. She has diabetes mellitus, hypertension, and hypothyroidism and is in atrial fibrillation. She has never been in the hospital before.

Her current medications include metformin (250 mg twice a day), losartan (50 mg/day), levothyroxine sodium (Synthroid) (50 mcg/day), digoxin (0.125 mg/day), furosemide (Lasix) (10 mg/day), aspirin (81 mg/day), simvastatin (20 mg/day), and warfarin (Coumadin) (4 mg/day, with 6 mg on Sundays). Allergies are to penicillin (hives) and to metoprolol (hypotension and dizziness). M. J. stopped smoking 5 years ago, but until then she smoked one-half pack a day.

Last laboratory test results (1 week ago) were: hemoglobin A1C (Hgb A1C) 8.3, international normalized ratio (INR) 1.7, sodium 129, potassium 5.8, chloride 102, CO_2 20, blood urea nitrogen (BUN) 45, creatinine 1.5, glucose 289, white blood cell (WBC) count 6.8, Hgb 10.1, hematocrit 30.2, platelets 215,000.

The home health nurse calls you from the patient's house, where she notes that the patient had a 5-minute spell of visual loss in her right eye. It has not recurred. During this period, M. J. noted that her left hand and left leg felt "funny," and her left foot and leg were so weak that she could not walk.

M. J. has a heart murmur, described by the home health nurse as loudest over the right sternal border and more prominent in the systolic phase. Furthermore, the home health nurse tells you that she hears bruits on both sides of the neck, with the right being louder than the left. The blood pressure in the right arm is 135/72 mm Hg and 110/66 mm Hg in the left arm. Heart rate is irregular at 75 to 90 beats per minute. The left hand and fingers have always been cooler than the right. Lungs are remarkable for wheezes. The patient has no fever. Oxygen saturations at room temperature are 90% to 92%, which has been her baseline.

1. What concerns do you have regarding M. J. at this point?
2. Do you need to see M. J. fairly soon, or can she come to see you at her regularly scheduled appointment in 3 weeks?
3. If you were to see M. J. in the next 24 hours, what additional tests would you perform?
4. Based on the laboratory results given, what changes would you make in her medication profile?
5. Which arm will you use for blood pressure recordings in the future?
6. What systolic blood pressure range would you order for M. J., as a general target?
7. If M. J. has a repeat episode of right eye blindness, lasting 30 minutes this time, what would you do?

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CHAPTER 13

Gastrointestinal Disorders

Laurie Kennedy-Malone

ASSESSMENT

Accurate history taking of gastrointestinal (GI) complaints is essential for completing an assessment of the older adult. The physical examination is often unremarkable, and laboratory findings may not provide diagnostic information because the presentation of illness in an older adult is usually subdued (Vonnes & El-Rady, 2021). GI conditions common in older adults include esophageal, gastric, and motility disorders such as Barrett's esophagus, gastric cancer, GI bleeding, *Clostridioides difficile* colitis, inflammatory bowel disease, diverticular disease, constipation, and colon cancer (Dumic et al., 2019; Soumekh & Katz, 2021).

Gathering the Gastrointestinal History

Generally, the chief complaints of GI conditions can be categorized into symptom cluster areas for further exploration: abdominal pain/discomfort, gastroesophageal reflux disease (GERD)/regurgitation symptoms, nausea/vomiting, diarrhea/incontinence, and difficult defecation and constipation (Koloski et al., 2017). Explore with the patient any episodes of change in appetite, anorexia, involuntary weight loss, dyspepsia, dysphagia, heartburn, nausea, regurgitation, vomiting, painful or difficult defecation, diarrhea, tenesmus, or constipation. Inquire if there has been any associated trauma with the presenting symptom, any hematemesis, hematochezia, or melena (Malagelada et al., 2017; Mealie et al., 2020; Wilkinson et al., 2019). If the patient's chief complaint is abdominal pain, differentiate between organic and functional origins of pain (Dunlap & Patterson, 2020).

Determine the sequence of events that triggered each symptom. Inquire about precipitating factors, such as an introduction of new foods or beverages (intolerance), meal consumption, position of the body, use of caffeine, alcohol use, or smoking. Were any other symptoms present that can be clustered to form a differential diagnosis? It is important to discern from patients what therapeutic measures they have initiated to alleviate the symptoms (McGee, 2020; Mealie et al., 2020). Determine whether the treatment is a previously prescribed regimen, an over-the-counter (OTC) medication, an herbal product, or a home remedy. Ask the patient when the last time a fecal occult blood test was performed and whether they recently had a colonoscopy.

Abdominal Symptoms

Although abdominal pain is a common acute problem with which patients present to their health-care providers, older adults may not experience the typical symptoms of abdominal disorders that younger patients report. If patients present with abdominal pain, it is important to discern the characteristic of the pain. How quickly did the pain begin? Was the pain abrupt? Is the pain progressive or intermittent? Has the patient ever experienced this type of pain before and, if so, what was the diagnosis and treatment? Has the patient noted any improvements with self-treatment, positioning, vomiting, or defecation? What is the referral pattern? Is the pain worse at night or during the day? Is it relieved or aggravated by food? If the patient reports triggers to abdominal pain by food, ask more specific questions pertaining to food to discern if the patient is having a specific food intolerance(s) or possible food poisoning. Does the patient have any associated symptoms of regurgitation, reflux, cough, nausea, vomiting, constipation, or diarrhea? (McGee, 2020). Ask about the severity of pain by having the patient rate the pain on a scale from 1 to 10; however, realize that in older adults' pain may be blunted despite the underlying pathology (Dumic et al., 2019; Vonnes & El-Rady, 2021). Determine the patient's family history of GI disorders, including malignancies. Gather a history of previous abdominal surgeries. Inquire about alcohol use or drug abuse. Ask the patient if they are taking any medications to decrease or stimulate appetite depending on the chief complaint. Inquire about any history of jaundice, heart disease, or peripheral vascular disease. Review all current medications (Mealie et al., 2020).

Inspection

The physical examination of the abdomen begins with inspection, checking for overall symmetry while observing the patient lying down. The practitioner can consider the abdomen to be divided into four quadrants, visualizing an imaginary vertical line from the sternum to the pubis passing though the umbilicus and a horizontal line drawn through the umbilicus.

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In addition to being familiar with the underlying organ systems and referred pain in the four quadrants, the nurse practitioner should be familiar with other anatomical landmarks, such as epigastric, periumbilical, suprapubic, and McBurney's point, which is one-third of the distance from the right anterior superior iliac spine to the umbilicus (Mealie et al., 2020).

Carefully examine for scars, lesions, stomas, striae, discoloration, dilated veins, or other marks. If surgical scars are detected, review with the patient their surgical history if not documented. Determine whether the abdomen is concave or protuberant. Is an umbilical, abdominal wall, incisional, or inguinal hernia present? If a hernia is suspected, have the patient raise the head and note if there is presence of a bulge (Shakil et al., 2020). Is a lift noticeable? Is there abdominal distention? If so, is the distention local or generalized? Causes of generalized distention include abdominal fat, peritoneal fluid, or gaseous distention, whereas local distention often is indicative of obstruction or organ or structural enlargement. Examine the umbilicus. Signs of ascites include a flat or everted umbilicus (Williams, 2009). Check for any bulging in the flanks as a sign of ascites.

Examine the skin of the abdomen for color, noting if there is any jaundice (as found in liver disease) or biliary tract obstruction, bruising, or telangiectasias (Suneja et al., 2020). A bluish discoloration detected around the umbilicus is known as Cullen's sign, which is often found in patients with bleeding in the peritoneum. If the bluish discoloration is on the flanks, this is known as Grey Turner sign and is often indicative of retroperitoneal bleeding, as in pancreatitis (Mealie et al., 2020; Rastogi, 2019). Jaundice in the area of the umbilicus is known as Ransohoff's sign and is a result of a ruptured common bile duct (Rastogi et al., 2019). Note whether there are any pulsatile movements across the abdomen. If present, this sign may be indicative of a vascular aneurysm or a wide arterial pulse pressure. Visible intestinal peristalsis may be indicative of bowel obstruction (Shimizu & Tokuda, 2013). If pink or purple striae appear on a pendulous abdomen, consider underlying Cushing syndrome (Mealie et al., 2020). Examine for any evidence of a pulsatile mass, which may be present in an abdominal aortic aneurysm or in muscle diastasis (Dunlap & Patterson, 2020).

Auscultation

Auscultations follow inspection of the abdomen. Using the diaphragm, place the stethoscope lightly against the skin. Listen for bowel sounds, vascular bruits, and rubs. Bowel sounds are produced by peristalsis. A murmur heard in the abdomen may be an aortic aneurysm. A constant systolic-diastolic bruit may occur when the patient has an arteriovenous fistula in the renal vessels. Other sites to auscultate for bruits during abdominal examination include the iliac arteries and the femoral arteries (Mealie et al., 2020)

Take the time auscultate for presence or absence of bowel sounds. Generally, people who are hungry have active bowel sounds. Bowel sounds described as high pitched, rumbling, or tinkling are known as borborygmi. A rushing sound is associated with bowel obstruction. If bowel sounds are absent, listen for 5 minutes. Listen for a loud succussion splash over the abdomen of a patient in whom you suspect a gastric obstruction or dilations (Williams, 2009). Suspect peritonitis, mesenteric thrombosis, or advanced intestinal obstructions when bowel sounds are absent (Jackson & Cruz, 2018). Nurse practitioners should not, however, rely on auscultation alone for diagnostic purposes; studies have refuted the usefulness of auscultation when differentiating patients who have normal versus pathological bowel sounds (Felder et al., 2014).

Percussion

Percussion of the abdomen is performed to determine the density of tissue of the abdominal organs by the sounds emitted when tapped (Rastogi et al., 2020). It is normal to hear tympanic sounds over the stomach, whereas dullness is expected over a distended bladder, the liver, and the spleen (Suneja et al., 2020). Dullness noted over other areas of the abdomen is a deviation from the norm. Definitive percussion is used to ascertain the size and shape of the liver and spleen. Because the liver decreases in size starting at about age 50 years, the normal range of the liver size in an older person is 6 to 12 cm (Williams, 2009).

Palpation

Perform light palpation to discern abdominal masses; enlarged organs such as liver, spleen, and kidneys; and areas of tenderness. If a mass is detected, the nurse practitioner needs to determine whether the mass is intra-abdominal or within the abdominal wall. Using the palm and extended fingers of the right hand, press about 21 cm deep. If a patient has complained of abdominal pain, always palpate in a quadrant away from the identified location. (Suneja et al., 2020). If noted tenderness is elicited over the epigastrium, consider gastritis or early acute cholecystitis from visceral nerve irritation (Mealie et al., 2020).

Once you discover the tender area, maintain pressure over the area to determine the consistency of the pain. Try to note if there is any voluntary guarding by the patient during palpation. If the pain diminishes despite the applied pressure to the area, inflammation is unlikely. If you suspect intra-abdominal tenderness, proceed to deep palpation. Check for referred rebound tenderness by applying pressure with the tips of the fingers to a site distant from the areas of questionable tenderness, and then quickly remove them from the abdomen (Suneja et al., 2020). Assessment of the patient's facial expression is warranted, especially in older adults who have difficulty with communication (Williams, 2009). Specific maneuvers to detect tenderness can lead the examiner to making a differential diagnosis; for instance, tenderness medial to McBurney's point suggesting a Meckel diverticulum should be distinguished from typical appendicitis tenderness. If tenderness is elicited remote from the areas palpated after release of pressure, consider peritoneal irritation (Mealie et al., 2020); a positive Rovsing's sign suggests right-sided peritoneal irritation if pain is reported when the examiner has performed deep palpation on the lower left quadrant (Rastogi et al., 2018). Although it is known that older adults may present with a subdued presentation of appendicitis, two maneuvers may elicit signs of an inflamed appendix. Pain may be elicited when the patient lifts the right knee as the examiner presses on the knee at the same time (psoas sign) and or by internal rotation of the flexed right thigh (obturator sign) (Hirsch, 2017).

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BOWEL OBSTRUCTION

Signal Symptoms: Cramping abdominal pain, dehydration, nausea, vomiting, obstipation, restlessness.

Description: Bowel obstructions are classified as mechanical or nonmechanical and partial or complete and are located in either the small or large intestine (Jackson & Cruz, 2018).

Etiology: Normal flow of gastric and intestinal contents is interrupted (Jackson & Cruz, 2018). A mechanical bowel obstruction results when there is a complete or partial blockage of the lumen of the bowel by an adhesion, tumor, or hernia. Additionally, adynamic ileus and colonic pseudo-obstruction occur because of a lack of enteric propulsion resulting from trauma, medications, metabolic disturbance, and postoperatively (Catena et al., 2019). Postoperative adhesions cause approximately 60% to 70% of small bowel obstruction (SBO) (Ozturk et al., 2018).

Occurrence: The incidence of SBO annually in the United States is about 350,000 (Reddy & Cappell, 2017), and large bowel obstruction occurs approximately four to five times less frequently than SBO (Jaffe & Thompson, 2015). Bowel obstruction occurs equally in men and women.

Age: Bowel obstruction from all causes, except intussusception, is more prevalent in older adults (Panzera et al., 2021).

Ethnicity: Not significant.

Contributing Factors: Most common causes include adhesions from previous abdominal or pelvic surgery, neoplasms, and herniation (Jackson & Cruz, 2018). Additional causes for mechanical obstruction include diverticulitis, foreign bodies (including gallstones, although uncommon), volvulus (twisting bowel on its mesentery), and intussusception (telescoping of one segment of bowel into another), fecal impaction, endometriosis, inflammatory bowel disease stenosis (Catena et al., 2019; Jackson & Cruz, 2018; Ozturk et al., 2018).

Signs and Symptoms: Patients should be asked about last bowel movement, ability to pass gas, previous episodes of diverticulosis or chronic constipation, any evidence of rectal bleeding or unexpected weight loss. Question the patient about medications to include any taken to relieve symptoms of pain and bloating (Catena et al., 2019). Older adults often present for evaluation late in their illness and often have atypical or nonspecific complaints (Ozturk et al. 2018). Older patients may present restless, show dehydration, sepsis, dry mucous membranes (Reddy & Cappell, 2017); underlying signs of prefrailty or frailty may be evident (Ozturk et al., 2018). The most common symptoms reported are bloating, colicky cramping abdominal pain, nausea, vomiting, abdominal distention, cessation of flatulence, and obstipation (Jackson & Cruz, 2018). It is important to note in patients with incomplete obstruction, watery diarrhea may be present initially (Ten Broek et al., 2018).

Inspect the abdomen for evidence of surgical scars and external hernias; the level and the location of the obstruction determines the amount of abdominal distention (Jackson & Cruz, 2018). Observe for visible peristalsis, which is a sign of bowel obstruction (Shimizu & Tokuda, 2013). Auscultate bowel sounds. In acute mechanical bowel obstruction, the bowel sounds are hyperactive and are described as "high-pitched tinkling" (Jackson & Cruz, 2018). Bowel sounds may be absent with advanced obstruction in the intestinal tract (Jackson & Cruz, 2018). Palpation of the abdomen may reveal abdominal wall or groin hernias. In mechanical obstruction of the large bowel, symptoms are similar to an SBO, but they appear more gradually. Perform a digital rectal examination to determine whether fecal impaction or rectal mass is a source of the obstruction (Jackson & Cruz, 2018). Given the possibility of dehydration and/or sepsis, monitor the vital signs for evidence of tachycardia and hypotension (Jackson & Cruz, 2018).

Diagnostic Tests: Standard laboratory evaluation includes a complete blood count (CBC) with differential and a metabolic panel to assess the patient for presence and severity of hypovolemia, hypokalemia, hypochloremia, metabolic alkalosis (may be evident in patients with emesis). Leukocytosis may be evident in patients who have had intestinal bacterial transmission or bowel perforation (Jackson & Cruz, 2018). Presence of leukocytosis, especially in frail older adults, may be delayed (Ozturk et al., 2018). Obtaining a serum lactate and C-reactive protein (CRP) should be considered in patients with suspected mesenteric ischemia or peritonitis (Ten Broek et al., 2018).

The initial imaging of a patient with a suspected bowel obstruction is the plain abdominal x-ray with flat and upright views, although the results may be normal in patients early in the obstruction phase or in those with a proximal obstruction (Catena et al., 2019; Jackson & Cruz, 2018). Plain films can identify multiple air-fluid levels, distention of small bowel loops, and the absence of gas in the colonic section (Ten Broek et al., 2018). If x-rays do not show an obstruction and there is a high index of suspicion, a computed tomography (CT) scan should be used to further evaluate. CT scan is found to have as much as a 90% sensitivity in identifying the presence of bowel strangulation and can identify the etiology and the site of the obstruction (Ten Broek et al., 2018). A water-soluble contrast enema may be ordered if a bowel obstruction is suspected (Catena et al., 2019). Ultrasonography may be used in the evaluation of acute abdominal pain and can be used to identify obstruction along with its cause (Catena et al., 2019; Jackson & Cruz, 2018).

Differential Diagnosis:

- Cholecystitis
- Constipation
- Diverticulitis
- Gallstones
- Abdominal hernia
- Narcotic bowel
- Appendicitis (stump appendicitis)
- Pelvic inflammatory disease
- Mesenteric ischemia
- Pseudo-obstruction (Ogilvie's syndrome)
- Medication adverse effects
- Postoperative paralytic ileus
- Perforated viscus/intra-abdominal sepsis
- Renal colic (Catena et al., 2019, p. 2; Jackson & Cruz, 2018, p. 346, Reddy & Cappell, p. 28)

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Treatment: Acute intestinal obstruction is a common reason for older adults to be admitted for evaluation by a general surgery service and to be treated by nonoperative management (NOM) or surgery (Catena et al., 2019; Jackson & Cruz, 2018). Initial treatment of a bowel obstruction consists of hospitalization for nasogastric suctioning and IV fluid administration to correct fluid and electrolyte imbalance (Ozturk et al., 2018). Bladder catheterization may be considered to monitor urine output (Jackson & Cruz, 2018). In the absence of clinical sign of strangulation or peritonitis, the patient can be treated with NOM up to 72 hours. Systematic signs of tachycardia, fever, focal tenderness, and elevated lactate levels can indicate intestinal ischemia (Ten Broek et al., 2018). Immediate surgical intervention is indicated for suspected vascular insufficiency, perforation, or strangulation of the bowel or in patients whose condition deteriorates from the time of admission (Jackson & Cruz, 2018). Bowel obstruction caused by tumors is treated with surgical resection and anastomosis when the patient's condition permits (Catena et al., 2019).

Follow-Up: Ten Broek and colleagues (2018) recommend NOM should be attempted for 3 to 5 days, then surgical management used for unresolved obstructions.

Sequelae: Complications from bowel obstruction include wound dehiscence, aspiration, short bowel syndrome, pneumonia, bowel perforation, anastomotic leak, and renal failure (Smith et al., 2021). Delay in surgery may increase morbidity and mortality outcomes in older adults (Ozturk et al., 2018). Recurrence of adhesive small bowel obstruction is common with nonoperative treatment (Catena et al., 2019; Jackson & Cruz, 2018). In older adults with a diagnosed malignancy as the cause of the bowel obstruction, consideration of the patient's wishes and quality of life need to be forefront (Ozturk et al., 2018).

Prevention/Prophylaxis: Caregivers must understand the importance of avoiding fecal impactions in patients at risk for this condition.

Referral: Consider referring to surgical service upon admission to the hospital (Jackson & Cruz, 2018).

Education: Inform older adults with diagnosed untreated internal and external hernias of the possible complication of bowel obstruction.

Clinical Recommendation	Evidence Rating	References
In the absence of emergent surgery for bowel obstruction, a trial of nonoperative management can be implemented for up to 72 hours.	B	Ten Broek et al., 2018
Continued research is needed on older adults who present with small bowel obstruction (SBO) to determine the impact of comorbidities on the optimal management of SBO resulting from adhesions.	C	Ten Broek et al., 2018
SBO is a leading cause of morbidity, death, and health-care expenditure for abdominal surgical emergency.	A	Ten Broek et al., 2018
When looking at hospital admission at 122 hospitals for adhesive SBO, the hospitals with a higher proportion of adhesive SBO patients treated with an early operation had a lower likelihood of serious complications, bowel resection, and death, independent of hospital type and number of adhesive SBO admissions.	A	Behman et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CHOLECYSTITIS

Signal Symptoms: Acute onset of right upper quadrant and/or epigastric pain that is persistent, with radiation to back or shoulders, and usually related to history of fatty meal intake prior to onset (Vagholkar, 2020).

Description: May fall into one of three categories: acute gallbladder inflammation related to cystic duct obstruction by gallstones, acalculous cholecystitis without presence of stones or sludge, or chronic gallbladder inflammation (Mou et al., 2019; Vagholkar, 2020).

Etiology: Gallstones are mainly composed of cholesterol, and stone formation is associated with pregnancy, rapid weight loss, diabetes mellitus, dyslipidemia, obesity, genetics, female sex, medications, older age, and metabolic syndrome (Zhao et al., 2019). Cholecystitis usually occurs when a gallstone obstructs the cystic duct; however, acalculous cholecystitis may be found in approximately 10% of cases, specifically in critically ill states (Vagholkar, 2020). Trapped bile caused by the blockage of the cystic duct leads to inflammation, impaired circulatory flow, and ischemia. The risk of bacterial infection climbs, with increased complications after 72 hours of symptoms (Mou et al., 2019). Common culprit organisms are *Escherichia coli*, *Klebsiella pneumonia*, and *Bacteroides fragilis* (Pisano et al., 2020). *Enterococcus* species may be found in immunocompromised patients (Pisano et al., 2020). Acute acalculous cholecystitis (AAC) is precipitated by stagnant bile and ischemic states; the critically ill patient who has suffered trauma, recent surgery, shock, sepsis, cardiac complications,

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sickle cell disease, diabetes, and total parenteral nutrition is at risk for AAC (Alshargi et al., 2018; Vagholkar, 2020).

Occurrence: Gallstones' prevalence ranges between 10% and 15% among adults, and 10% to 15% of these individuals will develop acute symptoms (Mou et al., 2019; Pisano, et al., 2020). ACC comprises the majority of all cases, with only 10% AAC (Vagholkar, 2020). Gallstones may be an incidental finding via imaging, and 80% of those with gallstones are asymptomatic (Mou et al., 2019). In the older adult, cholecystitis can present with atypical features and likely a complicated disease course (Chhoda et al., 2021).

Age: During reproductive years, women are more prone to gallstones than men (Mou et al., 2020; Vagholkar, 2020). As age increases, the risk for gallstones increases regardless of gender (Chhoda, 2021; Vagholkar, 2020). The risk of biliary disease is from 14% to 23% for the older adult, with increasing prevalence to 80% if older than 90 years (Chhoda et al., 2021).

Ethnicity: A high prevalence for cholecystitis exists among Hispanics and Native Americans; in the United States, biliary disease is greater in Hispanics compared to all other ethnicities (Figueiredo et al., 2017).

Contributing Factors: Nonmodifiable risk factors for cholecystitis include advancing age, female sex, race, and family history of gallbladder disease (Vagholkar, 2020). Females less than age 50 have a threefold likelihood of developing ACC compared to men (Mou et al., 2019). Obesity is a known predisposing factor to cholecystitis (Vagholkar, 2020). Diabetes, alcoholic cirrhosis, inflammatory bowel disease, chronic hemolysis, pancreatic insufficiency, and hyperlipidemia predispose patients to gallstone development. Gallstone formation may be attributed to use of exogenous estrogens prescribed for postmenopausal hormone replacement and hormonal contraceptives (Figueiredo et al., 2017). Gallbladder stasis, a precursor to gallstone formation, occurs with extended total parenteral nutrition (Vagholkar, 2020). Patients who experience rapid weight loss are at high risk for the development of gallstones, placing those with history of bariatric surgery at greater risk for gallstones.

Signs and Symptoms: The most common type of presentation includes the acute onset of right upper quadrant and/or epigastric pain that is moderate to severe in nature, persistent, and without any relieving factors (Mou et al., 2019; Vagholkar, 2020). Associated symptoms may include nausea, vomiting, malaise, fever, and poor appetite. A change in mental status, incontinence, and falls in the older adult may be the only outward sign (Chhoda et al., 2021). Physical examination may reveal right upper quadrant subcostal tenderness, guarding, and pain on inspiration (Murphy's sign) (Pisano, 2020; Vagholkar, 2020). The absence of Murphy's sign does not exclude the acute illness; the older adult may not exhibit Murphy's sign (Chhoda et al., 2021). Biliary colic pain can initially start in the epigastric region, then radiate to the right upper quadrant (RUQ); thus, it is important to question the patient about generalized upper abdominal pain (Vagholkar, 2020). In a patient who reports experiencing symptoms for days, rebound tenderness may suggest perforation. Jaundice on examination would raise concern for possible complications including obstruction; however, 15% of presentations will have jaundice (Vagholkar, 2020).

Diagnostic Tests: Mild leukocytosis with increased band formation is the most common abnormality seen on laboratory studies; however, white blood cell (WBC) counts may not be elevated in the older adult (Vagholkar, 2020). Significant leukocytosis would raise concern for complicated cholecystitis secondary to perforation, gangrene, and sepsis (Vogholkar, 2020). Elevation in lipase, amylase, and elevated liver function tests would prompt further evaluation for gallstone pancreatitis (Chhoda et al., 2021). In chronic cholecystitis, however, laboratory values may be normal. Elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) are common, and the total bilirubin and alkaline phosphatase can have a lag effect, increasing through the acute clinical course.

Real-time ultrasonography of the gallbladder and biliary tree is the diagnostic procedure of choice for both acute and chronic cholecystitis, showing gallstones, thickening of the gallbladder wall and, if the common bile duct is obstructed, dilation of the biliary tract (Pisano et al., 2020). An additional imaging modality called the hepatobiliary iminodiacetic acid scan (HIDA) is useful if there is concern for cystic duct obstruction or biliary dyskinesia. A computed tomography (CT) scan is often performed to evaluate acute abdominal pain when diagnosis is unclear; yet it is less sensitive at identifying gallstones than an ultrasound (Alshargi et al., 2018; Pisano et al., 2020). In situations where choledocholithiasis is questioned, a magnetic resonance cholangiopancreatography (MRCP) is highly sensitive and specific (93% and 96%, respectively) for biliary tree obstruction (Pisano et al., 2020). In cases with high suspicion for choledocholithiasis, MRCP can reduce the need for unnecessary endoscopic retrograde cholangiopancreatography (ERCP) (Pisano et al., 2020). Liver functions tests (LFTs), including bilirubin, may be elevated due to inflammatory gallbladder and biliary tree without any presence of choledocholithiasis; therefore, serologies are not sufficient to diagnosis choledocholithiasis, and further imaging is needed (Pisano et al., 2020). An endoscopic ultrasound (EUS) and MRCP are useful preoperatively if there is moderate concern for choledocholithiasis; an ERCP or intraoperative cholangiography (IOC) is necessary for patients with high risk for choledocholithiasis for both diagnostic and therapeutic purposes (Pisano et al., 2020).

Differential Diagnosis:

- Perforated peptic ulcer in older adults
- Appendicitis
- Liver abscess
- Diverticulitis
- Hepatitis
- Acute pyelonephritis
- Gastrointestinal (GI) carcinoma
- Acute pancreatitis
- Myocardial ischemia
- Herpes zoster
- Gastritis
- Peptic ulcer disease
- Mesenteric ischemia
- Cholangitis
- Irritable bowel syndrome
- Gastroesophageal reflux disease (GERD) (Jones et al., 2021)

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Treatment: Acute episodes require hospital admission in preparation for cholecystectomy; at this time antibiotics are given intravenously and selected based on targeting enteric pathogens. Antibiotic resistance should be taken into consideration, with antibiotic therapy tailored according to identified pathogens. Antibiotic choices may include but not limited to piperacillin-tazobactam, ampicillin-sulbactam, meropenem, imipenem-cilastatin, and third generation cephalosporins combined with metronidazole (Vagholkar, 2020). Depending on surgical risk, laparoscopic cholecystectomy is the preferred method of surgical intervention and should be undertaken within 72 hours (Chhoda et al., 2020; Mou et al., 2019). Open cholecystectomy may be necessary if patients are morbidly obese, if they are at increased risk for adverse reactions to anesthesia, or if there is a concern for malignancy, or if the patient has peritonitis, advanced liver disease with cirrhosis and portal hypertension, sepsis with cholangitis, or pancreatitis (Vagholkar, 2020). Supportive measures include giving analgesics and antiemetics as needed. The risk of conversion to open cholecystectomy is linked with male sex, older age (greater than 60 years), and prior abdominal surgeries (Pisano et al., 2020).

A cholecystectomy for acalculous cholecystitis in the critically ill patient may be on hold and delayed until health improves, with a percutaneous cholecystostomy (PC) tube as an initial approach to treatment (Mou et al., 2019). PC should not be performed on patients with coagulopathy, with complications including biliary leak, peritonitis, vascular compromise, and dislodgement of catheter (Chhoda et al., 2021). The general surgeon may weigh risks and benefits of a PC versus interval cholecystectomy in a patient with multiple comorbidities; if PC is performed within 24 hours of symptoms, hospital length of stay may be reduced (Mou et al., 2019). The recurrence risk of events following conservative management of cholecystitis is high; therefore, surgical intervention should be undertaken if there are no contraindications. In the event of choledocholithiasis, an ERCP may be undertaken for stone extraction prior to cholecystectomy (Pisano et al., 2020). If the clinical status is unknown regarding choledocholithiasis, a cholecystectomy with intraoperative cholangiogram is indicated to ensure no occult stones remain. Cholangitis requires prompt recognition in order to provide IV antibiotics, biliary decompression via ERCP, and close monitoring for sepsis. Subsequent cholecystectomy is indicated after biliary decompression.

Although used less often now than in the past, oral ursodeoxycholic acid may be considered for dissolution of gallstones less than 10 mm for prophylactic purposes in higher risk patients; however, the gallbladder must be functioning and the cystic duct must be patent (Chhoda et al., 2021). Recurrence rate of stones is more than 50%, even with ursodeoxycholic acid. Extracorporeal shock wave lithotripsy is a possible alternative in nonsurgical candidates, yet potential complications, including biliary pancreatitis and hematomas, may raise concern for the procedure.

Follow-Up: Postoperative management of routine cholecystectomy includes monitoring for impending infection, adverse drug reactions and interactions, and changes in functional and mental status. For the frail older adult who has undergone percutaneous cholecystostomy, observation for complications is crucial. For older women, the dosages of estrogen preparations may need to be reduced, if applicable, due to the idea that estrogen may contribute to gallstone development (Figueiredo et al., 2017).

Sequelae: Complications of acute cholecystitis include gangrenous cholecystitis, perforation, emphysematous cholecystitis, cholecystoenteric fistula, gallstone ileus, choledocholithiasis leading to cholangitis, and acute biliary pancreatitis (Chhoda et al., 2021). Frail older adults, especially those who are diabetic, are at high risk for complications from cholecystitis (Pisano et al., 2020). Patients may develop diarrhea and/or bloating postprandially after ingesting higher fat and greasy foods postcholecystectomy, but symptoms may improve over time; however, symptoms may be long term.

Prevention/Prophylaxis: The importance of resting and avoiding risk factors after acute cholecystitis or an exacerbation of chronic cholecystitis needs to be emphasized.

Referral: A surgical consultation is necessary if acute cholecystitis is suspected. A gastroenterologist should be consulted for the frail older adult who is not a surgical candidate, or in the clinical scenario of choledocholithiasis. Biliary pain in patients with a prior history of a cholecystectomy should be evaluated for a retained common bile duct stone. Referral to a gastroenterologist for evaluation by ERCP, magnetic resonance imaging (MRI), or endoscopic ultrasonography is highly recommended (Pisano et al., 2020).

Education: To prevent complications, encourage patients with chronic cholecystitis and patients for whom surgery is contraindicated to report early signs and symptoms of an acute attack. Patients also should be educated that gallstones could recur in the common bile duct, despite prior cholecystectomy.

Clinical Recommendation	Evidence Rating	References
For patients with cumulative risk factors for cholecystitis, early cholecystectomy is recommended before there is a progression of the disease leading to complications of acute cholecystitis.	A	Chhoda et al., 2021 Mou et al., 2019
Laparoscopic cholecystectomy is the preferred treatment for cholecystitis, barring any clinical contraindications.	A	Chhoda et al., 2021 Mou et al., 2019
A positive Murphy's sign is a useful diagnostic tool when examining older adults presenting with symptoms of acute cholecystitis; a negative sign, however, should be cautiously interpreted.	C	Chhoda et al., 2021

Continued

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Clinical Recommendation	Evidence Rating	References
The general surgeon may weigh risks and benefits of a percutaneous cholecystostomy (PC) versus interval cholecystectomy in a patient with multiple comorbidities; if PC is performed within 24 hours of symptoms, hospital length of stay may be reduced.	A	Mou et al., 2019
Liver function tests, including bilirubin, may be elevated due to inflammatory gallbladder and biliary tree without any presence of choledocholithiasis; therefore, serologies are not sufficient to diagnosis choledocholithiasis, and further imaging is needed.	A	Pisano et al., 2020

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CIRRHOSIS OF THE LIVER

Signal Symptoms: Jaundice, fatigue, spider angiomas, palmar erythema, nodular liver, choluria, ascites, encephalopathy.

Description: Cirrhosis occurs when there is chronic insult to the liver, resulting in fibrous and nodular regeneration of the existing hepatocytes, resulting in significant scarring and impaired liver function. From 1999 to 2019, cirrhosis was the eleventh leading cause of death in the United States with an average annual death rate over 40,000 per year (Centers for Disease Control and Prevention National Center for Health Statistics, 2020). The annual health-care costs for cirrhosis and advanced liver disease in the United States are between $12 billion and $23 billion (Peery et al., 2019).

Etiology: The most common etiology for cirrhosis in the United States is viral hepatitis (mostly hepatitis C and hepatitis B), alcoholic liver disease, and nonalcoholic steatohepatitis (NASH, an advanced form of nonalcoholic fatty liver disease [NAFLD]) (Smith et al., 2019). Hepatitis C recently replaced alcoholic cirrhosis as the leading cause of cirrhosis in patients who are on the liver transplant list. However, with increasing prevalence of fatty liver disease, estimates suggests that NASH will replace hepatitis C as the leading cause of cirrhosis in transplant-listed patients between 2025 and 2035 (Smith et al., 2019). The cause of primary biliary cirrhosis, a chronic autoimmune inflammatory disease of the liver in which the intrahepatic bile duct is destroyed, is unknown. Other causes of cirrhosis include autoimmune diseases (such as autoimmune hepatitis and primary sclerosing cholangitis), abnormal storage diseases (such as hemochromatosis, Wilson's disease, and alpha-1 antitrypsin deficiency), cardiovascular diseases (such as right-sided heart failure, Budd-Chiari's syndrome, and Osler-Weber-Rendu's disease), medications, sarcoidosis, and schistosomiasis (Smith et al., 2019).

Occurrence: In the United States it is estimated that 630,000 Americans have cirrhosis, although many are asymptomatic. The asymptomatic nature of early cirrhosis is why true estimates are hard to derive and likely two-thirds of patients are unaware of their disease (Scaglione et al., 2015).

Age: Liver disease, including cirrhosis, is diagnosed most frequently between the ages of 65 and 74 and is the eleventh leading cause of death (Centers for Disease Control and Prevention, 2018; Centers for Disease Control and Prevention National Center for Health Statistics, 2020). Additionally, advancing age increases the risk of drug-induced liver injury, especially with medications such as nitrofurantoin, isoniazid, and amoxicillin-clavulanate; this is likely affected by a predisposing influence of polypharmacy (Chalasani et al., 2014).

Ethnicity: The overall prevalence of cirrhosis is higher in non-Hispanic African Americans and Mexican Americans (Scaglione et al., 2015).

Contributing Factors: Overall, being male is independently associated with cirrhosis (Scaglione et al., 2015). However, in individuals who consume alcohol and develop alcoholic liver disease, progression to cirrhosis occurs more frequently in women compared to men (Crabb et al., 2020; Singal & Mathurin, 2021). The most common cause of cirrhosis in the United States is viral hepatitis, most often chronic hepatitis C or hepatitis B infection (Scaglione et al., 2015; Smith et al., 2019). Chronic alcohol consumption, either by itself or with other cirrhosis risk factors, is the second leading cause of cirrhosis; however, only 10% to 20% of patients with alcohol-associated liver disease will progress to cirrhosis (Singal & Mathurin, 2021; Smith et al., 2019). Finally, NAFLD and NASH are the third leading cause of cirrhosis, although it is expected to surpass hepatitis C as the leading cause of liver transplant within the next 5 to 15 years (Smith et al., 2019). Risk factors associated with NAFLD and NASH include many of the components of metabolic syndrome such as obesity, type 2 diabetes mellitus, and dyslipidemia (Chalasani et al., 2018). Additionally, although liver disease is the eleventh leading cause of death in the general population, it is the second or third leading cause of death in patients with NAFLD (Younossi & Henry, 2016). It should be noted that in patients with these three leading causes of cirrhosis, approximately 10% to 20% will develop cirrhosis within 10 to 20 years (Smith et al., 2019).

Drug-induced liver injury (DILI), and subsequent cirrhosis, is affected by several variables including age, sex, malnutrition, comorbidities, alcohol consumption, metabolic profile, dose, class effect, polypharmacy, and duration (Chalasani et al., 2014). The most common medications implicated in DILI include amoxicillin/clavulanate, isoniazid, methotrexate, allopurinol, amiodarone, fluroquinolones, macrolides, and nitrofurantoin. Certain infectious diseases, including sarcoidosis and

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schistosomiasis, have predisposed patients to a risk of developing cirrhosis (Smith et al., 2019). Other common causes of cirrhosis include certain storage diseases (such as hemochromatosis, Wilson's disease, and alpha1-antitripsyn deficiency), immune-mediated diseases (such as autoimmune hepatitis, primary biliary cholangitis, primary sclerosing cholangitis), cardiovascular conditions (such as heart failure, veno-occlusive disease [Budd-Chiari's syndrome], hereditary hemorrhagic telangiectasia [Osler-Weber-Rendu's disease]), and chronic biliary disease (such as recurrent bacterial cholangitis and bile-duct stenosis) (Smith et al., 2019).

Signs and Symptoms: Many patients are asymptomatic until advanced disease and decompensated cirrhosis occurs. When patients do exhibit symptoms, they can include anorexia, fatigue, weakness, generalized pruritus, right upper quadrant discomfort, unexplained weight loss, jaundice, ascites, peripheral edema, and encephalopathy (confusion and altered sleep). When questioned, reports of weight loss, easy bruising, and gastrointestinal (GI) bleeding may be common (Butterworth, 2019; Martin et al., 2014; Smith et al., 2019).

There are several physical examination findings that may be present in patients with cirrhosis (Smith et al., 2019). These may include muscle wasting, asterixis, jaundice, scleral icterus, spider nevi, ascites, dilated abdominal veins (caput medusae), enlarged or shrunken liver, hemorrhoids, splenomegaly, edema, erythema, palmar erythema, Kayser-Fleischer's ring around the cornea of the eye (in Wilson's disease), xanthoma, spider angiomas, clubbing of fingers, changes in the nailbed (Terry's nails, with two-thirds of the nailbed appearing white), Dupuytren's contracture, and asterixis. In men there may be decreased body hair, gynecomastia, and testicular atrophy.

Diagnostic Tests: The U.S. Preventative Services Task Force (USPSTF) recommends screening all adults 18 years and older for unhealthy alcohol intake (USPSTF et al., 2018). All adults should be screened yearly with a single question to elicit even a single episode of binge-drinking (five or more drinks a day for men, four or more for women) in the past year (Crabb et al., 2020). For any who answer yes, an assessment tool, such as the AUDIT (Alcohol Use Disorders Identification Test) (Saunders et al., 1993), AUDIT-C (first three questions of the AUDIT tool), or CAGE Questionnaire (Ewing, 1984), is recommended to evaluate for and diagnose alcohol use disorder (AUD), which can lead to alcoholic liver disease and cirrhosis (Crabb et al., 2020). It allows the practitioner to explore the patient's history of chronic alcohol use and the status of functional impairment.

In early or compensated cirrhosis, laboratory results may be normal; suspicion of liver injury may be aroused by elevated liver transaminases (aspartate transaminase/alanine transaminase [AST/ALT]) or abnormal imaging results (Smith et al., 2019). Other serologies alluding to possible cirrhosis include thrombocytopenia (typically with portal hypertension), elevated transaminases with an AST:ALT ratio greater than 1, elevated serum bilirubin, prolonged prothrombin time/International Normalized Ratio (PT/INR), and low serum albumin. For patients with whom there is suspicion of cirrhosis, other pertinent laboratory tests may help elicit specific etiology including viral hepatitis serologies (primarily for hepatitis B and hepatitis C); ferritin and transferrin saturation (for hemochromatosis); fasting lipid panel and hemoglobin A1c (Hg A1c) (for metabolic syndrome and NAFLD/NASH cirrhosis); antinuclear antibody, antismooth muscle antibody, and antimitochondrial antibody (for autoimmune cirrhosis); and ceruloplasmin (for Wilson's disease) (Smith et al., 2019).

In cirrhosis patients, a complete blood count (CBC) with indices may reveal anemia, which depends on etiology but is often multifactorial in nature, and may include chronic GI bleeding, alcohol toxicity, folate deficiency, anemia of chronic disease, splenomegaly, suppression of bone marrow, and hemolysis. Serum ammonia level is elevated in patients with hepatic encephalopathy resulting in confusion, disturbed sleep, and asterixis. The alpha-fetoprotein (AFP) level is elevated in patients with hepatitis C and is also a tumor marker for hepatocellular carcinoma (Marrero et al., 2018). Finally, certain biomarkers have been developed to help discern the degree of fibrosis and presence of cirrhosis, including the Fibrosis 4 score, Fibrotest/Fibrosure, NAFLD fibrosis score, and AST to platelet ratio index score; however, these are mostly validated in hepatitis C, except for the NAFLD fibrosis score, although they may still be helpful (Smith et al., 2019).

Abdominal ultrasound, a cost-effective option, can be ordered initially when cirrhosis is suspected to evaluate for findings suggestive of cirrhosis including surface nodularity, coarseness, increased parenchymal echogenicity of the liver; it can also be used for screening of cirrhosis sequelae including ascites, splenomegaly, portal hypertension, hepatocellular carcinoma (in conjunction with serum alfa-fetoprotein [AFP]), and portal vein thrombosis (with the addition of Doppler scanning (Marrero et al., 2018; Smith et al., 2019)). However, it should be noted that while ultrasonography has high sensitivity and specificity for detection of steatosis (94% and 84%, respectively), it is less effective at detecting fibrosis and cirrhosis (40% to 57% sensitive) (Smith et al., 2019). This is why liver biopsy, either percutaneous or transjugular, remains the gold standard for diagnosing liver cirrhosis (Smith et al., 2019). However, biopsy may still have a 20% rate of error in staging level of fibrosis and may also be unnecessary if clinical assessment, laboratory findings, and imaging results significantly suggest cirrhosis and biopsy would not alter patient management (Afdhal, 2003; Smith et al., 2019).

Differential Diagnosis:

- Liver cancer
- Alcoholic hepatitis
- Acute viral hepatitis
- Congenital hepatic fibrosis
- Idiopathic portal hypertension
- Idiopathic thrombocytopenia purpura (ITP)
- Ischemic hepatitis
- Schistosomiasis (O'Shea et al., 2010)

Treatment: The overall goal of treatment in cirrhosis is based on preventing liver decompensation, preventing cirrhosis complications, and preventing death (Smith et al., 2019). To prevent further hepatic insult, all patients with cirrhosis, regardless of etiology, should be counseled on complete abstinence of alcohol (Crabb et al., 2020; European Association for the Study of the Liver, 2018; Singal & Mathurin, 2021; Smith et al., 2019). Additionally, patients should also avoid or

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have dose-reduction with certain medications either due to hepatotoxicity or adverse effects that can affect cirrhosis management. These can include acetaminophen, NSAIDs, angiotensin-converting enzyme inhibitors, and systemic antifungals; whereas statins can cause elevated transaminases, they may be safely used (Chalasani et al., 2014; Smith et al., 2019). Some herbal medications and supplements have also been shown to be hepatotoxic, including germander, mistletoe, green tea extracts, echinacea, kava kava, camphor oil, black cohosh, saw palmetto, skullcap, valerian, aloe vera, vitamin A supplements, Herbalife products, Hydroxycut, and others (Bunchorntavakul & Reddy, 2013; Pittler & Ernst, 2003). A review of the patient's immunizations should be completed regularly to determine the need for influenza, hepatitis A and B, and pneumococcal pneumonia vaccines (Smith et al., 2019).

Nutritional therapy is of the essence because it has been estimated that as high as 75% to 90% of cirrhosis patients have malnutrition, which is more prevalent in advanced and decompensated disease, and more likely in alcohol-associated cirrhosis (Palmer et al., 2019). Poor nutrition has also been associated with cirrhosis complications such as ascites, hepatic encephalopathy, poorer liver function, and mortality. Because of this, it is recommended that all patients undergo assessment of body composition utilizing body mass index (BMI) and assessment for sarcopenia, lipopenia, and volume overload (Palmer et al., 2019). In cirrhotic patients, BMI needs to be adjusted, typically due to ascites and volume overload, although there is no validated way to do this; calculation with post-paracentesis weight may help (Tandon et al., 2016). The liver is the primary organ for the production and storage of many essential nutrients including glycogen/glucose, iron, proteins, vitamin A, vitamin D, vitamin B_{12} coagulation factors, hormones, cholesterol, ammonia, and others (Palmer et al., 2019). Malnutrition in cirrhotic patients often presents with loss of skeletal muscle and decreased muscle strength (which can be easily assessed with handgrip strength) (Palmer et al., 2019). In addition to sarcopenia, poor protein intake and synthesis results in low serum protein levels, decreased colloid pressure, and subsequently peripheral edema and ascites. Nutritional support as an attempt to counter sarcopenia, ascites/edema, and malnutrition should be multifactorial. Patients with cirrhosis (who are not obese) should consume 35 kcal/kg body weight per day and 1.2 to 1.5 g protein/kg body weight per day (European Association for the Study of the Liver, 2019). Specifically branch-chain amino acids (BCAAs, including valine, leucine, and iso-leucine) are plant-based amino acids needed for protein synthesis. Data shows that supplanting with oral BCAAs can reduce hepatic encephalopathy (Gluud et al., 2017); limited data show they may also possibly improve the patient's nutritional profile, prevent hospitalizations, and improve quality of life (Petta et al., 2010). Finally, consumption of a protein-rich late evening snack can help prevent protein breakdown during fasting state and has been shown to improve serum albumin levels, reduce AST/ALT, PT/INR, and ammonia levels and subsequently reduce recurrence of hepatic encephalopathy and ascites; however, the best composition of late evening snacks has not yet been determined (Chen et al., 2019; Palmer et al., 2019). Cirrhosis patients with ascites should have a 2,000 mg daily sodium restriction to help prevent edema and ascites (Smith et al., 2019). Multiple vitamin and mineral supplements should be prescribed, including adequate intake of vitamins A, D, E, and K, as well as B vitamins (if deficient), zinc, copper, and magnesium; avoid supplements with manganese because manganese levels are often high in patients with cirrhosis, and manganese can subsequently accumulate in the brain (Palmer et al., 2019). It is recommended, however, that a multiple vitamin without iron be used, unless iron-deficiency anemia is present (O'Shea et al., 2010).

Treatment for complications of cirrhosis may include antibiotics for infections such as spontaneous bacterial peritonitis (and possibly prophylactic antibiotics for recurrent episodes), diuretics if the patient has ascites or edema, and nonselective beta blockers for portal hypertension and variceal prophylaxis (European Association for the Study of the Liver, 2018; Smith et al., 2019). For hepatic encephalopathy treatment or prevention, lactulose and/or rifaximin are commonly used (Smith et al., 2019). Therapeutic paracentesis with albumin infusion may be needed for recurrent, especially large volume, ascites and eventually a transcutaneous intrahepatic portosystemic shunt (TIPS) may be necessary (European Association for the Study of the Liver, 2018; Smith et al., 2019). Guideline-based esophagogastroduodenoscopy (EGD) should be performed to screen for esophageal varices, especially in patients who cannot undergo nonselective beta blocker prophylaxis (Smith et al., 2019). Variceal banding can be utilized to prevent or treat variceal hemorrhage, which has been associated with a mortality rate near 15% (Cabrera et al., 2017).

Finally, as 80% of patients with hepatocellular carcinoma (HCC) are found to have pre-existing cirrhosis, all patients with cirrhosis should undergo HCC screening with liver ultrasound (Marrero et al., 2018). Serum AFP tumor marker is often added because it increases ultrasound sensitivity for HCC detection from 78% to 97% and from 45% to 63% in detection of early HCC and has a lower cost than computed tomography (CT) or magnetic resonance imaging (MRI) (Colli et al., 2006; Tzartzeva et al., 2018). However, any suspicious findings should be followed with CT or MRI for definitive diagnosis (Marrero et al., 2018).

Follow-Up: Surveillance of the older adult with cirrhosis depends on the stability of the patient and the presence of complications. Patients should be seen at least every 6 months to assess for problematic or worrisome signs or symptoms. Stable older adults should have repeat CBCs, complete metabolic profile, PT/INR, and liver ultrasound/AFP 6 months to 1 year after initial diagnosis, and then every 6 months thereafter to identify cirrhosis complications such as anemia, thrombocytopenia, coagulopathy, metabolic derangements, HCC, and others. Additionally, model for end-stage liver disease (MELD) and Child-Pugh scores should be calculated every 6 months on all cirrhosis patients (Smith et al., 2019). Unstable patients may need to be monitored more frequently.

Sequelae: Complications from decompensated cirrhosis commonly includes ascites, spontaneous bacterial peritonitis resulting from uncontrolled ascites, abdominal hernia from uncontrolled ascites, malnutrition, esophageal variceal bleeding, hepatocellular carcinoma (incidence from 1% to 8% per year depending on cirrhotic etiology), hepatic encephalopathy, portal hypertension (Marrero et al., 2018; Smith et al., 2019). Less common complications include

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hepatopulmonary syndrome, portopulmonary hypertension, renal failure, hepatorenal syndrome, cirrhotic cardiomyopathy, and relative adrenal insufficiency (European Association for the Study of the Liver, 2018). It should again be stressed that any cirrhotic patients who develop decompensated cirrhosis or complications should be referred to a specialist such as gastroenterology or hepatology (if available).

Alcoholic hepatitis may occur with cirrhosis with continued alcohol consumption and is generally defined as alcohol-related acute onset of symptomatic hepatitis. Severity is measured with calculation of the Maddrey discriminant function (DF), which is a score based on PT and serum bilirubin and can assess for mortality risk and guide treatment (Crabb et al., 2020; Singal et al., 2018; Singal & Mathurin, 2021). General management of these patients includes alcohol abstinence, fluid management, nutritional support, ulcer prophylaxis with proton-pump inhibitors (PPIs), and possibly glucocorticoids (Crabb et al., 2020; Singal et al., 2018). Patients with moderate to severe alcoholic hepatitis have 1-month mortality rates as high as 50% (Crabb et al., 2020). In severe alcoholic hepatitis (DF greater than or equal to 32), the use of nonselective beta blockers has been associated with increased risk of acute kidney injury and should therefore be discontinued (Sersté et al., 2015). Additionally, patients with severe alcoholic hepatitis should be trialed on prednisolone (40 mg/day orally), unless steroids are contraindicated, followed by calculation of the Lile score on day 7; the Lile score determines whether the patient is responding to steroids, of which 60% do (Crabb et al., 2020; Singal & Mathurin, 2021). A Lile score of 0.45 or less indicates response and improved mortality risk, and the prednisolone is continued for 28 days followed by a 2-week taper; if greater than 0.45 the patient is nonresponsive to steroids, has a poor prognosis, and steroids are subsequently discontinued (Crabb et al., 2020; Singal & Mathurin, 2021).

Prevention/Prophylaxis: Cessation of alcohol consumption is crucial to the prognosis of cirrhosis. Avoidance of hepatotoxic medications, especially NSAIDs, is recommended for patients with cirrhosis. All patients with cirrhosis should be given the hepatitis A and B vaccines unless they are shown to be already immune based on serological testing. The polyvalent pneumococcal vaccine and annual influenza vaccines also are recommended for these patients. Preventive strategies for patients with cirrhosis need to focus on the prevention of complications by instituting measures such as routine follow-up with laboratory testing and abdominal imaging, as well as endoscopic screenings for varices and variceal prophylaxis, unless contraindicated.

Referral: A gastroenterologist should be consulted when varices are suspected, and variceal bleeding occurs. An EGD is performed to manage complicated patients. Patients presenting with a new onset of ascites need to be referred for consideration of diagnostic paracentesis (European Association for the Study of the Liver, 2018; Smith et al., 2019). Referral to a hepatologist for patients with cirrhosis should be considered early on to plan management for complications and formulate plans for end-stage liver disease. Cirrhotic patients with a MELD score of 15, or any complication of decompensated cirrhosis should be referred to a liver transplant center for transplant evaluation; in the absence of significant comorbidities, age alone is not a contraindication for transplant and should not prevent the primary care practitioner from referring elderly patients for transplant evaluation (Martin et al., 2014; Smith et al., 2019).

Education: Instruct patients to eliminate all alcohol consumption. Recommend an alcohol treatment program and provide the telephone number for the nearest chapter of Alcoholics Anonymous. Patients should be requested not to self-medicate with over-the-counter (OTC) medications, including herbal products to prevent drug-induced liver injury. Patients with cirrhosis should eat small, frequent meals of a balanced diet containing 1.2 to 1.5 mg protein/kg body weight per day. Three to four cups of coffee daily, unless contraindicated for other reasons, has been shown to help prevent fibrosis progression in patients with NAFLD and hepatitis C as well as reduce risk of HCC in cirrhosis (Smith et al., 2019). Additionally, because of risk of fatal *Vibrio vulnificus* infection, patients with cirrhosis should be educated to avoid brackish/salt water and consumption of raw seafood (such as found in sushi) (Smith et al., 2019). Patients with encephalopathy should not be driving or operating complex machinery. For patients with end-stage liver disease, palliative care measures should be initiated.

Clinical Recommendation	Evidence Rating	References
Patients who have cirrhosis associated with a MELD score of 15 or greater or with complications of cirrhosis should be referred to a transplant center.	A	Martin et al., 2014
Patients with severe alcoholic hepatitis should be treated with corticosteroids, unless contraindicated.	A	Singal et al., 2018
Patients with a history of spontaneous bacterial peritonitis should be treated with prophylactic antibiotics.	A	Smith et al., 2019
All adults with cirrhosis should undergo hepatocellular carcinoma (HCC) surveillance to improve survival.	B	Marrero et al., 2018
Patients with a first episode of moderate ascites should be first treated with a mineralocorticoid receptor antagonist (spironolactone) 100 mg/day with stepwise increases to a maximum 400 mg/day.	A	European Association for the Study of the Liver, 2018

Continued

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Clinical Recommendation	Evidence Rating	References
For patients with ascites not responsive to spironolactone alone, furosemide 40 mg/day should be added to their diuresis regimen and increased stepwise to a maximum of 160 mg/day.	A	European Association for the Study of the Liver, 2018
Persistent hepatic encephalopathy should be treated with lactulose or rifaximin (Xifaxan).	B	Smith et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CLOSTRIDIOIDES DIFFICILE (FORMERLY KNOWN AS *CLOSTRIDIUM DIFFICILE*)

Signal Symptoms: Profuse, watery, malodorous diarrhea; abdominal discomfort; nausea; fever

Description: *Clostridioides difficile* infection (CDI) is a consequence of the colonization and subsequent infection of the colon by this organism following a disruption of the normal flora of the gut by antibiotic exposure (Solanki et al., 2021). Once established in the colon, *C. difficile* produces two potent toxins, Toxin A and Toxin B, that cause fluid secretion, inflammation, and injury to the colonic mucosa, resulting in diarrhea and/or colitis. Toxin A is responsible for increased intestinal permeability and fluid secretions, whereas Toxin B produces inflammation of the colon (Solanki et al., 2021). Due to increasing antibiotic usage, new and dangerous strains continue to emerge (Solanki et al., 2021). Intestinal colonization by *C. difficile* strains does not always result in infection or clinical symptoms, meaning some individuals may be asymptomatic carriers. An estimated 4% to 15% of adults who are otherwise healthy may be a carrier, with carriage also estimated to be 21% in those hospitalized and up to 30% in residents of long-term care (Kelly et al., 2021). Clinical presentation of *C. difficile* diarrhea varies from mild diarrhea as the only symptom to fulminant, life-threatening colitis.

Etiology: CDI is no longer only a hospital-acquired infection, with an estimated 51.9 episodes per 100,000 people in communities affected (Solanki et al., 2021). Risk factors include antibiotic exposure, older adults, and health-care facility exposure; however, the presence of inflammatory bowel disease, compromised immunity, liver and kidney disease, cardiac disease, chemotherapy, prolonged hospital stays, and prior gastrointestinal (GI) procedures also play a role in increasing the risk for CDI (Johnson et al., 2021; Kelly et al., 2021; Sams & Kennedy-Malone, 2017). Less-known risk factors include intensive care admission, prior hospitalization within several months, ventilatory support, enteral feedings, malnourished states, Caucasian race, and hypoalbuminemia (Kelly et al., 2021; Sams & Kennedy-Malone, 2017).

Bacterial spores are spread via the fecal-oral route and thrive on surfaces such as toilets, hospital equipment, and door handles (Sams & Kennedy-Malone, 2017). These spores have the potential to survive for months, even in harsh circumstances. Asymptomatic carriage of the organism by patients is not uncommon and may hinder adequate infection control measures. Patients who are admitted to the hospital and already asymptomatically colonized with this organism have six times risk of developing CDI (Kelly et al., 2021).

Occurrence: Data from 2011 reported an estimated 453,000 cases of CDI annually, with 14,000 deaths (Kelly et al., 2021). However, cases have decreased between 2011 and 2017, with long-term care facilities reporting 55% decrease in CDI incidences for years 2011 to 2015 (Kelly et al., 2021).

Recurrence is most commonly found in those older than 65, multiple and severe comorbidities, and exposure to antibiotic use following an infection (Dumic et al., 2019). Inflammatory bowel disease (IBD), prior organ transplants, end-stage renal and chronic kidney disease, and stem cell transplants have significantly increased risk of recurrent CDI (McDonald et al., 2018). PPI use has been associated with initial and recurrent CDI, but judicious use is appropriate if patients require proton-pump inhibitor (PPI) therapy according to appropriate indications (Kelly et al., 2021). Recurrence of CDI is defined by the presence of diarrhea and a positive stool test, usually occurring 2 to 8 weeks after treatment (McDonald et al., 2018). Different strains of the bacteria may be responsible for recurrent infection; however, recurrence more often is actually relapse of the recent infection (McDonald et al., 2018).

Age: Although the infection is difficult to manage in all ages, older adult patients can be particularly challenging to treat. Individuals aged 65 years and older have an increased risk for CDI along with severe disease manifestations (Dumic et al., 2019). Advancing age correlates with difficulty in successful treatment, while recurrence risk also increases with advancing age. The concern for decreased immunity in the older adult population is felt to contribute to complicated disease course (Dumic et al., 2019).

Gender: Females have been shown to have higher incidence rate of CDI than males (Solanki et al., 2021).

Ethnicity: CDI occurs in all ethnic groups, but Whites have been found to have higher incidence rates than other ethnicities (Kelly et al., 2021).

Contributing Factors: The main contributing factor to the development of CDI is antibiotic exposure. All antibiotics, including antibiotics used in treatment for CDI, have the potential to stimulate the development of CDI. Advancing

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age is a known risk factor. Due to age-related changes in the gut microbiota, older adults are at increased risk for severe presentation, and decreased functional status is independently known as a risk factor for poorer outcomes (Dumic et al., 2019).

Signs and Symptoms: The incubation period has been estimated anywhere from 2 to 3 days to approximately 1 week, but the exact incubation period is unknown (McDonald et al., 2018). Symptoms can appear immediately after beginning antibiotic therapy, or they may not develop until several weeks to months after completion of antibiotic therapy (McDonald et al., 2018). Older adults can present atypically, with lack of fever, and alteration in mental status or confusion can be an early sign (Sams & Kennedy-Malone, 2017).

CDI is classified as non-severe, severe, or fulminant. Non-severe CDI is characterized by white blood cell count 15 g/dL or less and creatinine less than 1.5 mg/dL (Johnson et al., 2021). Increasing leukocytosis or worsening renal function would be considered severe; fulminant process would include hypotension, shock, ileus, or megacolon (Johnson et al., 2021). High suspicion for megacolon or perforation should be raised if marked tenderness to palpation; toxin injury to the colon results in lost functionality and decreased/absent peristalsis (Sams & Kennedy-Malone, 2017). Sepsis secondary to bacteremia may occur, with mortality estimated from 4.5% to 16.7% for initial episode, whereas recurrent CDI has 33% increased risk of mortality (McDonald et al. 2018). Endoscopic evaluation via colonoscopy or flexible sigmoidoscopy may be undertaken when diagnosis is uncertain if patient does not clinically improve with standard therapies; however, endoscopy would be reserved on a case-by-case basis. The presence of adherent white and yellowish plaques that may coalesce, termed pseudomembranous colitis, are highly specific for *C. difficile* infection (Sams & Kennedy-Malone, 2017). However, the absence of pseudomembranous colitis does not exclude the presence of *C. difficile.*

Diagnostic Tests: Complete blood count and complete metabolic panel are useful for identifying leukocytosis, worsening renal function, and electrolyte abnormalities. Additional laboratory studies should include thyroid panel, lactic acid, stool cultures, and a two-step process for diagnosis of CDI. Computed tomography (CT) scan should be ordered if concerning abdominal examination or subjective symptoms to exclude megacolon or perforation. Stool testing is indicated in those with symptoms concerning for CDI, with three or more watery stools in a 24-hour period (Kelly et al., 2021). Stool testing should not be withheld if there are fewer than three watery stools in 24 hours, specifically if this is a high-risk individual for CDI. Diagnostic testing with stool samples should be a two-step process, whereby a test for glutamate dehydrogenase (GDH) or nucleic acid amplification testing (NAAT) is performed and, if positive, a toxin enzyme immunoassay (EIA) is performed (Kelly et al., 2021). Peri-rectal swabs for diagnosis of infection may also be used in the clinical scenario of paralytic ileus. If suspicion remains high for CDI despite negative testing, providers must use their best clinical judgment and treat appropriately.

Endoscopic evaluation via colonoscopy or flexible sigmoidoscopy may be indicated if persistent diarrhea and/or worsening clinical status occurs despite appropriate medical treatment. Diagnostic endoscopic evaluation is also helpful when the diagnosis is unclear, such as negative stool studies but persistent symptoms despite medical therapy.

Differential Diagnosis:

- Acute diarrhea caused by salmonella
- *Shigella*
- *Campylobacter jejuni*
- *E. coli* O157:H7
- *Cryptosporidium*
- *Giardia*
- *Microsporidia*
- *Isospora*
- *Cyclospora*
- Diarrhea associated with hyperthyroidism or diabetic neuropathy
- Irritable bowel syndrome
- Dietary causes, including nonabsorbable carbohydrates, caffeine, lactose intolerance, and gluten sensitivity
- Microscopic and collagenous colitis
- Pancreatic insufficiency
- Antibiotic-induced chemical effects
- Known antibiotic effects of bacterial and fungal overgrowth
- Food poisoning
- Bacterial or viral gastroenteritis
- Inflammatory bowel disease (IBD) (Kelly et al., 2021)

Treatment: Contact isolation must be employed for hospitalized individuals at first suspicion for CDI or known CDI (McDonald et al., 2018). Contact precautions should be continued until at least 48 hours after resolution of diarrhea; however, maintaining contact precautions while hospitalized can be continued if CDI rates are high in the area (McDonald et al., 2018). Patients with CDI in long-term care facilities should be in isolated rooms; however, if this is unavailable, patients should only be in a cohort with others who have the same organism (McDonald et al., 2018). Supportive measures to include oral and IV fluid replacement, low residue diet, and pharmacological therapy such as antiemetics are indicated. The offending antibiotic agent must be discontinued if clinically possible. A coexisting infection (e.g., urinary tract infection, pneumonia) would preclude complete discontinuation of all antibiotic therapy, as these conditions would still need treatment. Antidiarrheals and anti-motility agents have historically been avoided due to risk of megacolon, although further studies are needed to evaluate safety (McDonald et al., 2018).

Antibiotic treatment should be started empirically for those presenting with likely fulminant CDI instead of waiting on stool testing for confirmation; however, all other presentations need verification of positive CDI via testing so as to avoid unnecessary antibiotic therapy. Treatment of choice for initial non-severe and severe episodes is fidaxomicin 200 mg orally twice daily for 10 days (Johnson et al., 2021). If fidaxomicin is unavailable, vancomycin 125 mg orally four times a day for 10 days may be used; if neither are available, metronidazole 500 mg three times daily by mouth for 10 to 14 days may be used for non-severe episodes (Johnson et al., 2021). A fulminant presentation, which would be characterized by shock, ileus, hypotension, or megacolon, would require vancomycin 500 mg orally or nasogastric tube four times a day and IV metronidazole 500 mg three times a day (Johnson et al.,

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2021). If an ileus is present or the individual is unable to receive oral medications, vancomycin enemas would be indicated for direct topical therapy (Johnson et al., 2021; Kelly et al., 2021). Subsequent recurrences are treated similarly to initial recurrence, with the option of tapered/pulsed regimens of fidaxomicin or vancomycin (Johnson et al., 2021). If CDI recurrence within 6 months, adjunctive treatment using bezlotoxumab 10 mg/kg IV one-time dosing along with standard of care antibiotics is indicated; however, caution is advised, weighing risks and benefits in patients with history of congestive heart failure, if bezlotoxumab is to be used (Johnson et al., 2021). Fecal microbiota transplantation (FMT) should be offered after second recurrence of CDI (Johnson et al., 2021). FMT should also be considered in cases of severe or fulminant CDI, whereby antibiotic therapy has not been successful and/or patient is not an appropriate surgical candidate (Kelly et al., 2021).

Metronidazole and vancomycin are best absorbed via the oral route, but complicated clinical courses may require administration via other routes. Vancomycin is not highly effective intravenously, which leads to the need for colonic enemas. FMT should be delivered via colonoscopy or by oral capsules; enemas are reserved if no other methods available (Kelly et al., 2021).

PPI therapy does not have to be discontinued in patients with CDI, as long as benefits outweigh risks and there is an appropriate indication for PPI therapy (Kelly et al., 2021). Probiotic therapy is not indicated, as there is insufficient data to support their use in CDI prevention (McDonald et al., 2018). Surgical intervention may be indicated for those with fulminant CDI if an appropriate surgical candidate; total colectomy with end ileostomy or diverting loop ileostomy is performed if necessary. IBD patients with CDI should have minimum of 14 days antibiotic therapy, and FMT discussed in recurrent CDI (Kelly et al., 2021).

Follow-Up: The first month following treatment has been shown as crucial due to colonic flora disruption, raising concern for recurrence (McDonald et al., 2018). Risks of CDI continues for three months following prior antibiotic exposure (McDonald et al., 2018). Recurrence is identified as prior resolution with new onset diarrhea and a positive stool sample. Repeated stool testing during the same episode is not necessary, and stool testing to document a negative finding is not appropriate (McDonald et al., 2018). Those older than 65, immunocompromised, or with severe CDI on initial presentation are at highest risk for recurrence (Johnson et al., 2021). Therapeutic response should be based on clinical signs and symptoms, not repeat diagnostic testing.

Sequelae: Chronic colonization, paralytic ileus, toxic megacolon and fulminating colitis, chronic diarrhea, electrolyte imbalances, hypoalbuminemia, and reactive arthritis are complications of CDI.

Prevention/Prophylaxis: Infection control in health-care settings and reduction of risk factors are paramount. Contact isolation should be implemented without delay. Dedicated hospital equipment for the individual is necessary to prevent spread of infection. Proper hand washing is imperative. Equipment and rooms must be sanitized with bleach cleaning agents to kill spores, per facility protocol.

Referral: Signs and symptoms of ileus or fulminant disease, failure to respond to conventional therapy, and persistent diarrhea that is unexplained require referral. Inpatient older adults with signs of acute abdomen need a surgical referral. Gastroenterology consultation is recommended for bloody diarrhea, concern for secretory diarrhea, fecal incontinence, and failure to improve symptomatically with pharmacological therapy.

Education: Avoid unnecessary antibiotics. Universal precautions include utilizing hand washing with soap and water, along with bleach cleaning agents to sanitize all surfaces at home and in hospital settings. Do not use antidiarrheal agents. Continue PPI therapy if an appropriate indication exists for patient, and probiotic therapy is not recommended. Contact provider if recurrent diarrhea persists after treatment for CDI.

Clinical Recommendation	Evidence Rating	References
Antibiotic therapy for suspected fulminant *Clostridioides difficile* infection (CDI) should not be delayed if stool testing is still pending.	C	Johnson et al., 2021
Fidaxomicin is the drug of choice for initial non-severe episodes of CDI.	C	Johnson et al., 2021 Kelly et al., 2021
PPI use has been associated with initial and recurrent CDI, but judicious use is appropriate if patients require PPI therapy according to appropriate indications.	A	Kelly et al., 2021
The first month following treatment has been shown as crucial due to colonic flora disruption, raising concern for recurrence.	C	McDonald et al., 2018
FMT is indicated for second recurrences or in fulminant cases that do not respond to conventional treatment	C	Johnson et al., 2021 Kelly et al., 2021
Bezlotoxumab 10 mg/kg IV for one dose is recommended along with standard of care antibiotic therapy for those with first CDI recurrence, with caution advised if history of heart failure.	C	Johnson et al., 2021

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COLORECTAL CANCER

Signal Symptoms: A change in bowel habits, persistent diarrhea, bleeding from the rectum, blood in the stool, unexplained anemia, bloating, unexplained abdominal pain, increased gas, frequent abdominal distention and/or bloating, frequent abdominal cramps, vomiting, weight loss, fatigue, weakness, persistent constipation or feeling that the bowels do not completely empty or a feeling of needing to have a bowel movement that is not relieved by having one, rectal pressure, rectal pain, and/or reduction in diameter of stool (National Cancer Institute, 2020).

Description: About 70% of all cancers of the large intestine occur below the midpoint of the descending colon (descending 10%, sigmoid 10%, rectum 50%) (SEER, 2022). The sigmoid colon is the most common site for cancer of the colon. Rectal carcinoma is the most common cancer of the lower gastrointestinal (GI) tract (SEER, 2022). Most colorectal cancers appear to arise in polyps. The risk of cancer increases with the size of the polyp; 30% to 50% of polyps over 2 cm in size are malignant (SEER, 2022). Approximately 90% to 95% of large bowel tumors are adenocarcinomas (SEER, 2022). Gastrointestinal stromal tumors (GISTs) are rare neoplasms that represent approximately 1% to 2% of primary GI cancers (Ottaiano, et al., 2022). Leiomyosarcomas, melanomas, neuroendocrine tumors, and colorectal lymphomas are rare diagnoses (Ottaiano et al., 2022).

Etiology: Colorectal cancer results from complex interactions between inherited susceptibility and environmental factors, but the exact nature and contribution of these factors continues to be researched (National Cancer Institute, 2016). Lifestyle, genetic, and environmental factors have been associated with increased colorectal cancer risk. Increased consumption of red and processed meats is strongly associated with increased colorectal cancer risk, whereas high fruit/vegetable intake is inversely linked to colorectal cancer (Fan et al., 2017). Additional risk factors include smoking, excessive alcohol consumption, physical inactivity, and being overweight (Brenner & Chen, 2018).

Occurrence: Colorectal cancer is the third most common malignant neoplasm worldwide and the second leading cause of cancer deaths in men and women combined in the United States (Siegel et al., 2020). Worldwide, 916,000 deaths occurred in 2020 from colon and rectal cancer according to the World Health Organization (WHO, 2022). In 2022, an estimated 151,030 adults in the United States will be diagnosed with colorectal cancer. Specifically, it is predicted that there will be 106,180 new cases of colon cancer and 44,850 new cases of rectal cancer (Siegel et al., 2020). Although the majority of colorectal cancers are in adults aged 50 and older, 17,930 (12%) are diagnosed in individuals younger than age 50 (Cancer.org, 2020). Approximately 4.4% of men (1 in 23) and 4.1% of women (1 in 25) will be diagnosed with colorectal cancer in their lifetime. Lifetime risk is similar in men and women despite higher incidence rates in men because women have longer life expectancy (Siegel et al., 2020). Colorectal cancer incidence rates have been declining, largely attributable to the contribution of screening for prevention and early detection (Siegel et al., 2020)

Age: Although aging itself is a risk factor for the development of cancer, colorectal cancer incidence rates have been increasing since the mid-1980s in adults aged 20 to 39 years and since the mid-1990s in adults aged 40 to 59 years, with younger age-groups experiencing the steepest increase (Siegel et al., 2017). The median age of diagnosis has dropped from 72 years during 2001–2002 to 66 years during 2015–2016. The median age at colorectal cancer diagnosis is younger for rectal cancer (63 years) than for colon cancer (69 years) (Siegel et al., 2020).

Ethnicity: Colorectal cancer incidence and mortality are highest in non-Hispanic Blacks, followed closely by Native Americans and Alaskan Natives, and lowest in Asians/Pacific Islanders. During 2012–2016, colorectal cancer incidence rates in African Americans were about 20% higher than those in non-Hispanic Whites and 50% higher than those in Asians/Pacific Islanders. The disparity for mortality is twice that for incidence; colorectal cancer death rates in African Americans are almost 40% higher than those in non-Hispanic Whites and double those in Asians/Pacific Islanders (Cancer.org, 2020).

Contributing Factors: As previously discussed, lifestyle and dietary factors have been associated with the development of colorectal cancer. Additionally, there are hereditary risks. Lynch syndrome, a failure of cellular DNA repair genes that produces gene mutations, leads to an increased risk for colon cancers and other cancers (Sinicrope, 2018). Familial adenomatous polyposis is another genetic disorder in which the colon polyps and ultimately cancers can develop (Dinarvand et al., 2019). Genetic risk is suspected if someone is diagnosed with colon cancer at a much earlier age than is typical and/or has a strong family history of colon cancer that occurs at younger ages.

Signs and Symptoms: Clinical symptoms can include rectal pressure, passing bright red blood, constipation, bloating, diarrhea, weight loss, melenic stools, nausea, and loss of appetite. Patients presenting in the clinic with microcytic anemia should be evaluated for rectal bleeding and possible colorectal cancer.

Diagnostic Tests: According to U.S. Preventive Services Task Force USPSTF 2021 guidelines, colon cancer screening should begin at age 45 and continue through age 75 in individuals at average risk for colorectal cancer and with no personal or family history of colorectal cancer (U.S. Preventative Services Task Force [USPSTF] et al., 2021). Guidelines from the American College of Gastroenterology continue to screen for colorectal cancer for patients 50 and over but recommend screening for patients 45 years and older who are at average risk (de Kanter et al., 2022).

Individuals at moderate risk for developing colon cancer and/or with a personal or family history of colon cancer may need earlier or more frequent screening. People at high risk for colon cancer, such as those with Lynch's syndrome

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or polyposis syndromes (i.e., classic familial adenomatous polyposis [FAP]; attenuated FAP; MUTYH-associated polyposis [MAP]; Peutz-Jeghers' syndrome; juvenile polyposis syndrome; serrated polyposis syndrome) require enhanced colorectal surveillance and should be screened and monitored for other disorders as well, depending on the syndrome (Patel et al, 2022).

Several recommended colorectal cancer screening tests are available, and clinicians may consider many factors in deciding which test may be best for each person. Patient preference, screening method, preparation (e.g., bowel preparation), frequency of screening, location of screening, and follow-up procedures for abnormal findings may all play a role in determining which screening test is ultimately chosen. According to the USPSTF (USPSTF et al., 2021), recommended screening strategies include:

- High-sensitivity guaiac fecal occult blood test (HSgFOBT) or fecal immunochemical test (FIT) every year
- Stool DNA-FIT every 1 to 3 years
- Computed tomography (CT) colonography every 5 years
- Flexible sigmoidoscopy every 5 years
- Flexible sigmoidoscopy every 10 years + annual FIT
- Colonoscopy screening every 10 years

For patients aged 76 to 85, the decision to screen should be based on patient preferences, life expectancy, overall health, and prior screening history (Patel et al., 2022). The U.S. Multi-Society Task Force on Colorectal Cancer does not recommend routinely screening patients older than 85 years for colorectal cancer. It should be noted that patients at increased or high risk of colorectal cancer might need to start colorectal cancer screening before age 45, be screened more often, and/or get specific tests (Patel et. al., 2022).

A newer screening method, CT colonography or virtual colonoscopy, is a procedure that provides a computer-simulated endoluminal perspective of the air-filled distended colon. CT colonography requires a mechanical bowel preparation like that needed for barium enema because stool can simulate polyps (Biller & Scharg, 2021). Screening for colorectal cancer using a flexible sigmoidoscope is one of the few modalities that have been proven through randomized controlled trials to reduce colorectal cancer mortality and incidence (Biller & Scharg, 2021). Colonoscopy is the most accurate and versatile diagnostic test for colorectal cancer (Biller & Scharg, 2021). Colonoscopies can detect cancer and advanced lesions and are used for biopsy and diagnosis.

There is no diagnostic role for other routine laboratory tests in the diagnosis of colorectal cancer (Biller & Scharg, 2021). However, the advanced practice provider may see additional laboratory tests ordered for routine monitoring. These may include:

- *Complete blood count (CBC) with differential:* It should be noted that although colorectal cancer is often associated with iron-deficiency anemia, its absence does not reliably exclude the disease.
- *Comprehensive metabolic panel (CMP):* It should be noted that liver function tests lack sensitivity for detection of liver metastases.
- Tumor markers: Serum markers that have been associated with colorectal cancer include carcinoembryonic antigen (CEA) and CA 19-9. However, all these markers have a low diagnostic ability to detect primary colorectal cancer due to significant overlap with benign disease and low sensitivity for early-stage disease (Biller & Schrage, 2021). Neither serum CEA nor any other marker should be used as a screening or diagnostic test for colorectal cancer. However, CEA levels have value in the prognosis and follow-up of patients with diagnosed colorectal cancer (Biller & Schrage, 2021).

Radiological tests for staging include chest, abdomen, and pelvic CT either before or after resection (Biller & Schrage, 2021). A meta-analysis concluded that magnetic resonance imaging (MRI) is the preferred first-line imaging study for evaluating colorectal cancer liver metastases in patients who have not previously undergone therapy. In current practice, liver MRI is generally reserved for patients who have suspicious but not definitive findings on CT scan, particularly if better definition of hepatic disease burden is needed in order to make decisions about potential hepatic resection (Biller & Schrage, 2021). Positron emission tomography (PET) scans can be used as an adjunct to other imaging modalities for purposes such as evaluating patients who are thought to be present or future candidates for resection of isolated colorectal cancer liver metastases and localizing sites of disease recurrence (Biller & Schrage, 2021).

Differential Diagnosis:

- Diverticulitis
- Weight loss
- Blood in the stool
- Mass in the colon
- Prostatic carcinoma
- Sarcoma
- Inflammatory bowel disease
- Hemorrhoids
- Benign colonic polyps
- Peptic ulcer disease (PUD)
- Functional bowel disorders
- Infection
- Kaposi's sarcoma (KS)
- GISTs
- Lymphomas
- Carcinoid (well-differentiated neuroendocrine) tumors

Staging and Treatment: The Tumor, Node, Metastasis (TNM) staging system of the combined American Joint Committee on Cancer (AJCC)/Union for International Cancer Control (UICC) is the preferred staging system for colorectal cancer (Vogel et al., 2017). Patients should be referred to a surgeon for consideration of resection. Presence of metastatic disease does not rule out surgery. Radiographic, endoscopic (including biopsy), and intraoperative findings can be used to assign a clinical stage, whereas assessment of the pathological stage (termed pT, pN, pM) requires histological examination of the resection specimen (Vogel et al., 2017). The extent of treatment for colorectal cancer depends on how invasive the cancer is in the colon and surrounding

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sites, and the condition of the patient at the time of diagnosis. Surgery for colon cancer (including laparoscopic resection) should not be denied simply based on age. A comprehensive geriatric assessment may be useful in formulating an appropriate, individualized treatment plan for the older adult patient (Dolin et al., 2021). For patients with stages I–III disease, the standard of care is surgical resection followed by adjuvant therapy where appropriate (Brown & Koh, 2020).

Follow-Up: During and after treatment for colorectal cancer, oncology follow-up is essential. This may include serial imaging and laboratory testing depending on the cancer stage, treatment pursued, and progression of disease, among other patient specific factors. Primary care providers (PCPs) play an important role across the cancer continuum, from encouraging screening and accurate diagnosis to providing care during and after treatment for cancer and any comorbid conditions (Triantafillidis et al., 2017). PCPs should closely monitor for symptoms such as fatigue, weight loss, and change in bowel habits. Annual physical examinations are encouraged. Additional, PCPs can be instrumental in providing the patient, family, and caregiver support that is essential along the cancer trajectory.

Sequelae: The consequences of colorectal cancer can be broad and include complications such as obstruction, perforation, and possible need for colostomy, to loss of function, independence, and psychological distress. Bowel adhesions and chronic pain may also be a complication. Post-resection recurrence of colorectal cancer is common. According to an article by Brown and Koh (2020), locoregional recurrence occurs in 4% to 11.5% of patients following treatment of primary colon cancer with curative intent. For those who have had radiation directed at their rectum or at areas around their rectum, radiation proctitis with burning and diarrhea may occur. The liver and bone are two sites known for metastasis after colorectal cancer.

Prevention/Prophylaxis: The ACS recommends starting screening at age 45 for those patients at average risk. This can be done either with a sensitive test that looks for signs of cancer in the stool or with an examination that looks at the colon and rectum (ACG, 2021). For stool-based tests, clinicians should educate patients that these tests require an annual commitment. The gold standard for screening is delineated in Table 13-1. The results of epidemiological studies regarding the relationship between calcium intake and colorectal cancer risk have not always been consistent. A 2018 study looking at vitamin D and colorectal cancer found that higher circulating 25-hydroxyvitamin D was related to a statistically significant, substantially lower colorectal cancer risk in women and non-statistically significant lower risk in men (McCullough et al., 2019). As previously stated, avoiding smoking, physical activity and maintaining a healthy weight, and a diet high in fruits, vegetables, and whole grains has been shown to lower risk of colorectal cancer.

Referral: A gastroenterologist should be consulted for colonoscopy and biopsies can be done during the procedure if needed. A consultation with a surgical oncologist, usually found at a major medical centers, is advised. A team including a radiologist, oncologist, cancer surgeon, advanced practice provider (nurse practitioner [NP] and/or physician assistant [PA]), nutritionist, pharmacist, and nurse will develop a plan of care individualized to the patient and type of cancer. Ultimately the patient (and/or family caregiver where applicable) will decide the best course of action. Palliative care may be an appropriate choice.

Education: Teach older adults about the importance of monitoring for signs of colorectal cancer and to report any change in bowel habits. Primary care providers (PCPs) should discuss available screening options with patients.

TABLE 13-1 United States Multi-Society Task Force Guidelines for Colonoscopy Surveillance Post-polypectomy

TYPE OF POLYP	NUMBER OF POLYPS	RECOMMENDED FOLLOW-UP
Adenoma ≥10 mm	Piecemeal resection	6 mo, then 1 yr, then 3 yr
Adenoma	>10	1 yr. Consider genetic testing
Adenoma ≥10 mm	1–10	3 yr
Adenoma with villous component	1–10	
Adenoma with high-grade dysplasia	1–10	
Adenoma <10 mm	5–10	3 yr
	3–4	3–5 yr
	1–2	7–10 yr
Sessile serrated polyps (SSPs) <10 mm	5–10	3 yr
	3–4	3–5 yr
	1–2	5–10 yr
SSP ≥10 mm or SSP with dysplasia	Any number	3 yr
Traditional serrated adenoma	Any number	3 yr
Hyperplastic polyp ≥10 mm	Any number	3–5 yr
Hyperplastic polyps <10 mm	<20	10 yr

Data from Gupta, S., Lieberman, D., Anderson, J. C., Burke, C. A., Dominitz, J. A., Kaltenbach, T., Robertson, D. J., Shaukat, A., Syngal, S., & Rex, D. K. (2020). Recommendations for follow-up after colonoscopy and polypectomy: A Consensus update by the US Multi-Society Task Force on Colorectal Cancer. Gastroenterology, 158*(4), 1131–1153.e5. https://doi.org/10.1053/j.gastro.2019.10.026 and*

Abu-Freha, N., Katz, L. H., Kariv, R., Vainer, E., Laish, I., Gluck, N., Half, E. E., & Levi, Z. (2021). Post-polypectomy surveillance colonoscopy: Comparison of the updated guidelines. United European Gastroenterology Journal, *9(6), 681–687. https://doi.org/10.1002/ueg2.12106.*

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Clinical Recommendation	Evidence Rating	References
The USPSTF recommends colorectal cancer screening for all adults aged 50 years and continuing until age 75 years.	A	USPSTF, 2021
The USPSTF recommends screening for colorectal cancer in adults aged 45 to 49 years.	B	USPSTF, 2021
The USPSTF recommends that clinicians selectively offer screening for colorectal cancer in adults aged 76 to 85 years. Evidence indicates that the net benefit of screening all persons in this age-group is small. In determining whether this service is appropriate in individual cases, patients and clinicians should consider the patient's overall health, prior screening history, and preferences.	C	USPSTF, 2021
Recommend colorectal cancer screening in average-risk individuals between 50 and 75 years old to reduce the incidence of advanced adenoma, colorectal cancer, and mortality from colorectal cancer.	A	Shaukat et al., 2021
Achieving and maintaining a healthy body weight throughout life, being physically active, following healthy eating patterns at all ages, and avoiding alcohol are recommended by the American Cancer Society as part of the guidelines on diet and physical activity for cancer prevention.	A	Rock et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CONSTIPATION

Description: Constipation is broadly defined as bowel disturbances including reduced defecatory frequency, hard stools, significant straining, incomplete evacuation, and others (Bharucha & Wald, 2019; Forootan et al., 2018; Jani & Marsicano, 2018; Mounsey et al., 2015). Constipation ranks in the top five for most common gastrointestinal (GI) disorders diagnosed by physicians, results in 8 million annual referrals to gastroenterology, and poses an economic burden at $230 million annually (Bharucha & Wald, 2019; Jani & Marsicano, 2018).

Etiology: Colonic motility depends on the integrity of nervous system impulses, circular smooth muscle tone, and motor complexes stimulated by increasing intraluminal pressure generated by bulk. Any pathophysiological process that interferes with this process can cause constipation. Primary constipation includes slow transit constipation (possibly due to motor dysfunction, inadequate food intake, or alterations of the gut microbiome), normal transit constipation (such as irritable bowel syndrome constipation type, IBS-C), and defecatory disorders (resistance to evacuation or inadequate propulsion such as in dyssynergia, obstruction, rectal hyposensitivity, and structural abnormalities like rectoceles) (Bharucha & Wald, 2019). Secondary constipation is caused by any of a number of issues such as dehydration, inadequate fiber intake, metabolic diseases (diabetes, hypothyroidism, hypercalcemia), medications (including opioid-induced constipation, anticholinergics, and antidepressants), neurological disorders (such as dementia, Parkinson's disease, and multiple sclerosis), myopathic disorders (such as scleroderma), and structural issues (such as colon cancer or strictures) (Jani & Marsicano, 2018).

Occurrence: The prevalence of chronic constipation is 15% to 16% of the general population and higher in older adults (Bharucha & Wald, 2019; Jani & Marsicano, 2018).

Age: Constipation is more common in older adults with a prevalence of 33.5% compared to 16% in the general population (Bharucha & Wald, 2019). Older adults residing in long-term care facilities have a greater prevalence of constipation of around 50%, although it has been described as high as 80% (Lucak et al., 2021). The increase in older adults is likely multifactorial in etiology, including various physiological changes, lifestyle changes, increased medication burden and polypharmacy, and increased chronic disease burden (Lucak et al., 2021). At all ages, constipation is reported more frequently in women with a prevalence ratio of 1.5:1 in women compared to men. Additionally, women utilize laxatives and seek care for their constipation more frequently than men (Bharucha & Wald, 2019).

Ethnicity: Constipation tends to be more common in non-Whites (Bharucha & Wald, 2019).

Contributing Factors: There are multiple factors that can contribute to constipation (Bharucha & Wald, 2019; Forootan et al., 2018; Jani & Marsicano, 2018; Lucak et al., 2021). Medications that may contribute to constipation include analgesics (NSAIDs and opioids), antihypertensives (calcium channel blockers, clonidine), calcium supplements, narcotics, iron supplements, aluminum- and calcium-containing antacids, anti-Parkinson drugs, bile-binding medications (cholestyramine), and any drug that has anticholinergic side effects (Forootan et al., 2018; Jani & Marsicano, 2018; Lucak et al., 2021). Certain types of laxatives also may be constipating, such as stimulant laxatives (especially when overused), which may cause cathartic colon and laxative dependency, and bulk laxatives taken with insufficient fluids. Other potential causes include neurological disorders, such as Parkinson's disease, stroke, spinal cord disorders, dementia, and depression; metabolic factors such as hypokalemia, hypercalcemia, and

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chronic renal insufficiency; and institutionalization (including nursing home placement) (Forootan et al., 2018; Lucak et al., 2021). Finally, some identified risk factors include lower socioeconomic status, lower education, less physical activity, stress, and physical and/or sexual abuse (Bharucha & Wald, 2019).

Signs and Symptoms: The first part of an assessment should include the use of a tool to determine the person's normal pattern of bowel function. The most common tool is the Bristol Stool Chart, which classifies stools as hard to pass, ideal consistency, or difficult to control. Descriptions and pictures make it easy for patients to identify the type of stool. It is also helpful to include a food diary to determine dietary sources of the problem, including water and fiber intake. Other considerations are mobility, which affects bowel transit and also impacts ability to easily get on and off the toilet; duration of symptoms (age of onset); whether onset was gradual or sudden; proper environment for defecation; underlying medical conditions; history of abuse; associated symptoms; medications, including over-the-counter (OTC) and herbal supplements; and remedies already tried for relief (Bharucha & Wald, 2019; Jani & Marsicano, 2018; Lucak et al., 2021).

A thorough abdominal and rectal examination is necessary to rule out physical abnormalities and any warning signs, and then the data is compiled (Bharucha & Wald, 2019; Jani & Marsicano, 2018). The ROME IV diagnostic criteria are helpful in confirming the diagnosis of constipation, which must include two or more of the following six criteria:

- Fewer than three bowel movements in a week
- Straining at least at 25% of defecations
- Lumpy or hard stools in at least 25% of defecations
- Sensation of incomplete evacuation for at least 25% of defecations
- Sensation of anorectal obstruction/blockage for at least 25% of defecations
- Manual maneuvers to facilitate at least 25% of defecations (digital evacuation, support of the pelvic floor) (Jani & Marsicano, 2018)

Diagnostic Tests: All individuals should have a fecal occult blood test at the initial visit of a complaint of constipation. Additional diagnostic tests should be done if they can inform contributing causes or alter the treatment. Laboratory tests should include a complete blood count (CBC) but then be individualized for each patient based on their history and physical. Testing may include complete glucose, thyroid-stimulating hormone, electrolytes (including calcium), blood urea nitrogen (BUN), creatinine. A digital rectal examination can elicit structural abnormalities as well as anal tone and sequela of constipation such as fissures, rectal pain, and hemorrhoids. An abdominal radiograph may help to determine the extent and distribution of feces. Sigmoidoscopy or barium enema or both may be indicated in patients with a recent onset of constipation when a lesion is suspected or to evaluate for anatomic abnormalities. Other tests include balloon expulsion testing with manometry to check for dyssynergy; colonic transit study to diagnose slow transit constipation; barium defecography or pelvic magnetic resonance imaging (MRI) defecography to evaluate pelvic floor function and evaluate for abnormal structural problems such as prolapse, rectoceles, and enteroceles that can affect constipation. A colonoscopy should be done if the patient presents with alarm symptoms, anemia, or positive fecal occult blood (Bharucha & Wald, 2019; Lucak et al., 2021).

Differential Diagnosis: Because the diagnosis of constipation is very subjective and often a symptom of other issues, evaluation should focus on etiology and contributing causes to rule out potentially more insidious issues such as obstruction, fecal impaction, irritable bowel syndrome, structural defects, diverticular disease, and colorectal cancer (Jani & Marsicano, 2018; Lucak et al., 2021).

Treatment: After the specific etiology is established and factors contributing to constipation are identified, the appropriate pharmacological and nonpharmacological interventions are initiated. The primary aim of treatment is for the patient to have regular, predictable, and comfortable bowel movements. Ideally, this should be accomplished with diet and lifestyle changes such as fiber, water, and exercise. Adults should eat 20 to 35 g of fiber per day. Insoluble fiber found in whole wheat, whole grains, vegetables, and wheat bran is the best choice. An increase in fiber intake should be done over several weeks to prevent adverse effects like bloating, flatulence, and abdominal cramping. An adequate fluid intake of 1.5 to 2 L/day is also important and shown to improve frequency of stools, although may not be possible in patients with chronic diseases such as heart failure and kidney disease who may be on fluid restrictions. Fruits and fruit juices, especially prune and apricot which are high in sorbitol, are an alternative for those who cannot increase the fiber intake. It may take up to 4 weeks for the fiber and water effects to be noted, so the patient may need laxatives in the interim. Finally, timed toileting may be especially helpful in patients who have declining cognitive function (Bharucha & Wald, 2019; Forootan et al., 2018; Jani & Marsicano, 2018; Lucak et al., 2021).

Pharmacological treatments are recommended when diet and lifestyle changes are not sufficient. The recommendation is to start with bulk-forming agents and soluble fiber supplements. Psyllium or polycarbophil are commonly recommended, but they require increased fluid intake, which may not be appropriate for some older adults with heart and kidney disease. There are also multiple OTC soluble fiber supplement options available. Patients who fail to respond should be trialed on osmotic agents, such as polyethylene glycol (PEG), magnesium citrate-based laxatives (magnesium citrate), and nonabsorbable carbohydrates (lactulose), as a second-line treatment; use caution with some of these agents in older adults because they can cause electrolyte changes. Stimulant laxatives, such as senna, cascara, or bisacodyl, increase peristalsis and mucus production, and are generally safe as rescue agents or even more regular use (Bharucha & Wald, 2019). Stool softeners are often prescribed for older adults. These are not laxatives and may contribute to constipation, "the mush without the push." Discontinuing inappropriately prescribed stool softeners is an option for medication reduction in polypharmacy (Bharucha & Wald, 2019; Jani & Marsicano, 2018; Lucak et al., 2021).

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Newer prescription agents can be considered, and selection should be based on the presenting symptoms, the nature of the complaint, the side effects, speed of action, and patient acceptability. For treatment of either chronic constipation or IBS-C options include glucocorticoid (GC) receptor agonists (plecanatide, linaclotide), chloride channel activator (lubiprostone), and serotonin (5-HT4) receptor agonist (prucalopride). For opioid-induced constipation (OIC), consider use of peripherally acting μ-opioid receptor agonists (naloxegol, naldemedine, and methylnaltrexone) (Bharucha & Wald, 2019; Lucak et al., 2021).

Finally, there are additional nonpharmacological treatments for select patients. Those with pelvic floor dysfunction, defecatory disorders, or dyssynergy who do not respond to other treatment options may benefit from biofeedback therapy to retrain pelvic floor muscles and improve colonic transit and symptoms. This approach has been shown to improve colonic transit time in approximately 65% of patients with defecation disorder (Chiarioni et al., 2005). This may be especially useful in older adults with limited medication options. Finally, surgery is a treatment of last resort for patients with refractory symptoms, who do not have global gut hypomotility or defecation dysfunction. This is accomplished with an abdominal colectomy with ileorectal anastomosis. Careful consideration should be given in older adults who may have higher surgical risk (Bharucha & Wald, 2019; Lucak et al., 2021).

Follow-Up: Chronically constipated individuals often need to have combined nonpharmacological with regular or periodic pharmacological intervention. When laxatives are prescribed, these individuals should be reevaluated every 3 months for the side effects and the responses to treatment as well as any new warning signs or symptoms (Bardsley, 2015; Jani & Marsicano, 2018; Lucak et al., 2021).

Sequelae: Constipation, although uncomfortable, is rarely life threatening. When associated with pain, distention, or vomiting, constipation may be a sign of a life-threatening mesenteric infarction or a partial or complete bowel obstruction. Straining in older adults may have serious effects on the cerebral, coronary, and peripheral arterial circulation. If stool is not eliminated from the colon and the patient becomes dehydrated, stool may harden, resulting in fecal impaction, a large mass of compacted feces at the intestinal level that cannot be evacuated spontaneously. It has been estimated that 7% of long-term residents suffer from impactions yearly (Falcón et al., 2016). Also, although worrisome for many patients, colon cancer occurs very infrequently in chronically constipated patients (Bharucha & Wald, 2019).

Prevention/Prophylaxis: Adequate dietary fluid and fiber and regular exercise habits help to promote colonic mobility. Bowel elimination patterns should be monitored regularly in individuals who are unable to report bowel habits or bowel discomfort.

Referral: Hospitalization may be necessary in some cases of severe constipation and/or impaction, anorexia, dehydration, or nausea or vomiting. In fact, constipation results in approximately 92,000 hospitalizations a year (Morley, 2007). Patients with recent-onset constipation associated with bleeding, anemia, or family history of colon cancer; patients with chronic constipation with anemia, abdominal pain, and weight loss; and patients with recent-onset fecal incontinence should be referred to a gastroenterologist. Referral to a specialist also should be considered when there is a failure to alleviate constipation despite escalating attempts (Roque & Bouras, 2015).

Education: In addition to giving instruction in the dietary measures appropriate in preventing constipation, encourage older patients to maintain regular bowel habits and respond to the urge to defecate rather than suppress it. Patients should be encouraged to keep a dietary journal for a week to understand their diet habits that may need adjustment. Patients should also be educated on the role of regular exercise/movement in preventing constipation. Patient education regarding diet and exercise is challenging when patients have cognitive impairments, mood disorders, uncontrolled pain, or significant muscle weakness. Patients should be taught to take advantage of the gastrocolic reflex, which is strongest about 30 minutes after meal consumption and may be assisted at breakfast time by consuming a hot beverage. Trial of a small stool under the feet during defecation may help ease stool passage. Stooling time should be around 3 to 5 minutes, and not more than 10 minutes, to help prevent sequela such as hemorrhoids. All individuals should avoid the excessive use of laxatives as well as OTC medications known to have constipating side effects (Bardsley, 2015; Lucak et al., 2021; Mounsey et al., 2015).

Clinical Recommendation	Evidence Rating	References
The prevalence of constipation increases with age.	A	Serra et al., 2020
Patients with red flags for malignancy or complicated disease should have a colonoscopy.	A	American Gastroenterological Association et al., 2013
Polyethylene glycol (PEG) is preferred over lactulose for the treatment of constipation because it is more effective and has fewer adverse effects.	B	Mounsey et al., 2015
Peripherally acting μ-opioid receptor agonists (PAMORA) have prokinetic properties by reversing the inhibitory effects of μ-opioid analgesics on gastrointestinal motility and are effective in the management of opioid-induced constipation.	A	Serra et al., 2020

Continued

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Clinical Recommendation	Evidence Rating	References
The GC receptor agonist linaclotide and chloride channel activator lubiprostone are both effective and safe in the management of chronic constipation and irritable bowel syndrome constipation.	A	Serra et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

DIVERTICULITIS

Signal Symptoms: Impaired cognitive status, lower quadrant pain, fever.

Description: Diverticulitis is an inflammatory condition that involves perforation of one or more colonic diverticula, which are herniations of the mucosa through the muscularis of the colon, usually occurring in the sigmoid or descending colon. Less commonly, right-sided colon diverticulitis may occur. Small bowel diverticulitis may also occur but is rare. Inflammation of the diverticulum begins at the apex when the narrow opening of the lumen is exposed to fecal residue. Mucosal erosion within the diverticulum also can occur, leading to diverticulitis.

Etiology: Diverticula are common in older adults. Age-related changes in the elastic matrix of the colon and the resulting sluggish fecal mass are thought to cause increased intraluminal pressure of the colon (Dumic et al., 2019). Diverticular disease is rare in societies that consume high-fiber diets. It is thought that a low-fiber diet produces less bulky stool and increased intracolonic pressure (Hanna & Kaiser, 2021). Diverticulitis is thought to develop when one or more diverticula are perforated (macroperforation or microperforation). Because this perforation is usually a localized process, free intraperitoneal air or diffuse peritoneal signs are usually not evident; their presence would indicate a more severe case and the possible need for surgical consultation. A pseudodiverticulum occurs when only the mucosa and submucosa of the colon are affected, such as in small bowel diverticulitis (Rangan & Lamont, 2020). Approximately 90% of all cases of diverticulitis involve the left colon and sigmoid (Dumic et al., 2019).

Occurrence: An estimated 70% of older adults develop diverticulosis by age 80 years (Dumic et al., 2019). Diverticulitis occurs more commonly in older women versus older men and younger males versus younger females (Hannah & Kaiser, 2021). Historically, development of diverticulitis in those with diverticulosis was felt to be approximately 10% to 25%; however, now estimates are lower ranging from 1% to less than 5% (Hanna & Kaiser, 2021).

Age: Diverticulitis is found most commonly in older adults aged 60 to 80 (Wan & Krisko, 2021).

Ethnicity: Diverticulitis confined to sigmoid and left colon is found more commonly in Westernized countries or populations that have begun to consume a refined Western diet; people of Asian descent are more likely to have right-sided diverticulitis (Dumic et al., 2019).

Contributing Factors: Although there are patients who may not have been diagnosed with diverticulosis prior to an acute case of diverticulitis, it is important for the nurse practitioner to recognize known risk for developing diverticulosis. Obesity, as well as sedentary lifestyle, has been found to contribute to diverticular disease. Advancing age is the primary nonmodifiable risk factor for developing diverticulitis (Dumic et al., 2019). Chronic constipation leading to colonic wall weakness raises intraluminal pressure (Hannah & Kaiser, 2021). Long-term use of NSAIDs, aspirin, antiplatelets, steroids, opioids, immunosuppressant drugs, and cigarette smoking increases the incidence of diverticulitis (Dumic et al., 2019; Hanna & Kaiser, 2021).

Signs and Symptoms: Clinical presentation of diverticulitis in an older adult may be suppressed despite the presence of severe disease. Mental confusion may be the first overt indication of diverticulitis in older adults with known diverticular disease. Most common grouping of signs and symptoms include escalating abdominal pain, fever, and elevated inflammatory markers (such as white blood cell [WBC] count and C-reactive protein [CRP]) (Hanna & Kaiser, 2021). Pain may be colicky in nature and reported in the flank, back, or right side of the abdomen. Patients may describe the pain as dull, aching, and intermittent. Patients may experience abdominal or perirectal fullness. If the bowel is inflamed adjacent to the bladder, the presentation may mimic a urinary tract infection, especially if the patient reports dysuria. Acutely ill patients with a moderate-to-severe episode of diverticulitis may present with lethargy, reflecting signs of fluid depletion and sepsis.

Bowel sounds may be normal in mild disease; however, bowel sounds become hypoactive until there is an obstruction, when a tinkling sound may be heard. Hyperresonance may reflect intestinal obstruction. Localized tenderness is usually present in the left lower quadrant. Rebound tenderness, involuntary rigidity, and guarding are signs of peritonitis. Bleeding and evidence of chronic anemia are not typically associated with diverticulitis, raising concern for underlying occult malignancy (Hanna & Kaiser, 2021).

Diagnostic Tests: A CBC, complete metabolic panel (CMP), amylase, lipase, urinalysis, CRP, sedimentation rate can initially be ordered (Wan & Krisko, 2021). A computed tomography (CT) scan is the best imaging modality with sensitivity of 93% to 97% and specificity near 100% for diagnosing diverticulitis and severity (Hanna & Kaiser, 2021). Normal

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amylase and lipase will help distinguish diverticulitis from other causes of acute abdominal pain. Urinalysis may reveal sterile pyuria due to adjacent colonic irritation; however, if mixed colonic flora are present, consider the presence of a colovesical fistula (Hanna & Kaiser, 2021). Endoscopic measures during acute episodes of diverticulitis are avoided due to risk of perforation.

Differential Diagnosis:

- Acute appendicitis—suspect if right lower quadrant symptoms or nonresolution with medical therapy
- Inflammatory bowel disease (Crohn's disease)
- Complicated peptic ulcer disease (PUD)—suspect if pneumoperitoneum or peritonitis
- Ischemic colitis—suspect if high-risk patient, bloody diarrhea, elevated lactic acid
- Pseudomembranous colitis—suspect if antibiotic use or diarrhea
- Vascular ectasia—consider leaking abdominal aortic aneurysm
- Carcinoma of the colon—suspect if weight loss or bleeding
- Urological disorders, such as infection or ureteric colic
- Gynecological carcinomas or abscesses
- Pelvic inflammatory disease
- Infectious colitis
- Small bowel obstruction
- Endometriosis
- Ovarian cyst
- Testicular torsion
- Gastroenteritis
- Bowel obstruction
- Irritable bowel syndrome
- Kidney stone (Hanna & Kaiser, 2021)

Treatment: Diverticulitis is found to be polymicrobial and results from bacteria normally found in the gastrointestinal (GI) tract; the selection of antibiotics for the treatment of diverticulitis needs to consider the most common bacteria found in the colon, which are gram-negative aerobic rods and anaerobic microorganisms (Hall et al., 2020). If diverticulitis is deemed uncomplicated, outpatient treatment consists of oral antibiotics that cover gram-negative organisms for 7 to 10 days. Options include ciprofloxacin and metronidazole, levofloxacin and metronidazole, trimethoprim-sulfamethoxazole and metronidazole, amoxicillin-clavulanate, and moxifloxacin (Hall et al., 2020). Inpatient treatment of diverticulitis is indicated if complicated presentation, older age with multiple comorbidities, sepsis, and failing a trial of outpatient management. Inpatient treatment consists of IV antibiotics for 3 to 5 days, transitioning to oral therapy to complete a total of 10 to 14 days (Hall et al., 2020). Additional supportive measures include IV fluids, pain control, and antiemetic therapy. Patients should be nothing by mouth (NPO) until pain improved, advancing diet slowly. Imaging should be repeated if no improvement in 48 to 72 hours (Hall et al., 2020). Percutaneous drainage may be necessary if large abscess. Before recommending outpatient treatment, ensure that there is a reliable support system available. Antibiotics may need to be adjusted if blood or fluid cultures obtained with specific organisms.

Follow-Up: Older adults with mild cases treated at home with prescribed therapy should expect improvement by the third day. If, however, patients are not able to tolerate fluids and/or fail to respond to antibiotics and pain control, refer for hospitalization. Hospitalized patients require daily monitoring for persistent signs and symptoms of diverticulitis, laboratory values, and response to treatment. Recurrence after diverticulitis episode is dependent on the initial severity of episode, ranging from 13% to 20%, with highest recurrent rates of 40% to 61% if abscess present (Hanna & Kaiser, 2021). Surgical consultation may be necessary if the patient does not respond to treatment and continues to have an elevated WBC count, fever, rebound tenderness, pain, and tachycardia during acute illness. Surgery performed electively is recommended for those with complicated features including strictures, smoldering diverticulitis, inflammatory mass, and fistulae (Hanna & Kaiser, 2021). Approximately 20% of patients with diverticulitis do not improve with medical treatment and will require surgical intervention (Hanna & Kaiser, 2021). A colonoscopy is recommended approximately 6 weeks after diverticulitis episode to exclude occult malignancy because a malignancy may mimic diverticulitis presentation (Hall et al., 2020; Hanna & Kaiser, 2021)

Sequelae: Complications include bowel perforation, peritonitis, abscess, fistulae to bladder, vagina, small bowel, or skin, stricture, and bowel obstruction (Hanna & Kaiser, 2021). Medical supportive management may fail in up to 20% of patients, requiring need for surgical intervention (Hanna & Kaiser, 2021). Older adults with known diverticulosis are at higher risk for ischemic colitis (Dumic et al., 2019). Complications from diverticulitis tend to be most severe in patients who are immunocompromised, including those with diabetes, chronic kidney disease, or cirrhosis or those on immunosuppressant therapies (Hanna & Kaiser, 2021). Risk of bleeding in diverticular disease increases in patients taking anticoagulants and antiplatelets, aspirin, steroids, and NSAIDs (Hanna & Kaiser, 2021). Bleeding is not typically seen in episodes of acute diverticulitis but may still occur although less common; bleeding and anemia should raise concern for occult malignancy (Hanna & Kaiser, 2021). Approximately 1% to 5% of patients with radiological imaging favoring diverticulitis could actually be heralding an underlying malignancy (Hanna & Kaiser, 2021). Patients may deal with post-infectious IBS following diverticulitis episode (Dumic et al., 2019).

Prevention/Prophylaxis: Recognition of early signs and symptoms of diverticulitis helps prevent severe cases. A high-fiber diet is helpful in reducing risk of diverticular disease (Hanna & Kaiser, 2021). Evidence does not support that the inclusion of nuts, seeds, corn, and popcorn in the diet contributes to the development of diverticulitis (Strate et al., 2008). Calcium channel blockers and statins have shown a protective effect in reducing risk of diverticulosis in older adults, so consideration should be made to use these agents in the older adult who could benefit from these agents for comorbidities (Dumic et al., 2019).

Referral: Severe episodes of diverticulitis require hospitalization with possible gastroenterology and surgery consultation. Patients with localized abscesses need to be referred for consideration of a CT scan–guided percutaneous drainage (Hanna & Kaiser, 2021). Repeated episodes or complicated

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presentation may require surgical consultation for an elective resection if appropriate surgical candidate.

Education: Provide information on a high-fiber diet or fiber supplementation or both (Hanna & Kaiser, 2021; Wan & Krisko, 2021). Teach patients to increase their fluid intake, unless otherwise cautioned, especially when taking fiber supplements. Diverticulitis recurs in approximately 13% to 20% of patients if uncomplicated episode with higher recurrence rates if abscess present (Hanna & Kaiser, 2021; Wan & Krisko, 2021). Encourage older adults with obesity to consider weight reduction, physical activity, and avoidance of tobacco products to reduce potential complications of diverticular disease (Wan & Krisko, 2021).

Clinical Recommendation	Evidence Rating	References
Despite long-time popular belief, current evidence is lacking to show that including nuts, seeds, corn, and popcorn in one's diet contributes to the development of diverticulitis.	B	Strate et al., 2008
Regular intake of fiber may be beneficial in the prevention and recurrence of diverticular disease.	B	Hanna & Kaiser, 2021 Wan & Krisko, 2021
Calcium channel blockers and statins have shown a protective effect in reducing risk of diverticulosis in older adults, so consideration should be made to use these agents in the older adult who could benefit from these agents for comorbidities.	B	Dumic et al., 2019
A computed tomography scan is the best imaging modality with sensitivity of 93%–97% and specificity near 100% for diagnosing diverticulitis and severity.	A	Hanna & Kaiser, 2021
Risk of bleeding in diverticular disease increases in patients taking anticoagulants and antiplatelets, aspirin, steroids, and NSAIDs.	A	Hanna & Kaiser, 2021

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ESOPHAGITIS

Signal Symptoms:Dysphagia, regurgitation, pyrosis.

Description: Esophagitis is an inflammation of the lining of the esophagus.

Etiology: There are several different causes for esophagitis. Patients may develop esophagitis if they ingest medication improperly (medication esophagitis); ingest caustic chemicals; are exposed to radiation treatments (radiation esophagitis); have a bacterial, viral, or fungal infection (especially those patients who are immunocompromised); or have a history of gastroesophageal reflux disease (GERD; reflux esophagitis) (Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018; Wilkinson & Halland, 2020). *Candida albicans*, herpes simplex virus, and cytomegalovirus are the most common infectious causes (Dumic et al., 2019; Wilkinson & Halland, 2020). Bacterial esophagitis is rare but can coincide with a fungal or viral infection, making it difficult to diagnose. In GERD, erosive esophagitis is a common complication. Hiatal hernia, an intrinsic factor to the development of reflux esophagitis, increases in incidence with increasing age (Richter & Rubenstein, 2018). Eosinophilic esophagitis is a relatively new disorder described as a chronic immune or antigen-mediated esophageal disorder characterized as esophageal symptoms with endoscopic biopsies with more than 15 eosinophils per high-powered field and lack of pathological GERD (Dellon et al., 2013; Richter & Rubenstein, 2018).

Occurrence: It is estimated that between 6.4% and 15.5% of the population has esophagitis of some form (Richter & Rubenstein, 2018). One study found as many as 19% of the population suffers from asymptomatic esophagitis (Lee et al., 2016).

Age: Esophagitis can occur at all ages, and it occurs equally in men and women (Abid et al., 2005). However, medication-induced esophagitis is more common in older adults and is more prevalent in females (Abid et al., 2005). Hiatal hernias, more prevalent in older adults, are a known risk for erosive reflux esophagitis, and severe reflux esophagitis has been found more prevalent in patients 70 or older compared to 21 and younger (37% vs 12%) (Dumic et al., 2019; Johnson & Fennerty, 2004).

Ethnicity: Not significant.

Contributing Factors: In older adults, normal aging changes such as decreased salivation, gastric motility, and delayed gastric emptying can contribute to the development of esophagitis. Contributing factors to reflux esophagitis via persistent GERD regurgitation includes obesity, smoking, conditions that contribute to limited upper body mobility (such as spinal cord injuries), substances that can weaken the lower esophageal sphincter (coffee, peppermint, alcohol, spicy foods, citric fruits, chocolate, nifedipine, verapamil, and progesterone) (Commisso & Lim, 2019; Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018).

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Infectious agents are known to cause esophagitis in patients with certain viral, bacterial, parasitic, and fungal infections, such as in *Candida* esophagitis. Predisposing factors for patients who develop *Candida* esophagitis include radiation therapy, chemotherapy, certain hematological malignancies, AIDS, alcoholism, and malnutrition.

Medication-induced esophagitis ("pill esophagitis") is the result of altered pill passage through the esophagus (e.g., the pill becomes stuck or opens up) and subsequent prolonged mucosal contact, resulting in chemical irritation and mucosal inflammation. This can be contributed to by polypharmacy and impaired esophageal motility, which are more common in older adults (Dumic et al., 2019). Additionally, swallowing certain medications such as aspirin, tetracycline antibiotics, bisphosphonates, ferrous sulfate, captopril, certain chemotherapeutic agents, NSAIDs, quinidine, steroids, alendronate, alprenolol, vitamin C, phenytoin, calcium preparations, theophylline, and potassium chloride contributes to pill esophagitis (Dumic et al., 2019; Otaki & Iyer, 2021). Patients often report that insufficient fluid intake and not remaining upright after the medication is taken contributed to the symptoms of esophagitis (Aparanji et al., 2012; Dumic et al., 2019). Patients with cardiomyopathy with left atrial enlargement can have compression of the lower esophagus and subsequent impaired motility resulting in increased risk for pill esophagitis (Dumic et al., 2019).

Finally, several systemic disorders place patients at risk for esophagitis, including pemphigus vulgaris, bullous pemphigoid, Stevens-Johnson syndrome, lichen planus, inflammatory bowel disease, sarcoidosis, scleroderma, chronic granulomatous disease, and motility disorders of the esophagus (Aparanji et al., 2012).

Signs and Symptoms: A history of dysphagia and pain on swallowing (odynophagia) is common. Associated pyrosis, regurgitation, coughing, wheezing, and progressive hoarseness may occur, especially if associated with GERD. A fever may be present in patients with an infectious process. Patients should be questioned about medication usage, history of radiation treatments, smoking, and intake of substances that weaken the lower esophageal sphincter; sleeping habits; and use of any tight or restrictive clothing. Review patient medical history for chronic conditions that can contribute to esophagitis (Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018; Wilkinson & Halland, 2020).

Physical examination usually produces no positive findings for simple esophagitis but can be used to rule out other etiologies of abdominal pain. Oral thrush may be found in patients with *C. albicans*. Palpate for any upper abdominal masses or tenderness. Perform a rectal examination to detect any frank bleeding and stool guaiac to detect occult blood if gastrointestinal (GI) bleed is suspected, such as from erosive reflux esophagitis. Examine the oral cavity for sores and the skin for signs of immunosuppression or systemic diseases such as scleroderma or HIV/AIDS (Richter & Rubenstein, 2018; Zakharia & Tabibian, 2018).

Diagnostic Tests: If suspicion was aroused on the physical examination, stool should be checked using the guaiac test to determine whether there has been any intestinal bleeding. Laboratory studies are not required when antacids, position change, or both relieve pyrosis. For older adults who complain of persistent dysphagia or odynophagia with or without fever, a barium swallow or an endoscopy (with brush and biopsy if structural mucosal damage is suspected) or both are indicated. Also consider pH monitoring studies especially if the diagnosis is elusive or symptoms are refractory; however, in patients with eosinophilic esophagitis, the results are usually normal and, as such, pH monitoring can be utilized to rule out GERD over eosinophilic esophagitis in differential diagnosis (Akhondi, 2017; Otaki & Iyer, 2021).

Differential Diagnosis:

- Esophageal stricture (upper GI sinus)
- Esophageal carcinoma
- Cholecystitis and biliary colic
- GI foreign body
- Acute coronary syndrome
- Angina pectoris
- Myocardial infarction
- Peptic ulcer disease (PUD) (Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018)

Treatment: For infectious esophagitis, temporary symptomatic relief can be obtained with sucralfate slurry, 1 g/10 mL orally four times daily. Viscous lidocaine (2%), 15 mL orally every 4 hours as needed to swish and swallow, can be used for short-term temporary relief, unless contraindicated by potential drug interactions or history of cardiac or hepatic disease. For candida esophagitis, systemic therapy is the first-line treatment, rather than topical therapy; usually with fluconazole 200 mg to 400 mg daily for 14 to 21 days (Mohamed et al., 2019). For cases of herpes simplex virus–induced esophagitis in immunocompetent patients, spontaneous resolution is common, although oral acyclovir may be given to speed recovery. In immunocompromised patients, oral acyclovir is first-line treatment; for severe cases, IV antiviral therapy may be needed (Hoversten et al., 2019; Kadayakkara et al., 2016). Esophagitis from radiation can be treated with viscous lidocaine. For erosive esophagitis, use of proton pump inhibitors (PPIs) is recommended for 4 weeks, followed by reevaluation. In moderate to severe cases, PPIs have been found to be consistently superior to other options, including H_2 receptor blockers, in esophageal healing; however, agent selection and dose should be tailored to each patient (Kroch & Madanick, 2017).

Follow-Up: Patients should report progress at least 1 week after treatment. An endoscopy may be repeated if the patient is still symptomatic despite treatment compliance. Yearly endoscopy is recommended thereafter for patients with severe cases of esophagitis. Patients with eosinophilic esophagitis generally do not respond to treatment with PPIs and endoscopy with biopsy is completed to elicit the infectious etiology (Akhondi, 2017).

Sequelae: Ulceration and bleeding can occur if esophagitis is present. Barrett's esophagus with possible adenocarcinoma may be a long-term complication (Bujanda & Hachem, 2018; Dumic et al., 2019; Otaki & Iyer, 2021).

Prevention/Prophylaxis: Because of the high recurrence rate of esophagitis, patients should be instructed to follow all nonpharmacological measures unless otherwise instructed. Maintenance therapy for esophagitis may be prescribed for an extended time, although the dose and need should be periodically evaluated (Freedberg et al., 2017). Patient with

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Barrett's esophagus should take indefinitely a daily or twice daily PPI and undergo surveillance endoscopy with timing based on the dysplasia grade (Bujanda & Hachem, 2018).

Referral: A gastroenterologist should be consulted for the endoscopy and for patients with severe or nonresponsive esophagitis symptoms.

Education: Patients with reflux esophagitis should be instructed to raise the head of the bed 4 to 6 inches with shock blocks. Factors that increase abdominal pressure, such as wearing tight restrictive clothing, should be avoided. The patient should avoid smoking and ingestion of fatty foods, coffee, chocolate, mints, citric juices, alcohol, and large quantities of fluids with meals. Remind patients not to break or crush extended-release or delayed-release tablets. Teach the patient the importance of swallowing medications with an adequate amount of fluids. Patients with Barrett's esophagus should be educated on the need for indefinite PPI therapy and regular endoscopic surveillance (Commisso & Lim, 2019; Otaki & Iyer, 2021).

Clinical Recommendation	Evidence Rating	References
Topical steroids are the first-line treatment for eosinophilic esophagitis, rather than systemic steroids.	A	Dellon et al., 2013
Screening for Barrett's esophagus can be considered in men with more than 5 years of gastroesophageal reflux disease (GERD) symptoms and/or frequent GERD symptoms who also have two or more risk factors: age >50, White, central obesity, smoking history, and history of Barrett's esophagus and/or esophageal adenocarcinoma in a first-degree relative.	B	Shaheen et al., 2016
An 8-week course of proton pump inhibitors (PPIs) is the first-line treatment for symptoms relief and healing of erosive esophagitis.	A	Katz et al., 2013
PPIs have been found to be superior to H_2 receptor blockers in esophageal healing, preventing relapse of symptoms at 6 months, and maintaining symptom remission for more than 6 months.	A	Kroch & Madanick, 2017

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GASTRIC CANCER

Signal Symptoms: The most common symptoms at diagnosis of gastric cancer are weight loss (62%) and ongoing abdominal pain (52%) (Mansfield, 2021). Weight loss is usually due to decreased caloric intake as a consequence of other reported presenting symptoms including nausea, early satiety, and dysphagia. Patients reported vague pain in the epigastric area which increased in both frequency and severity as the disease progressed. A palpable abdominal mass is the most common physical finding in gastric cancer and is usually indicative of advanced disease (Mansfield, 2021).

Description: Gastric cancer develops when cells in the stomach begin to grow rapidly and uncontrollably. Eventually, this rapid cell growth will begin to interfere with the normal functions of the stomach. Adenocarcinomas account for approximately 95% of gastric cancers (National Comprehensive Cancer Network [NCCN], 2021). Adenocarcinomas arise from the stomach mucosa, and they are classified as either intestinal type or diffuse type. Intestinal type adenocarcinomas tend have a better prognosis and are more likely to have gene mutations which allow for targeted therapies. Diffuse type adenocarcinomas tend to be more aggressive, spreading more quickly than intestinal type, and are usually harder to treat (American Cancer Society [ACS], 2021c).

Other, less common types of gastric cancers include gastrointestinal stromal tumors (GISTs), neuroendocrine (carcinoid) tumors, lymphomas and (even less commonly) squamous cell carcinomas, small cell carcinomas, and leiomyosarcomas (ACS, 2021c). GISTs develop in the stomach walls cells called interstitial cells of Cajal. These are the cells that communicate with the muscles of gastrointestinal (GI) tract, which are responsible for the movement of food and fluid. Some GISTs are more likely to grow and spread to other sites of the body (ACS, 2019). Neuroendocrine tumors (NETs) can be either slow or fast growing. NETs tend to act like both nerve cells and endocrine cells, controlling the release of digestive enzymes, the movement of food through the GI tract, and regulating the growth of other cells of the digestive tract (ACS, 2018). Lymphomas are a type of cancer that arise from lymphocytes. These usually originate in other parts of the body but can rarely begin in the walls of the stomach.

Cancers of the stomach tend to develop more slowly when compared to other cancers. Early-stage stomach cancer begins in the innermost layer of the stomach—the mucosa. Patients with tumors invading through the mucosa or with suspicious local lymph nodes on imaging are considered to have locoregional disease and may or may not be surgically resectable. Sometimes gastric cancer invades or wraps around blood vessels or other vital structures. Although cancer at this stage is still considered locoregional, it cannot be safely removed surgically and is therefore no longer curable (ACS, 2021d). Gastric cancers can spread through the lymphatic system, circulatory system, peritoneal seeding, and

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direct extension through the gastric wall (Mansfield, 2021). Gastric cancer that has invaded other organs is considered metastatic.

Etiology: The etiology of gastric cancer is multifactorial. The differences in types of gastric cancer may also yield different etiologies. The Lauren classification of gastric cancer was established in 1965 and is still the most frequently used by clinicians. This system divides gastric cancer into intestinal type and diffuse type; an indeterminate type was later added to include gastric cancers with rare histology (Machlowska et al., 2020). Despite type, the etiology of gastric cancer is associated with the interaction of bacterial, dietary, environmental, lifestyle and host risk factors.

Intestinal type gastric cancer is the most common, and has been associated with gastric mucosa metaplasia, progressing from chronic gastritis to atrophic gastritis, intestinal metaplasia, dysplasia, and finally, adenocarcinoma. *Helicobacter pylori* infections, pernicious anemia, and perhaps a diet high in salt all may lead to gastritis, which initiates the cascade (Shah et al., 2020). A reduction in hydrochloric acid caused by gastric atrophy leads to an increase in gastrin, which induces gastric epithelial cell proliferation. This can also happen after gastric resections, where the increase in gastric pH may allow settlement of bacteria that can produce mutagenic compounds. Inflammation from chronic gastritis can also damage epithelial cells causing an increase in free radicals and increased cell turnover (Chan & Wong, 2021c). Intestinal type tumor cells tend to group together in tubular formations (Lauwers & Kumarasinghe, 2020). These tend to be slow growing, occur more often in men, older people, and are predominately found in high-risk areas (Canadian Cancer Society, 2021; NCCN, 2021).

Diffuse type gastric cancer tends to arise from normal gastric mucosa, having no clear precancerous lesion (Chan & Wong, 2021c). The lack of cohesiveness allows individual cells to grow and invade neighboring tissues aggressively, metastasizing much faster than intestinal type gastric cancers (Lauwers & Kumarasinghe, 2020; Machlowska et al., 2020). This is caused by the acquired or hereditary mutation of E-cadherin, a cell adhesion protein, causing disorganization of gastric cells (Lauwers & Kumarasinghe, 2020). Diffuse gastric cancers have also been found to have a higher incidence in females, younger patients, and are more frequently found in low-risk areas (Machlowska et al., 2020; NCCN, 2021).

Occurrence: Each year, approximately 990,000 people are diagnosed with gastric cancer worldwide. Of those, it is estimated that 738,000 will die (Machlowska et al., 2020). In the United States, around 22,220 patients are diagnosed annually, of whom 10,990 are expected to die (Chan & Wong, 2021a). Gastric cancer accounts for approximately 1.5% of all new cancer diagnosis each year in the United States (ACS, 2021a). Men are two to three times more likely than women to be diagnosed with gastric cancer (Machlowska, 2020). The American Cancer Society (2021a) estimates that in 2021 within the United States 16,160 men and 10,400 women will be diagnosed with gastric cancer, with 6,740 men and 4,440 women dying from the disease.

The worldwide incidence of gastric cancer has declined since the 1980s; however, this is with wide geographic variability. Decreased incidence is noted in Western Europe, sub-Saharan Africa, Australia, and North America, while East Asia, South and Central America, and Eastern Europe have the highest incidence rates. Gastric cancer is the most commonly diagnosed cancer in men in Japan and Korea and is the leading cause of cancer death in China (NCCN, 2021).

Age: Gastric cancer affects older people most often. The average age at diagnosis is 68 years. Of patients diagnosed with gastric cancer, approximately 60% are older than 65 years (ACS, 2021a).

Ethnicity: Within the United States, gastric cancer has been found to disproportionately affect non-White minority groups. The annual incidence of gastric cancer is highest in Asian and Pacific Islanders (10/100,000) and non-Hispanic African Americans (10/100,000), followed by Hispanic Americans (9.6/100,000), Native Americans and Alaskan Natives (8.8/100,000), and non-Hispanic European Americans (5.3/100,000) (ACS, 2020).

Contributing Factors: As previously mentioned, gastric cancer is associated with bacterial, dietary, environmental, lifestyle and host risk factors. *H. pylori* is a gram-negative bacteria that causes inflammation to gastric mucosa, and DNA changes to gastric cells over time. (Shah et al., 2020). *H. pylori* infections additionally damage the gastric microenvironment, making it more susceptible to carcinogens (Machlowska et al., 2020). Chan and Wong reported that "*H. pylori* infection has been associated with an approximately sixfold increase in the risk of adenocarcinomas distal to the cardia, including both the intestinal and diffuse types" (2021c).

Numerous studies have been done to correlate dietary factors and the risk of gastric cancers. Diets high in salt and salt-preserved foods (salted fish, cured meats, salted vegetables) have been strongly linked with gastric cancer development because salt is thought to damage the stomach mucosa, which increases its susceptibility to carcinogens. The decline of gastric cancer worldwide has been partly attributed to refrigeration practices that eliminate the need for salt preservation of foods. Additionally, diets high in fried foods, processed meats, and alcohol and low in fruits and vegetables have been associated with a high risk of developing gastric cancers in epidemiological studies (Chan & Wong, 2021c).

There has been some linkage proposed between occupations in coal and tin mining, steel and iron processing, and manufacturing rubber with an increased risk of gastric cancer; however, further research is needed to determine the overall effect of these environmental effects and developing gastric cancer. Cigarette smoking has been contributed to a 1.53-fold increase in the risk of gastric cancer; however, this risk decreased after 10 years of smoking cessation (Chan & Wong, 2021c). Regular ingestion of alcohol has not consistently been shown to cause a direct increased risk of gastric cancer; however, most studies show a positive correlation between heavy alcohol consumption and gastric cancer (Machlowska et al., 2020). The data for this correlation are greatest among people who have three or more drinks per day (ACS, 2021b). Individuals with a low socioeconomic status have a twofold increase in risk of distal gastric cancers, while those with a higher socioeconomic status are at a higher risk of proximal gastric tumors.

Obesity, defined as having a body mass index (BMI) greater than or equal to 25 kg/m^2, was correlated with an increased

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risk of gastric cancer, and there was a positive correlation with occurrence of gastric cancer and the individual's BMI increasing (ACS, 2021b). Other medical conditions associated with an increased risk for gastric cancer include gastric polyps, gastric ulcers, pernicious anemia, and Epstein-Barr virus (EBV). The EBV has been associated with 5% to 10% of gastric cancers worldwide. The pathogenesis of gastric cancers caused by EBV is unclear; the virus may inhibit the expression of certain tumor suppressing genes (Chan & Wong, 2021c). History of previous abdominal radiation and having undergone gastric surgery, especially a partial gastrectomy (Billroth I or II), also increases an individual's risk for developing gastric cancer. Lastly, individuals with blood type A have a 20% increase in developing gastric cancer when compared to those with blood types O, B, or AB (Chan & Wong, 2021c).

Although most gastric cancers are sporadic, having a positive family history is an important risk factor and can account for a threefold increase in risk compared to persons without a family history. Aggregation of gastric cancers within families account for 10% of incidences, whereas gastric cancers that are truly hereditary are culpable for 1% to 3% worldwide. The ratio of those diagnosed with gastric cancers that have a family history is greater in Asian areas than in Europe and North America. This concludes that environmental factors more than genetic agents affect the risk of gastric cancer development in countries with higher incidences (Machlowska et al., 2020).

Signs and Symptoms: Early detection of gastric cancer is often difficult because of the typically ambiguous clinical presentation. Patients often describe a vague sensation of fullness after a meal that is relieved by belching, nonspecific complaints of abdominal pain of varying intensities, nausea, anorexia, dyspepsia, vomiting, and evidence of GI blood (hematemesis and melena), and changes in bowel habits. Dysphagia is most commonly reported by those with cancers in the proximal stomach and esophagogastric junction (EGJ) (Mansfield, 2021). Epigastric discomfort is present in more than 75% of patients, and the presentation may be similar to that of a gastric ulcer further complicating the presentation, as 25% of patients diagnosed with gastric cancer have previously had gastric ulcers (Mansfield, 2021). Weight loss and pallor, if the patient is anemic, may be the only signs noted during physical examination. Examination of the skin may reveal diffuse seborrheic keratosis (sign of Leser-Trèlat). A palpable mass in the abdomen is felt in less than 20% of patients.

Many patients with gastric cancer often do not become symptomatic until their disease becomes metastatic. Metastatic distribution most commonly involves the liver, peritoneal surface, and distant lymph nodes. Liver involvement is usually diffuse and not singularly palpable; however, it is often associated with an elevated serum alkaline phosphatase level. Ascites is often the first sign of peritoneal spread. Because gastric cancers can be spread through the lymphatic system, patients with metastatic disease often have enlargement of the left supraclavicular lymph nodes (Virchow node), a periumbilical nodule (Sister Mary Joseph's node), and left axillary node (Irish node). Additionally, in advanced disease a rigid rectal mass may be palpated (Blumer's shelf) and/or an enlarged ovary may be detected in females (Krukenberg's tumor) (Mansfield, 2021).

Diagnostic Tests: For patients presenting with symptoms of gastric cancer, the following laboratory studies should be considered: complete blood count (CBC) with indices to determine presence of anemia, comprehensive chemistry profile, and fecal occult blood test (FOBT) to detect bleeding in the intestinal tract if suspected. Patients will need to be referred for an endoscopy (EGD) to determine the location of the tumor, measurement of tumor size, determination of macroscopic stage (T1–T4) and to obtain biopsies to confirm histological type (Shah, et al., 2020; Smyth et al., 2020).

Once diagnosis has been confirmed by biopsy on EGD, the remaining work-up is used to establish disease stage based on the American Joint Committee on Cancer and the Union for International Cancer Control system based on tumor, node, metastasis (TMN) (Mansfield, 2021). On EGD, macroscopic type (T stage) characterizes the depth the primary tumor has grown into the layers of the stomach (Smyth et al., 2020). A chest abdominopelvic computed tomography (CT) scan with oral and IV contrast should be used to evaluate for metastatic disease (M stage). In the absence of distant metastatic disease, endoscopic ultrasonography (EUS) is the preferred tool to determine the depth of invasion of primary gastric tumors (T stage), as well as to accurately evaluate for nodal staging (N stage) and occult metastases (M stage) (Mansfield, 2021; NCCN, 2021). A pretreatment, staging laparoscopy with cytology is recommended to monitor for peritoneal dissemination in patients with a lesion greater than T1a who are surgical candidates, even if no signs of metastatic disease have been previously discovered (NCCN, 2021).

If metastatic disease is found on CT scan, the suspected lesion must be confirmed by biopsy due to the risk of false-positive findings. A paracentesis should be performed on patients with ascites, and the fluid should be examined for cytology and chemical evaluation. CT scans can miss peritoneal and hematogenous metastases smaller than 5 mm and do not precisely evaluate the depth of primary tumor invasion and existence of lymph node involvement. The use of positron emission tomography (PET) scans is controversial. The NCCN (2021) recommends PET scans if no evidence of metastatic disease has been found previously, as PET scans have can detect radiographically occult metastatic lesions in up to 10% of those with locally advanced disease (Mansfield, 2021).

Microsatellite instability (MSI) testing is recommended on all newly diagnosed patients. Human epidermal growth factor receptor 2 (HER2) and programmed death-ligand 1 (PD-L1) testing should be performed on the tumor biopsy if metastatic adenocarcinoma is documented or strongly suspected (NCCN, 2021). Next-generation sequencing (NGS), with included tumor mutation burden (TMB) testing should be done if enough tissue is available after the previously recommended testing. MSI, HER2, PD-L1 and TMB determination can be used to guide treatment choices in advanced disease.

Differential Diagnosis:

- Bacterial/viral gastroenteritis
- Crohn's disease
- Chronic/acute gastritis
- Esophageal cancer
- Esophageal stricture
- Esophagitis

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- Gastric ulcers
- Gastroesophageal reflux disease (GERD)
- Irritable bowel syndrome
- Malignant neoplasms of the small intestine
- Mesenteric ischemia
- Non-Hodgkin's lymphoma
- Peptic ulcer disease (PUD) (Recio-Boiles & Babiker, 2020)

Treatment: Endoscopic resection is used to treat early-stage gastric cancers that have not yet invaded the submucosa (<T1b). For gastric cancers that have penetrated the submucosa but not yet mediatized to the lymph nodes (T1bN0) a partial or complete gastric resection is recommended with lymphadenectomy (NCCN, 2021). In the United States typically at least 16 lymph nodes are removed with a gastrectomy, whereas in East Asian countries more lymph nodes are removed (ACS, 2021d). Surgery may be considered in the noncurative or palliative setting to treat or prevent complications such as bleeding, pain, or obstruction.

Patients with gastric cancers that have invaded the muscularis propria or deeper at presentation (≥T2) or have any lymph node involvement but no metastatic disease (any N, M0) are recommended to undergo perioperative chemotherapy with fluorouracil (5-FU) based treatment. If no perioperative chemotherapy is given, postoperative 5-FU based chemotherapy and/or radiation with a fluoropyrimidine base (IV 5-FU or oral capecitabine) is recommended depending on the pathological findings at surgery, lymph node involvement, and surgical margins (NCCN, 2021). Although certain regimens are favored, agents used should be chosen after considering the patient's performance status, comorbidities, and toxicity profile of each medication. The NCCN (2021) recommends a multidisciplinary team including all relevant disciplines discuss all cases of patients without metastatic disease be prior to the finalization of treatment plans.

Patients with unresectable, metastatic, or recurrent gastric cancer (if localized therapies are not indicated) should be treated with systemic agents to alleviate symptoms, improve quality of life, and extend survival. Again, 5-FU based regimens are preferred in the first line. For patients with HER2 overexpression, trastuzumab (Herceptin) can be added to the regimen for additional benefit without adding cytotoxic side effects. For patients with a PD-L1 score ≥5, nivolumab (Opdivo), an immunotherapy agent, can be added as well in the first line. Additional therapies include the vascular endothelial growth factor (VEGF) inhibitor ramucirumab (Cyramza), which attacks the cancer cells' ability to make blood vessels without affecting healthy cells, unlike standard chemotherapy. There are many other chemotherapy agents from different classes that can be used beyond the first line as single agents or in combination. An additional immunotherapy recommended for gastric cancer is pembrolizumab (Keytruda), an immunotherapy based on microsatellite high status, PD-L1 expression ≥1, or tumor mutation burden high (NCCN, 2021).

Follow-Up: Most gastric cancer recurrences (70% to 80%) happen within the first 2 years after completion of therapy, with almost all (90%) of recurrences occurring within 5 years (NCCN, 2021). Follow-up, or surveillance, is important to detect recurrence early, when burden of disease is likely to be small allowing for more treatment options.

In general, surveillance visits should occur every 3 to 6 months for the first 2 years, then every 6 to 12 months for the next 3 years, then annually. Evaluation with a CBC and chemistry profile should be obtained as needed. Patients with stage II or III disease should be monitored with a CT scan of the chest, abdomen, and pelvis with oral and IV contrast every 6 to 12 months for the first 2 years, then yearly for up to 5 years. Early-stage gastric cancers should be monitored with serial EGDs. Patients with stage I disease and greater should be monitored with EGDs as clinically indicated (NCCN, 2021).

Additionally, patients who underwent surgical resection should be monitored for nutritional deficiencies, including B_{12} and iron insufficiency (NCCN, 2021).

Sequelae: Malnutrition, hemorrhage, obstruction, possibly evasive cancer, metastases, pain, nausea, vomiting, fatigue, chemotherapy-related neuropathy and recurrence are complications from gastric cancer and its treatment. Additionally, patients may experience reflux, dumping syndrome, hypoglycemia, and diarrhea following a gastric resection (NCCN, 2021).

Prevention/Prophylaxis: Patients should restrict the use of food products that contain nitrates and are highly salted. Consumption of fruits, especially citrus fruits, and vegetables has been found to protect against gastric cancer, possibly because they contain vitamin C, folate, carotenoids, and phytochemicals, which may provide protection against carcinogenesis (Machlowska et al., 2020). As previously stated, infection with *H. pylori* has been associated with an increased risk of gastric cancer. According to Choi and associates (2018), in the setting of early gastric cancers status post resection, the incidence of metachronous gastric cancer was 50% lower among patients treated for *H. pylori* versus placebo over a 5.9-year period. Screening for gastric cancer is controversial and not currently recommended in the United States. In countries with a high incidence of gastric cancer, screening has contributed to earlier detection and a decline in gastric cancer mortality; however larger, randomized trials are needed (Chan & Wong, 2021b).

Referral: A gastroenterologist should be consulted for the endoscopy and complicated management problems, including annual follow-up endoscopy. Patients with stages I to III disease should be seen by a surgeon for possible resection. After receiving a surgical resection, patients may need to be followed by a nutritionist. Additionally, patients with gastric cancer should see a medical oncologist to evaluate for the role of neoadjuvant, adjuvant, or palliative chemotherapy and to follow the patient for surveillance visits if not done by the surgeon. Given the commonly advanced age, comorbidities, and the cognition of patients with gastric cancer, careful attention to emotional support and their quality of life need to be considered when caring for older adults. Referral to counseling or psychiatry should be considered on an as needed basis. For patients with advanced disease, referral for palliative care or local hospice should be made.

Education: After partial and complete gastrectomy, patients should be taught about the importance of adequate nutrition. Consuming six small meals throughout the day and not drinking liquids with meals may help with weight loss and symptoms of dumping syndrome. Gastrectomy patients

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should also be educated to avoid foods that cause acid production (tomatoes, spicy foods, caffeine, peppermint, chocolate, and citrus fruits) because these can increase indigestion. Regular, moderate exercise can help improve fatigue. Antidiarrheal medications and an increase in dietary fiber can improve diarrhea. Chemotherapy-induced neuropathic pain can be permanent; however, symptoms can be improved with duloxetine (Cymbalta). Supplementation with vitamins, especially vitamin B_{12} and vitamin D, and minerals, such as calcium and iron, should be prescribed (NCCN, 2019).

Clinical Recommendation	Evidence Rating	References
Patients with early-stage gastric cancer who received *H. pylori* treatment had lower rates of metachronous gastric cancer and improvement in baseline gastric corpus atrophy when compared to placebo.	A	Choi et al., 2018
Patients with gastric intestinal metaplasia (GIM) should undergo endoscopic surveillance to determine extent of GIM and rule out any neoplasia.	C	Shah et al., 2020
Gastric resection should include the regional lymphatics with the goal of examining at least 16 lymph nodes.	A	NCCN, 2021
Universal testing for microsatellite instability (MSI) by polymerase chain reaction/mismatch repair by immunohistochemistry is recommended for all newly diagnosed patients.	A	NCCN, 2021
Perioperative chemotherapy or postoperative chemotherapy plus chemoradiation is the preferred approach for localized gastric cancer.	A	NCCN, 2021

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GASTRITIS

Signal Symptoms: Anorexia, nausea and vomiting, epigastric pain, gastroesophageal reflux disease (GERD) symptoms, or epigastric discomfort with tenderness.

Description: Gastritis is an acute or chronic inflammation of the mucosal lining of the stomach, established by histological findings on biopsy of inflammatory cells in the lamina propria, with further delineation of chronic gastritis as either atrophic or nonatrophic (Azer & Akhondi, 2021; Rugge et al., 2020). A number of conditions can cause gastritis including infection, autoimmune disorders, systemic disease, chemical (both endogenous and exogenous), radiation, and stress (Azer & Akhondi, 2021; Rugge et al., 2020). Patients may be asymptomatic; however, dyspepsia, iron-deficiency anemia, and macrocytic anemia may be found in older adults with atrophic gastritis (Lahner et al., 2020).

Etiology: Gastritis represents a group of disorders characterized by inflammation of the stomach lining. Each disorder has distinct clinical attributes, pathogeneses, and histological features; diagnosis must be done with histological interpretation of gastric tissues. Gastritis may be caused by parasitic, fungal, bacterial, or viral infectious agents; *Helicobacter pylori* is the most common culprit for gastritis globally (Azer & Akhondi, 2021). Chemical gastritis may occur secondary to bile reflux, alcohol use, NSAIDs, and doxycycline; physical agents such as radiation may also cause gastritis (Rugge et al., 2020). Autoimmune gastritis, resulting from chronic inflammatory processes, may lead to chronic atrophic gastritis; other autoimmune disorders such as thyroid disease, type 1 diabetes, and myasthenia gravis are associated with autoimmune gastritis (Azer & Akhondi, 2021; Lahner et al., 2020). Additional causes of gastritis that are rare include Crohn's disease, collagenous gastritis, eosinophilic gastritis, sarcoidosis-associated gastritis, lymphocytic gastritis, vasculitis-associated gastritis, and ischemic gastritis, which results in high mortality rate (Azer & Akhondi, 2021; Rugge et al., 2020). Atrophic gastritis is most often a result of chronic *H. pylori* and autoimmune gastritis (Lahner et al., 2020).

Occurrence: Exact incidence of gastritis is unknown.

Age: Although gastritis occurs in all ages, gastritis, specifically atrophic forms, are more common in the older adult (Dumic et al., 2019). Autoimmune gastritis is found more commonly in older adult women (Azer & Akhondi, 2021). Patients of all ages can be infected with *H. pylori*, with extensive atrophic damage no longer related only to older ages but rather with persistent *H. pylori* infection (Dumic et al., 2019).

Ethnicity: *H. pylori* infection is most common among Asians and Hispanics (Sonnenberg et al., 2020).

Contributing Factors: Many factors can precipitate the development of gastritis. Gastritis may be acute, chronic, or an exacerbation of chronic presenting acutely. Acute gastritis can be caused by physiological stressors, hypovolemic shock, portal hypertension, aspirin, NSAIDs, smoking, steroid use, alcohol, radiation, chemotherapy, gastric lymphoma, Crohn's disease, alcohol, bile reflux, autoimmune disorders, *H. pylori* and other bacterial, viral, and fungal infections (Azer & Akhondi, 2021). Stress, trauma, and burns can trigger this

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acute condition (Azer & Akhondi, 2021; Rugge et al., 2020). Autoimmune gastritis is related to the loss of parietal and chief cells and includes achlorhydria, hypergastrinemia, loss of pepsin and pepsinogen, and anemia (Azer & Akhondi, 2021). Chronic gastritis is predominantly a result of *H. pylori* infection. Autoimmune gastritis is seen with other autoimmune disorders that include thyroid diseases, myasthenia gravis, Addison's disease, type 1 diabetes, vitiligo, and oral lichen planus (Azer & Akhondi, 2021).

Signs and Symptoms: Anorexia, nausea (with or without vomiting), dyspepsia, epigastric pain worsened by eating, belching, and bloating are common with gastritis (Rahmawati, 2020). Physical examination may be unremarkable in cases of chronic gastritis. Palpate for abdominal masses and liver tenderness. Perform a rectal examination to test for occult blood if concern for occult blood loss. Any unexplained weight loss should be noted. Gastrointestinal (GI) bleeding may be exhibited by coffee-ground emesis, melena, hematochezia, or the passing of bright red blood in a nasogastric tube. Iron-deficiency anemia should raise suspicion for early autoimmune gastritis, but it may also be seen in other forms of gastritis (Azer & Akhondi, 2021; Lahner et al., 2020). Vitamin B_{12} deficiency is associated with atrophic gastritis; atrophic gastritis has also been linked with risk for osteoporosis (Clements et al., 2021).

Diagnostic Tests: Diagnostic studies include complete blood count (CBC) with indices to detect blood loss and anemia, stool guaiac test, and esophagogastroduodenoscopy (EGD) with biopsy, which is the definitive diagnostic test for gastritis and remains the gold standard. Histological examination of tissue specimens obtained during EGD assesses for *H. pylori* via stains, cultures, rapid urea test, or polymerase chain reaction (PCR) test (Azer & Akhondi, 2021). Noninvasive tests include urea breath test (UBT), fecal antigen test, and serologies; proton pump inhibitor (PPI) use will need to be restricted for 14 days and antibiotics for 28 days before UBT and fecal antigen testing (not serology) to ensure more accurate diagnosis and avoid false-negative results (Azer & Akhondi, 2021; Rugge et al., 2020). The serological testing for *H. pylori* is not able to distinguish between prior exposure or active infection; therefore, the utility of this test is limited in clinical scenarios. Noninvasive tests for *H. pylori* may be falsely negative in those with atrophic gastritis, so EGD with biopsy would be required to rule out infection (Lahner et al., 2020). Atrophic and autoimmune gastritis requires EGD with biopsy for histopathological diagnoses. Serum gastrin levels and pepsinogens assist in screening patients with concern for atrophic gastritis, followed by EGD for confirmation.

Differential Diagnosis:

- GERD
- Biliary tract disease
- Food poisoning
- Functional dyspepsia
- Peptic ulcer disease (PUD)
- Perforated or penetrated ulcer
- Gastric carcinomas
- Pancreatic disease
- Esophageal rupture
- Myocardial infarction (atypical presentation)
- Inflammatory bowel disease
- Zollinger-Ellison's syndrome
- Celiac disease
- Viral infections (Rugge et al., 2020)

Treatment: Patients with acute gastritis should avoid offensive agents that contributed to gastritis. If treatment for *H. pylori* is indicated, treatment options are delineated in Table 13-2. Iron or B_{12} supplementation may be necessary for iron-deficiency anemia and B_{12} deficiency. Dietary changes may be necessary

TABLE 13-2 ***Helicobacter pylori* Regimens for First-Line Treatment**

PATIENT CHARACTERISTICS FOR TREATMENT	MEDICATION AND DOSAGE
Patients who are not allergic to penicillin and have not previously received a macrolide	Standard dose PPI twice daily plus clarithromycin 500 mg twice daily, and amoxicillin 1000 mg twice daily for 10–14 days
	Or
	Bismuth quadruple therapy: PPI twice daily, bismuth subcitrate or subsalicylate 300 mg four times daily, tetracycline 500 mg four times daily, and metronidazole 500 mg three times daily
Patients who are allergic to penicillin and who have not previously received a macrolide	Standard dose PPI twice daily, clarithromycin 500 mg twice daily, metronidazole 500 mg twice daily for 10–14 days
	OR
	Bismuth quadruple therapy: PPI twice daily, bismuth subcitrate or subsalicylate 300 mg four times daily, tetracycline 500 mg four times daily, and metronidazole 500 mg three times daily
Patients who are allergic to penicillin, failed a course of prior therapy, or have previously received a macrolide	Bismuth quadruple therapy: PPI twice daily, bismuth subcitrate or subsalicylate 300 mg four times daily, tetracycline 500 mg four times daily, and metronidazole 500 mg three times daily
Patients who are not allergic to penicillin but have had macrolide exposure	Bismuth quadruple therapy: PPI twice daily, bismuth subcitrate or subsalicylate 300 mg four times daily, tetracycline 500 mg four times daily, and metronidazole 500 mg three times daily, or
	Standard dose PPI twice daily, levofloxacin 500 mg daily, amoxicillin 1000 mg twice daily

Source: *Chey et al., 2017*

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in those with eosinophilic gastritis (Azer & Akhondi, 2021). Lon-term PPI use may worsen atrophic gastritis precipitated by *H. pylori*, so patients should be assessed on a case-by-case basis for PPI necessity (Lahner et al., 2020). PPI therapy should be avoided in those with impaired gastric acid secretion due to atrophic damage (Lahner et al., 2020). Further studies are needed regarding prokinetic therapy in atrophic gastritis due to delayed gastric emptying in setting of reduced gastric acid (Lahner et al., 2020).

Follow-Up: *H. pylori* eradication should be documented after treatment, typically with noninvasive testing, but EGD with biopsy may be indicated if the presentation is complicated. Both PPI therapy and antibiotics should be held prior to noninvasive testing to avoid false-negative results. Surveillance EGD is recommended in extensive atrophic gastritis and intestinal metaplasia varying from 1 to 3 years, with earlier surveillance timing determined by presence of gastric cancer in a first-degree relative (Lahner et al., 2020). However, surveillance for atrophic gastritis without intestinal metaplasia located only in gastric antrum does not require EGD surveillance (Lahner et al., 2020).

Sequelae: *H. pylori* is a known risk factor for development of gastric cancer, and those with autoimmune atrophic gastritis are also at risk for gastric cancer and neuroendocrine tumors (Lahner et al., 2020). Vitamin B_{12} and iron absorption is affected in atrophic gastritis, leading to iron-deficiency anemia and pernicious anemia (Lahner et al., 2020). Iron-deficiency anemia may also be present in other forms of gastritis. Atrophic gastritis increases risk for osteoporosis (Azer & Akhondi, 2021; Lahner et al., 2020). Untreated, gastritis could progress to PUD, gastric bleeding, chronic gastritis, neuroendocrine tumors, mucosa-associated lymphoid tissue (MALT) lymphoma, depending on the etiology of gastritis (Azer & Akhondi, 2021).

Prevention/Prophylaxis: Prophylaxis with acid-suppressive drugs can reduce the incidence of acute stress gastritis. Older adults who are high-risk intensive care unit patients, including those with severe burns, central nervous system trauma, coagulopathy, sepsis, shock, multiple traumas, mechanical ventilation for longer than 48 hours, hepatic or renal failure, and a history of peptic ulcer or GI bleeding, benefit from prophylaxis medication to prevent acute gastritis. Alternative anti-inflammatory or nonnarcotic analgesics should be considered in the treatment of pain or inflammation in older adults with a history of gastritis, dyspepsia, or other upper GI clinical events

Referral: Consultation with a gastroenterologist for endoscopy and management of persistent dyspepsia is recommended.

Education: Advise patients to report any black, tarlike stools or frank bleeding to the health-care practitioner immediately. All alcohol, caffeine, salicylates, tobacco, and NSAID product use should be discontinued.

Clinical Recommendation	Evidence Rating	References
Atrophic gastritis is a result of chronic *Helicobacter pylori* and autoimmune gastritis.	A	Lahner et al., 2020
Vitamin B_{12} deficiency was found in patients diagnosed with atrophic gastritis.	B	Clements et al., 2021
H. pylori is a known risk factor for development of gastric cancer, and those with autoimmune atrophic gastritis are at risk for gastric cancer and neuroendocrine tumors.	C	Lahner et al., 2020

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GASTROENTERITIS

Signal Symptoms: Sudden onset of diarrhea, abdominal pain with distention, nausea, vomiting.

Description: An infectious response of the gastrointestinal (GI) tract to various microorganisms that can be viral, bacterial, or parasitic in origin.

Etiology: Caused by exposure to toxins and drugs or viruses, bacteria, and parasites:

- Viruses such as norovirus, formerly called the Norwalk-like virus and astrovirus
- Bacteria such as *Salmonella, Campylobacter, Shigella, Escherichia coli*, and *Vibrio cholerae*
- Parasites such as *Giardia lamblia*

Occurrence: Approximately 30% to 40% of gastroenteritis diarrhea in the United States is thought to be viral in origin. Exact incidence of infectious gastroenteritis is unknown because of underreporting of symptoms. Noroviruses cause approximately 19 to 21 million cases of acute gastroenteritis each year and are the leading cause of outbreaks of gastroenteritis. Norovirus outbreaks peak in the winter months. Norovirus accounts for 56,000 to 71,000 hospitalizations, and 570 to 800 deaths annually (Stuempfig et al., 2021).

Age: Occurs at all ages, but its incidence and the mortality rate from infectious diarrhea are higher in older adults. Epidemic cases of gastroenteritis occur in nursing home populations and long-term care facilities are the most frequently reported settings of outbreaks transmitted through person-to-person contact or environmental contamination (Stuempfig et al., 2021).

Ethnicity: Not significant.

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Contributing Factors: Specific to the older adult population, age-related factors such as decreased motility, mucosal atrophy, and decreased gastric acidity inhibit natural defense mechanisms against infectious agents, as well as age-related changes in B-cell and T-cell function (Cardemil et al., 2017). The use of H_2 blockers, proton pump inhibitors (PPIs), antacids, anticholinergic drugs, and narcotics increases the potential for developing gastroenteritis. Gastroenteritis also can be caused by viral or bacterial infection, food intolerance, and organic (shellfish, certain mushrooms) or inorganic (sodium nitrate) poisons. Travel to another country with a change in surroundings or to an area of poor sanitation standards and facilities can contribute to the development of gastroenteritis. Nursing home populations are susceptible to epidemics because of contact with health-care workers who may not use proper hand washing techniques. Some viruses, such as norovirus, can be transmitted by an airborne route, particularly through aerosolized particles. Fecal-to-oral contact has been identified as a mode of transmission of organisms. Person-to-person contact is responsible for greater than 90% of norovirus outbreaks in health-care settings (Chen et al., 2017).

Signs and Symptoms: History of possible fecal-to-oral contact; exposure to other patients with gastroenteritis; and ingestion of certain food products such as mayonnaise, custards, fried rice, vegetables, beef, poultry, bean sprouts, or raw seafood should be explored. Try to estimate the length of time that has elapsed since the patient ingested the food product suspected of contamination. Travel to a foreign country or region that may have contaminated water should be recorded, as should any previous history of diarrhea and related symptoms, and the duration of the current episode. A sudden onset of diarrhea, abdominal pain with distention, flatulence, and vomiting may be reported; however, diarrhea is more common in women. Associated anorexia, headache, fatigue, dizziness, and myalgias are also symptoms of gastroenteritis. Fever may or may not occur in the older adult. Mental confusion may result from dehydration. The stool's color, odor, amount, and frequency should be described, and the presence of any blood or mucus in the stool should be discerned. Patient use of prescription drugs, over-the-counter (OTC) medications, and home remedies need to be included in the history. In the physical examination, the skin is checked for signs of rashes or dehydration, and the lymph nodes are assessed for lymphadenopathy. Abdominal examination may reveal distention, hyperactive bowel sounds, and tenderness. Rectal examination may be performed to check for bleeding, stool character, and presence of any fecal impaction (Stuempfig et al., 2021).

Diagnostic Tests: Complete blood count (CBC) with differential should be ordered. White blood count (WBC) shift to the left may suggest an infection, and a decreased hemoglobin value indicates anemia from possible blood loss. Serum electrolyte evaluation shows an increased sodium level in dehydrated patients and decreased potassium resulting from the diarrhea. Elevated serum creatinine and blood urea nitrogen (BUN) levels also occur in dehydration. Stool samples for blood, ova and parasite, leukocytes, and bacteria are ordered to try to identify the microorganism in patients with bloody diarrhea, dehydration, or signs of inflammatory disease, and symptoms lasting more than 3 to 7 days. Cultures in immunosuppressed patients are also warranted. Cultures may be obtained in traveler's diarrhea (Acree & Davis, 2017).

Differential Diagnosis:

- Fecal impaction
- Fecal incontinence
- Colorectal cancers
- Adverse reaction to medications
- Diverticulitis
- Malabsorption
- Pseudomembranous colitis if the patient has been prescribed an antibiotic within 2 months of onset of symptoms
- *Clostridioides difficile* (Sattar & Singh, 2021)

Treatment: Lost fluids and electrolytes must be replaced. Clear liquids and specially formulated rehydration liquids, such as Pedialyte, should be given as tolerated. Clear broths and crackers may be added to the diet as tolerated. Early refeeding decreases symptom duration and improves nutritional outcomes (Sattar & Singh, 2021). Patients should avoid caffeine, dairy products, alcohol, fruits, bran, vegetables, and red meats. Solid foods should be added gradually, starting with rice or potatoes. Physical activity should be limited to avoid unnecessary exertion. Care should be taken to prevent any skin excoriation or pressure sores. Antibiotic therapy is specific to the bacterial or parasitic organisms identified from the stool culture:

- *Campylobacter* strains have been shown to have fluoroquinolone resistance and are best treated by azithromycin or other macrolides. For all antibiotics, either single-dose therapy or 3 days of therapy are sufficient for resolution of symptoms.
- *G. lamblia* infection is treated with metronidazole, 250 mg three times daily for 5 to 7 days.
- Severe cases of traveler's diarrhea (enterotoxigenic *E. coli*) can be treated with azithromycin 500 mg daily for 3 days (Acree & Davis, 2017).

Follow-Up: Contact outpatients 4 days after the onset of symptoms to determine progress. Request nursing home staff to provide a verbal report of the patient's condition on the third or fourth day. Note any further outbreak of gastroenteritis. When contacting the patient at home, question if there have been any additional symptoms, including fever and neurological developments such as paresthesia, motor weakness, and cranial nerve palsies. For older adults with chronic diarrhea or other persistent GI symptoms, refer to a gastroenterologist. Reactive arthritis may occur after infections from *Shigella, Salmonella, Campylobacter*, or *Yersinia* (Sattar & Singh, 2021).

Sequelae: Dehydration, anemia, metabolic acidosis, and hypovolemic shock and sepsis can occur in untreated cases of severe infectious diarrhea.

Prevention/Prophylaxis: Older adults with travel plans to foreign destinations should be counseled to avoid contaminated water and other high-risk beverages and foods to prevent traveler's diarrhea (Shane et al., 2017)

Referral: Refer to a specialist when symptoms persist beyond 4 days, when severe dehydration develops, or when the patient has bloody stools.

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Education: Gastroenteritis, although generally self-limiting, can be debilitating. Infections with some microorganisms, such as *G. lamblia*, can become chronic and result in lactose intolerance, which is common in older adults. Any new case of diarrhea not resolved in 3 to 4 days requires health-care provider intervention. Use of OTC antiperistaltic agents, such as loperamide, is contraindicated in infectious diarrhea, but may be used in immunocompetent adults with acute watery diarrhea (Shane et al., 2017).

Clinical Recommendation	Evidence Rating	References
Oral rehydration solution (ORS) is first-line therapy of mild to moderate dehydration in all ages with acute diarrhea from any cause.	A	Shane et al., 2017
Oral rehydration is the first, preferred step in treating acute diarrhea.	A	Shane et al., 2017
Antibiotics reduce the duration and severity of traveler's diarrhea.	A	Acree & Davis, 2017
Testing for *Clostridioides difficile* toxins A and B should be performed in patients who develop diarrhea after antibiotic use or hospitalization, or persistent diarrhea without an etiology.	C	Shane et al., 2017
People with fever or bloody diarrhea should be evaluated for enteropathogens for which antibiotic treatment may be beneficial: *Salmonella, Shigella, Campylobacter.*	A	Shane et al., 2017
Probiotics may be offered to reduce symptom severity and duration in immunocompetent adults with infectious diarrhea.	C	Shane et al., 2017

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GASTROESOPHAGEAL REFLUX DISEASE

Signal Symptoms: Regurgitation, heartburn (retrosternal burning), hoarseness, chronic cough, water brash, globus sensation, atypical chest pain.

Description: Gastroesophageal reflux disease (GERD) is a common disorder characterized by heartburn (epigastric/retrosternal burning) and regurgitation (reflux of gastric contents into the esophagus and/or pharyngeal tissues) (Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018). Symptoms are often postprandial with more atypical, including respiratory manifestations, and atypical symptoms more common in older adults (Commisso & Lim, 2019; Dumic et al., 2019; Richter & Rubenstein, 2018). Multiple factors contributing to the presence and severity of GERD have been identified, such as lifestyle factors, obesity, stress, and others (Commisso & Lim, 2019).

Etiology: The presentation of GERD is a complex problem than involves reduced lower esophageal sphincter (LES) tone, transient relaxation of the lower esophageal sphincter relaxation (TLESR) at inappropriate times, and decreased peristalsis (Otaki & Iyer, 2021; Richter & Rubenstein, 2018).

Occurrence: The lack of a diagnostic standard makes defining prevalence of GERD difficult. However, in the United States GERD has been estimated to affect anywhere from 6% to 30% of patients, accounting for the most common outpatient GI presentation and an average of over 100,000 hospital admissions from 2003–2006 (Dumic et al., 2019; Richter & Rubenstein, 2018; Thukkani & Sonnenberg, 2010). Additionally, it is estimated that 20% of U.S. adults have GERD symptoms weekly and 15 million reporting daily symptoms (Soumekh et al., 2014). There does not appear to be difference in occurrence of GERD between genders in North America, although men tend to have a higher risk of erosive esophagitis, Barrett's esophagus, and esophageal adenocarcinoma (Richter & Rubenstein, 2018).

Age: While the prevalence of GERD in older adults is thought to be equivalent to younger ages, it is felt that older adults tend to be less symptomatic or manifest with atypical symptoms due to factors such as decreased pain perception, less acidity of gastric contents, or increased in atrophic gastritis. However, older adults tend to suffer more complications; GERD remains prevalent and is one of the most common disorders in nursing home patients (Commisso & Lim, 2019; Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018; Sandhu & Fass, 2018)

Ethnicity: Prevalence of GERD appears to be similar across racial and ethnic backgrounds in the United States, although Whites tend to have a higher rate of complications, such as Barrett's esophagus, erosive esophagitis, esophageal adenocarcinoma, and strictures (Richter & Rubenstein, 2018).

Contributing Factors: Although some have proposed a minor genetic link to GERD, the overall contribution seems to be more related to environmental factors (Richter & Rubenstein, 2018). Intrinsic factors that contribute to the development of GERD include LES incompetence, alterations in GI tract bicarbonate levels, hiatal hernia, esophageal motility disorders, delayed gastric emptying, and gastric distention (Commisso & Lim, 2019; Dumic et al., 2019; Otaki & Iyer, 2021; Richter & Rubenstein, 2018). Patients with certain medical conditions

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that affect gastric motility such as stroke, diabetes, scleroderma, myasthenia gravis, and Parkinson's disease are also at risk for developing GERD (Bashashati et al., 2014).

There have been several environmental factors linked to GERD, including medications, obesity, tobacco, diet, and alcohol. Medications that can trigger GERD include nitrates, calcium channel blockers, benzodiazepines, antidepressants, lidocaine, tricyclic antidepressants, beta agonists, theophylline, sedatives, narcotics, anticholinergics; often they lower the LES tone. NSAIDs, aspirin, steroids, iron sulfates, gelatin capsules, antibiotics, potassium chloride tablets, vitamin C, quinidine, and bisphosphonates contribute to esophagitis, local erosions, or ulcers, which can present similarly to GERD. Obesity is a major risk factor for GERD (odds ratio [OR] 1.73), and abdominal obesity specifically is associated with many GERD complications (Eusebi et al., 2018; Richter & Rubenstein, 2018). Foods that can induce GERD include caffeine, mints, chocolate, carbonated drinks, alcohol, spicy foods, and citrus fruits; low-fiber diet has also been associated with increased GERD symptoms (Commisso & Lim, 2019; Ness-Jensen et al., 2016; Richter & Rubenstein, 2018). Other lifestyle factors associated with GERD include smoking, alcohol consumption, and stress (Commisso & Lim, 2019; Eusebi et al., 2018; Richter & Rubenstein, 2018). Exercise and GERD have a complex relationship with increased leisurely exercise being found protective, but certain exercises (such as stooping, weightlifting, and others that increase intra-abdominal pressure) are associated with increased GERD symptoms (Commisso & Lim, 2019).

Signs and Symptoms: Determine patients' precipitating factors related to the development of GERD, length of time they have been experiencing symptoms, description of the symptoms, and what regimens and/or lifestyle changes they have tried. Patients should be questioned about medication usage, smoking, alcohol, and intake of substances that can weaken the LES; sleeping habits; and use of any tight or restrictive clothing. Determine whether any activity triggers GERD, such as bending over, exercise, or being recumbent. Review the patient's dietary habits and elicit if there are food products that the patient regularly ingests that aggravate symptoms of GERD.

Question the patient about history of heartburn and regurgitation such as, pyrosis, belching, halitosis, nausea, atypical chest pain (radiation of pain to back, neck, and/or jaw), hoarseness, recurrent laryngitis, cough, choking, pharyngeal tightness, globus sensation, persistent clearing of the throat, sore throat, and chronic obstructive pulmonary disease (COPD) exacerbations (Otaki & Iyer, 2021; Richter & Rubenstein, 2018). Question about the presence of warning symptoms such as dysphagia, odynophagia, anorexia, weight loss, vomiting, or symptomatic anemia that could represent GERD complications such as erosive esophagitis with bleeding, Barrett's esophagus, esophageal adenocarcinoma, or others (Otaki & Iyer, 2021; Richter & Rubenstein, 2018). Review the medications the patient is taking to determine whether any medications reduce the LES pressure, decrease the LES pressure, and/or irritate the esophageal mucosa, such as NSAIDs. Question the patient about any previous history and/or treatment for *Helicobacter pylori*. Ask about any family history of esophageal cancer or hiatal hernia (Bashashati et al., 2014).

Physical examination usually produces no positive findings. Conduct a thorough examination of the oral cavity and a respiratory examination. Palpate for any upper abdominal masses or tenderness. If warranted by the patient's symptoms, perform a rectal examination to detect any melena.

Diagnostic Tests: If suspicion was aroused on the physical examination, stool should be checked using the guaiac test to check for intestinal bleeding. Laboratory studies are not required when antacids, position change, or both relieve pyrosis. Esophageal pH and manometry testing can be informative, although a proton pump inhibitor (PPI) trial is more appropriate in primary care as it is non-invasive, inexpensive, with sensitivity of 68% to 83% (Otaki & Iyer, 2021). For older adults with atypical symptoms, barium swallow or an endoscopy can be considered. Any patient presenting with laryngopharyngeal symptoms of GERD should be considered for a laryngoscopy (Otaki & Iyer, 2021; Vaezi et al., 2018). Additionally, patient's with extraesophageal symptoms such as chest pain or pulmonary symptoms, should be evaluated for other causes of these because symptoms are often multifactorial (Vaezi et al., 2018). Although a majority of GERD patients have a negative endoscopy, this should be considered for refractory symptoms, atypical symptoms, or warning symptoms.

Differential Diagnosis:

- Nonulcer dyspepsia
- Esophageal spasms
- Esophagitis
- Gastritis
- Eosinophilic esophagitis
- Functional dyspepsia
- Gastroparesis
- Esophageal stricture (upper gastrointestinal (GI) sinus)
- Esophageal carcinoma
- Cholecystitis
- Peptic ulcer disease (PUD)

(Richter & Rubenstein, 2018)

Treatment: The goals for the treatment of GERD include reducing symptoms, healing esophagitis, managing esophageal healing, improving quality of life, and preventing complications (Kroch & Madanick, 2017). Lifestyle changes and other nonpharmacological measures are key to symptom management, even though patients can be doubtful about their effectiveness (Commisso & Lim, 2019). These include weight management, avoidance of smoking, alcohol, trigger foods/beverages (such as high-fat, spicy, or acidic foods; mint; carbonated drinks; and caffeine), increased dietary fiber, and avoidance of late-night intake. Medications to suppress acid, such as antacids, H_2 receptor blockers, and PPIs, should be initiated for patients felt to have GERD (Otaki & Iyer, 2021; Wilkinson & Halland, 2020). Of these, PPIs remain the mainstay of treatment, given the rapid relief of GERD symptoms and esophageal healing that result from PPI treatment, and are one of the most prescribed classes of medication (Brisebois et al., 2018; Hussain et al., 2018; Otaki & Iyer, 2021). Once-a-day dosing is beneficial to aid in medication compliance, although increased frequency may be required depending on clinical response. A step-down approach can be initiated in patients with GERD by reducing

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the dosage of the PPI or by adding an H_2 blocker in the evening. While PPIs can be used long-term in patients who are unable to sustain remission without them, there are potential adverse effects, such as risk for *Clostridioides difficile* infection, vitamin and mineral deficiencies (magnesium, B_{12}, iron), and decreased bone mineral density (increased risk for fracture) (Brisebois et al., 2018; Commisso & Lim, 2019; Hussain et al., 2018; Otaki & Iyer, 2021). Subsequently, agent and dosage should be tailored to the individual patient with the dosage and need for the drug periodically reviewed to use the lowest effective dose (Freedberg et al., 2017; Kroch & Madanick, 2017). Pharmacological recommendations are listed in Table 13-3.

Follow-Up: Review lifestyle changes and the impact modifications have had on the patient's symptoms of GERD, presence of potential complications or warning symptoms (Maret-Ouda et al., 2020). Evaluate compliance with the medication regimen. Decisions should be made about any medication adjustments or plans for further testing or referral.

Sequelae: Several sequelae of GERD are possible, especially if left untreated or undertreated. These can include esophagitis with/without erosion and bleeding, esophageal stricture, Barrett's esophagus, and esophageal adenocarcinoma (Maret-Ouda et al., 2020). GERD is a risk for Barrett's esophagus with significant odds ratios (ORs) for weekly versus infrequent symptoms (OR 2.33), duration of 5 years versus less than a year (OR 3.0), and age of onset with weekly symptoms before age 30 versus later (OR 31.4) (Shaheen et al., 2016). Additional identified risks for Barrett's esophagus include obesity, smoking, family history of Barrett's, and hiatal hernia. Older adults are also at risk for developing pulmonary complications of GERD, such as chronic cough, recurrent pneumonitis, and aspiration pneumonia. Given the reflux of gastric content to the pharynx, dental erosions are also a possible sequela.

Prevention/Prophylaxis: Prevention of GERD should be aimed at eliminating or at least modifying the extrinsic factors that contribute to the development of the condition. Patients should be encouraged to make lifestyle adjustments and avoid potentially harmful medications or lifestyle choices (such as smoking) to prevent further complications.

Referral: A gastroenterologist should be consulted for the endoscopy and for patients with anemia, severe or nonresponsive reflux disease, dysphagia, odynophagia, unexplained weight loss, or evidence of hemorrhage. When a patient presents with laryngopharyngeal reflux, they should be referred for an indirect or direct laryngoscopy. If a patient presents with dysphagia, odynophagia, unexplained weight loss, or GI bleeding, or if a patient did not respond to initial therapy, refer to a gastroenterologist for further testing and evaluation/treatment.

TABLE 13-3 Pharmacological Recommendations for Gastroesophageal Reflux Disease

Treatment of Erosive or Nonerosive Gastroesophageal Reflux Disease

Proton Pump Inhibitors

DRUG	GERD DOSAGE
Dexlansoprazole	30–60 mg daily
Esomeprazole	20–40 mg daily
Lansoprazole	15–30 mg daily
Omeprazole	20–40 mg daily
Pantoprazole	20–40 mg daily
Rabeprazole	10–20 mg daily
H_2-RECEPTOR ANTAGONISTS	**GERD DOSAGE**
Nizatidine	150–300 mg q12hr
Famotidine	10–20 mg q12hr
Cimetidine*	400 mg q6hr or 800 mg q12hr
Ranitidine**	N/A

**Cimetidine is not recommended for use in older adults.*

***All ranitidine formulations (prescription and over-the-counter) were pulled from the U.S. market in 2020 by the Food and Drug Administration due to concerns of N-nitrosodimethylamine (NDMA) contamination (U.S. Food and Drug Administration, 2020)*

Education: Patients with GERD should be instructed to raise the head of the bed 4 to 6 inches with shock blocks or a foam wedge that can be placed at the head of the bed. The patient should avoid smoking and ingestion of coffee, mint, chocolate, and fatty, spicy, and acidic foods; increased dietary fiber may also be protective against GERD (Commisso & Lim, 2019; Otaki & Iyer, 2021). A food diary can help identify individualized trigger foods and substances that should be avoided. Remind patients not to break or crush extended-release or delayed-release tablets and to take medications with a full glass of water. Patients should avoid eating a meal for at least 3 hours before becoming recumbent. Decreasing abdominal pressure, such as avoiding restrictive clothing, may be helpful although evidence is limited. Oral PPIs should be administered 30 to 60 minutes before a meal (Katz et al., 2013).

Clinical Recommendation	Evidence Rating	References
A presumptive diagnosis of gastroesophageal reflux disease (GERD) can be made in the presence of typical symptoms of heartburn and regurgitation.	B	Katz et al., 2013
Weight loss is recommended in the treatment of GERD for patients who are overweight or have had recent weight gain.	B	Katz et al., 2013

Continued

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Clinical Recommendation	Evidence Rating	References
Screening for Barrett's esophagus can be considered in men with more than 5 years of GERD symptoms and/or frequent GERD symptoms who also have two or more risk factors: age >50, White, central obesity, smoking history, and history of Barrett's esophagus and/or esophageal adenocarcinoma in a first-degree relative.	B	Shaheen et al., 2016
For patients with diagnosed Barrett's esophagus without dysplasia, endoscopic surveillance should occur every 3–5 years.	B	Shaheen et al., 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

HEPATITIS A, B, AND C (VIRAL)

Signal Symptoms:

Acute Hepatitis A, B, and C: Can include fever, fatigue, abdominal pain, nausea, vomiting, jaundice, loss of appetite, diarrhea, dark urine, joint pain, clay-colored stool (Abutaleb & Kottilil, 2020; Centers for Disease Control and Prevention [CDC], 2020a, 2021a; Foster, 2019; Linder & Malani, 2017)

Chronic Hepatitis B and C: Most with chronic hepatitis B are asymptomatic, although some may develop cirrhosis or hepatocellular carcinoma (HCC) with symptoms associated with those conditions (CDC, 2020b, 2021a).

Description: The virus is transmitted primarily via the fecal-oral route after close contact with an infected person, although contact with feces or consumption of contaminated food or water are known vectors (Abutaleb & Kottilil, 2020; CDC, 2020a; Foster, 2019; Linder & Malani, 2017). After the virus is taken up in the gastrointestinal (GI) tract, it circulates to the liver where viral replication and pathology occurs followed by transaminitis 7 days later and (possible) symptoms a month later that peak 7 to 10 days after onset (Lemon & Walker, 2019; Walker, 2019). Some patients may only show mild symptoms or no symptoms, although asymptomatic hepatitis A is more common in children than adults (Linder & Malani, 2017; Shin & Jeong, 2018). Acute hepatitis A typically self resolves after 2 months, with no chronic disease or carrier state and typically no reinfection due to antibody production from initial exposure (Abutaleb & Kottilil, 2020; CDC, 2020a; Linder & Malani, 2017). However, as many as 15% of patients can have relapsing infection with recurrent symptoms within 6 months of initial infection (Abutaleb & Kottilil, 2020; CDC, 2020a). Acute liver failure is rare, occurring in 1 out of every 300 infections, and death can occur in approximately 10% of hepatitis A liver failure patients; these are more common in patients with pre-existing liver disease (Abutaleb & Kottilil, 2020; CDC, 2020a; Linder & Malani, 2017; Shin & Jeong, 2018).

Hepatitis B (HBV) is a partly double-stranded DNA virus with ten distinct genotypes and is transmitted through infected body fluids like semen, blood, and saliva (CDC, 2020b; Lin & Kao, 2017; Wilkins et al., 2019). Once in the person's system, hepatitis B makes its way to the liver and infects hepatocytes, where it causes acute infection and can damage the liver. After HBV exposure, symptoms typically present an average of 90 days later (if at all). Approximately 95% of adults will recover completely, while the remaining 5% progress to chronic hepatitis B infection (CDC, 2020b). The partly double-stranded DNA of the HBV can be repaired by the host cell into a covalently closed circular DNA (cccDNA), which is what allows chronic hepatitis B to persist despite antiviral treatment (Li et al., 2018; Lin & Kao, 2017). Hepatitis B carries with it a high level of morbidity and mortality, with 15% of adults dying prematurely from cirrhosis or HCC, although treatment helps reduce this risk (Wilkins et al., 2019).

Hepatitis C virus (HCV) is an RNA-based virus that is transmitted primarily through blood-blood contact or through body fluids that contain blood and is the only chronic viral disease that is consistently curable with the use of antiviral medications (Andrews, 2018; CDC, 2021a; Wilkins et al., 2015). HCV is responsible for more deaths in the United States than the next 60 reportable diseases combined, including tuberculosis and HIV (Andrews, 2018). Patients who contract HCV develop acute HCV infection, which can be either eradicated by the body or progress to chronic hepatitis C infection. It is estimated that about half of people who contract HCV will clear the infection spontaneously while half will progress to chronic infection (Seo et al., 2020). Of those with chronic hepatitis C infection, 5% to 25% will develop cirrhosis within 10 to 20 years; among these patients there is a 1% to 4% risk of HCC and 3% to 6% risk of developing decompensated cirrhosis; in patients with decompensated HCV cirrhosis, the 1-year mortality rate is 15% to 20% (Thomas & Seeff, 2005). Hepatitis C has been the number 1 etiology for liver transplantation for a number of years but fell to number 3 in 2016, likely due to development of highly effective and well-tolerated treatment regimens (Vyhmeister & Enestvedt, 2021).

Etiology: Hepatitis A is caused by ingestion of the viral particles via fecal-oral route, typically after close contact with an infected individual. Other means of transmission and infections are through sexual contact with an infected individual or ingestion of contaminated food or water (Abutaleb & Kottilil, 2020; CDC, 2020a; Foster, 2019; Linder & Malani, 2017). Transmission and infection are more common in certain individuals who are at higher risk, as discussed below.

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Hepatitis B is transmitted by infected body fluids, such as blood, semen, and saliva, that are able to enter the system through breaks in the skin or mucous membranes (CDC, 2020b). Such transmission activities include sex with an infected person, injection drug use, sharing of injection drug paraphernalia, maternal-newborn transmission during childbirth, infected body fluid contact with an open wound, or sharing items that can break the skin/mucous membranes (such as a razor or toothbrush) with an infected person. Individuals considered high risk for HBV include infants born to mothers who are infected with HBV, men who have sex with men (MSM), sex partners of infected persons, people who inject drugs (PWID), household contacts of infected persons, individuals at risk for occupational exposure (such as health-care workers and public safety workers), and patients on hemodialysis (CDC, 2020b).

For HCV, the primary means of transmission are through injection drug use and birth to an HCV-infected mother (Andrews, 2018; CDC, 2021a) with vertical transmission during childbirth responsible for the highest risk of HCV in children (Baden et al., 2014). Injection drug use accounts for 60% of annual acute HCV infections and approximately 65% of PWID are positive for hepatitis C, indicating exposure or active infection (Guss et al., 2018; Wu et al., 2019). Other less common means include having sex with an HCV-infected partner (especially MSM), sharing personal care products, undergoing health-care procedures, getting tattooed with contaminated supplies, receiving blood products (very rare after 1992), and being exposed to occupational hazards such as needle sticks. Although transmission through sex is uncommon, the risks increase in sexual contact where blood is exposed, such as anal sex, sex during menses, and sex with a partner with open lesions; however, HCV is more infectious than HBV or HIV when transmitted through IV drug use or intranasal drug use (Andrews, 2018).

Occurrence: Hepatitis A is more common in developing countries, although unvaccinated adult individuals in developed countries are at higher risk of becoming ill from hepatitis A infection (Abutaleb & Kottilil, 2020). In the United States, infections tend to occur as outbreaks, such as in food service via contaminated food (especially fruits and vegetables), daycare centers (from infants and children transmitting to unvaccinated adults), in specific communities (such as Native American tribes in the United States), and in areas with poor sanitation (Abutaleb & Kottilil, 2020; Cheek et al., 2011; Linder & Malani, 2017; Purpari et al., 2019). An outbreak in San Diego, California, among mostly boys and men who experienced frequent homelessness, injection drug use, and MSM behavior may indicate a shift in hepatitis A infection from food and water contamination to poor sanitation related to homelessness, overcrowding, and injection drug use (Abutaleb & Kottilil, 2020; Wooten, 2019). Other outbreaks have also been linked to homelessness, which seems to support this notion (Linder & Malani, 2017). Although the rate of hepatitis A infection in the United States had declined 95% from 1996–2011, the CDC noted approximately 15,000 cases from 2016–2018, which is a 294% increase compared to 2013–2015 (Foster, 2019).

In 2019, there were an estimated 20,700 cases of acute hepatitis B with an incidence rate of 1.0 per 100,000 people (CDC, 2021c). This is a slight decrease from an estimated 21,600 cases (incidence 1.0 per 100,000) in 2018 and 21,900 cases in 2015 (incidence 1.1 per 100,000) in 2015 (CDC, 2020b; Wilkins et al., 2019). Overall, the incidence of hepatitis B has been relatively stable from 2011 to 2018 fluctuating from 0.9 to 1.1 per 100,000 persons (CDC, 2020b). It is estimated there are between 850,000 to 2 million persons in the United States living with chronic hepatitis B (CDC, 2020b; Wilkins et al., 2019). Finally, in 2018 there were 1,649 deaths with HBV listed as an underlying or contributing cause of death on death certificates in the United States, although this is felt to be a conservative estimate with the actual deaths from HBV likely higher (CDC, 2020b).

In 2019, for hepatitis A and B, males had nearly twice the incidence of infection than females, which has been the case for hepatitis B for 15 years (CDC 2021f, 2021i). With hepatitis A, however, there are no differences in disease severity between sexes after the infection is contracted (Chang & Liaw, 2019).

In 2019, 4,136 cases of acute hepatitis C were reported, although the estimate for the true number of cases is around 57,500 with an incidence rate of 1.3 per 100,000 people (CDC, 2021d). This represents an increase in both reported and estimated cases each year since, starting in 2012 with 1,778 reported and 24,700 estimated (CDC, 2021k). It is estimated that 2.4 million people were living with hepatitis C from 2013–2016 (CDC, 2021a). Since 2011, males have had an accelerated increase in incidence compared to females, and in 2019 the incidence in males was 60% higher than females (CDC, 2021m). However, data for hepatitis C are difficult to ascertain due to the asymptomatic nature of the disease and the fact that many patients with chronic HCV are unaware of their infection (Office of Infectious Disease and HIV/AIDS Policy, 2016). In 2018, a total of 15,713 deaths had HCV as an underlying or contributing cause, although this is also a conservative estimate as most people who die lack HCV documentation on their death certificates (CDC, 2021a).

Age: In 2019, adults aged 60 and older in the United States represented the lower end of the incidence rates based on age for Hepatitis A, B, and C (CDC, 2021e, 2021h, 2021l; Shin & Jeong, 2018). However, patients older than age 40 who contract hepatitis A have a higher risk of severe disease and poor outcomes (Shin & Jeong, 2018). In hepatitis B, the younger the age of infection, the more likely a person is to develop chronic hepatitis B infection rather than clear the virus (Trépo et al., 2014). Finally, in hepatitis C, contracting the virus at an older age does not eliminate the associated risk of HCC.

Ethnicity: In 2019, the incidence rate for acute hepatitis A in the United States was highest in the White, non-Hispanic population (6.8/100,000) (CDC, 2021g). The lowest incidence rate of acute hepatitis A was in individuals of Asians/Pacific Islander descent at 0.7/100,000.

In 2019, the highest incidence rate of acute hepatitis B was in the White and non-Hispanic population of the United States (at 1.0/100,000), although this was closely followed by Black, non-Hispanic groups at 0.9/100,000 (CDC, 2021j). The lowest incidence rate of acute hepatitis B in the United States in 2019 was in those of Asian/Pacific Islander descent

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(similar to hepatitis A) at 0.3/100,000. Although the incidence rates for various ethnic groups have been relatively stable since 2004, the Native American/Alaskan Native population dropped from a peak rate of 1.8/100,000 in 2008 to 0.6/100,000 in 2019. Likewise, the Black, non-Hispanic population has dropped from a peak of 3.0/100,000 in 2005 to 0.9/100,000 in 2019 (CDC, 2021j).

In the United States in 2019, the Native American/Alaskan Native population had the highest incidence rate for acute hepatitis C at 3.6/100,000, with the second highest rate among the White, non-Hispanic population at 1.4/100,000 (CDC, 2021n). The lowest incidence of acute hepatitis C in 2019 was found in the Asian/Pacific Islander population at 0.2/100,000.

Contributing Factors: Although hepatitis A is primarily transmitted via the fecal-oral route by close contact with infected individuals (including sexual contact) and consumption of contaminated food or water, there are multiple risk factors for hepatitis A. These include MSM, travel to a country where hepatitis A is endemic, occupation with exposure risk, homelessness, and IV drug use (CDC, 2021d). Patients at risk for severe disease such as acute liver failure and death are older patients (>40 years old), those with pre-existing liver disease, and those who are immunocompromised (such as patients who are HIV positive) (CDC, 2020a; Linder & Malani, 2017; Shin & Jeong, 2018).

Because hepatitis B is transmitted by contaminated body fluids such as semen, saliva, and blood, the risk factors are easily understood (CDC, 2020b). Individuals at high risk for contracting hepatitis B via body fluids/blood include PWIJ because of potential of sharing infected or used needles or drug preparation paraphernalia. Also, household contacts of people who are infected with hepatitis B are at increased risk because of the potential for inadvertently contacting blood from open wounds, shared razors, toothbrushes (with gingival bleeding), and others. Health-care workers and public safety workers are at increased occupational exposure because of the potential for inadvertent needle sticks, spitting, and splatter of body fluids. Infants born to mothers infected with hepatitis B can contract hepatitis B through placental exchange or passing the infection from body fluids during childbirth. Finally, sexual partners of HBV-positive persons are at high risk due to body fluid exchange during sex; this is especially true with the MSM population, especially if sex is vigorous enough to have potential blood exchange (CDC, 2020b).

Because hepatitis C is transmitted by blood and blood-containing body fluids the individuals at risk are those who share blood or body fluids (Andrews, 2018; CDC, 2021a; Guss et al., 2018; Wilkins et al., 2015). One of the largest at-risk populations includes individuals born between 1945 and 1965, likely due to no universal precautions and other processes in vaccination, medical equipment sterilization, and dental care at that time. This population has a sixfold increased prevalence compared to other age-groups, and they represent 81% of persons with chronic HCV (Reilley et al., 2016). People who have used injection drugs (even long ago) are at increased risk for HCV because of the potential for sharing needles or drug preparation paraphernalia, which can introduce contaminated blood to an uninfected individual. Anecdotally, pockets of populations with high levels of HCV infection often have the same HCV genotype because the virus is spread among injection partners. People with HIV are also at increased risk for HCV, primarily PWID, because both viruses are transmitted through blood if needles are shared. Blood transfusion or organ/tissue transplant recipients are currently at low risk due to adequate blood and tissue testing for HCV. However, this testing was initiated in 1992; therefore, people who received blood or tissue/organ donations before then are at high risk. Those with occupational risk such as health-care or public service workers are at increased risk because of potential needle sticks, bleeding wounds, and others. Finally, children born to mothers who are positive for HCV are at high risk for HCV infection due to body fluid and blood transmission during the birth process and mother-baby placental exchange during fetal maturity (CDC, 2021a).

Signs and Symptoms: Although hepatitis A, B, and C are different viruses with different modes of transmission, risk groups, and rates of complication, they all affect the liver. Therefore, signs and symptoms are common amongst them. Symptoms that patients may have from acute viral hepatitis (from hepatitis A, B, C) include fever, fatigue, abdominal pain, nausea, vomiting, loss of appetite, diarrhea, dark urine, joint pain, and clay-colored stool (Abutaleb & Kottilil, 2020; CDC, 2020a, 2021a; Foster, 2019; Linder & Malani, 2017). Many of these symptoms are nonspecific and therefore unless more obvious or ominous symptoms or signs develop, many patients may not seek care. This is the basis for why, for example, approximately 40% of people with hepatitis C are unaware of their infection status (Office of Infectious Disease and HIV/AIDS Policy, 2016).

Physical examination and routine laboratory testing elicit signs such as jaundice or bilirubinemia and, because they are more ominous, should trigger testing for liver diseases including acute viral hepatitis. With chronic hepatitis B and C, patients are often asymptomatic until their disease progresses enough to result in advanced liver disease, which presents with its own set of signs and symptoms such as encephalopathy, palmar erythema, splenomegaly, hepatomegaly, spider telangiectasias, abdominal swelling (from ascites), lower extremity edema, anorexia, easy bruising/bleeding (from thrombocytopenia), and others (Butterworth, 2019; Martin et al., 2014; Smith et al., 2019). Additionally, there have been previously reported extrahepatic manifestations of hepatitis A, including rash, kidney injury, myocarditis, and Guillain-Barré syndrome (Allen et al., 2018).

Diagnostic Tests: Laboratory diagnosis of hepatitis A is accomplished with serological testing for anti-hepatitis A IgM antibodies (Abutaleb & Kottilil, 2020; CDC, 2020a). Hepatitis A immunoglobulin M (IgM) typically peaks a month after exposure and can last up to a year, and it can also be found in cases of recent immunization; false positives have been reported in certain patients, including some with autoimmune diseases (Abutaleb & Kottilil, 2020). Hepatitis A IgG follows after about 1 week, lasts for life, and confers immunity to future hepatitis A infection (Abutaleb & Kottilil, 2020). Hepatitis A RNA levels can be ordered, although is typically not necessary given availability of antibody testing. Finally, in the absence of hepatitis A antibody testing, a clinical diagnosis can be made in the presence of acute illness with any sign/symptoms of acute viral hepatitis AND the

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presence of jaundice or serum bilirubin >3.0 mg/dL or elevated alanine aminotransferase (ALT) levels >300 IU/L, and the absence of a more likely diagnosis (CDC, 2020a). Additional testing, including hepatic function panel, prothrombin time (PT) test/International Normalized Ratio (INR), imaging of the liver, and others can be investigated for decompensating disease and subsequent liver failure, although this is out of the scope of primary care.

Certain individuals should undergo screening for hepatitis B as recommended by both the U.S. Preventative Services Task Force (USPSTF) and/or the CDC. Screening is recommended for high-risk individuals as well as individuals who are HIV positive, those who are pregnant, persons born in regions of the world with a ≥2% HBV prevalence (such as Africa, Asia, and Eastern Europe), U.S.-born persons not vaccinated as infants whose parents were born in regions with a very high prevalence of HBV infection (i.e., ≥8%), patients on immunosuppression, infants born to people who are positive for hepatitis B surface antigen (HBsAg), patients on hemodialysis or chemotherapy, persons who are potential source of hepatitis B that could be spread to others (such as blood and/or tissue donors), and individuals with unexplained transaminitis (elevated aspartate aminotransferase [AST] or ALT) (CDC, 2020b; Wilkins et al., 2019). Screening involves testing for HBsAg and, if positive, a follow-up test for hepatitis B surface antigen antibody (anti-HBs) and hepatitis B core antigen antibody (anti-HBc) to differentiate infection versus immunity (Abara et al., 2018; Weinbaum et al., 2009; Wilkins et al., 2019).

Additionally, patients with certain risk factors should undergo routine, ongoing screening if those risk factors/behaviors are persistent. This includes PWID, intranasal drug use, persons who have sex with HCV-infected persons (especially MSM and unprotected sex) and persons who have certain medical conditions such as end-stage renal disease with ongoing hemodialysis (CDC, 2021a; Wilkins et al., 2015).

For patients with acute hepatitis B, testing and monitoring for clearance versus development of chronic state should be undertaken by a specialist. Evaluation for clearance versus chronic infection typically involves testing for hepatitis B e-antigen (HBeAg), detectable in early acute disease, and serum HBsAg, which indicates chronic hepatitis B if present for more than 6 months. Routine follow-up for signs of chronic HBV, reactivation of quiescent HBV (sudden flare-up of hepatitis B DNA in previously inactive chronic disease or resolved hepatitis B), fibrosis, cirrhosis, and liver failure can include trending AST/ALT levels, various ratios of antigen and antibody testing, HBV DNA levels, complete blood count (CBC) with platelets, INR (CDC, 2021c; European Association for the Study of the Liver, 2017; Terrault et al., 2016; Wilkins et al., 2019).

The CDC recommends one-time screening for all adults as well as screening for pregnant women during each pregnancy (CDC, 2021a).

Testing for hepatitis C beings with testing for hepatitis C antibodies (anti-HCV) through any of a number of assays (CDC, 2021a; Guss et al., 2018; Wilkins et al., 2015). Hepatitis C antibody testing has a sensitivity and specificity of 95% and 99%, respectively (AASLD/IDSA HCV Guidance Panel, 2015). If the HCV antibody test is positive, confirmation with a quantitative or qualitative test for HCV RNA should be performed, although quantitative testing will be required to determine viral load if treatment is desired (CDC, 2021a; Guss et al., 2018; Wilkins et al., 2015). If a patient has a negative HCV antibody test and may have been exposed within the last 6 months, then HCV RNA should be tested every 4 to 8 weeks for a minimum of 6 months or repeat HCV antibody testing should be performed at least 12 weeks later (likely more cost-effective) (Wilkins et al., 2015). Further testing and work-up will be required prior to initiating treatment.

Differential Diagnosis:

- Liver cancer
- Alcoholic hepatitis
- Autoimmune hepatitis
- Drug-induced liver injury
- Nonalcoholic steatohepatitis
- Shock-induced liver injury
- Congenital hepatic fibrosis
- Portal hypertension
- Schistosomiasis

Treatment: There is no treatment for routine, nonsevere hepatitis A infection (Abutaleb & Kottilil, 2020; Linder & Malani, 2017; Shin & Jeong, 2018). Rather, care is typically supportive including hydration and symptomatic management of fever and nausea/vomiting, and other symptoms until they resolve. For patients who develop liver failure, which is typically rare, liver transplant may be the only treatment available to prevent death and quick referral to a transplant center is critical (Abutaleb & Kottilil, 2020; Shin & Jeong, 2018). Certain direct-acting antiviral medications have shown promise in cell culture studies, although there has been difficulty in identifying and enrolling patients in clinical trials before acute infection resolution (Abutaleb & Kottilil, 2020).

Treatment of hepatitis B can be quite complex. Additionally, because of the HBV cccDNA accumulation in hepatocytes, patients can have persistent chronic hepatitis B despite antiviral treatments (Li et al., 2018; Wilkins et al., 2019). Because of this complexity, treatment is best undertaken by gastroenterology specialists who treat hepatitis B, infectious disease specialists, or hepatology specialists. Treatment need should be evaluated through ALT and HBV DNA as well as liver disease presence/severity and should be individualized to each patient (Ghany, 2017). The goal of HBV treatment is immunological cure, defined as loss of HBsAg with sustained suppression of HBV DNA, and normalization of ALT; these goals are correlated with improved outcomes and are possible with current therapies (Wilkins et al., 2019). It has been shown that treating pregnant women who are HBsAg positive can reduce the risk of perinatal transmission (Wilkins et al., 2019). Treating patients with chronic hepatitis B who develop decompensated cirrhosis can improve liver function, increase survival, and prevent need for liver transplantation, especially if treatment is initiated early in their decompensation; like any patient with decompensated cirrhosis, they should be referred to a liver transplant center for evaluation for liver transplant (European Association for the Study of the Liver, 2017).

There are eight approved hepatitis B treatment medications in the United States that span two classes: peginterferon alfa-2a agents (given subcutaneously) and oral nucleoside/nucleotide analogues (Terrault et al., 2016). There are multiple contraindications and precautions associated with each

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medication, such as renal function impairment, history of seizure disorders, diabetes, cardiovascular diseases, neuropsychiatric disorders, and hemorrhagic cerebrovascular events (CVA). Potential adverse effects range from mild to severe and can include flu-like symptoms, headache, fatigue, bone marrow suppression, acute renal failure, Fanconi's syndrome, lactic acidosis, pancreatitis, and others (Terrault et al., 2016). Primary care providers who have patients with hepatitis B undergoing treatment should monitor for potential adverse effects and contact the treating specialist as needed.

Treatment of hepatitis C has evolved tremendously in recent years. Prior to initiating treatment, several other work-up tests need to be completed. Serological testing pretreatment includes CBC, complete metabolic panel (CMP), HCV genotype, HIV testing, and quantitative HCV RNA (if not already completed) (Guss et al., 2018). CBC and CMP should be done at baseline and 4 weeks after treatment initiation. Genotype (1a, 1b, 2, 3, 4, 5, or 6) testing impacts the specific medications that can effectively treat the patient. The most common genotypes in the United States are genotypes 1a/1b (75%), genotype 2 or 3 (20% to 25%); genotypes 4 to 6 are rarer in this country (Guss et al., 2018). The viral load (determined with quantitative HCV RNA) impacts the length of treatment required. Additionally, patients should be evaluated for liver fibrosis or cirrhosis with either liver biopsy (gold standard) or noninvasive methods such as ultrasound elastography as degree of fibrosis/cirrhosis impacts treatment options (Guss et al., 2018).

Although primary care treatment is becoming more common, patients with complicated disease as with advanced fibrosis/cirrhosis, HIV co-infection, and renal disease should be referred to gastroenterology (with HCV treatment experience) or hepatology (Guss et al., 2018). Patients should be evaluated for likely compliance before initiating treatment (Wilkins et al., 2015). The standard of "cure" is sustained viral response at 12 weeks after treatment (SVR-12), although HCV RNA should be tested 4 weeks into therapy as well as 12, 24, and 48 weeks after completion of treatment (Guss et al., 2018). Patients should also be warned that re-infection, typically through high-risk behaviors, is possible after cure. Treatment duration ranges from 8 to 12 weeks depending on patient-specific factors, and medications involve 1 to 3 pills a day depending on the treatment option selected.

In regard to age, treatment for HCV should not be withheld solely due to age, and treatment should be offered to all patients older than 18 years who are eligible for treatment based on patient-specifics, except those with a life expectancy of 12 or fewer months (Ghany et al., 2020; Guss et al., 2018; Pan et al., 2020). A study was done that examined the efficacy of direct-acting antiviral (DAAs) in a large cohort of older adults in the United States. This study found that older patients represent a large, increasing population of patients with HCV and have strong indications for treatment because they tend to present with more advanced liver disease (Pan et al., 2020). It has been found that the efficacy of DAAs on treating hepatitis C in older patients is not significantly impacted (Pan et al., 2020). Table 13-4 shows approved DAA hepatitis C treatment regimens.

TABLE 13-4 Hepatitis C Treatment Medications

MEDICATION	GENOTYPE(S) TREATED
Sofosbuvir/velpatasvir	1–6
Elbasvir/grazoprevir	1, 4
Daclatasvir	1, 3
Glecaprevir/pibrentasvir	1–6
Ombitasvir, paritaprevir, ritonavir	4
Ombitasvir, paritaprevir, ritonavir, dasabuvir	1
Ledipasvir/sofosbuvir	1, 4, 5, 6
Simeprivir	1
Sofosbuvir	1–6
Sofosbuvir/velpatasvir/voxilaprevir	1–6 (with prior treatment experience)

Source: *Guss et al., 2018.*

Follow-Up: Follow-up for acute hepatitis A is focused on reevaluating liver function and serological testing, checking for any decompensation of the liver, and ensuring resolution of symptoms and the causative infection. Referral to gastroenterology or hepatology may be indicated depending on the clinical course.

Patients with chronic hepatitis B who are not treatment candidates require ongoing monitoring including ALT levels every 3 months for the first year and every 6 months after that, as well as HBV DNA levels for any elevated AST or ALT; patients who are not treatment candidates may become candidates in the future depending on their clinical progression (Ghany, 2017; Terrault et al., 2016, 2018). These patients should also undergo regular HCC screening because nearly half of all cases of HCC are in patients with chronic HBV (Tang et al., 2018). Screening with alpha fetoprotein (AFP), liver ultrasound, or both has mixed reviews. A randomized controlled trial found 37% reduction in mortality for these patients who did undergo routine screening, but a Cochrane review found insufficient evidence to support screening with ultrasound and/or AFP (Aghoram et al., 2012; Zhang et al., 2004). Regardless, if either test is abnormal, then computed tomography (CT) or magnetic resonance imaging (MRI) should be ordered (Tang et al., 2018). Patients should also be seen regularly to assess for HBV reactivation, signs and symptoms of cirrhosis, and signs and symptoms of decompensation.

Follow-up for patients with hepatitis C can vary depending on whether the patient has been treated or not. For patients currently on treatment, they should be monitored for compliance with therapy, adverse effects, and newly developing comorbidities (Wilkins et al., 2015). For patients who were treated, follow-up HCV RNA levels at 12 weeks after treatment (SVR-12/"cure"), 24 weeks after treatment, and 48 weeks after treatment should be performed (Guss et al., 2018). Additionally, patients should be monitored for any ongoing high-risk behaviors that could justify ongoing, yearly testing for HCV antibody/reinfection. It should be noted, however, that liver fibrosis and/or cirrhosis due to HCV can be improved or reversed after treatment and

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therefore reevaluation for level of fibrosis can be evaluated in the future after treatment (Hytiroglou & Theise, 2018).

Prevention/Prophylaxis: The best prevention for hepatitis A is vaccination. There are two types of vaccines currently available, including single-antigen hepatitis A vaccines (2 doses, 6 months apart) and combination vaccines (hepatitis A and hepatitis B; 3 doses given at month 0, 1, and 6) (Abutaleb & Kottilil, 2020; CDC, 2020a). Hepatitis A vaccination is currently recommended by the CDC Advisory Committee on Immunization Practices (ACIP) for all children younger than 18 years old, those at increased risk for hepatitis A infections, people at increased risk for severe disease from hepatitis A infections, those with occupational exposure hazards, unvaccinated individuals in areas experiencing a hepatitis A outbreak, and any individual who requests a vaccination (CDC, 2020a). Additional prevention measures include proper sanitation measures, especially hand hygiene in food services, as well as enteric precautions for patients with hepatitis A requiring hospitalization (Abutaleb & Kottilil, 2020).

Prevention of hepatitis B is best accomplished with high-risk behavior avoidance, vaccination, or both. In general, avoiding high-risk behaviors, such as not using injection drugs, practicing safe sex, using universal precautions in high-risk occupational settings, and not sharing personal care products (razors, toothbrushes, and others), can help decrease the risk of HBV exposure. ACIP also recommends HBV vaccination in several populations. These include all infants within 24 hours of birth, unvaccinated children younger than 19 years old, people with hepatitis C or HIV, people with chronic liver disease of other etiology (alcoholic liver disease, fatty liver disease, autoimmune hepatitis, etc.), people who are incarcerated, people traveling internationally to regions with ≥2% prevalence of HBV, patients at high risk of HBV exposure, and any individual seeking HBV protection (CDC, 2020b; Schillie, Vellozzi, et al., 2018; Wilkins et al., 2019). The hepatitis B virus (HBV) can survive outside the body for 7 or more days but can be killed with bleach and other viricidal cleaning solutions (CDC, 2020b).

There are currently three single-antigen (HBV only) vaccines and one combination vaccine (HBV/HCV) available for adults in the United States (CDC, 2020b). The vaccine schedule is usually 3 doses initially, 1 month after the initial doses, and 6 months after the initial doses. One formulation (Heplisav-B) is approved for 2 doses separated by 1 month (CDC, 2020b, 2021b; Schillie, Vellozzi, et al., 2018). Post-vaccination testing for immunity (anti-HBs >10 mIU/mL) is only indicated in patients who are at risk for being a nonresponder, such as immunocompromised patients, hemodialysis patients, health-care workers, and sexual partners of persons who are HBsAg positive (Kao, 2015; Schillie, Harris, et al., 2018). For nonresponders, revaccination can be completed with either a full repeat series followed by post-vaccination testing or a single dose followed by post-vaccination testing and completion of the series if still a nonresponder. More than two vaccine series is not recommended except in hemodialysis patients who should undergo annual testing and booster if anti-HBs <10 mIU/mL (CDC, 2020b; David et al., 2015; Schillie, Harris, et al., 2018).

There is currently no vaccine available for hepatitis C. Patients with hepatitis C should be assessed for alcohol intake and encouraged to decrease or abstain from alcohol to prevent accelerating progression of liver disease (European Association for Study of Liver, 2014; World Health Organization [WHO], 2014). Treatment should not be withheld from patients who do consume alcohol (Wilkins et al., 2015); however, some feel this is controversial. Finally, patients with hepatitis C or at risk for hepatitis C should be encouraged to receive vaccination against hepatitis A and B to prevent further liver injury (AASLD/IDSA HCV Guidance Panel, 2015).

Referral: In most cases of acute hepatitis A, referral is not usually necessary, especially in mild or asymptomatic cases. However, the patient may benefit from a referral to gastroenterology or hepatology to evaluate and monitor liver serologies, liver function, and to check for other liver diseases that may increase the patient's risk of chronic liver disease and eventual liver failure.

All patient who are positive for hepatitis B should be referred to gastroenterology, infectious disease, or hepatology for evaluation and consideration of HBV treatment. Additionally, they should be referred to a transplant center for evaluation of possible liver transplant if they develop decompensated cirrhosis (Wilkins et al., 2019). Although primary care is invaluable in education, prevention (vaccination), and ongoing evaluation for complications of hepatitis B, treatment of the virus and management of potentially complex liver disease is a specialty domain.

Patients requiring treatment of hepatitis C should be referred to gastroenterology (with experience treating HCV) or hepatology if the primary care provider is not experienced in treatment. Additionally, patients with complicated disease (advanced fibrosis, cirrhosis, renal disease, HIV co-infection, and others) should be referred to gastroenterology or hepatology (Guss et al., 2018) because they should begin lifetime screening for HCC and monitoring for decompensation. Patients who have hepatitis C as well as other comorbidities that predispose them to ongoing liver damage or reinfection, such as excessive alcohol intake, injection drug use, metabolic syndrome (risk for nonalcoholic fatty liver disease [NAFLD] and nonalcoholic steatohepatitis [NASH]) should be referred to the appropriate specialists as needed.

Education: Patients with hepatitis A should be educated on proper hygiene and sanitation. They should be given information on preventing the spread of hepatitis A, the possibility of relapse within 6 months when they will again be contagious, and symptoms of worsening liver function. They should also be informed of the importance of testing, possible vaccination, and possible postexposure prophylaxis in individuals with whom they have had close contact. Finally, they should be educated on means of risk reduction, both for infection and for spreading the infection while they are shedding viral particles.

Patients with hepatitis B should receive counseling on high-risk behavior avoidance, such as practicing safe sex, abstinence from IV drug use, and proper hygiene (such as not sharing personal care products with others). Also, these patients should be advised to avoid or at least limit alcohol intake to prevent further liver injury that can hasten cirrhosis and/or decompensation. For similar reasons, they should be counseled on lifestyle management to reduce excess body weight and metabolic complications that can also lead to NAFLD (Terrault et al., 2018). Finally, they should be

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educated on signs and symptoms that could herald worsening liver disease, reactivation of HBV, and/or decompensated cirrhosis and to seek care immediately.

Patients who are candidates for treatment should be educated about the need for medication compliance as well as compliance with follow-up visits and laboratory testing. Patients with hepatitis C, either active or posttreatment, on the transmission, risk factors, pathophysiology, and prevention of hepatitis C. HCV cure does not eliminate the risk of reinfection, so patients should be educated to abstain from high-risk behaviors (Wilkins et al., 2015). Finally, those with liver fibrosis or cirrhosis should be educated on signs and symptoms of advanced fibrosis, cirrhosis, and their associated sequelae.

Clinical Recommendation	Evidence Rating	References
One-time screening for hepatitis C is recommended for all adults aged 18 years and older.	B	Ghany et al., 2020
Periodic hepatitis C virus (HCV) testing is recommended in all adults at high risk for infection.	B	Wilkins et al., 2015
Hepatitis C antibody testing with reflex to HCV RNA testing is recommended for initial HCV screening.	A	Ghany, 2017
Abstinence from alcohol and/or alcohol cessation should be advised to all patients with hepatitis C.	B	Ghany et al., 2020
Antiviral treatment is recommended for all HCV patients except those with a short life expectancy not able to be remediated by HCV treatment or liver transplant.	A	Ghany et al., 2020
Vaccination against hepatitis A and B should be given to all susceptible patients with hepatitis C.	C	Wilkins et al., 2015

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

HERNIA

Signal Symptoms: A dull dragging sensation with an inguinal hernia; male patients may report pain and swelling in the scrotum; patients with strangulated abdominal hernia usually have a tender mass with associated fever, nausea, and vomiting.

Description: A hernia is the protrusion of tissue through a weakened section in the abdominal wall. Abdominal wall hernias usually occur at the groin (inguinal and femoral) and abdominal (umbilicus, epigastric, spigelian, pelvic, flank, and incisional) (Ansari, 2020; Shakil et al., 2020, Suneja et al., 2020). Hernias are classified by their severity as reducible, incarcerated, or strangulated. A reducible hernia moves easily through the anatomical defect. An incarcerated hernia does not return to a normal position automatically or when manipulated externally. A strangulated hernia results when an incarcerated hernia develops edema with ischemia to the entrapped bowel (Ansari, 2020); strangulation is more common with femoral hernias than inguinal hernias (HerniaSurge Group, 2018).

In addition to these classifications, inguinal hernias may be either direct or indirect. A direct inguinal hernia passes through the posterior inguinal wall, whereas an indirect or congenital inguinal hernia enters in through the internal abdominal inguinal ring along the spermatic cord through the inguinal passage, to exit out the external inguinal ring (Shakil et al., 2020).

Etiology: Hernias may be either acquired or present from birth. Hernia development has been linked to recurrent Valsalva's maneuvers and dysfunctional connective tissue resulting from malnutrition or long-term steroid use. In older women, a history of multiple pregnancies and relaxation of the pelvic musculature, combined with loss of extraperitoneal fat, are considered etiological factors in the development of an obturator hernia (Mindaye et al., 2020).

Occurrence: In the United States, more than 700,000 herniorrhaphies for inguinal and femoral are performed annually. The most common type of hernia is the inguinal hernia, which accounts for 96% of all cases, followed by the femoral hernia, which accounts for 4% of groin hernias (Shakil et al., 2020). Approximately 175,000 patients annually in the United States are scheduled for umbilical hernia repair (Netto et al., 2021).

Age: The incidence of femoral and obturator hernias in women increases with age. The incidence of male indirect (congenital) hernias decreases with age, but that of direct inguinal hernias increases (Shakil et al., 2020). The incidence of abdominal wall hernias in older adults has been on the increase (Buretta et al., 2020).

Ethnicity: Not significant.

Contributing Factors: Family history, previous contralateral hernia, male sex, older age, abnormal collagen metabolism, radical prostatectomy, radiation therapy, and low body mass index (BMI) are known risk factors for the development of an inguinal hernia (HerniaSurge Group, 2018; Shakil et al., 2020). In fact, indirect inguinal hernias are eight to ten times more common in men than in women. (Shakil et al., 2018). Abdominal hernias often develop in patients with a history of chronic cough, ascites, abdominal surgery, and chronic peritoneal dialysis, and symptomatic prostatism can

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contribute to development of a hernia because of the associated risk factor of increased intra-abdominal or intrathoracic pressure (Ansari, 2020; HerniaSurge Group, 2018). Increasing body mass index (BMI) and older age were found to directly related to incarceration of noninguinal abdominal wall hernias in patients hospitalized for hernias (Sneiders et al., 2019). Incisional abdominal hernias can be found in patients with abdominal organ transplants (Singh et al., 2020). Chronic straining for bowel movements, straining to urinate, and lifting heavy objects may be precursors to hernia formation. For women, a weakened pelvic floor after childbirth can contribute to the development of femoral herniation. Additionally, older women are three to five times more likely than men to develop a femoral hernia than an inguinal hernia (HerniaSurge Group, 2018). Older women who are underweight and have a history of chronic illness can develop obturator hernias, a rare condition (Mindaye et al., 2020). Hernias also may form at the site of a surgical incision or a large scar. Patients with known liver cirrhosis with ascites have a 20% chance of developing an umbilical hernia (Ansari, 2020). Family history of organ herniation is also recognized as an intrinsic factor contributing to the development of hernias.

Signs and Symptoms: Patients with hernias of the groin (femoral or inguinal) may initially be asymptomatic (HerniaSurge Group, 2018). When patients present with signs and symptoms suggestive of a hernia, question them about how long the discomfort (swelling, pain, mass) has been present. Ask whether the pain is aggravated by any activity, such as heavy lifting or positioning. Inquire about abdominal surgical history. Question whether there is a family history of hernias (Ansari, 2020). Patients may report a dull dragging sensation with an inguinal hernia (Shakil et al., 2020). Male patients may report pain and swelling in the scrotum. Hernias may be asymptomatic, only to be discovered during a routine physical examination. A reducible hernia presents as a nontender mass that becomes more pronounced after a Valsalva's maneuver. An incarcerated hernia, also a nontender soft mass, is found in the abdominal, femoral, or inguinal area and remains even after gentle manipulation. Patients with strangulated abdominal hernia usually have a tender mass with associated fever, nausea, and vomiting. No attempt should be made to reduce a strangulated hernia.

Physical examination reveals decreased flatus, high-pitched or tinkling bowel sounds, abdominal distention, and tenderness of the mass. When examining a patient with a suspected hernia, assess the patient in both the supine and standing position, first observing the suspected mass before change in position. Have the patient also perform the Valsalva's maneuver. If possible, attempt to identify the location of the hernia sac and the fascial opening of the hernia when palpating the abdomen (Shakil et al., 2020). Identify the border of the suspected hernia. Although rare, a patient with a chest wall bulge on the lower chest wall may have an abdominal intercostal hernia (Sagar et al., 2019). For a suspected inguinal hernia, ask the patient to flex the leg on the side you will examine and then gently palpate the groin area. Then, with fingertips placed over the femoral area, external ring and internal ring should be inserted up into the inguinal canal (Shakil et al., 2019; Suneja et al., 2020).

Gross screening for an inguinal hernia in a male patient is made easier with the patient coughing because "hernia bulges can be felt either against the examining finger (direct hernia) or at the tip of the finger, as it approaches the internal ring (indirect hernia)" (Amerson, 1990, p. 484). A femoral hernia can often be elicited by having a patient cough or strain; the bulge will be felt below the inguinal ligament (Suneja et al., 2020). A positive Howship-Romberg's sign, which is pain experienced with internal rotation of the hip along with intestinal obstruction, has been found in patients diagnosed with an obturator hernia (Saeed et al., 2019). A mass is detected in the femoral triangle; patients experience pain down the medial aspect of the thigh all the way to the knee as a result of compression of the obturator nerve (Suneja et al., 2020).

Diagnostic Tests: In an uncomplicated asymptomatic hernia, laboratory and diagnostic tests are unwarranted. The use of ultrasound should be avoided in evaluating an apparent inguinal hernia; however, remains useful in the diagnosis of occult hernias (Shakil et al., 2020). If there is questionable strangulation from a prolonged incarcerated hernia, laboratory studies for complications may reveal leukocytosis, elevated serum amylase, and guaiac-positive stool. The use of higher resolution multidetector computed tomography (CT) scan allows for a clearer image of the anatomy studied. Axial CT scan should be requested first if a hernia is suspected (Matzke et al., 2017). Abdominal series are done postoperatively to look for signs of perforation (free air) or obstruction of the bowel (multiple air-fluid levels).

Differential Diagnosis:

- Femoral lymphadenopathy
- Femoral artery aneurysm
- Psoas abscess
- Undescended testicle
- Vasitis
- Muscle strain (Ansari, 2020; Shakil et al., 2020)

Treatment: Small, direct inguinal hernias and painless, indirect inguinal hernias do not need immediate attention; however, surgery generally is recommended within 1 week of diagnosis. Patients who are not surgical candidates can be fitted for a truss and monitored for signs of prolonged incarceration. Patients with a small, direct, nonpainful hernia should be observed for reduction of the hernia when supine. Surgical repair of strangulated inguinal, umbilical, and femoral hernias is recommended immediately unless the patient is a poor surgical risk. For patients with cirrhosis and ascites, they benefit from elective umbilical hernia repair (Guo et al., 2021). These patients need to be hospitalized, receive IV solutions, and remain on nothing by mouth (NPO) status. Patients who are not surgical candidates can be fitted for a truss and monitored for signs of prolonged incarceration. For small umbilical hernias (<2 cm), a suture repair is often recommended whereas mesh is often used for larger umbilical hernias (Köckerling et al., 2021; Koebe et al., 2021).

Follow-Up: For patients with reducible hernias, observation of the hernia during subsequent physical examination is recommended. Patients suspected of having an incarcerated hernia should be followed up within 1 week to determine whether they are experiencing any tenderness of the mass

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and if a general surgeon has seen them. For the postoperative patient who has had a herniorrhaphy, assess for wound healing and recurrence of the hernia.

Sequelae: An untreated inguinal, umbilical, or femoral hernia may become incarcerated and strangulated, with subsequent intestinal gangrene. The likelihood of incarceration is greatest for femoral hernias (Ansari, 2020). Postsurgical complications of a herniorrhaphy include wound hematomas and superficial wound infections. Nerve entrapment is a serious complication of an inguinal herniorraphy. Additional complications from hernia repair include bowel, bladder, and vascular injuries (HerniaSurge Group, 2018). In one study, 17% of patients who had laparoscopic ventral hernia repair needed subsequent abdominal surgery for reasons such as unplanned bowel obstruction (Patel et al., 2017). Approximately 50% of hernia recurrence occurs within 5 years, and an additional 20% occurs 15 to 20 years after surgical repair (Slater et al., 2014). The mortality rate is increased for patients who have undergone an emergent abdominal wall hernia repair (Surek et al., 2021). For patients undergoing umbilical hernia repair, there is a slight risk (5%) of developing a concomitant paraumbilical hernia (Netto et al., 2021).

Prevention/Prophylaxis: Cessation of cigarette smoking is recommended to reduce intrathoracic pressure from chronic coughing. Encourage the use of fiber, fluids, and stool softeners for patients who strain with defecation. Patients should avoid lifting heavy objects without proper support. As a preventive measure, encourage weight reduction for patients with obesity, especially those who have had prior abdominal surgery.

Referral: Refer the patient to a general surgeon when a hernia is detected. A strangulated hernia requires immediate attention.

Education: Inform the patient with a reducible hernia of the potential complications of an untreated hernia and the importance of reporting immediately any new clinical signs and symptoms, such as increase in pain, swelling, and/or fever. Teach patients to avoid straining to defecate or urinate. Encourage smoking cessation to reduce the probability of a chronic cough. Instruct the patients on proper techniques for lifting heavy objects. Weight reduction should be encouraged for patients with obesity. Patients also should be advised to discuss with their surgeon postoperative restrictions and plan for rehabilitation and home support given the probable restrictions to activity (Shakil et al., 2020).

Clinical Recommendation	Evidence Rating	References
In a retrospective review of patients with laparoscopic ventral hernia repair, 17% of the 733 patients required a subsequent abdominal operation.	A	Patel et al., 2017
Both increasing body mass index and older age were found to be directly related to incarceration of noninguinal abdominal wall hernias.	A	Sneiders et al., 2019
A positive Howship-Romberg's sign, which is pain elicited with internal rotation of the hip, is common in older patients with an obturator hernia.	C	Saeed et al., 2019
Patients with cirrhosis and ascites benefit from elective umbilical hernia repair.	A	Guo et al., 2021

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IRRITABLE BOWEL SYNDROME

Signal Symptoms: Abdominal pain (may be described as colicky, pain relieved by defecation), altered defecation (constipation or diarrhea), abdominal distention, change in stool frequency, and the sensation of incomplete evacuation; patients often complain of associated symptoms such as bloating, fatigue, flatulence, passage of mucus, and abdominal distention (Wilkinson & Gill, 2021).

Description: Irritable bowel syndrome (IBS) is a chronic functional gastrointestinal (GI) disorder characterized by chronic abdominal pain and altered bowel function, in the absence of an attributable structural or biochemical cause (Ford et al., 2017). The subtypes of IBS are diarrhea prominent (IBS-D), constipation prominent (IBS-C), mixed diarrhea and constipation (IBS-M), and unspecified (IBS-U) (Aboubakr & Cohen, 2021; Ford et al., 2020).

Etiology: Although IBS is felt to be due to multiple interacting factors, the exact etiology remains uncertain and is likely multifactorial (Ford et al., 2017, 2020; Wilkinson & Gill, 2021). It has been proposed that IBS, as a functional disorder, is best understood in the context of the biopsychosocial model and alterations in the gut-brain pathway. Distortions in the normal gut-brain neuropathway can results in increased visceral hypersensitivity and altered bowel transit time and motility. Many IBS patients can also have coexisting psychological conditions such as depression or anxiety, as well as other chronic pain syndromes (fibromyalgia, chronic fatigue, and others) and other functional GI syndromes such as functional dyspepsia. (Wilkinson & Gill, 2021). While the focus remains on distortions of intestinal motility and altered visceral sensation, research has begun to investigate other contributing factors, such as immune causes, changes in

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intestinal flora (gut microbiota), food sensitivities, GI infections ("postinfectious IBS") and genetic predispositions (Aboubakr & Cohen, 2021; Ford et al., 2017, 2020; Wilkinson & Gill, 2021).

Occurrence: While IBS is a common GI complaint, its true prevalence is difficult to estimate due to a lack of biomarkers and a reliance on symptoms clusters for diagnosis (Ford et al., 2020; Wilkinson & Gill, 2021). However, estimates of prevalence range from 5% to 17% (Aboubakr & Cohen, 2021; Ford et al., 2020).

Age: The majority of patients with IBS are diagnosed at a younger age, typically younger than 50 years old (Ford et al., 2020). In fact, compared to the 5% to 17% prevalence in the general population, estimates are 7.3% of adults 60 and older (Lovell & Ford, 2012). Because most cases of IBS present by age 50 years, this syndrome is often a chronic condition in older adults for which treatment and management are still needed.

Ethnicity: IBS has a higher prevalence among Whites than among other ethnic groups (Minocha, 2005). However, comprehensive data are hard to find.

Contributing Factors: There have been multiple factors associated with IBS, including female sex (prevalence of IBS is significantly higher in women than in men [Sperber et al., 2017]), family history of IBS, and genetic contributors (Ford et al., 2017, 2020). Patients with IBS also tend to have coexisting psychiatric and/or psychological diagnoses, including stress and anxiety, and somatic disorders such as fibromyalgia and chronic fatigue syndrome (Aboubakr & Cohen, 2021; Ford et al., 2020; Wilkinson & Gill, 2021). Traumatic life events, such as physical or sexual abuse, may trigger the onset of IBS (Ford et al., 2017; Wilkinson & Gill, 2021). Certain food triggers have been identified, such as foods high in fermentable oligosaccharides, disaccharides, monosaccharides, and polyols (FODMAPs) which can include fructose, lactose, sorbitol, and other substances. Additionally, alterations in the gut microbiota (possibly from food triggers) have also been examined and associated with IBS (Ford et al., 2017, 2020).

A very common contributor to IBS is acute GI infection, such as bacterial, viral, or protozoa infections, which can result in postinfectious IBS (Aboubakr & Cohen, 2021; Ford et al., 2017, 2020; Wilkinson & Gill, 2021). While symptoms may be transient, they can morph into chronic IBS with one study finding 15% of postinfectious IBS patients having persistent symptoms 8 years after onset (Ford et al., 2020). Recent findings have indicated that the 5-HT (serotonin) concentration was higher in patients with IBS diarrhea type (IBS-D) and lower in those with IBS constipation type (IBS-C) than the general population (Camilleri, 2018). Various other contributors to IBS and symptom severity can include GI mucosal inflammation, abdominal or pelvic surgery, poor coping skills, lack of social support, and maladaptive thoughts (Ford et al., 2020).

Signs and Symptoms: A thorough dietary history is essential to establish a differential diagnosis of IBS, ruling out the possibility of food intolerances such as celiac disease or lactose intolerance. Review recent travel history with the patient for possible travel-related GI exposures. Explore the patient's psychosocial history to determine the relationships between stressful events and exacerbation of IBS as well as coexisting psychological/psychiatric diagnoses such as depression or anxiety. Determine when the symptoms initially began and typical symptoms pattern including the time of day when the pain and GI disturbances usually occur and any known triggers. A thorough GI review of systems is important in patients with IBS because GI conditions such as celiac disease and functional GI disorders such as functional dyspepsia, functional diarrhea, and functional bloating are often found in patients presenting with IBS symptoms (Ford et al., 2020; Wilkinson & Gill, 2021). A report of postprandial abdominal pain may suggest biliary tract disease, pancreatitis, or peptic ulcer disease (PUD). Patients often present with a change in stool pattern, such as constipation, diarrhea, or both that is associated with abdominal pain. However, patients with IBS rarely have nocturnal stools (Wilkinson & Gill, 2021).

Abdominal pain may be described as colicky, located in the lower abdomen, and associated with defecation or altered stool frequency/consistency. Pain is often relieved by defecation. Abdominal bloating and subsequent distention, mucus in the stool, and the sensation of incomplete evacuation are other presenting symptoms (Aboubakr & Cohen, 2021; Ford et al., 2020; Wilkinson & Gill, 2021). It should be noted that patient presentations with IBS can be highly variable (Wilkinson & Gill, 2021).

Patients should be assessed for extragastrointestinal symptoms, which are common and can include back pain, gynecological and urinary symptoms, headache, and fatigue. Older adults tend to have greater incidence of rectal urgency with fecal incontinence than younger patients (Minocha, 2005). Patients should be questioned for the presence of alarm symptoms, including onset after 50 years old, unintentional weight loss, family history of GI malignancy (such as colorectal cancer), GI bleeding, nocturnal diarrhea, and progressively worsening symptoms. The presence of any of these demands further investigation for the presence of more insidious pathologies (Aboubakr & Cohen, 2021; Wilkinson & Gill, 2021).

The physical examination is usually unremarkable, although there may be nonspecific abdominal tenderness on examination (Aboubakr & Cohen, 2021). Presence of an abdominal mass, lymphadenopathy, hepatosplenomegaly, or ascites in a patient with IBS should prompt further investigation (Wilkinson & Gill, 2021). A routine digital rectal examination generally reveals a tender rectum that is either empty or full of hard, firm feces. It is important to discern whether there are any disorders that may contribute to difficult or painful defecation, such as fissures, external hemorrhoids, or rectocele. Detection of a rectal mass on digital rectal examination is concerning and must be further evaluated to rule out malignancy. Additionally, the presence of any rectal bleeding is a warning sign and should be further investigated as is iron-deficiency anemia (Aboubakr & Cohen, 2021; Ford et al., 2020; Wilkinson & Gill, 2021).

Diagnostic Tests: IBS is often underdiagnosed because it is frequently not recognized (Wilkinson & Gill, 2021). IBS is not a diagnosis of exclusion, with current data recommending the use of a clinical diagnosis of IBS based on symptom application to Rome IV criteria. In the absence of warning signs or symptoms, exhaustive diagnostic work-up is typically of low

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yield, expensive, and of little other benefit (Ford et al., 2017, 2020). For example, a randomized controlled trial in Denmark compared suspected IBS patients with one group diagnosed with the symptom-based diagnostic approach with another group who underwent extensive serum and stool testing as well as flexible sigmoidoscopy to exclude an organic cause. The two approaches did not differ in patient quality of life, IBS symptoms, or patient satisfaction; however, costs were much lower in the symptom-based diagnosis approach (Begtrup et al., 2013).

The Rome IV criteria for the diagnosis of IBS is the most recent iteration of these criteria (see Table 13-5). A diagnosis of IBS based on Rome IV criteria requires recurrent abdominal pain with onset at least 6 months prior, occurring on average one day a week for the past 3 months, and association with two of three additional symptoms: the pain related to defecation, the pain is associated with a change in frequency of stool, or the pain is associated with a change in the form of the stool (Aboubakr & Cohen, 2021; Ford et al., 2017; Wilkinson & Gill, 2021). Again, the patient should be evaluated for warning signs or symptoms as discussed above. IBS can be further categorized into four subtypes, based on the predominant bowel habit utilizing the Bristol Stool Scale (see Table 13-6).

As previously discussed, an extensive work-up for IBS is not supported by current data. However, some limited testing may be appropriate, based on patient presentation, to rule out other possible etiologies. In general, it is reasonable to order a complete blood count (CBC) (for infection or anemia), C-reactive protein (CRP) and fecal calprotectin (for inflammatory bowel disease) (Ford et al., 2017, 2020; Wilkinson & Gill, 2021). Also, celiac disease serologies are justified in patients with suspected IBS because there is a near three times increased likelihood of celiac disease in patients with suspected IBS (Irvine et al., 2017). Additional testing should be based on the predominant bowel habit and further suspicions raised by the symptom review and examination.

If diarrhea is the presenting symptom, there are some additional testing options that may be useful, depending on the patient's particular presentation. For acute onset of symptoms, there should be consideration for *Clostridioides difficile* testing, especially in the setting of recent confinement to a health-care facility, recent antibiotic use, or other causes of altered GI flora, such as intestinal infection. Other testing that can be considered with diarrhea are stool culture and ova and parasite examination. Patients with IBS-D should have CRP and celiac serologies completed. Fecal calprotectin, in addition to CRP, can test for possible inflammatory bowel diseases. If there is the possibility of bile salt diarrhea, empiric trial of a bile salt sequestrant such as cholestyramine hydrogen breath testing can also be considered if small intestinal bacterial overgrowth (SIBO) is suspected, particularly in patients with high risk, such as previous gastric or intestinal surgery or intestinal structural abnormality (e.g., jejunal diverticulosis) (Aboubakr & Cohen, 2021; Ford et al., 2020; Wilkinson & Gill, 2021).

For patients with constipation who meet Rome IV criteria, the diagnosis is pretty certain unless there are obstructive symptoms. In addition to testing recommended for all IBS patients such as thyroid serologies, a plain abdominal x-ray series may elicit excessive stool burden or obvious masses. If obstructive symptoms are present (such as excessive straining or incomplete evacuation) or digital rectal examination suggests a defecatory disorder, then motility testing, anorectal manometry, or balloon expulsion testing can be pursued. If a possible rectal mass is detected on rectal examination, ultrasonography and/or flexible sigmoidoscopy should be pursued (Aboubakr & Cohen, 2021; Ford et al., 2020).

Colonoscopy is not generally warranted for patients suspected of IBS unless warning signs are present or endoluminal examination for screening purposes is due. In a study of 466 patients with IBS-D or IBS-M who underwent colonoscopy, inflammatory bowel disease was only detected in 2%, and no cases of colorectal cancer were discovered (Chey et al., 2010). Colonoscopy (and sometimes upper endoscopy) should be pursued in patients with a family history of colorectal cancer or irritable bowel disease or warning signs or symptoms, such as hematochezia or melena, heme-positive stool on examination, unintentional weight loss, or iron-deficiency anemia (Aboubakr & Cohen, 2021; Ford et al., 7, 2020). If a colonoscopy is being performed on patients suspected of IBS-D, whether due to family history, regular screening, or alarm symptoms, then random colon biopsies should be performed to evaluate for microscopic colitis (Aboubakr & Cohen, 2021). If upper endoscopy is being performed, regardless of cause, biopsies can be taken for celiac disease evaluation given the increased association between IBS patients and celiac disease (Ford et al., 2020). It should be reinforced that extensive testing on all IBS patients is not supported by the evidence and patients with diagnosed IBS have less than a 5% likelihood

TABLE 13-5 Rome IV Criteria for the Diagnosis of Irritable Bowel Syndrome

Symptoms present on average 1 day a week in the past 3 months (with symptom onset at least 6 months previously) with at least two of the following features:

- Related to (improved or worsened) with defecation
- Onset associated with a change in stool frequency
- Onset associated with a change in stool form or appearance

Source: *Ford et al., 2017*

TABLE 13-6 Irritable Bowel Syndrome Subtypes

TYPE	DESCRIPTION
IBS with predominant diarrhea (IBS-D)	Loose stool >25% of the time and hard stool <25% of the time
IBS with predominant constipation (IBS-C)	Hard stool >25% of the time and loose stool <25% of the time
IBS with mixed symptoms of constipation and diarrhea (IBS-M)	Hard stool >25% of the time and loose stool >25% of the time
Unclassified IBS (IBS-U)	Bowel movements cannot be accurately categorized as one of the other three subtypes

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of being given an alternative diagnosis in the future (El-Serag et al., 2004).

Differential Diagnosis:

- Food intolerances (lactose intolerance, fructose intolerance)
- Medication effects
- Parasitic infection
- Biliary tract disease
- Opioid-induced constipation (OIC)
- Neoplasms
- Chronic pancreatitis
- Narcotic abuse
- Celiac disease
- Crohn's disease
- Ulcerative colitis
- Ischemic colitis
- Microcytic colitis
- Thyroid dysfunction
- GI infection (viral, bacterial, protozoan)
- Chronic idiopathic constipation (CIC)
- Colorectal cancer
- Functional diarrhea
- Functional abdominal bloating/function abdominal distention (Aboubakr & Cohen, 2021; Wilkinson & Gill, 2021).

Treatment: The management of IBS depends on the presentation of the patient's condition, most bothersome symptoms, and with the goal of improving quality of life. For all patients with IBS, treatment should be individualized and start with reassurance and education including pathophysiology, natural history of the disease, and realistic expectations with current treatment limitations; care should be taken to be empathetic and nondismissive (Aboubakr & Cohen, 2021; Ford et al., 2020; Wilkinson & Gill, 2021). In all patients with mild symptoms that do not significantly impair quality of life, treatment tends to focus on diet, potentially exacerbating modifying medications, and use of over-the-counter (OTC) options for symptom flares. If symptoms do not respond, or are moderate to severe, pharmacological interventions can supplement mild treatment recommendations.

For patients of all IBS types, soluble or dietary fiber has been shown to be effective; insoluble fiber such as wheat bran can potentially increase bloating and cramping symptoms (Aboubakr & Cohen, 2021; Camilleri, 2018; Ford et al., 2017; Pietrzak et al., 2018). Dietary modifications include avoiding identified trigger foods and a low FODMAP diet (especially with IBS-D); trials of lactose and gluten elimination diets may be helpful, although strong evidence is lacking (Aboubakr & Cohen, 2021; Camilleri, 2018; Ford et al., 2017, 2020; Pietrzak et al., 2018; Wilkinson & Gill, 2021). Avoiding large meals, gas-producing foods (such as cruciferous vegetables), and caffeine may also be helpful (Böhn et al., 2015). Additional treatments that may improve global IBS symptoms include use of probiotics, exercise, and peppermint oil (Aboubakr & Cohen, 2021; Camilleri, 2018; Ford et al., 2020; Pietrzak et al., 2018). Finally, research has shown a benefit to tricyclic antidepressants (TCAs), selective serotonin reuptake inhibitors (SSRIs), and serotonin and norepinephrine reuptake inhibitors (SNRIs) as gut-brain neuromodulators to bring about improvement in abdominal symptoms as well as treat anxiety related to effects of the disease; specific classes tend to be favored for IBS-D or IBS-C and are further discussed below (Aboubakr & Cohen, 2021; Camilleri, 2018; Pietrzak et al., 2018; Wilkinson & Gill, 2021).

For IBS-D, first-line treatment should consist of fiber, dietary changes, and OTC antimotility agents such as loperamide (Aboubakr & Cohen, 2021; Pietrzak et al., 2018; Wilkinson & Gill, 2021). Loperamide (2 mg to 4 mg taken up to four times a day) acts as a opioid receptor agonist, increases colonic transit time, and reduces fluid secretion improving diarrhea, frequency, and urgency; however, loperamide has little effect on abdominal pain (Pietrzak et al., 2018; Wilkinson & Gill, 2021). Other common treatments for IBS-D not responsive to first-line treatments include antispasmodics such as dicyclomine (up to 20 mg up to four times daily before meals) and hyoscyamine (0.125 mg to 0.25 mg every 4 hours as needed). These are generally well tolerated, but their use in older adults should be cautious due to anticholinergic side effects (Aboubakr & Cohen, 2021; Pietrzak et al., 2018; Wilkinson & Gill, 2021). Peppermint oil (200 mg to 750 mg two to three times daily) has also been shown to be safe and more effective than placebo as an antispasmodic that can reduce pain, bloating, and urgency; it generally does not affect bowel habits, however (Aboubakr & Cohen, 2021). Rifaxamin (550 mg three times a day for 2 weeks) is a gut-limited antibiotic that is safe, even in older adults, and can improve symptoms; treatment can be repeated up to twice a year. Finally, eluxadoline (75 mg to 100 mg twice daily) is an opioid receptor agonist–opioid receptor antagonist that acts specifically on opioid receptors in the gut to improve both pain and diarrhea symptoms. However, it is contraindicated in patients who have had a cholecystectomy, sphincter of Oddi's disease, biliary obstruction, pancreatitis, or severe liver impairment and in those who consume three or more alcoholic drinks a day; it may cause pancreatitis, and any patients who develop pancreatitis-like symptoms should stop the medication and contact their provider (Camilleri, 2018; Pietrzak et al., 2018; Wilkinson & Gill, 2021).

Alosetron, a selective 5-HT_3 antagonist, is approved by the U.S. Food and Drug Administration (FDA) for IBS-D treatment in females only, but significant adverse side effects such as ischemic bowel and toxic megacolon limits this use in routine practice (Camilleri, 2018; Pietrzak et al., 2018). Historically, this drug resulted in adverse effects and was at one point pulled from the market. However, after prescribing guidelines were updated by the FDA, it gained an improved safety profile. Providers who choose to prescribe this drug must be aware of all risks and benefits and have a dedicated prescribing outline to meet safety requirements. Close follow-up is recommended, and prescribing should be done by an experienced provider who is familiar with the full ramifications of this drug. Because of the risks and limited prescribing indication, it is not a commonly used medication. Ondansetron (4 mg up to three times a day) is a less potent serotonin (5-HT_3) receptor agonist that can improve urgency and frequency of loose stools, and with a demonstrated excellent safety profile, is a good alternative to alosetron.

For IBS-C, like with IBS-D, first-line treatments should consist of medications for IBS regardless of subtype, diet, and other nonpharmacological treatments. Antispasmodics

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can also be effective with IBS-C in reducing abdominal pain (Pietrzak et al., 2018; Wilkinson & Gill, 2021); patients, especially older adults, should be cautioned against possible worsening anticholinergic effects, which can also worsen constipation, although they are generally well tolerated. Another initial option is polyethylene glycol (17 g once daily in 4 to 8 ounces of a beverage), an FDA-approved osmotic laxative used for short-term constipation; however, although it has been shown to improve constipation, it has little effect on abdominal discomfort. Other osmotic laxatives include lactulose, sorbitol, and mannitol (Aboubakr & Cohen, 2021; Pietrzak et al., 2018; Wilkinson & Gill, 2021). OTC stimulant laxatives are an option but may worsen abdominal cramping and are generally reserved for patients with dysmotility disorders or OIC (Aboubakr & Cohen, 2021).

There are a few second-line pharmacotherapeutics for patients with IBS-C who do not respond to first-line treatment. The first group is considered prosecretory agents. One class is the guanylate cyclase-C agonists linaclotide (72 mcg to 145 mcg daily for chronic constipation; 290 mcg daily for IBS-C, both on an empty stomach) and plecanatide (3 mg to 6 mg daily), which increase chloride secretion into the colon increasing stool softness, increasing colonic transit, and decreasing pain (Aboubakr & Cohen, 2021; Pietrzak et al., 2018; Wilkinson & Gill, 2021). While doses of linaclotide vary for indication, the medication is often titrated to a dose based on patient response rather than type of constipation. Another prosecretory agent is lupiprostone (8 mcg or 24 mcg twice daily on a full stomach) and is a chloride channel activator that increases stool softness, increases colonic transit, and decreases pain (Aboubakr & Cohen, 2021; Pietrzak et al., 2018; Wilkinson & Gill, 2021). Finally, tegaserod (6 mg twice daily in women younger than 65 years old) is a serotonin (5-HT_4) receptor agonist that has significant side effects including headache, abdominal pain, and a low risk for ischemic cardiac events and therefore is not often prescribed; it is contraindicated in patients older than 65 years, and renal function must be closely monitored in all patients (Aboubakr & Cohen, 2021; Wilkinson & Gill, 2021).

For patients with IBS-M, general treatment measures such as antidepressants (TCAs, SSRIs, SNRIs) as well as diet, trigger avoidance, probiotics, and other options discussed above can be initiated for symptom improvement. Often, these patients require recommendations from both IBS-C and IBS-D treatments as their stools are typically variable. They can utilize the recommendation needed at the time, based on if they are having predominantly constipation or diarrhea.

Follow-Up: For patients with chronic IBS, a positive relationship between the health-care provider and the patient is mutually beneficial. It should be the focus and intent of the provider to educate the patient on the disease and expected outcomes. The patient should be often reminded of the chronic nature of IBS with flares and remissions of symptoms; they will frequently report symptoms in different ways depending on their current state of control. The provider should be intentional about not being dismissive and should have empathy for the patient who can have symptoms that are debilitating and significantly affect quality of life. Dietary intervention and stress-reduction techniques (as well as other coping strategies) should be reviewed and evaluated on an ongoing basis. In patients with newly diagnosed IBS, evaluation of persistent symptoms and treatment response should be executed to ensure no further work-up is needed for possible missed diagnosis other than IBS, especially with the development of any warning symptoms (Pietrzak et al., 2018; Wilkinson & Gill, 2021).

Sequelae: Patients with IBS have been found to have multiple comorbidities that need to be considered. Functional dyspepsia, depression, and anxiety are common comorbidities in patients with IBS, often for similar biopsychosocial and brain-gut axis etiologies as IBS (Aboubakr & Cohen, 2021; Ford et al., 2017, 2020). Complications may develop because of other pathological processes mistaken for IBS symptoms. Patients with uncontrollable diarrhea are at risk for dehydration because of fluid and electrolyte loss; this is especially true in older adults. Fecal impaction may result from chronic constipation, especially in an immobile, cognitively impaired older patient.

Prevention/Prophylaxis: The patient should become familiar with stress-reduction techniques and coping mechanisms, which are especially useful during emotionally stressful situations. Patients should avoid all food products that are known to irritate their bowels (Wilkinson & Gill, 2021). Patients with known food intolerance must read nutrition labels and be informed of the inactive contents of medications, which may contain irritating substances.

Referral: Refer patients to a gastroenterologist for colonoscopic imaging as appropriate for screening or warning signs or symptoms. Refer again if patients exhibit persistent symptoms such as abdominal pain, severe constipation, or uncontrollable diarrhea despite compliance with treatment. Patients may benefit from psychotherapy to help with anxiety and depression symptoms, which can improve symptoms associated with gut-brain based disorders like IBS. Psychotherapy (such as cognitive behavioral therapy, hypnotherapy, mindfulness) can be an effective nonpharmacological treatment in patients with IBS (Aboubakr & Cohen, 2021). Biofeedback can be effective for patients who have IBS-C with obstructive symptoms (Ford et al., 2017).

Education: Inform patients that because the increase of dietary fiber could aggravate their IBS symptoms, they should increase it gradually to the recommended dose. This risk can be reduced with soluble or dietary fiber rather in insoluble fiber (Aboubakr & Cohen, 2021; Camilleri, 2018; Ford et al., 2017; Pietrzak et al., 2018). Eating smaller, frequent meals and avoiding known triggers and FODMAPs may ease the IBS symptoms in older adults and enhance overall quality of life; however, these ideas require education and explanation (Ford et al., 2020). Inform patients with chronic IBS that although the disease itself does not lead to a more serious illness, any change in symptoms should be reported to the health-care practitioner.

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Clinical Recommendation	Evidence Rating	References
Patients should be diagnosed with IBS based on positive diagnostic strategy rather than a diagnostic strategy of exclusion.	A	Lacy et al., 2021
Diagnosis of IBS should be based on the Rome IV criteria.	B	Pietrzak et al., 2018
Colonoscopy should only be offered in IBS diagnosis in justified cases (such as alarm symptoms or for scheduled routine screening).	A	Lacy et al., 2021
Soluble fiber, and not insoluble fiber, should be used to treat patients with all subtypes of IBS.	B	Lacy et al., 2021 Ford et al., 2020 Pietrzak et al., 2018
Rifaxamin should be used to treat IBS-D symptoms.	B	Lacy et al., 2021 Ford et al., 2020
The use of guanylate cyclase activators (linaclotide or plecanatide) is recommended for the treatment of IBS-C.	A	Lacy et al., 2021 Ford et al., 2020 Pietrzak et al., 2018
Tricyclic antidepressants (TCAs) can be used to treat global IBS symptoms.	B	Lacy et al., 2021 Ford et al., 2020
Chloride channel activators (lubiprostone) can be used to treat IBS-C.	B	Lacy et al., 2021 Ford et al., 2020 Pietrzak et al., 2018
Mixed opioid receptor agonist–opioid receptor antagonist medications (eluxadoline) should be used to treat IBS-D symptoms.	B	Lacy et al., 2021 Ford et al., 2020 Pietrzak et al., 2018

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LIVER CANCER

Signal Symptoms: Cachexia, jaundice.

Description: The liver is the most common organ in the body for metastasis from other cancers. Common sites of primary tumors that metastasize to the liver are the lungs, colon, pancreas, stomach, breast, and gallbladder. Hepatocellular carcinoma, intrahepatic cholangiocarcinoma, angiosarcoma and hemangiosarcoma, and hepatoblastoma are primary liver cancers. Hepatocellular carcinoma is associated with cirrhosis of the liver (American Cancer Society [ACS], 2021a).

Etiology: The hepatic filtration of arterial and portal venous blood is a major reason for the high prevalence of metastases from primary cancerous sites in the body to the liver. Metastases also may result from an extension from an abdominal tumor or through the lymphatic system. Malignant tumors of the liver are primarily adenocarcinomas.

Occurrence: Primary liver cancer, rare in the United States, accounts for about 2% of all cancers or approximately 42,000 cases per year (National Cancer Institute [NCI], 2021). It is more common for cancer in the liver to have metastasized from another part of the body rather than be a primary liver cancer. Men are about 2.5 times more likely than women to develop liver cancer (ACS, 2021b; NCI, 2021).

Age: Median age of diagnosis is 65 years (NCI, 2021).

Ethnicity: The incidence of liver cancer is highest in Native Americans/Alaskan Natives (ACS, 2021b; NCI, 2021).

Contributing Factors: The most common risk factor is chronic hepatitis B or C infection, which leads to cirrhosis. The risk increases in people who drink more than six alcoholic drinks per day (ACS, 2021b). Additional risk factors include hemochromatosis, obesity, type 2 diabetes, porphyria cutanea tarda, alpha-1 antitrypsin deficiency, and Wilson's disease (ACS, 2021b; National Comprehensive Cancer Network [NCCN], 2021).

Signs and Symptoms: Complaints of weakness, malaise, weight loss, sweating, and anorexia may be reported. Pain in the upper abdomen can be associated with the cancer and also may be reported. Physical examination reveals cachexia. Auscultation may reveal a bruit over the tumor and tenderness of the liver. Hepatomegaly and ascites may be present. A mass may be palpable. In more advanced cases, jaundice may appear (NCCN, 2021).

Diagnostic Tests: Patients at high risk for hepatocellular carcinoma (HCC) should be screened using ultrasound and alpha fetoprotein (AFP) every 6 months (NCCN, 2021). Identification of a liver nodule that is smaller than 1 cm

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should be reimaged with an ultrasound in 3 to 6 months. Nodules that are larger than 1 cm should be reimaged with abdominal computed tomography (CT) scan or contrast-enhanced magnetic resonance imaging (MRI). Nodules that demonstrate arterial hypervascularity and venous or delayed phase washout are diagnostic for HCC. Those nodules that do not demonstrate arterial hypervascularity and venous or delayed phase washout should be reimaged with another contrast-enhanced study such as a CT scan or MRI, and percutaneous biopsy should be completed. A CT of the chest and bone scan should be ordered if clinically indicated.

Laboratory testing should include a complete blood count (CBC), hepatitis panel, bilirubin, alkaline phosphatase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), prothrombin time (PT), International Normalized Ratio (INR), blood urea nitrogen (BUN), and creatinine. Laboratory findings may be nonspecific and are related to the underlying liver disease. Findings may include thrombocytopenia, hypoalbuminemia, hyperbilirubinemia, and hypoprothrombinemia. Additionally, patients may have mild anemia and electrolyte disturbances (NCCN, 2021). Serum alkaline phosphatase, AST, ALT, and gamma-glutamyl transpeptidase (GGT) are often abnormal in a nonspecific pattern. PT/INR may be elevated.

Differential Diagnosis:
- Cirrhosis
- Chronic hepatitis B or C infection
- Metastatic malignancy to the liver

Treatment: All patients should be evaluated by an experienced multidisciplinary team for available treatment options. Advancements in the surgical treatment of hepatic metastatic cancers include tumor ablation and microscopic glass beads containing a radioactive element. Surgical resection of the liver is beneficial only if the patient has a resectable tumor; even so, the survival rate remains low. Liver transplant may be considered in patients with early-stage liver cancer, as well as advanced disease. Systemic therapy may be considered as adjuvant treatment or in patients who are not candidates for surgery. Recommended first-line treatment includes atezolizumab plus bevacizumab, sorafenib, or lenvatinib. Checkpoint inhibitors may be considered in some circumstances (NCCN, 2021).

Follow-Up: Patients and family members should be given the opportunity to explore adjunctive methods of pain relief and relaxation. After diagnosis of liver cancer, the focus should be on holistic palliative care, including the intervention of hospice and services.

Sequelae: The prognosis is poor because the tumor grows rapidly and often metastasizes to the lungs or bones. The survival rate is only 4 to 6 months.

Prevention/Prophylaxis: The hepatitis B vaccine is recommended for high-risk patients. Treatment of hepatitis C is recommended. Avoidance of chemical exposure, as part of occupational safety, is suggested. Annual ultrasound screening for patients with chronic hepatitis B or cirrhosis should be considered as a preventive measure for liver cancer (ACS, 2021b).

Referral: Refer the patient to an oncologist when the diagnosis of liver cancer is suspected. Local hospice care services should be contacted for care for the patient and family.

Education: Although no further medical treatment is aimed at reversal of the disease, the patient needs to know that you will collaborate with the hospice nurses to provide for the patient's comfort throughout the disease process. The patient can be referred to http://www.liverfoundation.org/support/ for basic information about liver cancer.

Clinical Recommendation	Evidence Rating	References
Prevention of hepatocellular carcinoma (HCC) should focus on preventing infection with hepatitis B virus (HBV) and hepatitis C virus (HCV), treating patients with viral hepatitis who are candidates for treatment, avoiding environmental toxins, and attempting to prevent the development of cirrhosis in patients with liver disease.	A	ACS, 2021b
Patients with chronic HBV infection who are at increased risk for HCC should undergo routine surveillance.	A	ACS, 2021b NCCN, 2021
All patients with cirrhosis, regardless of etiology, should undergo surveillance for HCC.	B	NCCN, 2021
Surveillance in high-risk patients should be performed with ultrasonography every 6 months rather than annually.	B	NCCN, 2021

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NONALCOHOLIC FATTY LIVER DISEASE

Signal Symptoms: Fatigue, right upper quadrant pain or fullness, possible hepatomegaly.

Description: Nonalcoholic fatty disease (NAFLD) is the most common chronic liver disease in Western countries (Westfall et al., 2020). NAFLD refers to a spectrum of liver disorders that include simple steatosis (fatty liver) and nonalcoholic steatohepatitis (NASH). NASH is characterized by hepatocyte injury, inflammation, and fibrosis, which can ultimately lead

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to cirrhosis and end-stage liver disease (Patel & Siddiqui, 2019). Risk factors for the development of NASH include elevated fasting blood glucose, low high-density lipoprotein (HDL) and elevated fasting cholesterol (Sivell, 2019). Alcohol use must be minimal to meet the criteria for NAFLD (Chalasani et al., 2018). The maximum intake of alcohol is two standard drinks a day for men and one for women (USDA, 2020)

Etiology: While the exact mechanism for the NALFD is unknown (Wilkins et al., 2011), development of NAFLD has been associated with diabetes, obesity, insulin resistance, hypertension, and dyslipidemia (Kudaravalli, & John, 2021). Insulin resistance is the most important risk factor for the development of NAFLD. It has been suggested that there may be a genetic predisposition to NAFLD, especially in patients who also develop metabolic syndrome (Westfall et al., 2020).

Occurrence: NAFLD is the most common liver disease in the United States (Patel & Siddiqui, 2019). It has been predicted that NAFLD will become the most frequent indication for liver transplantation by 2030. In the United States, it is estimated that 100 million adults will be affected by NAFLD by 2030 and the prevalence will continue to rise (Westfall et al., 2020).

Age: The majority of patients diagnosed with NAFLD are in their 40s or 50s (Iqbal et al., 2019). The risk of nonalcoholic steatohepatitis, cirrhosis, and hepatocellular carcinoma (HCC) is increased in the older adults with NAFLD (Chalasani et al., 2018; Li et al., 2018).

Ethnicity: Hispanics have the highest rate of NAFLD while studies have shown an increase in metabolic syndrome in South Asian populations, which could progress to NAFLD (Sivell, 2019).

Contributing Factors: The most common risk factors associated with the development of NAFLD are obesity (body mass index [BMI] >30 kg/m^2)—especially central obesity—diabetes, metabolic syndrome, hypertension, dyslipidemia, and insulin resistance (Sivell, 2019; Westfall et al., 2020). NAFLD may be present in patients who have jejunoileal bypass or gastric bypass or who have experienced starvation and/or protein energy malnutrition. Also at risk are patients receiving parental nutrition (Mitra & Ahn, 2017). Drug-induced NAFLD can be caused by aspirin, cocaine, valproate, highly active antiretroviral, tetracycline, NSAIDs, amiodarone, tamoxifen, methotrexate, and corticosteroids. In patients with coexisting conditions, such as ulcerative colitis, Graves' disease, or type 1 diabetes, consider an autoimmune cause for NAFLD (Croke & Sampson, 2012). Genetic factors such as high-risk allele of the patatin-like phospholipase domain-containing protein 3 gene have been found in patients with NAFLD (Westfall et al., 2020). There is evidence that NAFLD is linked to other chronic disease such as sleep apnea, colorectal cancer, osteoporosis, psoriasis, and endocrine diseases such as polycystic ovary syndrome and hypothyroidism (Westfall et al., 2020). Increased age has been shown to be a risk factor for developing NAFLD and NASH and advanced fibrosis (Neuschwander-Tetri, 2017)

Signs and Symptoms: Most patients with NAFLD are asymptomatic (Sivell, 2019). Patients may present with fatigue, jaundice, pruritus, right upper quadrant discomfort or fullness (Westfall et al., 2020). Inquire about weight loss. On examination, look for evidence of jaundice of the skin, scleral icterus, and spider angiomas. Patients may have unexplained abnormal liver blood tests as part of a routine physical or drug monitoring such as statins. On physical examination, patients with NAFLD may have hepatomegaly (Kudaravalli & John, 2021).

Diagnostic Tests: NAFLD is a diagnosis of exclusion. The most common abnormal laboratory tests are elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) (Chalasani et al., 2018), especially in patients with type 2 diabetes (Sheng et al., 2018). ALT and AST may be elevated two to five times the upper limits. It is important to exclude other causes of elevated transaminase levels. Hepatitis A, B, and C need to be ruled out, as does autoimmune hepatitis. Check ferritin and iron levels to rule out hemochromatosis (Westfall et al., 2020). Consider ruling out Wilson's disease, thyroid disease, celiac disease, and alpha-1 antitrypsin deficiency. A fasting glucose or A1c level, lipid panel, prothrombin time (PT), albumin, and total bilirubin should be obtained (Sivell, 2019; Westfall et al., 2020). With a sensitivity of 82% to 89% and a specificity of 93% for identifying a fatty liver, an ultrasonography of the liver will assist in the diagnosis of NAFD by identifying fatty infiltration (Sivell, 2019). A transient elastography is routinely used to grade fibrosis based on liver stiffness (Li et al., 2018). A liver biopsy should be considered for patients who are likely to have a more advanced liver disease, including those with morbid obesity, diabetes, advanced age, and an AST/ALT ratio greater than 1. Liver biopsy remains the gold standard for the patient with suspected NASH, hepatic stenosis, and fibrosis and cirrhosis (Chalasani et al., 2018). Patients with persistent elevations in liver enzymes despite lifestyle changes may be considered for liver biopsy. Patients should be screened for alcohol and drug use.

Differential Diagnosis:

- Alcoholic hepatitis
- Autoimmune hepatitis
- Hepatitis B
- Hepatitis C, particularly
- Thyroid disease
- Alpha-1 antitrypsin disease
- Medication-induced hepatitis
- Wilson disease (Kudaravalli & John, 2021, Westfall et al., 2020; Wilkins et al., 2013)

Treatment: Management of NAFLD should focus primarily on risk factors such as insulin resistance and hyperlipidemia (Chalasani et al., 2018; Westfall et al., 2020). Patients who are overweight or obese with NAFLD should consider making lifestyle changes that include following a Mediterranean diet that focuses on weight loss (Neuschwander-Tetri, 2017). It has been shown that weight loss and exercise reduce liver enzymes levels and steatosis (Westfall et al., 2020). Weight loss should not exceed 1 to 2 pounds a week. For patients with end-stage liver disease, weight loss should not be recommended due to the risk of protein calorie malnutrition. Any alcohol use should be prohibited (Li et al., 2018).

Treatment for hyperlipidemia in patients with NAFLD cirrhosis is recommended to prevent cardiovascular disease; however, avoid this in patients with decompensated cirrhosis

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(Li et al., 2018). Medications for the treatment of insulin resistance (pioglitazone, rosiglitazone) have been shown to improve transaminases levels and decrease hepatic steatosis (Westfall et al., 2020). Obese patients who are unable to lose weight with lifestyle changes should be considered for bariatric surgery; individual risk for complications from surgery need to first be evaluated (Neuschwander-Tetri, 2017). Hepatitis A and B vaccine should be given to patients without serological evidence of immunity (Westfall et al., 2020). Patients should be monitored for weight loss.

Sequelae: NAFLD in older adults is often more severe and can carry a worse prognosis than in the younger population. Complications include portal hypertension, gastroesophageal varices, cirrhosis, hepatic failure, and HCC (Li et al., 2018; Maurice & Manousou, 2018; Neuschwander-Tetri, 2017; Sivell, 2019). Risk factors for the development of HCC in NAFLD include the older age, type 2 diabetes, and cirrhosis (Li et al., 2018). The most common cause of death in patients with NAFLD is cardiovascular disease (Maurice & Manousou, 2018).

Prevention/Prophylaxis: Weight loss and engaging in regular physical activity should be encouraged in patients with obesity (Westfall et al., 2020). Patients with diabetes, hypertension, and hyperlipidemia should be closely monitored and managed to help prevent the progression of NAFLD.

Referral: Consider referral to a specialist when the clinical parameters are indicating a severe disease state. Patients whose liver enzymes remain elevated despite weight loss, those who are morbidly obese, those with AST/ALT twice the upper limits of normal and those with NASH whose clinical picture suggests the likelihood of cirrhosis should be referred (Westfall et al., 2020).

Education: Patients should be advised that NAFLD is usually caused by the same conditions that cause an increased risk for cardiovascular disease. Lifestyle choices should be reviewed with the patient at each encounter as the management of NAFLD is directed at risk factors, specifically, diabetes, elevated lipids, and obesity and the patient's progress toward making changes toward a healthy diet and a regular exercise regimen (Kudaravalli & John, 2021).

Clinical Recommendation	Evidence Rating	References
Blood glucose control should be well controlled in patients with diabetes and NAFLD.	C	Chalasani et al., 2018
Patients with NAFLD should be encouraged to eat a healthy diet (Mediterranean) and encouraged to increase physical activity.	C	Chalasani et al., 2018
Liver biopsy is the gold standard for the diagnosis of NASH, hepatic stenosis and fibrosis and cirrhosis.	C	Chalasani et al., 2018

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PEPTIC ULCER DISEASE

Signal Symptoms:

Gastric Ulcers: History of dyspepsia, epigastric pain, pain that radiates to the back after the ingestion of a meal.

Duodenal Ulcers: Pain 1 to 3 hours after a meal (patients with gastric ulcers have pain immediately on eating), and resolution of pain at times with eating. Nocturnal pain may occur in duodenal ulcers in the older adult; definitive symptoms may be absent, and vomiting and anorexia may be reported instead of epigastric pain.

Description: Peptic ulcer disease (PUD) involves ulcerations of the mucous membrane of the stomach or duodenum into the submucosa (Lanas & Chan, 2017). The disease is classified according to the nature and anatomical location of the lesion. Gastric ulcers generally are found along the lesser curvature of the stomach between antral and acid-screening mucosa, occurring anywhere in the stomach, from the cardia to the pylorus. Duodenal ulcers develop in the duodenal bulb or in the immediate postbulbar area (Dunlap & Patterson, 2019).

Etiology: The etiology of PUD is characterized best as an imbalance between the noxious agents to which the gastrointestinal (GI) mucosa is exposed (primarily hydrochloric acid and pepsin) and the protective factors (mucus production, bicarbonate secretion) that the mucosa uses to resist destruction from such noxious agents. An increase in destructive influences (e.g., with NSAID use) can destroy the mucosa, leading to the development of an ulcer (Narayanan et al., 2018). *Helicobacter pylori* and NSAIDs or aspirin products are the predominant risk factors for PUD (Dunlap et al., 2019; Lanas & Chan, 2017; Narayanan et al., 2018). Historically, *H. pylori* was more prevalent as a culprit for PUD, but NSAIDs and other caustic substances have become more prominent (Malfertheiner & Schulz, 2020). Although rare, non–*H. pylori* bacteria have been found to contribute to PUD; identification requires special histological stains such as Giemsa,

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Steiner, or Whartin-Starry silver stain (Da Cunha & Dharan, 2021). Approximately 20% of cases will not be related to *H. pylori*, aspirin products, or NSAIDs (Lanas & Chan, 2017). Additional etiologies could include ischemic injury, medication-induced (alendronate, steroid therapy, potassium chloride, chemotherapy), viral etiologies (cytomegalovirus [CMV] and herpes simplex virus [HSV]), gastric bypass procedures with ulcers at anastomotic sites, tumors (such as lymphoma), Cameron's ulcer, Crohn's disease, eosinophilic gastroduodenitis, and idiopathic ulcers (Malfertheiner & Schulz, 2020; Narayanan et al., 2018; Sivakumar & Stubbs, 2021).

Occurrence: Approximately 4.5 million people will experience PUD annually, with an approximate 5% to 10% prevalence of PUD globally (Prasad & Friedman, 2018; Rothermel & Edwards, 2020). Gastric ulcers may be more prevalent in older women, with duodenal ulcer occurrence more common in men (Sivakumar & Stubbs, 2021).

Age: Majority of those affected by PUD are aged 25 to 64 years (Dunlap & Patterson, 2019).

Ethnicity: Prevalence of PUD secondary to *H. pylori* is higher in Mexican Americans (60%) compared to non-Hispanic Americans (30%) (Narayanan et al., 2018).

Contributing Factors: *H. pylori* infection is a factor in more than 90% of duodenal ulcers and 70% to 90% of gastric ulcers (Sivakumar & Stubbs, 2021). Use of aspirin and other NSAIDs—because of their ability to inhibit prostaglandin synthesis—has been shown to increase the risk of PUD (Malfertheiner & Schulz, 2020). Other medications, including selective serotonin reuptake inhibitors (SSRI)s, steroids, aldosterone antagonists, and anticoagulants combined with NSAIDs or aspirin result in increased risk of acute bleeding (Lanas & Chan, 2017).

Additional risk factors for developing PUD include tobacco and alcohol use, gastrinoma, family history of ulcers, and significant stressors on the body such as acute critical illness (Dunlap & Patterson, 2019).

Signs and Symptoms: Patients presenting with symptoms of PUD must be evaluated for alarm symptoms, which would prompt diagnostic endoscopy instead of empiric treatment, specifically if older than age 55 (Narayanan et al., 2018; Sarfraz, 2018). In older adults, definitive symptoms may be absent. Alarm signs and symptoms, known as red flags, would include overt GI bleeding (melena and/or hematochezia), iron-deficiency anemia, unintentional weight loss, dysphagia or odynophagia, persistent vomiting, palpable abdominal mass, family history of upper GI cancers, and symptoms present at age 55 and older (Dunlap & Patterson, 2019; Narayanan et al., 2018; Sivakumar & Stubbs, 2021). Overt GI such as melena or hematochezia may be the first sign heralding PUD, occurring in in almost 50% of patients, as classic symptoms may have been absent prior to presentation (Lanas & Chan, 2017; Sivakumar & Stubbs, 2021). Acute onset of epigastric pain that is persistent could be indicative of perforation (Lanas & Chan, 2017). Mortality for perforation may be up to 20%, depending on the patient's age at presentation and coexisting medical conditions (Lanas & Chan, 2017).

Approximately two-thirds of PUD presentations may have nonspecific or silent symptoms (Altwejry et al., 2020). Most common symptoms if present would include epigastric pain with characteristics of burning or gnawing, intermittent abdominal pain with periods of relief, nausea, vomiting, possible weight loss (Altwejry et al., 2020; Lanas & Chan, 2017; Sivakumar & Stubbs, 2021). Patients with gastric ulcers have a history of abdominal pain that is worsened by eating and may be relieved by antacids, whereas duodenal ulcers exacerbate pain at night or several hours after eating, and pain may resolve while eating (Dunlap & Patterson, 2019; Lanas & Chan, 2017; Sivakumar & Stubbs, 2021).

Physical examination of a patient with PUD may be normal (Dunlap & Patterson, 2019). If PUD is significant or advanced, tenderness of epigastric abdomen may be noted; however, 30% of older adults will not have palpation tenderness (Dunlap & Patterson, 2019; Sarfraz, 2018). Perforation signs would include rigidity of the abdomen and absence of bowel sounds; a gastric outlet obstruction would be suspected if succession splash heard upon auscultation (Dunlap & Patterson, 2019; Sarfraz, 2018). Digital rectal examination should be performed, with hemoccult testing obtained; findings of melena or hematochezia could indicate upper GI bleeding or rapid transit upper GI bleeding if the latter is appreciated (Dunlap & Patterson, 2019; Sarfraz, 2018).

Diagnostic Tests: Esophagogastroduodenoscopy (EGD) with a biopsy for the detection of peptic ulcer, malignancy, and *H. pylori* remains the gold standard in diagnostic testing for this disease, especially in patients 55 years or older and/or with alarm symptomatology (Dunlap & Patterson, 2019; Lanas & Chan, 2017). Patients younger than 55 without alarm signs or symptoms, no concern for gastric carcinoma, or living in area of increased prevalence of gastric carcinoma or *H. pylori*, may be tested for *H. pylori* and treated without undergoing diagnostic endoscopy (Dunlap & Patterson, 2019; Narayanan et al., 2018). EGD is still recommended for any patient with alarm signs or symptoms regardless of age.

Diagnostic tests for *H. pylori* include a stool antigen or urea breath test (UBT); however, serological antibody testing for *H. pylori* is not helpful for identifying active versus past infection and for this reason is not recommended to exclude presence of *H. pylori* (Altwhejry et al., 2020; Dunlap & Patterson, 2019; Narayanan et al., 2018). Serological antibody testing for *H. pylori* shows results as positive or negative, and this is not able to identify active versus past infection; therefore, it is not helpful in diagnosing the presence of active *H. pylori* infection. Proton pump inhibitor (PPI) use will need to be restricted for 14 days and antibiotics for 28 days before UBT and fecal antigen testing to avoid false-negative results (Sivakumar & Stubbs, 2021).

Laboratory tests including a complete blood count, serum chemistries, fecal occult blood testing, amylase, and lipase can be drawn to help exclude other differential diagnoses or confirm anemia and occult GI bleeding; however, there is no blood test that can determine the presence of PUD (Dunlap & Patterson, 2019; Sivakumar & Stubbs, 2021).

Differential Diagnosis:

- Abdominal aortic aneurysm
- Acute coronary syndrome
- Angina

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- Celiac disease
- Crohn's disease
- Esophagitis
- Gastritis
- Gastroenteritis
- Gastric carcinoma
- Gastroesophageal reflux disease (GERD)
- Gallbladder disease
- Mesenteric ischemia
- Irritable bowel syndrome
- Pancreatitis (acute or chronic)
- Zollinger-Ellison's disease
- Nonulcer dyspepsia (Dunlap & Patterson, 2019; Sarfraz, 2018; Sivakumar & Stubbs, 2021)

Treatment: PUD should be managed according to the etiology. NSAIDs and aspirin should be stopped if feasible, especially if the offending cause of PUD. For PUD not related to *H. pylori* infection, treatment with PPIs for at least 6 to 8 weeks should result in ulcer healing as long as the offending medication is no longer used; complicated PUD will require longer therapy up to 12 weeks (Narayanan et al., 2018). If NSAIDs/aspirin therapy is essential for the patient to continue, PPIs should be continued prophylactically to reduce recurrence (Dunlap & Patterson, 2019). Sucralfate has been shown effective for treatment of duodenal ulcers secondary to NSAIDs only and not effective for treatment of gastric ulcers (Narayanan et al., 2018).

Surveillance EGD around 6 to 8 weeks after diagnosis, should be performed for gastric ulcers due to potential risk of harboring malignancy (Dunlap & Patterson, 2019; Narayanan et al., 2018). Further biopsies should be undertaken if persistent ulcer disease is noted at surveillance EGD. Refractory ulcers greater than 5 mm that do not respond to 8 to 12 weeks of appropriate PPI therapy should raise concern for alternative etiology, including hypersecretory state, infectious or infiltrative processes, cocaine, Crohn's disease, carcinoma, or noncompliance (Sivakumar & Stubbs, 2021).

Acute GI bleeding due to PUD is associated with a mortality rate of 10% depending upon associated comorbidities, requiring inpatient treatment and IV PPI therapy (Altwejry et al., 2020). Fluid resuscitation with crystalloid solutions should be started immediately upon presentation to a medical facility, with the goal of maintaining hemoglobin above 7 g/dL (Lanas & Chan, 2017). IV PPI should be started upon presentation, as this reduces the risk of bleeding and rebleeding post EGD (Narayanan et al., 2018). PPI infusion should be continued following EGD if bleeding stigmata noted or intervention for hemostasis was performed (Narayanan et al., 2018). EGD is indicated for acute GI bleeding, with hemostatic intervention for therapeutic purposes; the first 72 hours following intervention are critical because recurrent bleeding is most likely during this time (Chiu, 2019). Angiography with embolization may be needed for persistent bleeding ulcers (Chiu, 2019). Surgery may be necessary if unable to perform endoscopic or embolization therapies fail. Perforated PUD carries a mortality rate of 30%, prompting surgical intervention emergently if appropriate surgical candidate; contained perforations may be appropriate for medical supportive treatment including IV PPI, nothing by mouth (NPO) status, and antibiotics (Altwejry et al., 2020; Narayanan et al., 2018). Finally, gastric outlet obstruction due to PUD requires IV PPI possible endoscopic therapy with dilation, or surgery (Altwejry et al., 2020).

H. pylori eradication is paramount to reduce the risk of recurrence of PUD and reduce risk of gastric cancer secondary to *H. pylori* (Chey et al., 2017; Narayanan et al., 2018; Sivakumar & Stubbs, 2021). The full course of therapy for 10 to 14 days should be taken to avoid incomplete therapy and potential persistent bacteria. Choice of regimen is based on prior antibiotic exposures and treatments. Multiple regimens are available, including rescue therapies for those who have failed prior treatment. Eradication testing should be performed 4 weeks following therapy via breath test, fecal test, or endoscopic biopsy (Chey et al., 2017). For those who have failed multiple regimens and providers are unable to document eradication, endoscopic biopsy for culture and sensitivity is recommended (Narayanan et al., 2018).

Follow-Up: Confirm eradication of *H. pylori* 4 weeks after treatment therapy via stool antigen test or urea breath test (Chey et al., 2017). It is important that PPI therapy be held for at least 14 days prior to documenting eradication. Surveillance EGD for gastric ulcers to document healing.

Sequelae: Complications originating from PUD in older adults include gastric bleeding with accompanying anemia, larger gastric ulcers than in younger counterparts, higher surgical risk with 30-day morbidity and mortality compared to younger patients, and increased risk of persistent ulcers and bleeding due to polypharmacy (Dumic et al., 2019).

Prevention/Prophylaxis: Any patients with previous history of GI bleeding, *H. pylori* infection, multiple and/or high NSAID use (including aspirin), corticosteroid use, or polypharmacy as well as older adults are at risk for developing PUD (Dumic et al., 2019). Signs and symptoms of impending recurrence of PUD, including epigastric pain, anorexia, melena, and weight loss, should be identified early. The use of NSAIDs and aspirin along with antiplatelets and anticoagulation lead to increased risk of bleeding (Malfertheiner & Schulz, 2020). Prophylactic PPI use may prevent PUD if NSAIDs/aspirin products are necessary to continue (Lanas & Chan, 2017).

Referral: Refer the patient to a gastroenterologist for initial endoscopy and for treatment of upper GI bleeding. PPI therapy, compared with histamine blockers and placebo, has been shown to reduce mortality after upper GI bleeding secondary to PUD (Narayanan et al., 2018). Refer again if epigastric pain and dyspepsia persist despite treatment and if signs of GI bleeding are present.

Education: Avoidance of aspirin and other NSAIDs and tobacco is essential. Reduction of stressful events, coffee (including decaffeinated forms) and other caffeine products, and alcohol is recommended. Caution patients about taking over-the-counter (OTC) medication preparations without professional advice. Patients with history of GI bleeding should notify the health-care provider of any recurrent symptoms and overt bleeding, such as melena or hematochezia. Patients treated for *H. pylori* should have eradication documented, and surveillance EGD should be completed for all gastric ulcers to ensure healing.

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Clinical Recommendation	Evidence Rating	References
Assess patients for NSAID use if they are ≥65 years, for prior GI clinical conditions including dyspepsia, and for low-dose aspirin use to determine whether medication should be avoided or used with protective measures to reduce GI bleeding.	A	Lanas & Chan, 2017
Medications including selective serotonin-reuptake inhibitors, steroids, aldosterone antagonists, and anticoagulation combined with NSAIDs/aspirin result in increased risk of acute bleeding.	A	Lanas & Chan, 2017
There is a decreased mortality rate from bleeding peptic ulcers when proton pump inhibitor (PPI) therapy is utilized for treatment after diagnosis.	A	Narayanan et al., 2018
Treat patients with peptic ulcer disease (PUD) symptoms and *H. pylori* infection with standard protocol to reduce the risk of ulcer recurrence and promote healing.	A	Chey et al., 2017 Narayanan et al., 2018 Sivakumar & Stubbs, 2021
Upper endoscopy is needed for patients with PUD who are older than 55 years and/or with alarm symptoms, or in those with ulcers who do not improve with therapy.	A	Narayanan et al., 2018 Sarfraz, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

A 71-year-old woman presents with a 4-week history of dyspepsia and abdominal pain that she describes as gnawing. She states that for years she has had occasional heartburn, but she cannot recall having abdominal pain like she is experiencing now. She states that she also has arthritis and has taken ibuprofen every day for the past 2 years. For her stomach pain she has been taking Tums extra strength a couple of times a day. She states that the pain began soon after visiting her sister, who is a nurse at a mission in Nicaragua.

Chief Complaint: "My stomach hurts and wakes me up from my sleep. I find myself belching after meals and I feel bloated."

Objective: Blood pressure (BP) 118/70 mm Hg, heart rate (HR) 90 beats/min, respiratory rate 18 breaths/min, BMI 29.

1. How will you use this information to prepare for today's visit?
2. What additional subjective data are you seeking?
3. What additional objective data will you be assessing for?
4. What are the differential diagnoses that you are considering?
5. What laboratory tests will help you rule out some of the differential diagnoses?
6. What is your treatment and specific information on the prescription you will give to this patient?
7. What are the potential complications from the treatment ordered?
8. What additional specific laboratory tests will you consider ordering?
9. What additional patient teaching may be needed?
10. What type of specialist will you be consulting for this patient?

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CHAPTER 14

Renal and Urological Disorders

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ASSESSMENT

Development of renal and urological conditions increases with age (Preminger, 2019). When assessing the renal and urological system, the practitioner needs to take into consideration the comorbidities that are often experienced by older adults, such as diabetes and hypertension, that can contribute to the development of kidney disease and alter urological function. Consider asking focused questions to determine changes in renal or urological system.

- Address urination pattern to include frequency, urgency, nocturia and incontinence.
- Determine whether there is any pain upon urination and the location of the pain.
- Inquire about the ability to start or maintain the stream of urine.
- Address the color of urine to include any evidence of blood.
- Assess daily fluid intake, including caffeine, and what time it is consumed.
- Note any medications that are either prescribed for or directly impact the renal or urological system.
- Inquire about family history of renal or urological disorders.

Pain that originates in the kidneys or ureters is often localized to the flanks or lower back and may radiate into the ipsilateral iliac fossa, upper thigh, testis, or labium. Typically, pain caused by obstructing calculi is colicky and may be prostrating; it is more constant if caused by infection (Capilouto & Williams, 2021). Patients with acute kidney injury may experience drowsiness, confusion, appear inattentive and speech may be slurred, whereas patients with chronic kidney disease often appear weak, experiencing malaise (Maddukuri, 2020a).

Acute urinary retention distal to the bladder causes agonizing suprapubic pain; chronic urinary retention causes less pain and may be asymptomatic. Dysuria is a symptom of bladder or urethral irritation. Prostatic pain manifests as vague discomfort or fullness in the perineal, rectal, or suprapubic regions. In men with bladder obstruction, a thorough history may reveal episodes of urinary hesitancy, straining, decrease in force and caliber of the urinary stream, and terminal dribbling. Incontinence has various forms in men (Andriole, 2020). If patients report passing air with urine, this is known as pneumaturia and could be a sign of vesicovaginal, vesicoenteric, or ureteroenteric fistula; Crohn's disease; abscess; colon cancer; or emphysematous pyelonephritis (Maddukuri, 2020b)

Health-Related Concerns of the Older Male

The genitourinary and reproductive systems of the older person assigned male sex at birth undergo more gradual changes. Pubic hair turns gray and becomes sparse. Penile size decreases slightly. Scrotal contents hang lower; the testes decrease in size and firmness, and less sperm are produced due to an increase in connective tissue in the tubules. Testosterone production declines slowly, resulting in slower arousal and more prolonged difficulty reaching orgasm. Ejaculation is less intense and shorter, with less seminal fluid and rapid detumescence. Prostatic tissue enlargement is common, frequently resulting in nocturia, urinary hesitancy, decreased urine flow, retention (sometimes with overflow incontinence), and less forceful ejaculation (Gunes et al., 2016).

When taking the history related to the genitourinary and reproductive systems of the older male patient, ask about difficulty urinating, hesitancy, decreased force of stream, frequency with decreased amount, dribbling, incontinence, or nocturia. If you suspect that the patient has developed benign prostatic hyperplasia, consider administering the American Urological Association Symptom Index (AUA-SI) which is an eight-item questionnaire addressing urological symptoms to determine the perceived severity of an enlarged prostate (Barry et al., 2017).

Ask about rashes or lesions that have developed or reoccurred. If nocturia is present, establish its onset and frequency, and explore possible contributing factors other than prostatic enlargement, such as sleep apnea, use of diuretics, caffeine or alcohol ingestion, increased fluid consumption in the evening, habit of frequent urination, mild heart failure, or dependent edema. Other pertinent questions concern such urinary symptoms as urgency, dysuria, hematuria, or documented urinary tract infection (UTI). Inquire about the older male's sexual health and, if he is experiencing erectile dysfunction (ED), whether he has sought any treatment (Savoy et al., 2020).

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Physical Examination of the Genitourinary System

The physical examination focuses on the skin, costovertebral angle, abdomen, rectum, groin, and genitals (Maddukuri, 2020a, 2020b). In women with urinary symptoms, pelvic examination is usually done, which is discussed in detail in Chapter 15, Gynecological Disorders.

Skin

For patients in whom you suspect chronic kidney disease, examine the skin for any evidence of xerosis due to sebaceous and eccrine sweat gland atrophy, any pallor due to anemia of chronic disease, hyperpigmentation due to increased melanin deposits, evidence of petechiae or ecchymoses due to platelet dysfunction or yellow to brown skin caused by urochrome deposits.

Costovertebral Angle

The costovertebral angle is formed by the 12th rib and lumbar spine. In severe infection, placing the palm of the hand on the area and applying pressure may be adequate to elicit pain. In other patients, pain may only occur with blunt striking of the back, flanks, and with a fist. Noted costovertebral tenderness may indicate pyelonephritis, calculi, or urinary tract obstruction.

Abdomen

While rare to view fullness of the upper abdomen, it can be a nonspecific finding of hydronephrosis or a kidney or abdominal mass. To test for bladder distension and urinary retention, percussion that elicits dullness suggests bladder distention. Under most circumstances even a full bladder cannot be percussed above the symphysis pubis (Maddukuri, 2020a) because over 1,000 mL of urine is required to result in a bladder extending above the symphysis pubis.

Prostate

Routine examination of the prostate is controversial, and there is limited evidence that it is useful in prostate cancer screening (Naji et al., 2018). For examination of the prostate through the rectum, the patient is placed in the left lateral decubitus position or standing and leaning forward over the examination table with toes pointed inward, for easier access to the anorectal area. The examiner uses a well-lubricated, gloved finger, advanced above the anal canal, to palpate the anterior wall of the rectum for the prostate gland. The gland is normally heart shaped with a central groove that can be felt. The normal surface is smooth, elastic, and nontender on palpation. Absence of the central groove in a smooth gland or protrusion of the gland more than 1 cm into the rectum is typical of benign prostatic hyperplasia (Andriole, 2020). A boggy, tender prostate is suspicious for prostatitis. A hard, irregular nodule may indicate carcinoma. Either finding requires further work-up.

Groin and Genitals

The inguinal canal is palpated for hernia and the inguinofemoral areas are palpated for lymphadenopathy. If an inguinal and/or genital hernia is suspected, the palpation should be done with patients standing. Inguinal hernia or adenopathy may explain scrotal or groin pain. The scrotum needs to be examined for any lesions and palpated for swelling or masses. Gross asymmetry, swelling, erythema, or discoloration of the testes may indicate infection, torsion, tumor, or other mass. Normally the left testicle is hanging lower than the right testicle; if elevation of one testis is noted, it may be indicative of testicular torsion (Marchese, 2016). Horizontal testicular lie (bell-clapper deformity) indicates increased risk of testicular torsion. Cremasteric reflex may be absent with testicular torsion (Mellick et al., 2021). Location of irregularities in relation to the testis and the degree and location of tenderness may help differentiate among scrotal irregularities (e.g., spermatoceles, epididymitis, hydroceles, tumors). If swelling is present, the area should be transilluminated to help determine whether the swelling is cystic or solid (Suneja et al., 2020).

The penis is examined with and without retracting the foreskin. Note if on the penis there are any lesions to include herpes simplex, chancre, or chancroid (Chipollini et al., 2019). If red, raised hyperkeratotic lesions on the scrotum are detected, consider Fordyce's disease, a benign condition. Look for evidence of intertrigo, which could be caused by *Candida* (Chipollini, 2019). Peyronie's disease can also be assessed with inspection of the penis. This disease results in fibrous plaques that can be felt in the penile shaft. If noted, inquire about any problems with priapism, curvature of erections, ulcers, and discharge.

ACUTE KIDNEY INJURY

Signal Symptoms: Decreased urine output, fatigue, anorexia, weakness, edema, pruritus

Description: Acute kidney injury (AKI) is defined as the abrupt loss and abnormality in kidney function over 6 hours to 1 week with a duration of less than 3 months (Levey, 2020). This decrease in estimated glomerular filtration rate (eGFR) leads to impaired control of acid-base balance and electrolytes and fluid balance. Acute renal disease (ARD) has been coined to define the continuing pathological processes and adverse events developing after AKI (Gameiro, 2018). According to the United States Renal Data System (USRDS) 2020 report, the rate of hospitalization of patients with AKI has increased by approximately 40% over the years of 2009–2018. Patients with AKI without prior diagnosis of chronic kidney disease (CKD) who were discharged alive from hospitalization had a 6-month probability of 0.4% of development of end-stage renal disease (ESRD) (USRDS, 2020). In patients with previous diagnosis of CKD who developed AKI, the 6-month probability of development of ESRD was 2.0% (USRDS, 2020). Patients hospitalized with AKI without pre-existing CKD survived for one year after discharge, the probability of being diagnosed with CKD within the year following discharge was nearly 50% (USRDS, 2020).

Etiology: Renal function with urine formation is based on four steps that occur in specific areas of the kidney. First, blood from the renal arteries is delivered to the glomeruli and filtered, resulting in an ultrafiltrate. The ultrafiltrate, free from protein and blood elements, then flows into the renal tubules, which reabsorb and secrete solute and/or water from the ultrafiltrate. The final tubular fluid, urine, leaves the kidney, draining through the renal pelvis and ureter and into the

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bladder, leaving the body through the urethra. Any disruption in the process of urine formation can result in the deterioration of renal function and AKI.

Further breakdown of the definition of AKI by Kidney Disease: Improving Global Outcomes (KDIGO) (2012) is any increase in serum creatinine (SCr) by greater than or equal to 0.3 mg/dL within 48 hours or increase in the SCr greater than or equal to 1.5 times baseline within the prior 7 days, or urine volume less than 0.5 ml/kg/hour for 6 hours. Serum creatinine is a by-product of muscle metabolism that is excreted unchanged by the kidneys. Changes in SCr and urine output are indicators of a change in eGFR. Normal eGFR varies according to age, sex, and body size. In young adults, it is 120 to 130 mL/min and declines with age starting after 40 years. Assessment of renal function is made by eGFR, and it is the most widely accepted and most useful overall index of kidney function (KDIGO, 2012). Patients who have extremes of muscle mass, such as the frail older adult, the critically ill, patients with cancer, body builders, or those with unusual diets, will have inaccurate eGFR. Creatinine clearance (CrCl), where urine is collected over 24 hours and the amount of creatinine is measured, is a better measurement in these patients and will give a much better indication of the GFR in patients recovering from AKI.

The RIFLE criteria (Risk, Injury, Failure, Loss and End Stage) were developed as a system of diagnosis and classification for the broad range of acute kidney impairment (KDIGO, 2012):

- **Risk:** 1.5-fold increase in SCr or 25% decrease in GFR, or urinary output <0.5 ml/kg/hr × 6 hours
- **Injury:** 2-fold increase in SCr or 50% decrease in GFR or urinary output <0.5 ml/kg/hr × 12 hours
- **Failure:** 3-fold increase in the SCr or 75% decrease in GFR, SCr >4.0 or acute rise in the Scr >0.5, urinary output <0.3 ml/kg/hr × 24 hours or anuria × 12 hours
- **Loss:** Complete loss of kidney function >4 weeks
- **End-Stage Renal Disease:** failure >3 months

Identification of the cause of AKI is important for proper management and treatment. Prerenal AKI is decreased renal perfusion precipitated by an abrupt change in volume status. Postrenal AKI is caused by obstruction in an area of the kidney that decreases elimination and removal of urine. Prerenal and postrenal causes can be determined by using fractional excretion of sodium (FENa), which measures the amount of filtered sodium in the urine. If the FENa is <1%, this indicates decreased perfusion to the kidney but no damage to the kidney because it is still able to absorb sodium and water. If the FENa is >2%, intrinsic or postrenal damage is indicated because the kidney is unable to hold onto to sodium and water. Postrenal AKI indicates obstruction of urine from the glomerulus into the bladder. Usually this can be caused by nephrolithiasis or an enlarged prostate but could also be caused by other conditions that would compress the ureter, such as pregnancy or abdominal tumor.

Occurrence: Although risk for AKI increases with age, it can occur at any age or ethnicity. Across age-groups, a higher percentage of men are affected by AKI than women (USRDS, 2020).

Age: Although AKI can occur at any age, its incidence is highly associated in patients 75 years of age or older (USRDS, 2020).

Ethnicity: Blacks were diagnosed with AKI 70% more frequently than Whites in 2018 (USRDS, 2020).

Contributing Factors: Patients with underlying CKD are more likely to develop AKI. The leading cause of CKD is diabetes, followed by hypertension. Having either condition or both increases the risk of the development of AKI. USRDS (2020) reports that 41.8% of patients hospitalized in 2018 had diabetes with CKD. Factors that predispose the patient to vascular diseases, such as smoking, hyperlipidemia, claudication, stroke, myocardial infarction, and atrial fibrillation, should be noted. Patients with new onset atrial fibrillation who are not anticoagulated are at high risk for renal artery emboli.

Prerenal AKI is a physiological response to renal hypoperfusion without tubular injury. It can be caused by depletion of intravascular volume resulting from vomiting, diarrhea, hemorrhage (either surgical or gastrointestinal [GI]), excessive diuresis, or burns. Sepsis, hypoxemia, anaphylactic shock, pancreatic disease, and liver disease will also cause AKI due to decreased intravascular volume. In addition, any condition that affects the renal vascular system, such as renal artery stenosis, renal vein thrombosis, hemolytic uremia syndrome, and sickle cell anemia will cause AKI. Medications, particularly cyclosporine, tacrolimus, angiotensin-converting enzyme (ACE) inhibitors, NSAIDs, radiopaque dye, and amphotericin, will also induce AKI due to reduction in renal blood flow.

Conditions that cause intrinsic AKI are focused on the area of the kidney that is damaged. This can be tubular damage, glomerular damage, interstitial damage, and vascular damage. The most common cause of damage to the structures of the kidney is prolonged hypoperfusion and destruction/damage to the cells by nephrotoxins. Vascular damage to the kidney caused by postinfectious or other type of glomerulonephritis leads to glomerular AKI. Interstitial damage is caused by systemic lupus erythematosus, sarcoidosis, certain viruses (Epstein-Barr, cytomegalovirus, and HIV), certain medications (NSAIDs, sulfonamides, proton pump inhibitors) and certain bacterial infections. Tubular damage can be causes by radiographic contrast dye, ethylene glycol, rhabdomyolysis, tumor lysis syndrome, and myeloma.

Postrenal causes of AKI include any condition in which there is an impediment of the excretion of urine anywhere from the collecting tubules to the urethra. In the tubules, crystal or protein particles can precipitate, causing obstruction. Ureteral obstruction can be caused by calculi, clots, fungus balls, tumors, or trauma. Bladder obstruction, either mechanical or chemical, will also cause postrenal AKI. Prostatic disease, either hypertrophy or cancer, is the most common type of postrenal AKI.

Signs and Symptoms: Predominant symptoms are usually those of the underlying illness or injury that precipitates the AKI. The patient may have symptoms directly resulting from alterations in kidney function, such as decreased urine output, flank pain, edema, or hypertension. The patient may have noticed a change in their urine consistency or color, such as foamy urine, which indicates proteinuria, or dark brown/red urine that could be indicative of red blood cells (RBCs). Patients may have nausea, vomiting, and diarrhea, leading to volume depletion. Specific questions regarding use of medications that can cause renal injury, including NSAIDs and antihypertensive medications such as ACE inhibitors (ACEIs) and angiotensin receptor blockers (ARBs) and recent antibiotic use, need to be asked of the patient. Factors that predispose the patient to vascular disease and a detailed history of hypertension, diabetes mellitus, smoking, hyperlipidemia, claudication,

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stroke, myocardial infarction, and atrial fibrillation should be noted. In addition, ask patients whether they have experienced any fatigue, arthritis, weight loss, cough, hemoptysis, arthralgias, or sinus symptoms, which may indicate a systemic illness, such as vasculitis or systemic lupus erythematosus. Use of illicit drugs, such as cocaine, ecstasy, and heroin, can also cause AKI. In addition, questioning about past history of drug use, tattoos, and piercings, which increase the risk for hepatitis B, hepatitis C, and HIV, can lead to glomerular disease.

Recent imaging studies requiring the use of radiographic contrast agents should be explored due the increased incidence of development of AKI with these agents (Davenport et al., 2020). A past history of cancer, specifically prostate, cervical, or bladder cancer, could be indicative of obstruction of the urinary tract. Any family history of kidney disease increases the risk of a patient developing kidney disease in their lifetime. Patients with signs and symptoms of renal failure, such as weakness, easy fatigability, anorexia, altered mental status, weight loss, dysgeusia, nausea, cold intolerance, neuropathy, tremor, asterixis, seizures, and uremic fetor (where the patient has an ammonia-like or urine-like odor to the breath) may be suffering from ESRD and need to be admitted to the hospital for further evaluation and treatment.

Physical examination includes assessment of weight, orthostatic blood pressure, mucous membranes, and skin turgor and neck veins for the presence of volume depletion or overload. A funduscopic examination positive for atrioventricular nicking, exudates, or arterial narrowing is indicative of hypertension. Cardiac examination may reveal an S_3, indicative of volume overload or heart failure. The presence of a pericardial rub may indicate pericarditis, a late finding in ESRD. Lung assessment may reveal tachypnea and rales. Skin assessment should include inspection for any rash, skin lesions, livedo reticularis, or purpura that may indicate vasculitis or autoimmune disease. Periorbital, pretibial, and presacral edema can indicate advancing renal disease from any cause. Abdominal assessment should include auscultation for renal or abdominal bruits as well as evaluation for abdominal masses, costovertebral angle tenderness, and bladder distention. Assess for asterixis, a tremor of the wrist when it is extended, which is commonly seen in patients with ESRD.

Diagnostic Tests: Urinalysis is a noninvasive tool that can provide information regarding AKI. Urine is analyzed for sediment, specific gravity, urine sodium, urine protein, and urine creatinine levels. The appearance of certain urinary casts, cylindrical particles associated with certain diseases, assists in determination of the cause of the AKI. Specific gravity reflects the ability of the kidney to concentrate urine and can reflect a patient's volume status. To determine prerenal or postrenal AKI, FENa should be utilized. Further laboratory tests may show hyperkalemia, hypocalcemia, hyponatremia, and acidosis. A complete blood count (CBC) should also be drawn to evaluate for leukocytosis and anemia.

Radiographic studies are performed to assist in the diagnosis and cause of AKI. Renal ultrasound is most common and can be used to assess kidney size, obstruction, and the presence of masses. Upon imaging of kidneys with AKI, they are usually normal size. If masses are noted on the kidneys with ultrasound, an abdominal computed tomography (CT) scan will help to identify the lesion. Renal biopsy is only performed when laboratory data have been unrevealing and no reversible causes are identified as the cause of AKI. The procedure is performed percutaneously, and the most common complication is bleeding. Assessment of the patient's activated partial thromboplastin time (aPTT), prothrombin time (PT)/International Normalized Ratio (INR), and platelet count must be performed before the biopsy. Renal biopsy is avoided in patients who have a "solitary" kidney, either from congenital absence or acquired absence, such as nephrectomy for renal cell carcinoma.

Differential Diagnosis:
- Gastroenteritis
- Sepsis
- Glomerulonephritis
- Benign prostatic hypertrophy
- Nephrolithiasis
- Lupus nephritis
- Atypical hemolytic uremic syndrome

Treatment: Treatment is based on the cause of AKI. In volume depletion, fluid resuscitation with isotonic saline and/or packed RBCs is used to reestablish circulating volume. Vasopressors to maintain blood pressure may also be needed. Withdrawal of the offending medication and avoidance of other nephrotoxic agents is extremely important. Dose adjustment of renally metabolized medications is also warranted. Antihypertensive medications should be judiciously titrated to avoid any further renal hypoperfusion. In obstructive AKI, treatment of the obstruction often results in renal recovery. Usually, rapid correction of prerenal and postrenal causes leads to full recovery of kidney function. Avoid exogenous sources of potassium, such as nutritional supplementation and IV fluids. Treatment of hyperkalemia includes administration of IV calcium gluconate, insulin, beta-2 agonists (albuterol), dextrose, and potassium-removing agents. Hyperphosphatemia may also occur in AKI, and calcium acetate or calcium carbonate can be used to reduce absorption of phosphorus from the GI tract. Platelets are often dysfunctional in AKI, and desmopressin (DDAVP) may be required to activate platelets. Due to lower levels of circulating erythropoietin and decreased bone marrow responsiveness, anemia is often found in AKI, requiring transfusion of RBCs to increase oxygen-carrying capacity to the kidney.

If there is no recovery in kidney function after correction of the cause of the AKI, hemodialysis may need to be initiated. This is especially important in the face of continued acid-base disturbances, electrolyte abnormalities, volume overload, and uremia. The risk of developing ESRD is higher in patients who already have CKD and sustain dialysis-requiring AKI.

Follow-Up: Patients who are unable to fully recover to their previous level of kidney function will need to be closely monitored and followed by a nephrologist. Follow-up with a nephrologist 3 to 4 weeks after discharge to evaluate serum creatinine is important. Patients who have a new diagnosis of CKD stages 1 through 5 will require follow-up with a nephrologist for the remainder of their lives. For patients with concomitant conditions of hypertension, diabetes, and strict disorders, it is highly advised that current practice guidelines be followed.

Sequelae: CKD is a direct result of AKI because a return to previous level of kidney function is low. Patients with CKD are at increased risk for progression to ESRD, which requires renal replacement therapy. In addition, they are at increased risk for cardiac sequelae, including coronary artery disease,

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heart failure due to fluid overload, electrolyte derangements, cerebrovascular accident (CVA), and peripheral vascular disease. A nephrologist will manage comorbidities associated with CKD, including anemia of chronic disease, secondary hyperparathyroidism, and hypertension. Tight glycemic control will also assist to slow progression of CKD.

Prevention/Prophylaxis: Prevention of AKI begins first with identifying those at risk for CKD, especially patients with underlying diabetes and hypertension. Close monitoring of serum creatinine and urine for albuminuria is paramount. Prompt referral to nephrology when there is an increase in creatinine is important. Patients with a past history of AKI should be educated on the avoidance of nephrotoxic medications, such as NSAIDs and radiopaque contrast, to prevent further progression of kidney damage. Clinicians should ensure that medication dosages, especially those that are renally secreted, are adjusted appropriately for a patient's glomerular filtration rate once their new GFR baseline is determined following AKI.

Referral: Patients who have AKI are usually hospitalized for management of the cause of the AKI. Prompt evaluation and management by a nephrologist is warranted to prevent further kidney damage. After resolution of the AKI and discharge from the hospital, follow-up with a nephrologist is strongly encouraged for ongoing assessment and management of serum creatinine and eGFR until recovery or plateauing occurs. Patients may not return to their previous level of creatinine after an AKI event.

Education: Patients should be educated on signs of heart failure as well as avoidance of certain over-the-counter (OTC) medications that would precipitate AKI. Patients should be instructed to avoid diets high in salt and to strive for less than 2 grams of sodium per day (KDIGO, 2012). In addition, tight glycemic control, with hemoglobin A1c (Hb A1c) of less than 7%, as well as optimal blood pressure control of 120/80 mm Hg or less is paramount. Smoking cessation and maintenance of healthy body weight are also important in maintaining healthy kidney function.

Clinical Recommendation	Evidence Rating	References
Urine output and serum creatinine continue to be the foundation markers for acute kidney injury (AKI).	C	Ostermann et al., 2020
Assessment of renal function is made by estimation of the glomerular filtration rate and is the most widely accepted and most useful overall index of kidney function.	C	Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group, 2012
AKI and chronic kidney disease (CKD) are increasingly recognized as related entities in the context of kidney disease.	C	Ostermann et al., 2020
Current practice guidelines should be followed in patients who have hypertension and diabetes in addition to CKD.	C	KDIGO, 2012
Renally excreted medications should be dosed on calculation of creatinine clearance.	C	KDIGO, 2012

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

BENIGN PROSTATIC HYPERPLASIA (BENIGN PROSTATIC HYPERTROPHY)

Signal Symptoms: Urinary frequency, nocturia, urgency, hesitancy, weak or intermittent urine stream, straining to void, sensation of incomplete voiding, dysuria, terminal dribbling, incontinence.

Description: Benign prostatic hyperplasia (BPH), also called benign prostatic hypertrophy, is the benign growth of the prostate that may lead to obstruction of the bladder outlet. Cellular elements of the prostate are involved, and dysfunction in normal cell apoptosis with excessive growth of epithelial and stromal cells within the prostate occurs (Ng & Baradhi, 2021).

Etiology: Originates in the transitional and periurethral zones of the prostate and is hormonally influenced by testosterone and dihydrotestosterone (DHT) production.

Occurrence: Occurs universally in older men; genetics is thought to play a part in males who develop it at a younger age.

Age: Seen in 50% of men older than 50 years and in 90% of men by age 85 years.

Ethnicity: A recent study found that Black men are significantly less likely than White men to undergo surgical treatment for lower urinary tract symptoms/BPH (Antoine et al., 2021).

Contributing Factors: Risk factors include age older than 40, metabolic syndrome, obesity, type 2 diabetes, genetic predisposition, high alcohol intake, and being inactive (Langan, 2019; Ng & Baradhi, 2021).

Signs and Symptoms: Lower urinary tract symptoms (LUTS) occur on a continuum and do not necessarily reflect the degree of prostatic enlargement. The onset of symptoms is gradual and includes increased frequency of urination, nocturia, hesitancy, urgency, and weak urinary stream. These

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symptoms are not specific for BPH and progress gradually over a period of years.

The American Urological Association (AUA) has developed a self-administered 8-measure Symptom Index (AUA-SI) helpful in addressing the occurrence and symptom severity (1 to 7 mild; 8 to 19 moderate; 20 to 35 severe) (Barry et al., 1992).

History elements should include:

- Urinary storage (frequency, urgency, nocturia), voiding symptoms (strength of stream, hesitancy, intermittency, straining to urinate), and post-void dribbling
- History of type 2 diabetes, which can cause frequency and diuresis
- Symptoms of neurological disease
- Sexual dysfunction, which is correlated with BPH
- Gross hematuria or pain in the bladder region suggestive of a bladder tumor or calculi
- Smoking history, which is a risk factor for bladder cancer
- History of bladder/prostate surgery, urethral trauma, urethritis, or urethral instrumentation that could lead to urethral stricture
- Family history of BPH and prostate cancer
- Treatment with drugs that can impair bladder function (anticholinergic drugs), increase outflow resistance (sympathomimetic drugs), or cause mobilization of fluids (diuretics)

Physical examination includes a digital rectal examination (DRE) and neurological assessment. The prostate may be enlarged or normal-sized. It should feel smooth, with a rubbery consistency and nontender. Nodularity or extreme hardness raises suspicions of malignancy whereas tenderness may indicate prostatitis. Prostate size does not correlate with degree of obstruction or severity of symptoms as the clinician cannot assess the periurethral zone where symptoms originate.

Diagnostic Tests: Urinalysis is recommended to rule out alternative diagnosis. If the urinalysis is positive for nitrates or large leukocytes and the patient has urinary tract infection (UTI) symptoms, a urine culture should be done. Ketones, blood, protein, or glucose could indicate other causes of the LUTS. Prostate-specific antigen (PSA) testing can be considered in those with a 10-year life expectancy and those patients who desire to be screened for prostate cancer. If screening is agreed upon, PSA is measured before starting a 5-alpha reductase inhibitor because this medication may lower future readings and can influence prostate cancer screening results. PSA may be elevated in BPH, prostatitis, acute urinary retention, catheterization, recent ejaculation, and prostate cancer (Ng & Baradhi, 2021). Creatinine and an ultrasound to check the bladder residual should be measured if renal insufficiency or obstructive uropathy is suspected. Upper tract imaging, transrectal ultrasound, flow studies, and cystourethroscopy are not indicated unless surgery is planned or there is a need to rule out other conditions.

Differential Diagnosis:

- Prostate cancer (may coexist with BPH)
- Bladder cancer
- Urethral stricture/bladder neck contracture
- Urinary infections (UTI, prostatitis)
- Cardiovascular disease (edema, diuretic use) can worsen urinary symptoms
- Neurogenic bladder
- Neurological disease causing voiding dysfunction (hyper/hypoactivity of the bladder, hypercontractility of the bladder neck)
- Endocrine disease (long-standing uncontrolled diabetes can cause decreased sensation, bladder underactivity, and incomplete bladder emptying; glucosuria can cause increased urine production worsening LUTS)
- Polydipsia from overintake of fluids

Treatment: For patients with mild symptoms and an AUA-SI score less than 8 or for those with moderate to severe symptoms who have not developed the complications of LUTS or bladder outlet obstruction (renal insufficiency, urinary retention, or recurrent infection), a program of watchful waiting and instruction to avoid medications known to worsen symptoms is prescribed (AUA Education and Research, Inc., 2010). Medication groups to be avoided include decongestants and other sympathomimetics and anticholinergics (Valladales-Restrepo & Machado-Alba, 2019). Patients should be instructed in lifestyle self-management such as limiting fluids in the evening, limiting alcohol and caffeinated beverages, Kegel exercises for urgency episode, timed voids, and double voiding to help with bladder emptying (Schreiber, 2017).

For mild-to-moderate symptoms, alpha-adrenergic blockers such as alfuzosin (Uroxatral), doxazosin (Cardura), terazosin (Hytrin), and tamsulosin (Flomax) relax smooth muscle of the bladder neck and prostate and can increase peak urinary flow rate; all alpha-adrenergic blockers are equally effective with symptom relief between 1 and 4 weeks (AUA Education and Research, Inc., 2010). Tapering terazosin, tamsulosin, and doxazosin as well as evening dosing minimizes postural hypotension. Those patients who are scheduled for cataract surgery in the next few months should not start an alpha blocker due to an increased risk of floppy iris syndrome. Alfuzosin has the lowest studied risk of causing floppy iris syndrome in the future (Silverstein, 2018). Dutasteride (Avodart) and finasteride (Proscar), and 5-alpha reductase inhibitors, block the conversion of testosterone to dihydrotestosterone, the major intraprostatic androgen in men, and are used when prostate enlargement is identified. Side effects include decreased libido, ejaculatory dysfunction, gynecomastia, and impotence. Treatment for 6 months or longer is needed for maximal benefit. Finasteride and an alpha blocker used concurrently slow the progression of BPH; the greatest effect is seen in patients with significantly enlarged prostates. Phosphodiesterase type 5 (PDE5) inhibitors have been shown to be beneficial with symptom relief. Tadalafil 5 mg has been approved for treatment of BPH/LUTS and is comparable in symptom relief to alpha blockers with rare side effects. In those patients with ED and BPH, this is a reasonable alternative to alpha blockers. Side effects are rare but can include headache, indigestion, back pain, flushing, and nasal congestion (Jung et al., 2017; Pattanaik et al., 2018). Tadalafil cannot be taken at the same time of day as an alpha blocker due to risk of hypotension.

For moderate to severe LUTS caused by BPH (AUA-SI score >20), surgery is an option. Surgery is recommended in those with renal insufficiency, recurrent UTIs, recurrent bladder stones, refractory urinary retention, or refractory gross hematuria (AUA Education and Research, Inc., 2018). In recent years, many treatments have proliferated in this category. Transurethral resection of the prostate (TURP) has been the standard for years, with open prostatectomy for glands of

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more than 40 g. Other treatment options include the transurethral incision of the prostate (TUIP) for gland enlargement of less than 30 g. Holmium laser enucleation (HoLEP), photoselective vaporization of the prostate (PVP), and thulium laser enucleation of the prostate (ThuLEP) use lasers for treatment of small to large prostates and in those patients who are at higher risk for bleeding. Urolift (prostatic urethral lift), which uses mechanical clips, and Rezum (water vapor thermal therapy), which uses steam to induce localized cell death, are newer options for those with smaller prostates (<80 g) that are sexual side effect sparing and can be done in the office with select patients. Aquablation is a newer therapy using high pressure water to resect the smaller prostate (30 to 80 g) that is done under general anesthesia but has limited data (Parsons et al., 2020).

Follow-Up: Scheduling of follow-up depends on the course of treatment. AUA symptom scores can assess treatments. Patients receiving alpha blockers should be followed in 2 to 4 weeks, whereas those started on 5-alpha reductase inhibitors should be seen in 6 months with a follow-up PSA if screening for prostate cancer. Depending on age, risk factors, and informed decision making regarding PSA testing (see prostate cancer section), consider annual PSA and DRE for prostate cancer. Annual urinalysis is typically done.

Sequelae: Untreated BPH can lead to urinary retention and bladder outlet obstruction requiring catheterization and/or surgery. Chronic issues can lead to renal insufficiency, UTIs, bladder stones, and bladder diverticula. Side effects of medical treatment include retrograde ejaculation, decreased libido, or orthostatic hypotension. Surgical sequelae can include retrograde ejaculation and urethral stricture.

Prevention/Prophylaxis: Prevention of obesity and diabetes can help reduce the risk of BPH.

Referral: BPH symptoms that do not respond to medical management, urinary retention, abnormality found on digital examination, incontinence, hematuria, and neurological disease that impacts LUTS should be referred to urology for evaluation. Consider collaborative management for drug therapy.

Education: Lifestyle measures to address include weight loss and diabetes control to reduce risks. Educate the patient about BPH and its treatment options and side effects. Instruct the patient to avoid any drugs that can increase retention or cause symptoms to flare up, including caffeine, alcohol, sedatives, over-the-counter (OTC) sleeping pills, and OTC cold and allergy remedies. Instruct the patient to report hematuria, UTI symptoms, or worsening LUTS. There is not enough evidence to support any herbal supplements for BPH.

Clinical Recommendation	Evidence Rating	References
Watchful waiting is an option; the need for medical treatment is based on symptoms (American Urological Association [AUA] symptom score) and the degree of patient bother.	C	AUA Education and Research, Inc. (2010)
Alpha-adrenergic antagonists are equally effective and work rapidly; patients can expect moderate improvement in symptoms.	A	Langan, 2019
5-alpha reductase inhibitors modestly improve AUA symptom score and reduce the risk of acute urinary retention or need for invasive surgery.	A	Langan, 2019
Combination therapy with an alpha blocker and a 5-alpha reductase inhibitor is superior to monotherapy, particularly in patients with higher prostate volumes and prostate-specific antigen (PSA) levels.	B	Langan, 2019
Tadalafil 5 mg has been approved for treatment of benign prostatic hyperplasia (BPH)/lower urinary tract symptoms that are comparable in symptom relief to alpha blockers. In those patients with erectile dysfunction and BPH, this is a reasonable alternative to alpha blockers.	B	Jung et al., 2017 Pattanaik et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

BLADDER CANCER

Signal Symptoms: Painless hematuria (most common presenting symptom), urinary frequency or urgency, urinary tract infection (UTI), flank pain, mild suprapubic pain; often asymptomatic.

Description: The majority of bladder cancers are urothelial carcinoma or transitional cell; 1% to 2% are squamous cell cancer; and the rest are adenocarcinoma, small cell carcinoma, or sarcoma (American Cancer Society [ACS], 2021a). In bladder cancer, the posterior and lateral walls of the bladder are involved more frequently than the superior wall. Bladder cancer can be categorized as *superficial*, *invasive*, and *metastatic*. Superficial, or early, bladder cancer occurs when the lesion is located on the surface of the mucosa or when the tumor penetrates the mucosa and submucosa only. Invasive bladder cancer develops when lesions pervade the bladder muscularis or the perivesical fat. Metastatic bladder cancer is characterized by lymph node, visceral, or bone tissue involvement.

Etiology: Bladder cancer has been linked to smoking, chemical exposure, and exposure to certain medications such as

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cyclophosphamide (ACS, 2021b). Squamous cell bladder cancer has been linked to chronic infection with *Schistosoma haematobium* (Saginala et al., 2020).

Occurrence: In the United States, each year more than 83,000 new cases of bladder cancer are diagnosed, and more than 17,000 deaths can be attributed to bladder cancer. Bladder cancer is the sixth most common type of cancer (National Cancer Institute [NCI], 2021) and is almost three times more common in men than in women (National Comprehensive Cancer Network [NCCN], 2021).

Age: Median age of diagnosis is 73 years. Bladder cancer is rarely diagnosed in patients younger than the age of 40 years (NCCN, 2021).

Ethnicity: In the United States, White males have the highest risk, with roughly twice the incidence seen in African American and Hispanic men (NCI, 2021). The incidence in White and Black women is about the same. Hispanic women have a lower incidence compared with White and Black women (NCI, 2021).

Contributing Factors: Smokers are three times more likely to develop bladder cancer as compared with non-smokers. Some industrial chemicals have been linked with bladder cancer, including benzidine and beta-naphthylamine. Additionally, painters, machinists, printers, hairdressers, and truck drivers are at increased risk due to chemical exposure. Use of the medication pioglitazone has been linked with an increased risk of bladder cancer. Dietary supplements that contain aristolochic acid have been associated with urothelial cancers. Infections of the urinary tract, long-term indwelling catheters, renal and bladder stones, and chronic bladder irritation have been linked to bladder cancer (ACS, 2021b). Family history of bladder cancer can also increase risk. Family members may share some changes in the *GST* and *NAT* genes. Inherited genetic syndromes such as Lynch's syndrome, Cowden's disease, and a mutation in the retinoblastoma gene (*RB1*) can also increase the risk (ACS, 2021b; Saginala et al., 2021). Pelvic irradiation, certain drugs (e.g., cyclophosphamide) can contribute to the development of bladder cancer. *S. haematobium* infection is prevalent in Africa and the Middle East and has been associated with the development of bladder cancer (Saginala et al., 2020).

Signs and Symptoms: Gross, painless hematuria, pyuria, burning, and urinary frequency are common in the presentation of bladder cancer. The presence of unexplained hematuria in a patient older than 40 years denotes urothelial cancer until proved otherwise. Symptoms of advanced cancer may include pelvic or flank pain and lower extremity edema, resulting from lymphatic or venous blockage. Patients also may complain of abdominal pain, anorexia, and bone pain.

The physical examination may be normal in most patients; however, the clinician should palpate the pelvic area to identify a solid pelvic mass, palpate and percuss for evidence of any kidney enlargement, and perform a prostate examination on men and a pelvic examination on women. Additionally, the examination should be directed toward searching for possible sites of metastasis in the lungs, liver, bone, and lymph nodes.

Diagnostic Tests: Cystoscopy is the gold standard for the initial diagnosis and staging of bladder cancer (NCCN, 2021). Cytology should also be considered. Examination under anesthesia (EUA) should be performed to determine whether or not a palpable mass is present and, if present, whether or not it is mobile. An EUA during cystoscopy is effective at identifying locally advanced disease, which may present as gross extravesical extension, invasion of adjacent organs, or pelvic sidewall involvement. If a mass is felt, the bimanual examination is repeated after the resection to see if it is still present. Urine biomarkers may be checked through a few commercially available tests. Advantages of these tests include high sensitivity, but these tests are also associated with higher costs (Zhu et al., 2019).

Imaging studies may be used to define the location and the extent of the tumor, as well as to detect sites of multifocal disease. A computed tomography (CT) scan of the abdomen and pelvis should be performed with and without contrast, including delayed images to identify defects in the collecting system. Although CT scan provides better visualization of tumors than ultrasound, it may miss tumors less than 1 cm in size, particularly those in the bladder trigone or dome, and it cannot differentiate depth of bladder wall invasion (i.e., mucosal versus lamina propria or muscularis propria). Magnetic resonance imaging (MRI) may be considered in patients with poor renal function or in patients with iodinated contrast allergy. A positron emission tomography (PET) scan may be performed in patients with at least cT2 disease or in high-risk patients in whom metastatic disease is suspected. MRI of the brain with and without contrast is reserved for patients who are symptomatic or with small cell histology (NCCN, 2021).

Differential Diagnosis:

- Neurogenic bladder
- Nephrolithiasis
- UTI
- Benign prostatic hypertrophy
- Other genitourinary cancers (Perazella, 2021)

Treatment: Management of bladder cancer depends on the stage of the disease. Neoadjuvant chemotherapy, concurrent chemoradiation therapy, or adjuvant chemotherapy may be given to patients who are a candidate for cystectomy. Patients who are not candidates for cystectomy may be given concurrent chemoradiation therapy or radiation alone. Checkpoint inhibitors are recommended as second-line therapy (NCCN, 2021). Advanced disease generally requires surgery, radiation, and chemotherapy with combination agents. The patient's age and health status at the time of diagnosis must be considered in the management of bladder cancer (NCCN, 2021).

Follow-Up: Patients with superficial low-grade bladder cancer require a cystoscopy at designated intervals, although the value of repeated testing has been questioned. The need for supplemental nutritional support, pain management, prevention of complications such as skin breakdown, and an advance directive should be discussed during future follow-up care. Patients with a urostomy may need assistance from an ostomy nurse.

Sequelae: Metastasis to other parts of the body can occur. Survival of the untreated patient may be less than 2 years.

Prevention/Prophylaxis: Encourage patients who smoke to quit and exhort all patients to decrease exposure to harmful chemicals.

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Referral: Refer patients with clinically significant hematuria to a urologist. An oncologist also may be involved in the patient's management of the disease. Patient and family support is important at this time; information pertaining to hospice services should be provided. Patients with a urostomy may seek support from a local chapter of the United Ostomy Associations of America (UOAA) at 1-800-826-0826 or https://www.ostomy.org/.

Education: Older adults with bladder cancer may need to be educated about palliative support measures with a diagnosis of metastatic bladder cancer or when the disease becomes terminal.

Clinical Recommendation	Evidence Rating	References
Urine dipstick is not recommended for screening of bladder cancer in the general population due to lack of specificity.	A	National Comprehensive Cancer Network (NCCN), 2021
Routine screening for bladder cancer is not recommended for the general population.	B	NCCN, 2021
Patients should be counseled to eliminate active and passive smoking for prevention of bladder cancer.	B	American Cancer Society (ACS), 2021b, NCCN 2021
Cystoscopy is recommended in all patients with symptoms suggestive of bladder cancer. It cannot be replaced by cytology or by any other noninvasive test.	A	NCCN, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CHRONIC KIDNEY DISEASE

Signal Symptoms: Fatigue, anorexia, altered mental status, weakness, dysgeusia, pruritis, nausea, vomiting, edema.

Description: Chronic kidney disease (CKD) continues to be a growing worldwide problem. According to Centers for Disease Control and Prevention (CDC) data, more than 1 in 7 Americans, or around 35 million people, have CKD in the United States (CDC, 2021). CKD, when left undiagnosed and untreated, will progress to end-stage renal disease (ESRD), requiring renal replacement therapy in order for the patient to survive. With the increased prevalence of diabetes and an aging population, incidence of CKD will continue to rise. Early detection of CKD remains paramount to decrease the progression to ESRD. CKD is a silent disease, and often patients are unaware they have it until it is too late.

Etiology: CKD is defined as abnormalities of kidney structure or function, present for more than 3 months (Kidney Disease: Improving Global Outcomes [KDIGO], 2012). This can be from long-term diseases, such as diabetes or hypertension, or by the development of acute kidney injury (AKI). Decrease in glomerular filtration rate (GFR) and the presence of albuminuria are indicative of kidney damage. Certain markers, such as urine sediment abnormalities, electrolyte abnormalities, abnormalities noted on imaging, can also be noted with CKD (Table 14-1). Criteria for defining CKD are shown in Box 14-1.

Diabetes continues to be the leading cause of CKD, followed by hypertension (United States Renal Data System [USRDS], 2020). Other causes of kidney disease include glomerulonephritis, inherited polycystic disease, autoimmune diseases, infections, excessive use of nephrotoxic medications, and urological diseases.

TABLE 14-1 Markers for Kidney Damage

Markers of kidney damage (one or more)	Albuminuria (AER ≥30 mg/24 hr; ACR ≥30 mg/g [≥3 mg/mmol])
	Urine sediment abnormalities
	Electrolyte and other abnormalities due to tubular disorders
	Abnormalities detected by histology
	Structural abnormalities detected by imaging
	History of kidney transplantation
Decreased GFR	GFR <mL/min/1.73 m² (GFR categories G3a–GS)

AER, albumin excretion rate; ACR, albumin-to-creatinine ratio; GFR, glomerular filtration rate

Reprinted with permission from Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. (2013). KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. Kidney International, *3(1), 1–150.*

Occurrence: According to CDC data, more than 1 in 7 Americans, or around 35 million people have CKD in the United States (CDC, 2021). CKD affect more females than males (USRDS, 2020).

Age: Although CKD can affect any age-group, CKD is four times more prevalent among older (aged greater than or equal to 65) than younger individuals (USRDS, 2020). Despite being more prevalent in the older population, CKD

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BOX 14-1
Criteria for Definition of Chronic Kidney Disease

- Duration greater than 43 months (documented or inferred)
- Glomerular filtration rate (GFR) <60 mL/min/1.73 m^2 (GFR categories G3a–G5)
- Evidence of kidney damage from structural abnormalities or functional abnormalities other than decreased GFR, such as albuminuria, urinary sediment abnormalities, renal tubular disorders, or pathological abnormalities

Source: KDIGO, 2013

has actually decreased in this age-group since 2003–2006 (USRDS, 2020).

Socioeconomic Factors: Prevalence of CKD is higher among individuals with lower income: 17.4% of those below the poverty line versus 14.4% among those above (USRDS, 2020). It also affects those with lower education: 17.2% among those with less than a high school education compared to 13.1% with some college (USRDS, 2020).

Geographic Location: CKD was least prevalent in the states of Wyoming, Alaska, and Vermont and most prevalent in the states of Louisiana, Alabama, Florida, and Hawaii (USRDS, 2020).

Ethnicity: Blacks have a higher prevalence of CKD than Whites, according to USRDS data. Hispanics/Latino Americans continue to have the lowest incidence of CKD.

Contributing Factors: Diabetes mellitus is the leading cause of CKD and is the leading risk factor in the development of CKD. Hypertension, both a cause and a consequence of renal disease, closely follows. Autoimmune disorders, such as systemic lupus erythematosus, and malignancy, such as renal tumors or multiple myeloma, also increase the risk of kidney dysfunction. Vascular disease, chronic pyelonephritis, nephrolithiasis, systemic infections, and gout will also predispose a patient to chronic kidney disease. Certain medications, such as NSAIDs, especially when used in excessively high doses, will cause CKD. Radiopaque dye will also cause kidney damage, either leading to AKI or further accelerating CKD. AKI often predisposes a patient to the development of CKD. A family history of renal disease is an important risk factor in the development of CKD. People of color have an increased risk of CKD and are more likely to progress from CKD to ESRD. In addition, the presence of inherited disease, such as autosomal dominant polycystic kidney disease, will lead to development of CKD.

Exposure to toxins can also play a role in the development of CKD. Exposure can be occupational, environmental, or recreational. There is a strong association between smoking and development of CKD. Chronic smoking causes nephrosclerosis, which is caused by microvascular atherosclerosis, resulting in hypertension. Illicit substances associated with CKD include heroin and cocaine. Recently, methamphetamines and ecstasy use have been associated with CKD. Methamphetamines cause accelerated hypertension, causing renal damage. Ecstasy use can lead to rhabdomyolysis, drug-induced vasculitis, and severe hyponatremia. Cocaine use is associated with acute rises in blood pressure, leading to AKI from hypertension. Rhabdomyolysis, either drug or exercise-induced, will cause kidney damage. Transmittable disease, such as hepatitis and HIV, will also cause kidney damage leading to CKD. Exposure to heavy metals such as lead, cadmium, mercury, and organic solvents has been strongly linked to CKD; thus, screening for occupational hazards is a must.

Signs and Symptoms: CKD is a silent disease and does not produce symptoms until renal injury is quite advanced. Many individuals are unaware that they have CKD until it progresses to stages 3 or 4. In stages 1 and 2, blood urea nitrogen (BUN) and creatinine levels are normal or nearly normal, and acid-base, fluid, and electrolyte balances are maintained through the adaption of remaining nephrons. In stage 3, there is moderate impairment of GFR, and BUN and creatinine levels begin to increase. The patient usually remains asymptomatic, but levels of erythropoietin and parathyroid hormone are abnormal. Early symptoms of kidney disease, if any, may be similar to other illnesses. Only when the patient develops stage 4 or 5 of kidney disease do more profound symptoms of CKD occur. These include fatigue, loss of appetite, weight loss, dyspnea, anascara, confusion and difficulty with concentration, pruritus, dysgeusia, and foul-smelling breath (KDIGO, 2012).

Although diagnosis of kidney disease is based heavily on laboratory data and diagnostic imaging, a careful and through history may lead to clues associated with the diagnosis of CKD. Careful review of any kidney disease in the family is imperative, including questions relating to any hereditary diseases, such as autosomal dominant polycystic kidney disease. If the patient has a past history of pregnancy, ask whether there were any complications, including proteinuria, pre-eclampsia, or gestational diabetes. Any past urological conditions could indicate postrenal causes of CKD.

Any history of diabetes mellitus or hypertension should immediately raise a strong suspicion for the presence of CKD. In addition, cardiac issues such as heart failure and liver issues such as cirrhosis can lead to cardio-renal and hepato-renal disease. Disorders of the urinary tract, recent systemic infections, unusual rashes, or skin lesions should also raise suspicion of CKD. A through medication history should also be obtained to identify medications that may be contributing or causing CKD.

Diagnostic Tests/Tools: As stated previously, estimation of GFR is the best indicator to level of kidney function and functioning renal mass (KDIGO, 2012). There are varying stages of estimated GFR (eGFR) which indicates the degree of kidney damage. Albuminuria is a defining marker of renal injury regardless of GFR, often occurring before any rise in serum creatinine.

Spot urine albumin/creatinine ratio is the preferred screen as it detects lower levels of proteinuria. Low levels of proteinuria (30 to 300 mg) were once thought to be insignificant, but it is now known that modest albuminuria is significant for CKD. Severe albuminuria is significant for increased mortality and ESRD. Dipstick urinalysis should not be used for screening. eGFR and albuminuria should be assessed yearly in patients with CKD and with increased frequency in those patients who have high risk of rapid progression of CKD.

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There are number of equations that are utilized to determine eGFR based on serum creatinine. The Cockcroft Gault equation is used to estimate GFR to determine dosing of medications. The Modification of Diet in Renal Disease study equation was developed in 1999 and is the current recommended eGFR calculator for reporting in adults (KDIGO, 2012). It uses serum creatinine, age, sex, and race for estimation of GFR based on body surface area (BSA). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) equation was developed in 2009 and the uses the same four variables as the Modification of Diet in Renal Disease equation but has less bias and greater accuracy at higher eGFR. The CKD-EPI equation is currently utilized by clinic laboratories in the United States for GFR reporting and is recommended by KDIGO to be used for calculation of eGFR. In addition, serum cystatin C is a filtration marker that has emerged as an alternative to serum creatinine. It has been found to more accurately estimate eGFR because it reaches a steady state much faster than creatinine. It is often used when there is a decreased eGFR without the presence of structural disease, risk factors for CKD, or albuminuria (Gaitonde et al., 2017). eGFR in CKD patients is more accurate because of their steady state of kidney function. AKI often has every fluctuating eGFR as the kidney recovers from the damage. A creatinine clearance (CrCl), in which a volume of urine is collected over 24 hours and the amount of creatinine secreted is measured, is a more accurate indicator of eGFR because it is a direct measurement.

Other markers are also used to determine damage to kidneys, such as abnormalities in urinary sediment and abnormal findings on imaging studies. Examination of the urinary sediment for white blood cells (WBCs), red blood cells (RBCs), or casts may indicate the presence of acute kidney disease (AKD) or CKD and requires further investigation. Imaging studies should also be performed to suggest the cause of CKD. Ultrasound examination may indicate the presence of kidney stones, hydronephrosis, cysts, or masses. Small kidneys on ultrasound suggest CKD, whereas "large" kidneys may indicate tumors, cysts, or infiltrating diseases. A computed tomography (CT) scan may reveal tumors, obstructions, cysts, or calculi.

Further laboratory data that should be assessed in patients with possible CKD include complete blood count (CBC) and electrolytes. Fasting lipids and hemoglobin A1c (Hb A1c) should be evaluated in patients with diabetes. Serum and urine protein electrophoresis, complement levels, antineutrophil cytoplasmic antibody, antinuclear antibody, and viral studies (including hepatitis B and C and HIV) should also be performed.

Differential Diagnosis:

- AKI
- Cirrhosis
- Uropathic obstruction
- Nephrotic syndrome
- Tubulointerstitial disease

Treatment: Referral to a nephrologist should occur if (1) GFR is less than 30 mL/min, (2) there is a decline in GFR greater than 3 mL/min, (3) albuminuria is present, (4) it is difficult to control hypertension, and (5) there is unexplained anemia with GFR less than 60 mL/min (Gaitonde et al., 2017). Further investigation using the previous diagnostic tests will assist the nephrologist in the determination of the cause of the CKD. A patient may also have to undergo renal biopsy to fully determine the level of severity/damage the illness has caused as well as to obtain a definitive diagnosis. Once the stage of CKD is identified, management of CKD is aimed primarily at preventing progression of the disease through medications, risk factor reduction, lifestyle changes, and education of the patient and family regarding kidney disease. Eventually there is decline in kidney function to ESRD. Patients then must decide between renal replacement therapy—hemodialysis or peritoneal dialysis—in order for the patient to survive or opt for no renal replacement therapy and end-of-life care.

Patients with CKD have a greater risk for cardiovascular disease than those without. As stated previously, hypertension is both a cause and a sequela of kidney disease. It is associated with a faster decline in kidney function by increasing albuminuria and furthering the development of cardiovascular disease. Thus, reducing the risk of progression of CKD and advancement of cardiovascular disease is paramount. Reduction of blood pressure to target levels is the most important treatment step in managing CKD. Patients who are at greatest risk for complications or already have evidence of cardiovascular disease may need more aggressive blood pressure control, ideally in the 120/80 mm Hg or less range.

Multiple medications are frequently required in CKD patients to achieve goal blood pressure. Angiotensin-converting enzyme inhibitors (ACEIs) and angiotensin-receptor blockers (ARBs) are first-line treatment in patients with CKD and increased albuminuria, with or without diabetes. These agents reduce albuminuria and slow the rate of decline in kidney function in both diabetic and nondiabetic kidney disease. When beginning a patient on an ACEI or ARB, serum creatinine and serum potassium should be measured within 2 to 4 weeks after initiation or increase in either the ACEI or ARB dosing (KDIGO, 2021). Continue the ACEI or ARB therapy unless serum creatinine rises by more than 30% within 4 weeks of initiation of treatment or increase in dose (KDIGO, 2021). Consider dose reduction or discontinuation of the ACEI/ARB with symptomatic hypotension or uncontrolled hyperkalemia (KDIGO, 2021). Furthermore, sodium restriction of less than 2 g per day is recommended for blood pressure control (KDIGO, 2021) and moderate-intensity physical activity greater than or equal to 150 minutes per week is also recommended.

Increased salt and water retention occur with CKD leading to edema, necessitating initiation of a diuretic. Thiazide diuretics often become less effective as GFR falls below 40 mL/min due to decreased renal blood flow. Usually a loop diuretic, such as furosemide, torsemide, or bumetanide, is used. Side effects of loop diuretics include hypokalemia and hypomagnesemia, which can lead to increased cardiovascular risk of arrhythmias. Thus, serum electrolytes should be monitored, and the patient should be instructed to report any paresthesias, rash, or tinnitus.

Calcium channel blockers (CCBs) are effective agents that can be used to lower blood pressure in CKD patients; however, there are differences between these medications' effects on reducing proteinuria. Nondihydropyridine CCBs (verapamil, diltiazem) reduce proteinuria among patients with advanced nephropathy, whereas dihydropyridine CCBs (nifedipine, felodipine, amlodipine) will not have this effect unless coupled with an ACEI or ARB. The major side effect of CCBs is lower extremity edema, which is usually not resolved with the addition of diuretic.

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Beta blockers such as carvedilol, metoprolol, or bisoprolol should be used in patients with CKD when a proper dose of ACEI, ARB, or CCB is not enough to lower blood pressure. Although these agents do not provide any renoprotective effects, they do assist in reducing cardiovascular mortality in high-risk patients. Beta blockers should be avoided in patients with bradycardia or heart block.

Central alpha-adrenergic agonists decrease the effects of sympathetic activity to lower blood pressure. Vasodilators such as hydralazine and minoxidil are often used as fourth-line agents when other antihypertensive treatments have failed. Vasodilator therapy does not reduce proteinuria and has not been shown to improve renal outcomes. Side effects of minoxidil include increased hair growth and risk of pericardial effusion. Hydralazine is the leading cause of drug-induced lupus syndrome and should be avoided in any patient with an autoimmune disease.

Tight glycemic control in CKD patients reduces cardiovascular disease and CKD progression risk in both type 1 and 2 diabetes mellitus. An Hb A1c of less than 7.0% is the goal of patients with diabetes and CKD (KDIGO, 2020). Although achieving this can be difficult for some patients and is associated with increased risk of hypoglycemia, tight control reduces not only albuminuria but also retinopathy and neuropathy. Patients with type 2 diabetes mellitus and CKD should first be treated with metformin and sodium-glucose cotransporter-2 inhibitor (SGLT2i) (KDIGO, 2020). If eGFR is less than 30 ml/min, then these should be discontinued (KDIGO, 2020). Insulin can be used to treat diabetes in CKD, and doses should be tailored to attain the goal Hb A1c while avoiding hypoglycemia. Insulin types and doses should be individualized to each patient and to the patient's level of CKD. If a patient is unable to achieve glycemic targets despite use of metformin and SGLT2i, KDIGO (2020) recommends use of glucagon-like peptide 1 (GLP-1).

Anemia is a common complication of CKD. It worsens as kidney function declines, becomes prevalent in CKD stage 3, and continues through stage 5 into ESRD. The primary cause of anemia is decreased secretion of erythropoietin from decreased functioning renal cells, resulting in fatigue, decreased exercise capacity, decreased cognition, and impaired immunity, leading to decreased quality of life. Workload of the heart is increased with anemia, leads to left ventricular hypertrophy and cardiomyopathy, and increases the patient's risk of death from ischemic heart disease and heart failure. Evaluation of patients with CKD and anemia, regardless of age or CKD stage, should include iron complete blood count, reticulocyte count, iron studies, serum ferritin, serum transferrin saturation, serum B_{12}, and folate level (KDIGO, 2020). Iron can be given either orally or intravenously. IV is usually reserved for severely depleted patients and those on hemodialysis. Erythropoietin-stimulating agents (ESA) can be given once iron deficiency is corrected, other causes of anemia have been excluded or treated, and hemoglobin is consistently below 10 g/dL. Epoetin alfa, darbepoetin alfa, and methoxy polyethylene glycol-epoetin beta are erythropoietin receptor activators for the treatment of anemia associated with CKD. All correctable causes of anemia should be addressed prior to initiation of ESA therapy (KDIGO, 2020).

Changes in mineral metabolism and bone structure begin early in CKD. This not only encompasses bone disease but also vascular and soft tissue calcification. As kidney function worsens and GFR continues to decline, the kidney must work harder to excrete phosphorus. This then reduces the formation of the active form of vitamin D (1,25D). Low levels of 1,25D, coupled with low serum calcium levels from decreased gut absorption, lead to a rise in parathyroid hormone. This leads to secondary hyperparathyroidism due to hypocalcemia, hyperphosphatemia, and low 1,25D levels. The increased parathyroid hormone affects bone metabolism and increased bone turnover, causing decreased cortical bone and bone strength. This increases risk of fracture and causes increased "bone pain" in patients with CKD. Development of secondary hyperparathyroidism can be decreased by dietary restriction of high-phosphate foods such as fast food, dairy products, colas, and processed food products. A phosphate binder, which binds to the phosphate in food and is eliminated in the bowel movement, is also prescribed. Calcium acetate, lanthanum carbonate, sevelamer carbonate, sucroferric oxyhydroxide, and ferric citrate are the common phosphate binders used today. Patients who have high levels of parathyroid hormone should be assessed for hyperphosphatemia, hypocalcemia, high phosphorus intake, and vitamin D deficiency (KDIGO, 2017).

Patients with CKD are also at increased risk for malnutrition and hypoalbuminemia. These are associated with poor outcomes when the time comes for the patient to initiate dialysis. The restriction of protein in the CKD population has been a topic of ongoing debate. Current recommendations from KDIGO (2012) include a protein intake of 0.8 g/kg/day in patients with CKD. Patients need to be monitored for malnutrition with serum albumin levels and body weight assessments.

Smoking cessation is strongly encouraged in patients with CKD. Smoking compounds the risk for cardiovascular mortality in patients with CKD and hastens progression of kidney disease. Smoking risks and smoking cessation should be addressed with each office visit.

Unfortunately, despite optimal treatment and practices by the patient, kidney disease may continue to progress until kidney failure occurs. Patients then develop uremia, which is the accumulation of toxins within the blood. This leads to anorexia, nausea, vomiting, asterixis, muscle weakness, platelet dysfunction, pericarditis, mental status changes, and possibly coma. At this point, dialysis is initiated to "clean" the blood of these toxins and will need to continue throughout the patient's lifetime.

Follow-Up: Care of the patient with CKD is in the hands of the nephrologist for the rest of the patient's life span. Unfortunately, timely referral to help keep the patient from progression to ESRD is often not done. In addition, some patients are not aware that they have CKD. It has been found that the worse the patient's kidney function is, the more aware they are of their disease (CDC, 2012). According to Levin et al., (2013), any patient with the following criteria should be referred to nephrology for further evaluation:

- AKI or abrupt sustained fall in GFR
- eGFR less than 30 mL/min/1.73 m^2
- A consistent finding of significant albuminuria (albumin-to-creatinine ratio greater than 300 mg/g [greater than 30 mg/mmol]) or albumin excretion rate greater than 300 mg/24 hours

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- Progression of CKD
- Urinary red blood cell (RBC) casts, RBC 420 per high-power field sustained and not readily explained
- CKD and hypertension refractory to treatment with four or more antihypertensive agents
- Persistent abnormalities of serum potassium
- Recurrent or extensive nephrolithiasis
- Hereditary kidney disease

The goal of the nephrologist is to avoid any further progression of CKD. Tight glycemic control, optimal blood pressure control, dietary phosphate restriction, and management of anemia are paramount. Patient education of CKD continues with every office visit as well. In addition, once the patient reaches stage 4, options classes are held with the family and the patient to discuss dialysis modalities (i.e., peritoneal dialysis or hemodialysis). Patients with CKD with GFR <30 mL/min who are expected to reach ESRD should be informed, educated, and referred for kidney transplantation regardless of socioeconomic status, sex, gender identity, or race/ethnicity (Chadban et al., 2020). If the patient chooses not to proceed with dialysis, referral should be made for palliative care to discuss end-of-life decisions.

Sequelae: The major sequela of CKD is ESRD. In addition, CKD is associated with an increased risk of cardiovascular disease. Thus, lifestyle changes, such as maintaining healthy body weight, restriction of salt and high-fat diet, active participation in an exercise program, smoking cessation, limited alcohol intake, and tight glycemic and blood pressure control are important, not only to reduce cardiac risk, but also to slow progression of kidney disease. For older adults with CDK and diabetes mellitus, there is an increased risk of developing cognitive impairment, dementia, sarcopenia, and frailty (Clemens et al., 2019).

Prevention/Prophylaxis: Early screening for albuminuria in patients at risk for CKD is paramount. In addition, risk factors associated with CKD, including level of GFR, level of albuminuria, age, sex, race/ethnicity, elevated blood pressure, hyperglycemia, dyslipidemia, smoking, obesity, history of cardiovascular disease, ongoing exposure to nephrotoxic agents, and others, should not be ignored (KDIGO, 2012). Tight glycemic control, optimal blood pressure control, tobacco cessation, low-salt diet, avoidance of nephrotoxic medications, and maintaining optimal weight with healthy lifestyle all assist in reducing the risk of CKD.

Referral: All patients with CKD should be referred to a nephrologist for ongoing monitoring.

Education: Patients with CKD are educated regarding their disease and the manifestations of this disease. Continued education regarding low-sodium and low-protein diet, compliance with medications, tight glycemic control, and avoidance of NSAIDs and contrast dye is important. Patients are encouraged to continue to follow up with their primary care physician for other aspects of their health care.

Clinical Recommendation	Evidence Rating	References
Assessment of renal function is made by estimated glomerular filtration rate.	C	Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group, 2012
Albuminuria of >30 mg/24 hr for 3 mo is indicative of chronic kidney disease (CKD).	C	KDIGO, 2012
Hb A1c target range should be from <6.5% to <8.0% in patients with diabetes and CKD who are not treated with dialysis.	C	KDIGO Diabetes Work Group, 2020
Patients with diabetes should be treated with an angiotensin-converting enzyme inhibitor or an angiotensin II receptor blocker (ARB) should be initiated in patients with diabetes, hypertension, and albuminuria; titrating these medications to the highest approved dose tolerated.	C	KDIGO, 2020
Physical activity of moderate intensity lasting at least 150 minutes a week or to a level compatible with their cardiovascular and physical ability is suggested for patients with high blood pressure and CKD.	C	KDIGO Blood Pressure Work Group, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CYSTITIS

Signal Symptoms: Dysuria, frequency, urgency, suprapubic tenderness, hematuria, new or worsening incontinence (Godbole et al., 2020). Fever and systemic symptoms usually are absent in infection limited to the lower tract.

Description: Cystitis is a pathogenic invasion of the mucosal wall of the bladder, causing an inflammatory reaction. It results from an ascending infection via the urethra of bowel flora organisms from the perineum (Cortes-Penfield et al.,

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2017). Cases of cystitis are classified as complicated or uncomplicated. Uncomplicated cases (the focus of this entry) are defined as acute genitourinary symptoms with evidence of pyuria and bacteriuria in a nonpregnant person with no history of abnormal urinary tract anatomy or function (Ashraf et al., 2020; Medina & Castillo-Pino, 2019). Complicated cystitis occurs in individuals whose urinary tract does not function properly due to structural or functional abnormalities. Many diseases and genitourinary interventions such as obstructive lesions, instrumentation, foreign bodies, and neurological diseases are contributing factors in complicated cystitis. In the older adult, there is considerable variation in the clinical characteristics of cystitis.

Asymptomatic bacteriuria (ASBU) is the presence of one or more species of bacteria growing in the urine at specified quantitative counts ($\geq 10^5$ colony-forming units [CFU]/mL or $\geq 10^8$ CFU/L), irrespective of the presence of pyuria, with no corresponding urinary tract symptoms. This condition is prevalent in older adults, especially those who live in nursing homes (Cortes-Penfield, 2017; Henderson et al., 2019; Nicolle et al., 2019). The U.S. Preventive Services Task Force (USPSTF), American Urological Association (AUA), and Infectious Disease Society of America (IDSA) have found that evidence does not support the routine screening of nonpregnant adults for ASBU and that no benefit is derived from it (Ashraf et al., 2019; Henderson, et al., 2019; Nicolle et al., 2019). Differentiating between ASBU and urinary tract infection (UTI) is a challenge in the older adult. In long-term care facilities, it is quite common to misdiagnose ASBU as a UTI. In cases where a urine culture is positive without urinary symptoms, it is recommended to evaluate for other causes before initiating antibiotics (Cortes-Penfield, 2017; Nicolle et al., 2019).

Etiology: The most common organism identified in the older adult with cystitis is *Escherichia coli* (Ashraf et al., 2019; Nicolle et al., 2019). Other commonly isolated organisms include *Klebsiella, Proteus*, and *Enterococcus* species, which are found in nursing home residents (Cortez-Penfield et al., 2017; Godbole et al., 2020; Scott & Liang, 2021). Older adults with indwelling catheters or anatomical abnormalities are susceptible to UTIs that are caused by gram-negative rods (*Proteus, Klebsiella, Serratia*, and *Pseudomonas*) (Medina & Castillo-Pino, 2019). It is not uncommon with indwelling catheters to isolate more than one species in a urine culture. The prevalence of multidrug-resistant organisms is higher in long-term care residents and is attributed in part to more frequent and inappropriate use of antibiotics (Scott & Liang, 2021).

Occurrence: UTIs cause 15.5% of hospitalizations and 6.2% of deaths attributable to an infectious disease in patients older than the age of 65 years (Biggel et al., 2019). Approximately 50% of antimicrobial use in hospitals and up to 75% of antibiotic use in long-term care facilities may be inappropriate or unnecessary (Morrill et al., 2016; Muhammad, 2020).

Age: Incidence of UTI increases with age but is difficult to calculate due to ASBU.

The incidence of ASBU increases with age, with 5% or fewer cases occurring among healthy premenopausal women, and a 15% or greater incidence in women and men between ages 65 and 80 years, and continues to climb after age 80 to as high as 40% to 50% of long-term care residents older than age 80 (Biggel et al., 2020; Cortez-Penfield et al., 2017; Godbole et al., 2020). Estimates suggest the overall incidence of UTIs in older men and women is in the range of 1 infection per 14 to 20 person-years (Cortez-Penfield et al., 2017). ASBU is found 100% of patients with long-term indwelling catheters and 3% to 5% of instances of short-term catheter use (Godbole et al., 2020).

Ethnicity: Not significant.

Contributing Factors: Predisposing factors to the development of cystitis in older adults include indwelling catheters, urethral or condom catheters, incontinence (urinary and fecal), poor perineal hygiene, cognitive impairment, neurological conditions that impair bladder emptying, diabetes, and neurogenic bladder (Soria & Khoujah, 2021). Other predisposing factors to cystitis include sexual intercourse, functional disability, sickle cell disease, prior antibiotic therapy, genetic predisposition, functional or structural genitourinary tract abnormalities (including urethral strictures, pelvic floor dysfunction, ureteral weakness, and vesicoureteral reflux or renal calculi) (Soria & Khoujah, 2021). Frail older adults in institutionalized settings are at additional risk due to lack of adequate fluids and immobility.

The older adult's compromised anatomical defenses related to decline of aging allow bacterial ascent of the genitourinary tract and subsequent colonization of pathogens (Badalato & Kauffman, 2016). Benign prostatic hyperplasia (BPH), incontinence, urinary retention, instrumentation, and institutionalization are all contributing factors to the increase in the prevalence of cystitis in older adult men (Soria & Khoujah, 2021). The length of the male urethra provides a protective barrier against ascending bacterial infection, especially before age 50 years (McLellan & Hunstad, 2016).

The woman's shorter urethra is an anatomical difference that explains why women are more susceptible to UTIs over their lifetime. Additionally, the urethra's proximity to rectal and vaginal flora increases the risk of cross-contamination. The loss of estrogen resulting in vaginal atrophy in older adult women and an increase in vaginal pH, leading to subsequent colonization with pathogenic bacteria are also factors (Zeng et al., 2020).

Signs and Symptoms: The older community-dwelling adult presents with similar symptoms of UTI as a younger person but may present with an atypical presentation of mental confusion, anorexia, malaise, and incontinence especially for patients with indwelling catheters or the frail older adults (Long & Koyfman, 2018). Nonspecific symptoms such as functional decline, increased confusion, and other nonspecific signs may be mistakenly attributed to cystitis in the absence of urinary tract symptoms and should be thoroughly examined in the differential (Long & Koyfman, 2018). Patient should be asked about their social history, including sexual activity, in the older adult. Sexually transmitted diseases and human immunodeficiency virus are increasing in the older adult, so it is important to evaluate carefully to rule out other potential diagnoses (Tran & Leonard, 2017). Women may report pelvic pain, vaginal or cervical discharge, bleeding that may indicate an ascending infection, sexually transmitted infection or disease, or a gynecological cancer.

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If fever, flank pain, and other systemic symptoms are reported, consider obstruction such as renal calculi, urinary retention, and hydronephrosis as differentials when ordering diagnostic tests.

The physical examination must include a detailed history when someone presents with dysuria. It is important to characterize the timing, severity, duration, and persistence of the symptoms. Pain at the beginning of urination suggests a urethral problem such as urethritis. Pain at the end of urination may arise from the bladder or prostate. Other bladder symptoms, such as frequency, urgency, incontinence, hematuria, malodorous urine, and nocturia must be explored. The history should include the presence of flank pain, nausea, fever, and other systemic symptoms which may represent a complicated UTI (Godbole et al., 2020). A history of dysuria, UTIs, sexually transmitted infections, and recent sexual activity should be included.

In addition to dysuria, men with prostatitis may have deep perineal pain and obstructive urinary symptoms, whereas those with epididymo-orchitis may have localized testicular pain. Lesions from herpes simplex virus of the vulvar or penile area may cause dysuria.

Vaginal examination in women should rule out discharge, irritation, and erythema in women who have recurrent symptoms or who do not respond to treatment (Ashraf et al., 2020). In men, the prostate gland should be examined gently to assess for enlargement, bogginess, and tenderness to rule out prostatitis, which is considered a complicated UTI.

Diagnostic Tests: Urine dipstick is used as a quick method for ruling out UTI as the cause of urinary symptoms. Urine dipstick testing detects the presence of leucocyte esterase also known as pyuria and nitrites which identifies gram-negative bacteria. Nitrites are unable to identify gram-positive bacteria, *Enterococci* and *Pseudomonas* because these organisms are unable to reduce nitrates to nitrites (Ashraf et al., 2020; Cortes-Penfield et al., 2017).

Testing for UTI should be ordered only when clinical symptoms such as dysuria are present (Cortes-Penfield et al., 2017). The presence of greater than 105 colony-forming units/mL of a single bacterium in a culture of freshly voided urine is generally considered to be a significant bacteriuria (Pipili & Grapsa, 2019). Collection of a urinalysis and culture specimen without contamination is critical. A patient must be able to give a clean specimen with less than 15–20 epithelial cells per high power field (HPF) (Ashraf et al., 2020). If the epithelial cells are elevated, then contamination has occurred due to contact with the genital surface. Older adults may often have difficulty in collecting a clean-catch urine specimen due to coordination, mobility, or cognitive issues (Ashraf et al., 2020; Cortes-Penfield et al., 2017). If unable to collect a clean-catch specimen, an in-and-out catheterization of the bladder is acceptable the risk of a UTI developing is about 1% (LaRocco et al., 2016). Staff collecting urine specimens may use methods that are not recommended such as obtaining the urine from a chronic urinary catheter, urine collection bag, urinal, or bedpan that are contaminated with bacteria, which may affect the integrity of the urine culture results. Urine specimens should be sent to the laboratory immediately or refrigerated because bacteria grow rapidly when the specimen is left at room temperature.

The diagnosis of UTI cannot be solely based on urine culture results because bacteriuria may be present in asymptomatic patients. In older adults, the rate of ASBU is so high that bacteriuria cannot be excluded as an abnormal finding (Ashraf et al., 2020). The presence of bacteria in the urine may indicate one of the following conditions: contamination of the specimen, UTI, or ASBU (Nicolle et al., 2019). Use test results coupled with history and examination findings to derive a diagnosis. The accepted standard for bacteriuria is at least 10^5 colony-forming units (CFUs) per one mL of a single organism in the urine of an uncatheterized patient or $\geq 10^3$ CFU/mL greater than or equal to one bacterial species in the urine of a catheterized patient (Ashraf et al., 2020; Nicolle et al., 2019). Lower bacteria counts may be reflective of a UTI in patients with urinary symptoms.

Pyuria is the presence of an increased number of polymorphonuclear leukocytes which indicates an inflammatory reaction in the urinary tract, and is generally defined as a positive leukocyte esterase on urine dipstick or greater than or equal to 10 white blood cells (WBCs) per HPF (Ashraf et al., 2020). Pyuria is sensitive but not specific for UTI, particularly among catheterized patients. Pyuria can be seen in patients with catheter use, sexually transmitted diseases, renal tuberculosis, interstitial nephritis, or ASBU (Nicolle et al., 2019). The absence of pyuria is a strong indicator that a UTI is not present (Cortes-Penfield et al., 2017). The presence of pyuria is not an indication to initiate antibiotics. Dependence on pyuria alone for diagnosis of UTI would lead to inappropriate antibiotic prescribing because pyuria is a common finding in ASBU (Ashraf et al., 2020; Cortes-Penfield et al., 2017; Nicolle et al., 2019).

Although considered a complicated UTI, catheter-associated UTI (CAUTI) is widely recognized as the most common healthcare-associated infection (Anger et al., 2019). Careful consideration needs to be taken to differentiate between ASBU and CAUTI. The AUA stresses the need for careful surveillance because of the potential risk of multidrug-resistant organisms (Anger et al., 2019). Experts agree that ASBU in the face of an indwelling catheter does not require antibiotic treatment, even though administration rates remain as high as 32% (Ashraf et al., 2020; Cortes-Penfield et al., 2017). McGeer criteria were developed in 1991 to provide standardized guidance for epidemiological surveillance in long-term care facilities. Updates to the guidelines were made in 2012, making significant changes to the diagnosis of UTI with and without the presence of an indwelling catheter. All symptoms must be new or acutely worse, alternative noninfectious causes of symptoms should be evaluated/considered before deemed an infection, and identification of infections are not to be based on a single piece of evidence and should always consider the clinical presentation (Cortes-Penfield et al., 2017).

Older adults are at a high risk of adverse events from antibiotic use; using active monitoring while waiting for urine culture results is acceptable if the patient is clinically stable (Cortes-Penfield et al., 2017). Active monitoring requires frequent vital sign monitoring, assessment for early sepsis, ongoing hydration, and nursing staff reporting changes in condition. If the patient begins to decline, implementation of empirical antibiotics is recommended pending availability of urine culture sensitivities.

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Differential Diagnosis:
- Urethritis
- Prostatitis
- Epididymitis
- Vaginitis
- Obstructive uropathy
- Sexually transmitted infections
- Complicated pyelonephritis

Treatment: In 2010, Infectious Disease Society of America (IDSA) published guidelines for the treatment of UTI recommending four antibiotics for the treatment of uncomplicated UTIs in women: nitrofurantoin, fosfomycin, pivmecillinam (which is not available in the United States), and trimethoprim-sulfamethoxazole. There were no recommendations made for UTI in men or in the treatment of complicated UTI. Choosing an antibiotic should be based on the susceptibility from the urine culture results. Other considerations are allergy history, drug interactions, renal function, frequency of dosing, side-effect profile, local antibiogram data, and insurance coverage and cost (Godbole et al., 2020).

First-Line Agents: Nitrofurantoin-(monohydrate/macrocrystalline) is indicated in uncomplicated UTI, recurrent UTI, and UTI prophylaxis. Nitrofurantoin is well tolerated and has good susceptibility to uropathogens, but it is not appropriate in those with upper urinary tract disease due to poor levels in tissue and blood (Cortes-Penfield et al., 2017). Dosing of nitrofurantoin is 100 mg by mouth for 5 days for uncomplicated and recurrent UTI. Although the U.S. Food and Drug Administration (FDA) recommended against using nitrofurantoin in patients with a creatinine clearance (CrCl) of 60 mL/minute, recent data suggest that nitrofurantoin can be used effectively for cystitis regardless of renal function (Cortes-Penfield et al., 2017). The risk of pulmonary toxicity is greater in adults with a creatinine clearance (CrCl) <30 mL/min, and the Beers criteria recommend against use of nitrofurantoin in older adults >65 years with a CrCl <30 mL/min (Ashraf et al., 2020; Cortes-Penfield et al., 2017).

Trimethoprim-sulfamethoxazole (TMP/SMX) is indicated for uncomplicated UTI and recurrent UTI where resistance rates to *E. coli* are less than 20% (Cortes-Penfield et al., 2017). Dosing of TMP/SMX is 800 mg/160 mg twice daily for 3 days.

Fosfomycin is indicated in the treatment of UTI. Unfortunately, its use is limited by availability, cost, and lack of standardized susceptibility testing (Ashraf et al., 2020; Babiker et al., 2019). It should be reserved for treatment of acute simple UTI. It is a single dose oral agent that is mixed with water to administer. Fosfomycin is susceptible in extended spectrum beta-lactamase uropathogens (Ashraf et al., 2020; Babiker, 2019).

Second-Line Agents: Fluoroquinolones to treat UTIs has become very common due to their high oral bioavailability, broad spectrum, and its short course treatment. The FDA in 2016 advised that due to the serious side effects associated with fluoroquinolones use, they are not recommended in uncomplicated UTI when other treatment options are available (Ashraf et al., 2020; Buehrle et al., 2021; Cortes-Penfield et al., 2017; Cowart et al., 2019). The serious risks of fluroquinolone use outweigh the benefits. Black box warnings by the FDA include tendinitis/tendon rupture, peripheral neuropathy, central nervous system effects, exacerbation of myasthenia gravis, aortic dissection, retinal detachment, QT prolongation, hypoglycemia/hyperglycemia, and *Clostridioides difficile* (Buehrle et al., 2021; Cowart et al., 2019).

Uropathogens are known to have high susceptibility to aminoglycosides but the lack of oral formulations of these drugs; the need to monitor serum drug levels; and the risk of major adverse events including nephrotoxicity, vestibular toxicity, and ototoxicity limit the role of this class in treating UTIs outside of the inpatient setting (Ashraf et al., 2020, Cortes-Penfield et al., 2017).

Duration of Treatment: There is more evidence that demonstrates short-course antibiotics for treatment of CAUTI and therapy lasting longer than 7 days do not prevent recurrence and increase the risk of *C. difficile.* Longer treatment is still recommended in those with UTI with bacteremia, pyelonephritis, and perinephric abscess (Ashraf et al., 2020; Cortes-Penfield et al., 2017).

Treatment recommendations have been changing to reflect trends in pathogen resistance, antibiotic adverse effects, and best evidence-based practice. Current recommendations include multiple treatment regimens based on the needs of the patient. All providers should be aware of the patient's renal function or pre-existing renal disease before prescribing an empirical antibiotic (or any medicine for that matter). Always encourage good hydration and the use of analgesics such as acetaminophen and short-term NSAID therapy for fever and pain. Phenazopyridine 100 to 200 mg by mouth every 8 hours for 3 days can be added to these regimens for the relief of dysuria.

Follow-Up: Follow-up test-of-cure urinalysis and urine cultures are not indicted for uncomplicated cases of cystitis in which symptoms resolve on antibiotics (Ashraf et al., 2020). Relapse occurs when symptoms persist despite antimicrobial treatment. Additional evaluation is warranted for other potential causes that may be causing ongoing symptoms. Cystitis treated with the correct antimicrobial therapy is resolved in 90% of the cases. Recurrence is seen in about 25% to 50% of women after a UTI (Ashraf et al., 2020; Peck & Shepherd, 2021). Change in treatment is warranted if the organisms are resistant to the original treatment.

Sequelae: Untreated symptomatic cystitis can lead to kidney damage, pyelonephritis, sepsis, shock, and death.

Prevention/Prophylaxis: Strategies for prevention of recurrent uncomplicated cystitis include reduction of frequency of intercourse, abstaining from spermicidal use, proper perineal hygiene and voiding habits, and removal of unnecessary indwelling urinary catheters. Prophylactic use of antibiotics by patients with indwelling catheters is not recommended (Assadi, 2018). For older adults who require frequent instrumentation of the lower genitourinary tract or who have frequent cystitis, suppressive antimicrobial therapy may be considered on an individual basis (Assadi, 2018).

Antibiotic use is a driver of antibiotic resistance. A systematic review of randomized trials looked at long-term antibiotics for prevention of recurrent urinary tract infection in older adults. Long-term use was defined as at least 6 months. Researchers reviewed 53 studies; only four were eligible for inclusion and no studies included older men. Three studies

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found long-term antibiotics reduced the risk of recurrence of UTI by 24% (Ahmed et al., 2017). There was not statistically significant increase in risk of adverse events. One trial showed 90% of urinary and *Escherichia coli* isolates were resistant to trimethoprim-sulfamethoxazole after 1 month of prophylaxis use (Ahmed et al., 2017). The outcome revealed that although long-term use helps with recurrence the benefit when the antibiotic is discontinued is lost. The studies that were reviewed were not definitive about length of treatment, risks of antibiotic resistance, or effects in the older male. More studies need to confer the risk versus benefit of long-term use. Antibiotic prophylaxis should be compared with nonantibiotic prophylaxis with evidence of efficacy (such as vaginal estrogen creams).

Cranberry supplements have been publicized as a remedy for prevention of UTI. It is thought that cranberry products acidify the urine thereby preventing UTI. Another mechanism may be that they may inhibit *E. coli* from adhering from the lining of the bladder wall. Current evidence does not support the use of cranberry products in the prevention of UTI (Ashraf et al., 2020).

Methenamine is approved by the FDA for prophylaxis or suppression of recurrent UTI. Methenamine works as an antiseptic and has not shown that organisms develop resistance. In an acidic environment, methenamine is hydrolyzed to ammonia and formaldehyde (Chwa et al., 2019; Snellings et al., 2019). The urine pH must be acidic (pH below 5.5) for it to convert to formaldehyde; if urine acidification is not possible, then its use should be discouraged (Chwa et al., 2019; Snellings et al., 2019). Patients who are chronically catheterized and unable to retain urine are poor candidates because methenamine works in the bladder. Avoid use of sulfanomides in patients taking methenamine. Also avoid using methenamine in those with renal or hepatic dysfunction and in those with gout. Studies have shown efficacy as an antibiotic-sparing alternative (Chwa et al., 2019). In a retrospective, observational study, methenamine use was associated with a longer time to develop a UTI in older adults with varying degrees of kidney function. In fact, the effectiveness of methenamine appeared to be similar regardless of kidney function (Snellings et al., 2019). Future research is needed to determine an effective dose and duration of use in the older adult.

Postmenopausal women often experience vaginal atrophy manifested by vaginal dryness, itching, urinary incontinence, and painful sexual intercourse. These symptoms may imitate UTI, resulting in being treated with unnecessary antibiotics. Vaginal estrogen preparations may help reduce the incidence of UTI and associated symptoms that may reflect UTI. Concerns that using estrogen in the postmenopausal woman may potentially increase cancer risk and cardiovascular disease have existed, particularly in those women using systemic estrogen (Fox et al., 2021). However, an observational study found that the risk of cardiovascular disease and cancer did not increase in postmenopausal women using vaginal estrogen (Ferrante et al., 2021.) A randomized clinical trial found vaginal estrogen was effective in prevention of UTI in postmenopausal women with an active diagnosis of recurrent UTI (Ferrante et al., 2021). Local estrogen therapy may be helpful in reducing recurrent UTI and to treat atrophic vaginitis.

Referral: In complicated cystitis that has progressed to pyelonephritis or urosepsis, consultation with a urologist, urogynecologist, or infectious disease specialist is recommended for hospitalization. This recommendation can also be applied to recurrent UTI.

Education: Adequate hydration remains a cornerstone in the prevention and treatment of any infectious process. Have the patient perform timed and double voiding to lower the postvoid residual of those suspected of urinary retention serving as a nidus for infection. Patients should also be instructed to complete the full course of antibiotic therapy prescribed unless notified by their provider.

Clinical Recommendation	Evidence Rating	References
Evidence does not support the routine screening of nonpregnant adults for asymptomatic bacteriuria. No benefit of screening has been found.	A	Ashraf et al., 2020 Nicolle et al., 2019
The presence of more than 10^5 colony-forming units/mL of a single type of bacteria in a culture of freshly voided urine is consistent with significant bacteriuria in symptomatic subjects.	A	Godbole et al., 2020
Antimicrobial selection for empirical therapy should be based on the patient's individualized history and requirements (including prior antibiotic use, symptoms, urine culture results, and institutional susceptibilities). Treatment should be reevaluated and modified as appropriate.	A	Cowart et al., 2019 Buehrle et al., 2021 Ashraf et al., 2020 Cortes-Penfield et al., 2017 Godbole et al., 2020
Fluoroquinolones should not be used for first-line empiric treatment of uncomplicated urinary tract infections.	A	Cowart et al., 2019 Cortez-Penfield et al., 2017 Buehrle et al., 2021 Ashraf et al., 2020
Follow-up test-of-cure urinalysis and urine cultures are not indicted for uncomplicated cases of cystitis.	A	Ashraf et al., 2020

Continued

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Clinical Recommendation	Evidence Rating	References
Careful infection surveillance and special attention to special population groups (older adults, individuals with neurogenic bladders, etc.) in those at risk for catheter-associated urinary tract infection.	B	Ashraf et al., 2020
Consider prophylactic antimicrobial prophylaxis for recurrent cystitis and those who undergo frequent lower urinary track instrumentation.	B	Assadi, 2018
In patients with complicated, unresolved, recurrent, or worsening cystitis, specialist referral is recommended. In complicated cystitis that has progressed to pyelonephritis or urosepsis, urgent evaluation and consultation with a specialist is recommended for further testing and hospitalization as appropriate.	B	Ashraf et al., 2020 Nicolle et al., 2019 Cortez-Penfield et al., 2017
Urine culture is preferred but not required in the treatment of acute, uncomplicated cystitis.	B	Cortes-Penfield et al., 2017
Cranberry products can be helpful to reduce recurrent cystitis.	B	Ashraf et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

ERECTILE DYSFUNCTION

Signal Symptoms: None; noncompliance with medication regimen, responses on sexual history query or questionnaire.

Description: Erectile dysfunction (ED), previously known as impotence, is the consistent inability to achieve and maintain an erection sufficient for sexual satisfaction (McCabe et al., 2016). In a broader sense, ED encompasses problems with arousal, libido, orgasm, sensation, and relationships (Khera, 2020).

Etiology: ED may be caused by medications, vascular, endocrine, neural, psychological issues, and lifestyle and interpersonal stressors (see Contributing Factors).

Occurrence: An estimated 20 to 30 million U.S. men experience chronic ED (Irwin, 2019).

Age: Incidence of ED increases with age. The prevalence is approximately 52% for men between ages 40 and 70 years; in men older than 70 years, prevalence is increased further. Men older than 70 years with chronic medical problems, such as diabetes, have a prevalence of more than 90%. Because the condition is often underreported, the percentage is probably higher. Approximately 25% of erectile problems are related to drugs (Irwin, 2019).

Ethnicity: Not significant.

Contributing Factors: ED causes are often multifactorial (Irwin, 2019):

- Stress
- Long-term alcohol use
- Tobacco use
- Sedentary lifestyle
- Obesity (Pizzol et al., 2020)
- Interpersonal conflict
- Pelvic surgery/trauma
- Underlying chronic issues (diabetes, hypertension, hyperlipidemia, sleep apnea, atherosclerosis, chronic kidney disease [CKD], depression).
- Recreational drug use (cocaine, marijuana, opiates)
- Antiandrogens, anticholinergics, anticonvulsants, antidepressants (including selective serotonin reuptake inhibitors, monoamine oxidase inhibitors, tricyclic antidepressants), antipsychotics, levodopa, lithium, centrally acting depressants (sedatives/hypnotics, tranquilizers, opiates)
- H_2 blockers, stimulants such as amphetamines, beta blockers, spironolactone, methadone, cytotoxic agents, antihypertensives (clonidine, methyldopa, thiazides, calcium channel blockers), urological drugs (alpha blockers), anti-inflammatories (baclofen, naproxen)

Various processes are involved, including effect on libido, neurochemical mediation, and drug side effects.

Signs and Symptoms: There may be no reported symptoms unless the provider includes a sexual history, is aware of the potential for ED when prescribing certain medications, and asks about baseline sexual activity at that time, then periodically reassesses this during follow-up visits. The patient should be asked about sexual interest, sexual ability, and sexual activity. Patients with a prior diagnosis of diabetes, hypertension, dyslipidemia, or depression are at increased risk (Irwin, 2019).

History should include prescribed and over-the-counter (OTC) medications and supplements, alcohol use, tobacco use, and use of recreational drugs. The CAGE test for alcoholism, a screening questionnaire for depression, or other psychological screens as needed may be included as part of the history. A history of surgical procedures, especially of procedures involving the prostate, bladder, or colorectal area, and including the lymphatic channels, may reveal potential sources of ED (Artemi et al., 2019). The Sexual Health Inventory for Men (SHIM) is a five-item questionnaire that can be used to assess the presence and extent of erection difficulties (Rosen et al., 1999).

Physical examination is performed to look for any systemic signs that could contribute to the ED. Evaluate the

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patient's overall appearance and mobility, then assess the vital signs, specifically checking for orthostatic hypotension. Severe obesity could be a risk for sleep apnea and lower testosterone. Palpation of the thyroid may reveal a goiter. Gynecomastia may be related to certain drugs or a decrease in overall testosterone.

Diminished peripheral pulses suggest a circulatory problem. Lack of sensation or inability to discriminate between sharp and dull may indicate peripheral neuropathy, especially if the history is positive for diabetes. Abnormal reflexes point to a neurological problem. Decreased mobility may indicate a neurological or musculoskeletal problem contributing to ED. Examination of the genital area may reveal testicular atrophy or penile plaques, as seen in patients with hypogonadism or Peyronie's disease. Assess for the bulbocavernosus reflex; absence of this reflex indicates penile neuropathy (Khera, 2020).

Diagnostic Tests: Laboratory testing is not necessary for a diagnosis but can help to determine the possible causes of ED and help expose other chronic issues that are often associated with it. Testosterone is one blood test that is not typically done with health maintenance screening, but if found to be unequivocally low, should be addressed. Diagnostics may include (Agronin, 2021):

- Fasting glucose and hemoglobin A1c (Hb A1c)
- Complete blood count (CBC)
- Comprehensive metabolic profile
- Thyroid-stimulating hormone
- Lipid profile
- Serum total testosterone fasting between 8 and 10 a.m.
- Serum prolactin

Treatment: Depends on patients' preferences, ideally improving quality of life and reducing the risk of chronic disease. Lifestyle recommendations should be advised for all, specifically diet and exercise and tobacco cessation. Address untreated depression. Optimal treatment of chronic diseases that affect hormones, mental health, and the endothelium can help to improve treatment of ED.

If newer onset ED is thought to be related to a medication, decrease the dose, eliminate the medication, or substitute another medication from available drugs that do not cause ED. If this is not possible, or if the patient continues to experience the problem, treatment options include oral, intraurethral, or intracavernosal medications; vacuum erection devices; or penile prosthesis (Irwin, 2019).

Phosphodiesterase-5 (PDE-5) inhibitors may be considered after cardiac risk factors, chronic illness, medication assessment, and underlying etiology are examined. Medications in this classification include sildenafil citrate (Viagra), vardenafil (Levitra), tadalafil (Cialis), and avanafil (Stendra). Tadalafil has a longer duration and avanafil has a rapid onset. During sexual stimulation, nitric acid is released into the corpus cavernosum, resulting in increased cyclic guanosine monophosphate (cGMP) levels, which prevents smooth muscle relaxation and increases blood flow to the penis. PDE-5 inhibitors enhance this effect by inhibiting an enzyme that degrades cGMP in the corpus cavernosum. These medications are contraindicated with nitrates and in advanced heart disease; cytochrome influences include increased plasma levels with inhibitors of CYP3A4 or CYP2D9 and decreased plasma levels with inducers of CYP3A4. Side effects include headache, flushing, urinary tract infection (UTI), abnormal vision (blue-green, blurring, photosensitivity), nasal congestion, diarrhea, dizziness, and rash. PDE-5 inhibitors are effective in treating drug-induced ED in patients taking antidepressants/antipsychotics and antihypertensives/diuretics (Burnett et al., 2018; Khera, 2020).

Follow-Up: Individualize follow-up according to cause and treatment. Periodic reassessment of treatment for recurrence of the problem is helpful. For medication treatment, monitor for side effects and response.

Sequelae: Disruption of sexual function may result in depression or relationship problems. Complications may arise from treatment.

Prevention/Prophylaxis: Avoid prescribing medications with a high risk for causing ED and include a sexual history in routine history and physical examination whenever prescribing a new medication with ED as a potential side effect. Optimize overall cardiovascular health through encouragement of Mediterranean diet and regular exercise.

Referral: Refer patients to a urologist to evaluate for other causes or multifactorial causes of ED. If blood work indicates lower testosterone levels, consider referral to endocrinology or urology to discuss possible supplementation because decreased testosterone has been found to impact erections. For other types of treatment, such as penile implants or injection, refer the patient to a urologist specializing in this area. Also refer patients who are experiencing the problem to a support group. Refer for psychological services when indicated.

Education: Teach the patient about possible medication side effects and that they cannot be used in conjunction with nitrates. Educate the patient about normal age-related changes in sexual functioning and how to adapt.

Clinical Recommendation	Evidence Rating	References
There is no recommended diagnostic testing to serve as a gold standard for erectile dysfunction (ED); history and physical examination are sufficient in making an accurate diagnosis in the majority of cases.	C	Irwin, 2019
The phosphodiesterase-5 inhibitors are the most effective drugs in the treatment of ED, including ED associated with diabetes and spinal cord injury, and in men with sexual dysfunction secondary to antidepressants.	A	Burnett et al., 2018

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NEPHROLITHIASIS

Signal Symptoms: Vague flank pain, hematuria, renal colic, abdominal pain.

Description: In the Western Hemisphere, most cases of nephrolithiasis (the presence of calculi [kidney stones]) result from calcium salts, uric acid, cystine, struvite, and medications forming crystals that become attached to the kidney, eventually developing into stones. Calculi range in size from microscopic to several centimeters in diameter. Calculi often attempt to travel through the urinary system and out through the urine. Pain occurs when the calculi become lodged (Curhan et al., 2021).

Etiology: Kidney stones develop from the supersaturation of urine with stone-forming material. The abundance of solutes begins to develop into crystals. The crystals adhere to one another forming stones. Approximately 80% of diagnosed kidney stones contain calcium; 10% to 15% are struvite stones, resulting from urinary tract infections; 3% to 10% are uric acid calculi; 1% contain cystine: and 1% are formed from medications (Alelign & Petros, 2018).

Occurrence: One out of 11 Americans will be diagnosed with a kidney stone in their lifetime. Approximately 50% of patients who have had previous urinary calculi have a recurrence within 10 years.

Age: Men 60 and older have the highest incidence of nephrolithiasis in the male population. The episodes of kidney stones in females aged 20 to 39 have doubled and now surpass their male counterparts in this age-group (Chen et al., 2018). Men are more likely than women to form uric acid stones; struvite stones are more common in women due to the higher incidence of urinary tract infections (Alelign & Petros, 2018).

Ethnicity: The incidence of kidney stones is most prevalent among Whites followed by Mexican Americans. The lowest occurrence is found in Blacks.

Contributing Factors: A major contributing factor to the development of calculi is decreased fluid intake leading to high concentration of urine. Certain food substances that increase the likelihood of kidney stone formation include dairy products, chocolate, green leafy vegetables (calcium oxalate stones), and meat and fish (cystine stones). Certain medications, such as triamterene, indinavir, guaifenesin, and sulfa, can also contribute to the development of nephrolithiasis (Alelign & Petros, 2018). A history of hyperparathyroidism, sarcoidosis, Cushing's syndrome, Paget's disease, and immobilization may contribute to the development of calcium phosphate stones. Chronic urinary tract infections (UTIs) are precursors to struvite stone formation. Family history has also been found to contribute to stone development. Bowel disorders that cause chronic acidic urine states, such as patients that have undergone bariatric surgeries, can increase nephrolithiasis frequency. Increased urine calcium and uric acid with decreased urine pH has been found in individuals with obesity. Patients with diabetes tend to excrete more oxalate increasing risk of development in calcium oxalate stones (Chen et al., 2018).

Signs and Symptoms: Patients may experience abrupt, severe, colicky pain in the abdomen or flank that radiates to the groin. The pain sensation can begin as vague flank pain (Capilouto & Williams, 2021). Pain spreading downward suggests movement of the stone along the ureter. Associated nausea and vomiting may occur. Hematuria is also common (Fontenelle & Sarti, 2019). Physical examination may reveal local abdominal and costovertebral angle tenderness. Men complaining of groin pain should have a testicular examination to rule out testicular torsion or epididymitis. Women with pain radiating to the labia should have a pelvic examination to rule out possible ovarian torsion, cysts, pelvic inflammatory disease, and tumors.

Diagnostic Tests: For patients who have not yet passed a stone, urine collection for recovery of stones or gravel should be ordered. Urinalysis can reveal the presence of leukocytes, bacteria, and blood, which can be indicative of UTI. The presence of crystals in urinalysis can aid in the determination of the type of stone present. A computed tomography (CT) scan of the abdomen and pelvis without contrast using low-radiation protocols is the preferred imaging study. It is readily available at most facilities and presents the highest diagnostic accuracy of stone size, location, and potential complications. Ultrasound of the kidneys and bladder are recommended second-line to minimize radiation exposure. Although abdominal plain films are inexpensive and quick, they can fail to detect radiolucent stones, small stones, or obstructions (Curhan et al., 2021).

Differential Diagnosis:

- Papillary necrosis
- Hydronephrosis
- Ileus
- Diverticulitis
- Appendicitis
- Bowel obstruction
- Mesenteric ischemia
- Ovarian cyst
- Testicular torsion
- Constipation
- Arterial aneurysm
- Cholecystitis
- Acute cystitis
- Pyelonephritis
- Ectopic pregnancy
- Prostatitis
- Renal cell carcinoma
- Narcotic seekers

Treatment: Size and location of the stone, coupled with the length of time since the onset of symptoms, directs treatment. Stones less than or equal to 5 mm usually pass on their own without intervention. A stone larger than 10 mm requires referral to a urologist for possible intervention that may include extracorporeal shock-wave lithotripsy, ureteroscopy stone removal, or percutaneous nephrolithotomy. Patients not in distress and without obstruction may benefit from the use of alpha blockers, which have been shown to aid in the passage of 44% of stones 5 to 10 mm (Rule et al., 2020). NSAIDs have been found to be more effective in pain management than narcotics with fewer side effects (Fontenelle & Sarti, 2019).

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Follow-Up: For those at high risk of recurrence, a repeat CT scan or ultrasound is recommended in 1 to 2 years. At this time, also review with the patient the need for metabolic work-up, family history, health conditions associated in stone formation, and compliance with dietary restrictions and fluid requirements.

Sequelae: Immediate complications of unresolved kidney stones include obstruction, urinary tract infection, and sepsis. A high incidence of recurrence of kidney stone formation exists. Metabolic causes of kidney stones need to be ruled out when dietary measures are unsuccessful. Patients with nephrolithiasis are also commonly afflicted with chronic health conditions including chronic renal failure, hypertension, diabetes, and cardiovascular disease (Alelign & Petros, 2018).

Prevention/Prophylaxis: An adequate daily fluid intake is essential. Patients should be encouraged to drink 2 to 3 liters daily. To prevent recurrent stones, review the patient's dietary habits to discern if there are any excessive food products that may be factors in kidney stone formation (calcium, purine, protein).

Referral: Refer the patient to a urologist when:

- Obstruction is detected.
- The stone is more than 10 mm.
- The stone has not passed within 4 weeks of conservative measures for stones <10 mm.
- The patient has complicated diagnostic reports.
- The patient has severe nausea and vomiting, intractable pain, urosepsis, anuria, or renal failure.

Education: Inform all patients with nephrolithiasis that there is a high probability of a second occurrence of a kidney stone. Advise the patient, if possible, to strain urine with the provided strainer when experiencing symptoms of kidney obstruction. A daily fluid intake of 2 to 3 L is recommended. Provide information about any food restrictions that may be deemed necessary to prevent specific stone formation (Alelign & Petros, 2018).

Clinical Recommendation	Evidence Rating	References
Computed tomography (CT) without contrast using low radiation is the preferred imaging study for nephrolithiasis detection; however, if a low radiation CT is not available, then ultrasound occasionally in combination with x-rays is recommended.	B	Curhan et al., 2021
Alpha adrenergic blockers have been shown to be 44% successful in the passage of stones 5–10 mm.	A	Rule et al., 2020
There has been a significant increase in kidney stone development among women of childbearing ages.	A	Chen et al., 2018
NSAIDs are more efficient with fewer negative outcomes than narcotics.	A	Fontenelle & Sarti, 2019

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PROSTATE CANCER

Signal Symptoms: Early stage often asymptomatic. Obstructive voiding symptoms (hesitancy, intermittent urinary stream, decreased force of stream) are generally indicative of advanced disease.

Description: Prostate cancer is a malignant neoplasm of the prostate, which is a male sex accessory gland. The prostate has been equated to the size of a walnut, encircling the urethra like a doughnut. The role of the prostate is to secrete fluid into the ejaculate that accompanies sperm and seminal fluid to make up semen. Ninety-five percent of prostate cancers are adenocarcinomas.

Etiology: Approximately one-half of prostate cancers demonstrate a genetic component. Testosterone has been identified as a prerequisite for the development of prostate cancer. Prostate cancers exhibit high levels of androgen receptors (Leslie et al., 2019).

Occurrence: Prostate cancer is the second leading cause of cancer death in men, second only to lung cancer (American Cancer Society [ACS], 2021). Prostate cancer is the most common cancer in men, with approximately 1 in 8 being diagnosed. The older adults are more frequently affected, with 60% of cases diagnosed after age 65 years; 45% of cancer deaths are between ages 60 and 79 and 50% at 80 and above (Seigel, 2021).

Age: Mean age at diagnosis is 66 years (ACS, 2021).

Ethnicity: Black men in the United States have the highest incidence of prostate cancer in the world, with Asian and Hispanic men at lower risk than White men (ACS, 2021). Diagnosis in Black men tends to be at a more advanced stage, and disease-specific survival is lower in this group (ACS, 2019).

Contributing Factors: Age greater than 50 years, being African American, and diets high in fat are contributing factors. Family history appears significant with a 2.5-fold increased risk with a first-degree relative affected before age 50 years. The risk is even greater if the affected relative is a brother rather than a father, if the affected relative is younger than 55 years, or if two or more first-degree relatives are affected. (ACS, 2021; Leslie et al., 2019). Individuals with a first- or second-degree family member with a history of

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metastatic prostate, ovarian, male breast cancer, female breast cancer below 46, colorectal cancer or endometrial cancer at age younger than 51, or pancreatic cancer are considered at a higher risk. Familial genetic carriers of the *BRCA2* or *HOXB13* gene are at increased risk for prostate cancer. (National Comprehensive Cancer Network [NCCN], 2021)

Signs and Symptoms: There are usually no symptoms with early disease. Symptoms generally occur in advanced stages, making early detection desirable. Obstructive voiding symptoms (hesitancy, intermittent urinary stream, decreased force of stream) generally reflect locally advanced disease with growth into the urethra or bladder neck. Locally advanced tumors may result in hematuria and hematospermia. If rectal obstruction occurs, a large bowel obstruction or difficulty in defecation may be present. Prostate cancer that has spread to the regional pelvic lymph nodes occasionally causes edema of the lower extremities or discomfort in pelvic or perineal areas. Metastasis occurs most often to the bone, resulting in pain and pathological fractures.

Diagnostic Tests: Screening discussion should be held with men around the age of 50 years who do not possess comorbidities that restrict life expectancy to less than 10 years, unless risk factors dictate earlier. Controversy continues in terms of screening recommendations. Table 14-2 reflects current screening statements by expert groups and the date declared.

A digital rectal examination (DRE) is the only method for physically examining the prostate, with awareness that only part of the gland can be palpated, allowing for irregularities to be missed. DRE is considered abnormal if the prostate is enlarged, asymmetrical, nodular, or tender. The effectiveness of DRE for prostate cancer screening is not well established and is considered to have low sensitivity. A prostate-specific antigen (PSA) blood test and a DRE may detect cancer at an earlier stage than if no screening is performed.

A PSA is a glycoprotein expressed by normal and neoplastic prostate tissue and is excreted in the ejaculate to liquefy semen (Freedland, 2021). Escape of PSA in large amounts into the bloodstream occurs when the basement membrane of the prostate epithelial cells is disrupted. Both the PSA and DRE may produce false-positive or false-negative results. A PSA level of 4.0 ng/mL or greater historically has been used to recommend referral for further evaluation or biopsy, which remains a reasonable approach for men at average risk for prostate cancer. Five-alpha reductase inhibitors finasteride and dutasteride are known to lower PSA levels. If a PSA is noted to be elevated, a DRE (if not done before), a repeat PSA 4 to 6 weeks after elevation, and work-up for benign disease are done.

Parametric magnetic resonance imaging (MRI), if available is now recommended and utilized pre-biopsy to help image for aggressive lesions in those with an elevated PSA. If the MRI is used for detection, the area can then be targeted on the biopsy. Biopsies are taken on each side with specific focus on the lesion if imaged with the MRI (Eklund et al., 2021; NCCN, 2021).

Differential Diagnosis:
- Benign nodule prostate growth
- Subacute prostatitis
- Prostatic intraepithelial neoplasia
- Prostate stones

Treatment: Treatment depends on stage of the tumor, anticipated effects of treatment, and the age, general health, and life expectancy of the patient. The Gleason score determines the grade of prostate cancer. The Gleason score grades tumors on a 1 to 5 range based on the degree of glandular differentiation and structural architecture. Grade 1 represents the most well-differentiated appearance, and grade 5 represents the most poorly differentiated. The primary and secondary architecture are added together to create the score (i.e., 3 + 4 = 7). Treatment options include active

TABLE 14-2 Recommendations for Prostate Cancer Screening

GROUP / SOCIETY	RECOMMENDATION
American Cancer Society (2018)	• Beginning at 50 years of age, asymptomatic men who have at least a 10-year life expectancy should have an opportunity to make an informed decision with their physician about screening. • Men at high risk, including African American men and men who have a first-degree family history (father or brother) of prostate cancer diagnosed before 65 years of age, should receive this information beginning at 45 years of age. • Men at highest risk with more than one first-degree relative with prostate cancer should have conversation about screening at age 40. • When screening is performed, PSA testing should be used with or without digital rectal examination. Frequency of testing depends on PSA level.
American Urological Association (Carter et al., 2013; Reconfirmed 2018)	• Use shared decision making for men 55 to 69 years of age. • Individualize screening decisions for higher-risk men 40 to 54 years of age. • Do not screen men younger than 40 years, older than 70 years, or who have a life expectancy of less than 10 to 15 years.
National Comprehensive Cancer Network (2021)	• General screening starts at 45 for average risk patients. • Screen earlier at age 40 if patient is of African ancestry; 40 if carrying germline mutations or if there is a suspicious family history. • Continue screening until 75 (continue in select cases).
U.S. Preventive Services Task Force (2018)	• Use shared decision making for men 55 to 69 years of age. • Do not screen men older than 69 years.

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surveillance for a tumor of incidental histological findings, to radical prostatectomy, radiation, or androgen deprivation therapy. Gleason score 6 cancer should be handled conservatively using active surveillance, a practice involving PSA monitoring, and repeat biopsies with the goal of delayed treatment unless the Gleason score changes.

Follow-Up: Follow-up depends on current treatment and patient-specific risk. It may be best shared by the cancer specialist and the primary provider. Routine history and physical examinations, cardiovascular health screenings, surveillance for diabetes, depression screening, annual quality of life assessment, and evaluation and management of any sexual dysfunction should be considered.

- PSA: The frequency is dependent on whether on active surveillance (every 3 months) or has been treated with prostatectomy, radiation, or androgen deprivation therapy.
- DRE: Annually after radiation but may be discontinued if PSA is undetectable. Discontinue after radical prostatectomy (NCCN, 2021).

For patients with radical prostatectomy, any PSA greater than 0.2 ng/mL is abnormal and raises concern for recurrence or progressive cancer. Patients with radiation therapy often do not have a PSA that drops to an undetectable level. Surveillance is based on the nadir. There is concern for recurrence if the PSA raises 2 ng/mL above the nadir or is continually rising after radiation treatment. (NCCN, 2021)

Sequelae: Complications of treatment may include incontinence, erectile dysfunction (ED), mild colitis, and radiation cystitis. After nerve-sparing prostatectomy, urinary continence returns in under 6 months in about 50% of men. The rate of ED after radiation ranges from 10% to 80%.

Prevention/Prophylaxis: PSA screening remains controversial because many of the prostate cancers detected are low-grade and slow-growing. In 2012, the USPSTF recommended against screening for prostate cancer, with the American Urological Association (AUA) (Carter et al., 2013) opting for PSA testing after a discussion with shared decision making. In 2018 the U.S. Preventive Services Task Force (USPSTF) adjusted recommendations for shared decision making with initial potential screening at age 55. The American Cancer Society (ACS) (2018) recommends that asymptomatic men who have at least a 10-year life expectancy have an opportunity to make an informed decision with their health-care provider about whether to be screened for prostate cancer. Men at average risk should receive this first information beginning at age 45 to 50 years. Men at higher risk, including African Americans and men with a first-degree relative (father or brother) diagnosed with prostate cancer before age 65 years, should receive this information at age 45 years. Men with an appreciably higher risk (multiple family members diagnosed with prostate cancer before age 65 years) should receive this information at age 40 years. Asymptomatic men with less than a 10-year life expectancy based on age and health status should not be offered prostate cancer screening. Screening, when completed, is recommended with PSA with or without DRE.

Referral: Because the major harm with PSA screening is overtreatment and given the variability in how prostate cancer is handled, referral to academic urology practice and providers that treat most low-grade prostate cancer with active surveillance is preferred.

Education: Review risk factors and significance of reporting family history. Used informed decision making prior to testing.

Clinical Recommendation	Evidence Rating	References
Participate in informed decision making after shared discussion of risks and benefits of screening.	C	American Cancer Society, 2018
Health-care providers should periodically discuss prostate cancer screening with men who are expected to live at least 10 years and are old enough to be at significant risk for prostate cancer.	B	Carter et al., 2013 (Reconfirmed, 2018)
When screening, perform with prostate specific antigen testing every 2 to 4 years in those of average risk.	B	Carlsson & Vickers, 2020
Stop screening after age 69 or earlier if comorbidities limit life expectancy to less than 10 years.	C	Hoffman, 2021

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PROSTATITIS

Signal Symptoms: Myalgia, cloudy urine, and urinary symptoms such as dysuria, frequency, and urgency are classic symptoms and may be associated with fever, chills, and malaise. Swelling of the prostate can also cause complaints of pain at the tip of the penis, hesitancy, and intermittency (Coker & Dierfeldt, 2016). Sexual dysfunction, psychological issues, and urogenital pain may occur in chronic cases (Khan et al., 2017; Su et al., 2020).

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Description: Prostatitis includes both acute and chronic bacterial prostatitis and prostatitis syndrome, also termed chronic pelvic pain syndrome (CPPS). The National Institutes of Health Consensus Classification of Prostatitis identifies four categories of prostatitis based on clinical presentation: type I, acute bacterial prostatitis; type II, chronic bacterial prostatitis; type III, CPPS with either type IIIA inflammatory components or type IIIB noninflammatory components; and type IV, asymptomatic prostatitis. Acute bacterial prostatitis is an acute bacterial infection of the prostate and, if left untreated, it can progress to sepsis or development of prostatic abscess. By definition, an organism must be identified with culture. Chronic prostatitis is defined by symptoms being present for at least 3 months and urine cultures obtained over the course of the illness repeatedly growing the same bacterial strain. CPPS is pelvic pain in the absence of bacteria localized to the prostate (Su et al., 2020).

Etiology: Most common pathogens in prostatitis include *Escherichia coli, Klebsiella, Proteus mirabilis, Enterococcus faecalis*, and *Pseudomonas aeruginosa* (Coker & Dierfeldt, 2016; Su et al., 2020).

Occurrence: Prevalence of prostatitis in men is approximately 8% to 16%; however, only 5% to 10% were found to have a bacterial source (Davis & Silberman, 2021). Men who have had one occurrence of bacterial prostatitis have an increased chance of having a recurrence and 10% chance of developing chronic pelvic pain.

Age: Bimodal incidence peaks between 20 and 40 years and older than 60 years (Gill & Shoskes, 2016).

Ethnicity: Not significant.

Contributing Factors: History of urinary tract infection (UTI), history of sexual abuse, functional or anatomical anomalies (phimosis, stricture), presence of indwelling catheter, unprotected vaginal/anal intercourse, recent prostate or transurethral biopsy/surgery. Diabetes and other immunocompromised states increase the risk for developing (Davis & Silberman, 2021).

Signs and Symptoms: The predominant symptom is pain in the prostate, perineum, scrotum, testes, penis, urinary bladder, or lower back. Acute bacterial prostatitis frequently includes symptoms similar to acute cystitis or pyelonephritis, including malaise, low back and perineal pain, high fever, chills, dysuria, inability to empty the bladder, nocturia, and urinary retention. Men are acutely ill and may look toxic (Davis & Silberman, 2021). In chronic bacterial prostatitis, symptoms can be subtle and variable and are similar to those of an acute bladder infection, such as frequency, urgency, dysuria, perineal discomfort, low back pain, and urinary dysfunction (Khan et al., 2017; Su et al., 2020).

Physical examination may reveal a tender, boggy prostate on rectal examination. The prostate gland may be warm, swollen, firm, or irregular. Prostatic massage with acute infection is contraindicated because it increases the risk for bacteremia, is very painful, and has no benefit. Suprapubic tenderness should be evaluated for retention and costovertebral tenderness should be assessed due to the differential of pyelonephritis (Davis & Silberman, 2021).

Diagnostic Tests: Diagnosis of acute bacterial prostatitis is often done by report of symptoms. Suspected acute prostatitis diagnostics include midstream urinalysis and urine culture. If a patient has urethral discharge or has risk for sexually transmitted infection, test for urine gonorrhea and chlamydia. If the patient meets sepsis criteria, send them to the emergency department where a complete blood count (CBC) with differential, basic metabolic panel, lactic acid, and blood cultures will be run. Urine should be a midstream collection, and the presence of more than 10 white blood cells (WBCs) per high-power field (HPF) suggests a positive diagnosis. Suspected chronic prostatitis/CPPS tests include urinalysis, urine culture, and postvoid residual, if sensation of incomplete emptying of bladder is present. Persistent suspected chronic bacterial prostatitis should be referred to a urologist, who may do further testing that includes two-glass preprostatic and post prostatic massage test. In most cases, imaging is not required unless an abscess is suspected, and a computed tomography (CT) scan or ultrasound can be ordered. If prostate-specific antigen (PSA) screening is planned, it should be deferred for at least a month until acute symptoms have resolved (Meyrier & Fekete, 2020).

Differential Diagnosis:

Acute Bacterial Prostatitis:

- Acute cystitis: rapid onset and rapid response to antimicrobial therapy
- Urethritis: clinical diagnosis, mucopurulent or purulent urethral discharge; typically no prostatic tenderness
- Pyelonephritis: positive costovertebral angle tenderness, may have hematuria, may have abdominal pain; more common in younger patients; no prostatic tenderness.
- Acute urinary retention: physical assessment of distended bladder; if acute prostatitis not strongly suspected, straight catheterization should relieve most symptoms
- Benign prostatic hyperplasia (BPH) (see BPH in this chapter): prostate enlarged but not tender
- Urinary tract stones: acute, crampy pain on urination; sludge or gravel may be seen in urine specimen, especially if the specimen is strained; may be accompanied by nausea, vomiting; prostate not tender
- Bladder cancer: voiding symptoms present but prostate not tender
- Prostate cancer: enlarged possibly nodular prostate that may cause lower urinary tract symptoms, but prostate not tender

Chronic Bacterial Prostatitis:

- Chronic prostatitis/chronic pelvic pain syndrome with no evidence of bacterial source
- Noninflammatory bladder, prostate, or pelvic floor issues can present with similar symptoms (BPH, high tone pelvic floor, lower back issues)

Treatment: Empiric antibiotics are indicated in acute bacterial prostatitis while awaiting culture results; they are culture-based in chronic bacterial prostatitis, with empiric therapy started while awaiting any results of the culture (Meyrier & Fekete, 2020). Predominant infectious organisms are gram negative, so Bactrim DS twice daily, ciprofloxacin (Cipro) 500 mg twice a day, or levofloxacin (Levaquin) 500 mg daily are first-line therapy. Because the prostate has lower absorption abilities, antibiotics for acute infections without hospitalization or risk factors should be continued for 2 to 4 weeks. Those with a history of a prostate abscess, a persistently painful rectal examination, or bacteriuria should

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be continued on antibiotics for at least 4 weeks and up to 6. If the patient is acutely ill on presentation with fever, intolerance of oral medications, urinary retention, or concern for sepsis, the health-care provider should consider hospitalization and parenteral antibiotics (Su et al., 2020)

Patients should be evaluated for need of stool softeners if defecation is painful or difficult. Evaluate the need for analgesics, antipyretics, or anti-inflammatory medications and warm water baths.

Patients with chronic prostatitis or relapse should also receive extended antimicrobial therapy for 2 to 6 weeks. (Davis & Silberman, 2021; Su et al., 2020).

Follow-Up: For patients with acute bacterial prostatitis, a repeat urine culture a week after initiating treatment is recommended. If positive, consider changing antibiotics based on culture. Refer patients with symptoms of BPH, intractable infection, or prostatodynia to urology.

Sequelae: Unresolved acute prostatitis can lead to bacteremia or pyelonephritis. If acute prostatitis is not completely treated it can lead to chronic prostatitis and pelvic pain. Prostatic abscess rarely occurs as a complication of acute bacterial prostatitis except in patients who are immunocompromised.

Prevention/Prophylaxis: Reduce the need for catheterization. Educate on use of protection if participating in anal sex. Compliance with antibiotics in acute infections is important for prevention of chronic prostatitis and CPPS.

Referral: Refer patients with symptoms of BPH, intractable infection, or prostatodynia to a urologist.

Education: Educate the patient and family regarding the cause of symptoms and treatment. Explain the need for extended antibiotics and importance of adherence with treatment. Emphasize that prostatitis can recur and to report symptoms at onset.

Clinical Recommendation	Evidence Rating	References
Antimicrobial therapy should be guided by bacterial cultures and sensitivities for chronic bacterial prostatitis.	B	Su et al., 2020
Optimal duration of antibiotic treatment for acute bacterial prostatitis is 2–4 weeks.	C	Davis & Silberman, 2021 Su et al., 2020
Initial outpatient treatment is with trimethoprim-sulfamethoxazole or a fluoroquinolone unless a specific resistant organism is suspected.	C	Su et al., 2020
Refer to the hospital if elevated temperature, inability to tolerate oral medications, signs of sepsis, or urinary retention is present.	C	Davis & Silberman, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

Mrs. C., a 66-year-old woman, presents to your practice with a complaint of recent onset of leaking urine. She has no prior history of this. On further questioning you discover that she is newly married, after being widowed for 15 years, during which time she had no sexual partners. She and her new husband have just returned from a cruise, and she reports that he is a "passionate" lover and she is having difficulty meeting his needs for daily intercourse. Other symptoms that Mrs. C. reports are vaginal burning and general discomfort "down there."

Medications: Takes fish oil at bedtime, vitamin D_3 1,000 IU daily. No known drug allergies.

Vital signs: Blood pressure (BP) 128/76 mm Hg, pulse 82 (regular), respiratory rate 16 breaths/min, temperature 98.2°F (oral), BMI 23.4.

A staff member has obtained a urine specimen for dipstick. Findings are as follows:

Nitrite—negative

Leukocyte esterase—negative

Blood—trace

Protein—trace

Glucose—negative

Ketones—negative

Specific gravity—1.015

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What national guidelines are appropriate to consider?
4. What tests will you order?
5. Are there any screening tools that you want to use?
6. What are the differential diagnoses that you are considering?
7. What is your plan of care?
8. What additional patient teaching may be needed?
9. Will you be looking for a consultation?

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CHAPTER 15

Gynecological Disorders

Evelyn Duffy and Mary Franklin

ASSESSMENT

Assessment of the sexual and reproductive systems is best accomplished using a framework of trauma-informed care. Trauma-informed care encompasses six principles: psychological safety, trustworthiness and transparency, peer support, collaboration, empowerment, and humility and responsiveness (Trauma Informed Care Implementation Resource Center, 2021). Implementing these principles in the assessment of sexual and reproductive health includes measures such as obtaining history questions with the patient dressed, conducting the interview seated so that patient and provider are at eye level, starting with less-sensitive questions first, explaining the rationale for questions and physical examination procedures, and having the patient decide what clothing to remove or leave on for the physical examination.

A comprehensive medical, surgical, social, and family history may reveal medications, conditions, or historical factors that affect the reproductive system. Although a comprehensive obstetrical history is generally not relevant to the care of the older adult, historical factors that should be elicited include number of births (increased risk pelvic organ prolapse), gestational diabetes (increased risk of type 2 diabetes) and pre-eclampsia (increased risk of hypertension and stroke). The review of systems (ROS) should include specific questions about vasomotor symptoms, urinary incontinence, vaginal bleeding, and issues with sexual activity such as decreased libido or pain. Older adults are often hesitant to discuss these sensitive issues. Establishing a relationship with the patient, having a nonjudgmental approach, and explaining the purpose of history questions all help reduce patient discomfort with this section of the ROS. Reassuring patients that not only are issues such as decreased libido or incontinence common, but that there are treatment options, encourages the report of bothersome symptoms.

A complete sexual history for the older adult includes eliciting information about 4 Ps: sexual Practices, number and types of Partners, Protection against and history of sexually transmitted infections, and Pleasure in sexual practice (Savoy et al., 2020). The clinician should record the timing and results of cervical cancer screening and mammograms.

Physical examination related to the reproductive system will vary based on the presenting symptom. Routine clinical breast examinations are not universally recommended. If clinical breast examinations are performed, they can be discontinued when screening mammograms are discontinued. Age-related changes in the female breast include the atrophy of glandular breast tissue and replacement with fat and connective tissue. There may be a decrease in breast size or breasts may become pendulous and less firm, due to loss of elasticity. Areolar nipple ducts may be palpable, feeling stringy and firm. The inframammary ridge assumes more prominence. Axillary hair decreases. Age-related changes in the male breast may include gynecomastia.

Physical examination of the breast includes both inspection and palpation. Inspection is performed in the seated position and the patient performs three maneuvers: hands on hips, hands over head, and leaning forward. The examiner is assessing for symmetry, skin changes, lumps, dimpling, and nipple retraction. Palpation of the breasts is done in a supine position and includes both light and deep palpation and examining all of the breast tissue from the clavicle to the top of the rib cage, including the axillary area. Palpation using a stripe pattern has been shown to provide the most reliable results.

Atrophic changes related to age are common in the reproductive system of those assigned female sex at birth. Pubic hair becomes gray and sparse, and the labia flatten. Vaginal epithelium is thinner, drier, and itchy, with less rugae; decreased secretions and alkalinity predispose patients to painful intercourse, friability, and vaginitis (Alvisi et al., 2019; Angelou et al., 2020; Faubion et al., 2017; Manda, et al., 2021; Mitchell & Waetjen, 2018; Nappi et al., 2019; Scavello et al., 2019). The vagina becomes shorter, narrower, and less elastic; tissue is pale pink and shiny. Sexual abstinence intensifies atrophic changes. Undergarments and incontinence often irritate sensitive external structures (Manda et al., 2021). The uterus becomes smaller, and ovaries are not palpable due to atrophy. The pelvic floor muscles, sacral ligaments, and other supporting structures relax, increasing the risk of pelvic organ prolapse.

Routine examination with a speculum and bimanual examination is not recommended. If an examination is needed for symptoms, accommodations may be needed to accomplish the examination. Alternatives to the lithotomy position include examining in the side-lying position with one leg straight or bending the knees with heels against the

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buttocks (avoids use of stirrups). Patients with arthritis may be more comfortable if pain medication is taken before the examination. Equipment should be assembled and ready to limit time spent in the examining position. Applying a water-soluble lubricant to the speculum before insertion is important for comfort. The narrow Pederson speculum, in an adult or pediatric size, may be chosen for those with a narrow introitus. To examine for pelvic organ prolapse, a half speculum is used, retracting the anterior vagina and the posterior vagina separately (American College of Obstetricians and Gynecologists [ACOG] & The American Urogynecologic Society, 2019).

On bimanual examination, the ovaries should not be palpable, and the uterus should be small and firm. Cervical cancer screening with Pap or human papillomavirus (HPV) testing is no longer recommended for those older than age 65 who have had adequate prior screening and are not at high risk for cervical cancer and those younger than age 65 who have had a complete hysterectomy for noncancerous reasons (U.S. Preventive Services Task Force [USPSTF], 2018).

BREAST CANCER

Signal Symptoms: None; breast mass, axillary mass, skin changes, unilateral black or bloody nipple discharge.

Description: Breast cancer is the most common noncutaneous cancer in U.S. women, accounting for 30% of all new cancer cases and 15% of all cancer deaths in 2021 (American Cancer Society [ACS], 2021a). Breast cancer was estimated to affect 49,290 with *in situ* disease and 281,550 with invasive disease and to result in 43,600 deaths in 2021 (ACS, 2021a). Men represent approximately 1% of breast cancer incidence and deaths (ACS, 2021a). Incidence and death rates for breast cancer increase with age, peaking at ages 70 to 74. The incidence of breast cancer decreases after age 80, possibly due to reduced screening (ACS, 2019a; U.S. Cancer Statistics Working Group, 2020). Currently, women living in the United States have approximately a 13% or one in eight lifetime risk of developing breast cancer (Breastcancer.org, 2021). At the time of diagnosis, 64% of cancers are localized, and only 6% of initial diagnoses are for metastatic disease. The 5-year survival rate for localized breast cancer is 99%, for regional disease is 86%, and for metastatic disease is 26% (ACS, 2019a).

Breast cancers are classified as malignant, neoplastic tumors that start in the tissue of the breast. The two most common types are ductal and lobular carcinomas, with ductal carcinomas having a higher prevalence (ACS, 2019a). Breast cancers may be invasive or noninvasive (also called *in situ*). Ductal carcinoma *in situ* (DCIS) is a condition in which abnormal cells replace the normal epithelial cells of the breast ducts and is considered a noninvasive form of breast cancer (ACS, 2019a). Lobular carcinoma *in situ* (LCIS) is considered a benign condition, although LCIS does increase the risk of invasive breast cancer (ACS, 2019a; Giuliano et al., 2018).

Most breast cancers are invasive, which means cancer cells have broken through the walls of the glands or ducts where they originated and subsequently grow into surrounding breast tissue. The prognosis of invasive breast cancer is influenced by disease stage at first diagnosis. This is determined clinically by a classification of tumor stage by the American Joint Committee on Cancer (AJCC) Tumor-Node-Metastasis (TNM) staging system (ACS, 2019a). Staging using the AJCC TNM system includes information about tumor size, spread within the breast and to adjacent tissues (T), the extent of spread to nearby lymph nodes (N), presence or absence of distant metastases (spread to distant organs) (M), receptors for estrogen (ER), progesterone (PR), human epidermal growth factor (HER2) and extra copies of the HER2 gene as well as grading how closely the microscopic appearance of the cancer resembles normal breast tissue (ACS, 2019a). Once all the factors are determined, a stage of 0, I, II, III, or IV is assigned, with stage 0 being *in situ,* stage I being early stage invasive cancer, and stage IV being the most advanced disease with distant organ metastases (Giuliano et al., 2018).

Receptors for estrogen, progesterone, and HER2 are crucial in breast cancer staging and prognosis. If tumors are positive for either or both estrogen and progesterone receptors, the term hormone receptor (HR) positive is used. The most common breast cancer with the best prognosis is HR receptor positive and HER2 negative. Tumors positive for both HR and HER2 are generally diagnosed at a higher grade and have a less positive prognosis. Tumors negative for both HR and HER2, called triple negative cancers, have a poorer prognosis than other cancers, primarily because there is a lack of effective treatments. Triple negative cancers are twice as likely to occur in non-Hispanic Black women compared to non-Hispanic White women in the United States and are also more common in premenopausal women and those with *BRCA* mutations (ACS, 2019a). Other types of breast cancer involving tissues other than lobes or ducts are less common and include inflammatory breast cancer and Paget's disease (ACS, 2019b).

Etiology: The exact cause of breast cancer is unknown, with environmental and genetic contributions.

Occurrence: Excluding cancers of the skin, breast cancer is the most common cancer among U.S. women and accounts for 30% of newly diagnosed cancers (ACS, 2021a). An estimated 281,550 cases of breast cancer were predicted among U.S. women in 2021. At the same time, 43,600 women were expected to die from breast cancer in 2021, which is second only to lung cancer deaths. In men, 2,650 new cases of breast cancer and 530 deaths were predicted in 2021 (ACS, 2021a).

Age: The median age of diagnosis of breast cancer is 62 years. Risk is positively related to increased age, placing older individuals at higher risk (ACS, 2021a).

Ethnicity: The incidence of breast cancer is highest in non-Hispanic White women, closely followed by non-Hispanic Black women. Hispanic, Native American/Alaskan Native, and Asian/Pacific Islander women have a lower incidence of breast cancer, although Hispanic women generally present at a later stage of disease (ACS, 2019a; Yedjou et al., 2019). Non-Hispanic Black women have a higher mortality rate at all ages and have a higher incidence of breast cancer under age 40 (ACS, 2019a; Yedjou et al., 2019). Disparities that

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factor into different outcomes in breast cancer include socioeconomic status (education, income, and employment), access to adequate health-care services, extent of mistrust of the health-care system, tobacco use, exposure to environmental toxins, prevalence of comorbidities (particularly obesity), nutritional and physical activity status, and rates of breastfeeding (Yedjou et al., 2019).

Contributing Factors: Female sex assigned at birth is a significant risk factor for developing breast cancer. Although family history is a strong contributing factor, most individuals with a first-degree relative with breast cancer will not develop breast cancer, and most individuals who develop breast cancer do not have a family history. Compared to women with no family history, the relative risk (RR) is 1.5 with one affected first-degree relative and the RR is 2.0 to 4.0 with two or more first-degree relatives (ACS, 2019a). The risk is increased if the affected relative developed breast cancer at an early age, in both breasts, or is male (ACS, 2019a). Another strong contributing factor is the presence of an inherited gene mutation such as *BRCA1* or *BRCA2*. In the general population, the risk of developing breast cancer by age 80 is around 10%. For individuals with *BRCA* mutations, the risk is about 70% (ACS, 2019a). In addition to *BRCA* mutations, there are about 300 identified gene mutations associated with increased breast cancer risk. A few of the more common genetic mutations are Partner and Localizer of *BRCA2* (*PALB2*), *TP53* (associated with Li-Fraumeni's syndrome), *PTEN* (Cowden's syndrome), *LKB1/STK11* (Peutz-Jeghers' syndrome), Checkpoint Kinase 2(CHEK2), *ATM*, and *CDH* (ACS, 2019a; Odle, 2017).

Dense breast tissue, present in up to one half of all women, is a contributing factor to breast cancer. Increased density identified on mammography is more common in young women and makes mammograms more difficult to read. Glandular and connective tissue are typically replaced by fatty tissue after menopause, making breasts less dense. The RR for developing breast cancer with heterogeneously or extremely dense breasts increases with age from 1.23 for those aged 40 to 49 to a RR of 1.30 for those aged 65 to 74 (Siu, 2016). At least 44 states have legislation addressing notification of patients when increased breast density is identified on mammography (Dense Breast-info, 2019).

Compared to those who were never diagnosed with breast cancer, individuals with a personal history have a 3% to 7% risk over 10 years of developing a new breast cancer. Rates of new primary breast cancers after a prior breast cancer diagnosis have decreased over the past 40 years, potentially because of an increase in hormonal therapy for HR positive cancers and an increase in bilateral mastectomy (ACS, 2019a). DCIS increases the risk of invasive breast cancer by a RR of 2.1 to 4.0. Although LCIS is a benign condition, it increases the risk of invasive breast cancer by a RR of >4. For this reason, LCIS may be surgically removed even though it is benign (ACS, 2019a). Previous chest radiation, a family history of ovarian cancer, and a personal history of ovarian or endometrial cancer increases the risk of breast cancer (ACS, 2019a). Other contributing factors include nulliparity or having the first child after age 30, early menarche, late menopause, use of postmenopausal hormones, obesity, alcohol consumption, tall height, and not breastfeeding (ACS, 2019a; American College of Obstetrics and Gynecology [ACOG], 2017). There is biological plausibility for environmental impacts. Recent immigrants from Asian countries have very low rates of breast cancer, whereas Asian Americans born in the United States have rates of breast cancer similar to non-Hispanic Whites (Yedjou et al., 2019).

Benign breast conditions are categorized into three general groups: nonproliferative lesions (overgrowth of breast tissue; little or no effect on breast cancer risk), proliferative lesions without atypia (abnormal cells; small increase in risk of breast cancer, RR of 1.5 to 2.0); and proliferative lesions with atypia (RR >4) (ACS, 2019a). Although not an independent risk factor for breast cancer, high bone mineral density in postmenopausal women has been associated with increased rates of HR positive breast cancer, potentially because of cumulative estrogen exposure (ACS, 2019a).

Signs and Symptoms: Signs and symptoms of breast cancer range from completely asymptomatic to a breast or axillary lump or mass, black or bloody nipple discharge, change in the size or shape of the breast, changes in the skin, and inversion or deviation of the nipple (ACS, 2019a).

Diagnostic Tests: For individuals at high risk or individuals who have noted a breast mass or other symptoms, history taking and clinical breast examination is the first stage of breast cancer diagnosis. A diagnostic mammogram is used to determine breast disease in those who have breast symptoms or abnormal screening mammography. This diagnostic procedure is distinguished from screening mammography. Suspicious findings on mammography must be confirmed by biopsy.

Standard setting agencies have published a number of different breast cancer screening guidelines. Although there are nuances in these different guidelines, for individuals at average risk for breast cancer or less than a 20% lifetime risk, there is consensus that screening mammograms should start by at least age 50, be performed at an interval of between one and two years, and that discontinuation be considered when life expectancy is less than 10 years (Narayan et al., 2020). Table 15-1 compares the recommendations for mammography for average risk women from various organizations.

To determine risk for breast cancer, several risk assessment tools are available (Table 15-2). Although these risk tools help identify individuals who might benefit from early or enhanced screening, they do not all include the detailed family history necessary to determine which individuals should be referred to genetic counseling or testing for *BRCA* gene mutations. Risk factors that are associated with *BRCA* gene mutations include a family history of any of the following: breast cancer prior to age 50, breast and ovarian cancer in the same family member, male breast cancer, bilateral breast cancer, multiple relatives with breast cancer or with ovarian cancer, and Ashkenazi Jewish ancestry (Smith et al., 2019). If these risk factors are present, then referral to genetic counseling should be offered. For individuals with a 20% or greater lifetime risk of breast cancer, annual magnetic resonance imaging (MRI) and mammography is recommended (Smith et al., 2019). A common screening protocol for individuals at increased risk is to alternate mammograms and MRIs every 6 months.

Breast ultrasound is used to further evaluate abnormal findings from a screening or diagnostic mammogram or from a clinical breast examination. It has been demonstrated that ultrasound detects more cancer than mammography alone in women with dense breast tissue, although it can increase the likelihood of false-positive results (ACS, 2019a; Monticciolo et al., 2018). Biopsy to obtain samples for cytology and

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TABLE 15-1 Mammography Screening Recommendations

AGE	RECOMMENDATION	ORGANIZATION(S)	REFERENCES
40–49	Individual decision	American College of Physicians (ACP)	Qaseem et al., 2019
		U.S. Preventive Services Task Force (USPSTF)	USPSTF, 2016
	Yearly screening	American College of Radiology (ACR)	Monticciolo et al., 2017
	Yearly screening starting at age 45	American Cancer Society (ACS)	ACS, 2021b
	Offer screening every 1–2 years	American College of Obstetricians and Gynecologists (ACOG)	ACOG, 2017
50–74	Screen every 1–2 years	ACOG, ACP, ACR, ACS, USPSTF	ACOG, 2017; Qaseem et al., 2019
			Monticciolo et al., 2017; ACS, 2021b
			USPSTF, 2016
75+	No recommendation	USPSTF	USPSTF, 2016
	Continue as long as overall health is good and life expectancy is >10 years	ACOG, ACP, ACR, ACS	ACOG, 2017; Qaseem et al., 2019
			Monticciolo et al., 2017, ACS, 2021b

TABLE 15-2 Breast Cancer Risk Assessment Tools

TOOL NAME	WEB SITE	COMMENTS
National Institutes of Health Gail Model	https://bcrisktool.cancer.gov/	Patient-friendly. Assesses personal and brief family history and four demographic questions—age, race/ethnicity, age at menarche, and age at first birth.
Tyrer-Cuzik or IBIS model	https://ibis-risk-calculator.magview.com/	Designed for health-care providers. Extensive family history, including the option to create pedigree. In addition to other demographics, includes height, weight, mammographic density, and results of genetic tests.
Bright Pink Risk Assessment	https://brightpink.org/	Patient-friendly. In addition to other demographics, includes height, weight, alcohol and tobacco consumption, amount of exercise, chest radiation, and family history.

histology is recommended to confirm the breast cancer diagnosis (Cardoso et al., 2019)

Differential Diagnosis: The majority of breast masses are benign. Benign conditions are classified as nonproliferating lesions, proliferating lesions without atypia, and proliferating lesions with atypia (ACS, 2019a). Mastitis is not a tumor and does not increase the risk of breast cancer.

- Benign nonproliferating breast mass: Nonproliferating lesions do not seem to affect future cancer risk. These include:
  - Adenosis
  - Benign phyllodes tumor
  - Duct ectasia
  - Epithelial calcifications
  - Fat necrosis
  - Fibrosis
  - Lipomas
  - Mild hyperplasia
  - Neurofibromas
  - Single papilloma
- Proliferating lesions without atypia: Increase cancer risk by approximately one to two times over average risk. These include:
  - Ductal hyperplasia without atypia
  - Fibroadenoma
  - Multiple papillomas
  - Radial scar
  - Sclerosing adenosis
- Proliferating lesions with atypia: Increase cancer risk by four to five times, and higher if there is a family history (ACS, 2019a). These include:
  - Atypical ductal hyperplasia
  - Atypical lobular hyperplasia

Treatment: The treatment for breast cancer confirmed by biopsy is ideally determined by shared decision making with a multidisciplinary team of surgeons, medical oncologists, and genetic specialists after consideration of patient's age, menopausal status, and preferences, and cancer staging and biological characteristics along with the risks and benefits of each treatment option. A variety of multi-gene testing panels are available and genetic testing is recommended to help determine prognosis and treatment (Telli et al., 2019). Depending on the stage of disease, hormone markers, and genetics, the treatment for an initial occurrence of cancer may include breast-conserving surgery (lumpectomy or partial mastectomy), mastectomy, chemotherapy, radiation, targeted therapies, selective estrogen

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receptor modulators, aromatase inhibitors, bisphosphonates, immune modulators, and monoclonal antibodies (ACS, 2019a; Cardoso et al., 2019; Telli et al., 2019; Waks & Winer, 2019). Ovarian suppression has become a standard part of breast cancer therapy for premenopausal women (Telli et al., 2019).

Follow-Up: Follow-up of breast masses and breast cancer is based on the specific diagnosis, cancer staging, and treatment rendered.

Sequelae: Adjusting for age, mortality rates declined 40% since 1989. Decline in breast cancer mortality is attributed to improved breast cancer treatment coupled with early detection (Smith et al., 2019). These trends have not affected all populations equally. From 2011 to 2016, rates of mortality were 41% higher for non-Hispanic Black individuals as compared to non-Hispanic White individuals (Smith et al., 2019). Factors contributing to this disparity include discrepancies in insurance status, tumor size and receptor status at diagnosis, presence of comorbidities, and disparity in breast cancer treatment (Dreyer et al., 2018; Waks & Winer, 2019).

Prevention/Prophylaxis: Screening mammography remains the most effective means of breast cancer screening and recommendations were discussed previously. It is no longer recommended to teach breast self-examination due to potential overdiagnosis and overtreatment (ACOG, 2017; Siu, 2016). Rather than the regimented, every month breast self-examination that used to be taught, breast self-awareness is recommended by the ACS and ACOG. Breast self-awareness means being familiar with how breasts normally look and feel so that changes can be reported. (ACS, 2019a; ACOG, 2017). Clinical breast examinations (CBE) by a health-care provider can also lead to overdiagnosis and overtreatment. Some organizations either recommend against CBE (ACS, 2019a; Oeffinger et al., 2015; Qaseem et al., 2019) or state there is insufficient evidence to recommend (Siu, 2016). Only ACOG guidelines recommend offering a clinical breast examination every 1 to 3 years from ages 25 to 49 and then yearly starting at age 50 (ACOG, 2017).

Genetic testing is recommended for individuals with a family history suggestive of a cancer gene mutation. Early and/or enhanced screening is recommended for those with a lifetime risk of 20% or greater (Monticciolo et al., 2018; Smith et al., 2019). Carriers of *BRCA* genes can be offered prophylactic oophorectomy (if childbearing is complete) and/or prophylactic mastectomy (Carbine et al., 2018). Chemoprevention using tamoxifen or raloxifene decreases breast cancer risk and breast cancer death for individuals at high risk, particularly those with *BRCA* mutations (Samadder et al., 2019). Enhanced screening including MRIs, prophylactic surgery, and chemoprevention are not recommended for individuals with a lifetime risk of less than 20% (ACOG, 2017).

Several strategies are suggested to help reduce the risk of breast cancer, and these include avoiding weight gain and obesity, engaging in regular physical activity, minimizing alcohol intake, and minimizing exposure to menopause hormone therapy (ACS, 2019a). Breastfeeding decreases breast cancer risk by 4% for every 12 months of breastfeeding (ACS, 2019a).

Referral: All breast masses should be further evaluated for malignancy. Referrals to surgeons, oncologists, geneticists, genetic counselors, mental health services, and appropriate support groups are made as necessary. A persistent palpable breast mass with a negative mammogram warrants further evaluation, especially in young women with dense breast tissue.

Education: A comprehensive plan of education empowers patients to put breast cancer risk in perspective with other health risks, to modify risk factors that can be controlled, and to be proactive about screening. Use of risk assessment tools and a detailed personal and family history can help individuals assess their breast cancer risks. A lack of clear consensus on screening guidelines necessitates shared decision making between patient and provider about when to start screening, the frequency of mammograms, and when it is prudent to discontinue screening. Providers have a role in educating patients on self-breast awareness, that self-breast examinations are no longer recommended, and that most guidelines also suggest against CBE. Educating patients on danger signs and when to report changes along with discussing modifiable risk factors such as weight management, physical activity, and alcohol consumption is a crucial part of the plan.

Clinical Recommendation	Evidence Rating	References
Mammography screening between the ages of 40 to 50 is an individual decision between the patient and provider.	C	Qaseem et al., 2019 USPSTF, 2016
Mammography screening should be performed every 1–2 years between the ages of 50 and 75.	B	ACOG,2017 Monticciolo et al., 2017 Qaseem et al., 2019 Smith et al., 2019 USPSTF, 2016
Individuals with a personal or family history of breast or ovarian cancer or a family history of known or suspected *BRCA* gene mutations should be offered genetic counseling.	B	USPSTF, 2019
Breast self-examination has increased harm without providing evidence of benefit and is not recommended.	A	ACOG, 2017 Smith et al., 2019 USPSTF, 2016

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ENDOMETRIAL CANCER

Signal Symptoms: Abnormal uterine bleeding, particularly postmenopausal bleeding.

Description: Endometrial cancer is the abnormal proliferation and neoplastic transformation of endometrial tissues. It is the most common gynecological malignancy in the United States. Endometrial cancer may be confined to the lining of the uterus, may spread to the myometrium or cervix, may have local spread to the pelvic region, or metastasize to remote tissues.

Etiology: Endometrioid tumors, which are comprised of an increased number of endometrial cells and are associated with excess estrogen, either endogenous or exogenous, account for 70% of all endometrial cancer (but only 40% of the deaths). These were historically labeled type 1 tumors and are associated with obesity and metabolic syndrome (Brooks et al., 2019; Gentry-Maharaj & Karpinskyj, 2020; Lu & Broaddus, 2020; McDonald & Bender, 2019). Non-endometrioid tumors may have serous, clear cell, or carcinosarcoma histology, are not associated with excess estrogen or obesity, are more aggressive, present at a higher stage, have a higher risk of recurrence and a worse prognosis. These were historically called type 2 tumors (Brooks et al., 2019; Gentry-Maharaj & Karpinskyj, 2020; Lu & Broaddus, 2020).

Occurrence: Endometrial cancer represents 7% of all cancers in women and 4% of all cancer deaths (American Cancer Society [ACS], 2021a); it is the most common gynecological cancer in developed countries, and rates have increased about 1% per year in the past 20 years (ACS, 2021a). Because of increased rates of obesity and increased life expectancy, this trend of increasing rates is expected to continue (Gentry-Maharaj & Karpinskyj, 2020). It is estimated that in 2021 there will be approximately 66,570 cases of uterine cancer and 12,940 deaths (ACS, 2021b). The lifetime probability of developing endometrial cancer for all women in the United States is 3% (Gentry-Maharaj & Karpinskyj, 2020). Most individuals present with early-stage disease and have an excellent prognosis (Brooks et al., 2019).

Age: Advancing age is the most important risk factor for endometrial cancer; 5% of tumors occur in women younger than 40 years old. Most tumors occur after menopause, with 60 years being the average age of diagnosis (ACS, 2021b).

Ethnicity: Incidence rates in the United States are higher in non-Hispanic White women, but the mortality rate is almost twice as high in non-Hispanic Black women. This discrepancy has been associated with non-Hispanic Black women having tumors with a more aggressive profile, presenting at a higher grade and more advanced stage, and not receiving comparable treatment to non-Hispanic White women (Brooks et al., 2019; Doll et al., 2018). Lack of access to appropriate care may contribute to this disparity (Lu & Broaddus, 2020).

Contributing Factors: Endometrial cancer occurs only in individuals assigned female sex at birth. Obesity, diabetes hypertension, and exposure to endogenous or exogenous estrogen are significant risk factors for endometrial carcinoma (Brooks et al., 2019; Gentry-Maharaj & Karpinskyj, 2020; McDonald & Bender, 2019). Nulliparity, early menarche, and late menopause are all associated with an increased risk of endometrial cancer (Gentry-Maharaj & Karpinskyj, 2020). There is a high incidence of this cancer in individuals with polycystic ovarian syndrome (Gentry-Maharaj & Karpinskyj, 2020). The use of tamoxifen increases risk by a relative risk (RR) of 2.0 to 3.0 (Gentry-Maharaj & Karpinskyj, 2020). The risk of endometrial cancer in individuals with Lynch syndrome is around 50%, accounting for 3% of all endometrial cancers. Lynch syndrome is a hereditary genetic mutation that places persons affected at higher risk for developing cancer and at a younger age. In addition to endometrial cancer, persons with Lynch syndrome are at risk for colorectal cancer, as well as several others. Multiparity, breastfeeding, and combined oral contraceptives decrease the risk of endometrial cancer (Gentry-Maharaj & Karpinskyj, 2020).

Signs and Symptoms: Postmenopausal bleeding is the most common symptom associated with endometrial carcinoma, occurring in 94% of all cases (Gentry-Maharaj & Karpinskyj, 2020). A finding of endometrial cells after menopause or atypical glandular cells on Pap testing should prompt further evaluation (Passarello et al., 2019).

Diagnostic Tests: For an individual with abnormal uterine bleeding, particularly postmenopausal bleeding, a thorough history and physical examination, including a pelvic and rectal examination, is essential to rule out pelvic masses and other urogenital causes of bleeding. Transvaginal pelvic ultrasound is the most common imaging modality, and magnetic resonance imaging (MRI) may also be ordered (Faria et al., 2019; Murali et al., 2018). Diagnosis of endometrial cancer is confirmed with endometrial sampling obtained by blind biopsy, hysteroscopy, or curettage (Murali et al., 2018). Detection of early endometrial cancer by evaluating endometrial epithelial cells from the cervical opening using a cytobrush is being investigated (Yen et al., 2020). Comprehensive surgical staging is based on extent of invasion into the myometrium and/or cervix, extent of local spread to the adnexal and /or peritoneal regions, extent of spread to lymph nodes, histology, type, and grade of tumor (Murali et al., 2018). There is no screening recommended for individuals at average risk (Gentry-Maharaj & Karpinskyj, 2020). For individuals with Lynch syndrome, routine endometrial biopsy starting at age 35 and hysterectomy with bilateral salpingo-oophorectomy at age 40 or when childbearing is complete is recommended by the American Cancer Society and the National Comprehensive Cancer Network (Bercow & Eisenhauer, 2019; Bristowe et al., 2018; Gentry-Maharaj & Karpinskyj, 2020; MacKintosh & Crosbie, 2018; Passarello et al., 2019).

Differential Diagnosis:

- Infection
- Atrophy
- Polyps
- Other causes of genital tract bleeding

Treatment: Treatment decisions are made primarily on the basis of stage, extent of lymph node involvement, histology, and grade. Genomic factors are not typically used in treatment decisions at this point (Brooks et al., 2019). The primary treatment for early-stage cancer is surgery (total hysterectomy and bilateral salpingo-oophorectomy and

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assessment/removal of lymph nodes), which also allows accurate staging of the cancer (Brooks et al., 2019). In select individuals who do not have Lynch syndrome and are younger than age 50, ovarian sparing surgery might be considered (Brooks et al., 2019). Radiation therapy, often targeted to the vagina rather than the whole pelvic region, is used for individuals with intermediate or high-risk disease (Brooks et al., 2019; Passarello et al., 2019). Chemotherapy may be used in advanced disease or for serous type histologies (Brooks et al., 2019; Faria et al., 2019; Passarello et al., 2019). Progestins alone, or in combination with tamoxifen, can be used for metastatic disease (Brooks et al., 2019).

Follow-Up: For individuals with low risk of recurrence, follow-up is every 6 months for 1 to 2 years and then yearly. For individuals with a higher risk of recurrence, follow-up is every 3 months for 2 years followed by every 6 months until year 5, then annual follow-up (Passarello et al., 2019).

Sequelae: Around 75% of cancers are diagnosed at an early stage, with a 5-year survival rate of 95%, and a 10-year survival rate of 77% (Gentry-Maharaj & Karpinskyj, 2020). Various factors influence the prognosis, including histological differentiation, depth of invasion, and lymph node metastases. Histological type also influences the outcome. Sexual side effects due to postoperative vaginal shortening and vaginal scar tissue post radiation are common (Passarello et al., 2019).

Prevention/Prophylaxis: Protective factors include combined hormonal contraceptives, breastfeeding, coffee consumption of more than four cups a day, physical activity, and regular use of aspirin (Gentry-Maharaj & Karpinskyj, 2020; MacKintosh & Crosbie, 2018). The progesterone-releasing intrauterine device decreases the risk of endometrial cancer by 19% (Gentry-Maharaj & Karpinskyj, 2020; MacKintosh & Crosbie, 2018). Individuals with a uterus who are prescribed estrogen therapy post menopause must also be prescribed a progestin.

Referral: All cases of suspected endometrial cancer are referred to a gynecologist for evaluation and treatment. Routine surveillance of the endometrium and prophylactic surgery should be considered for those at high risk.

Education: Explain the significance of postmenopausal bleeding to every individual at the time of menopause, and inquire about the presence of vaginal bleeding at visits after menopause. Estrogen should not be taken without progesterone in the postmenopausal period in the presence of an intact uterus.

Clinical Recommendation	Evidence Rating	References
Routine screening of average-risk asymptomatic women is not recommended	A	Gentry-Maharaj & Karpinskyj, 2020
90% of those diagnosed with endometrial cancer have symptoms, primarily postmenopausal bleeding	A	Gentry-Maharaj & Karpinskyj, 2020
First-line treatment for most women is surgical total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH-BSO), which is both therapeutic and prognostic (allows staging).	B	ACOG, 2015
Prognosis is good for most patients, with an overall 5-year survival rate of more than 75%; prognosis for uterine sarcoma is worse.	B	ACOG, 2015

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GENITOURINARY SYNDROME OF MENOPAUSE

Signal Symptoms: Dyspareunia vaginal dryness and pain, vulvovaginal irritation and burning, urinary frequency and dysuria, and recurrent urinary tract infections (UTI) (Shifren, 2018).

Description: The hypoestrogenic state after menopause causes chronic and progressive anatomic and physiological changes to the genital and urinary tissues that result in a variety of symptoms. Vulvovaginal atrophy with loss of lubrication and dyspareunia is the most common component of genitourinary syndrome of menopause (GSM), affecting up to 90% of individuals post menopause (Alvisi et al., 2019; Angelou et al., 2020; Mitchell & Waetjen, 2018; Shifren, 2018). GSM can have a significant negative effect on sexual health and quality of life, although it is often not addressed by either health-care providers or patients (Alvisi et al., 2019; Kagan et al., 2019; Nappi et al., 2019; Scavello at al., 2019).

Etiology: Estrogen deprivation post menopause causes GSM. The main physiological changes include drying and thinning of urogenital tissues with a loss of collagen, elasticity, and blood flow, increased pH, decreased vaginal discharge, and decreased bladder capacity and sensation (Alvisi et al., 2019; Angelou et al., 2020; Faubion et al., 2017; Manda et al., 2021; Mitchell & Waetjen, 2018; Nappi et al., 2019; Scavello et al., 2019). Decreased libido is common (Alvisi et al., 2019; Angelou et al., 2020; Scavello et al., 2019).

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Occurrence: This disorder affects all postmenopausal individuals assigned female sex at birth to some degree and depends on the length of time since menopause. More individuals report symptoms 5 years after menopause than in the first year after menopause (Angelou et al., 2020). Individuals assigned male sex at birth who have had vaginoplasty surgery in a male to female transition may have GSM symptoms. Maintaining a neovagina requires lifelong vaginal dilation and estrogen therapy (Mundluru & Larson, 2018).

Age: While GSM is most common after menopause, typically starting in the fifth decade of life, it can occur at any time if an individual has a lack of estrogen. Hypoestrogenic states are common in hypothalamic or pituitary dysfunction, after oophorectomy, and after chemotherapy or radiation therapy (Shifren, 2018).

Ethnicity: Not significant.

Contributing Factors: Menopause resulting in decreased estrogen is the main contributing factor. Any condition leading to a hypoestrogenic state can be associated with GSM. Premature ovarian insufficiency, premenopausal oophorectomy, alcohol abuse, tobacco use, sexual abstinence, physical inactivity, pelvic radiation, chemotherapy, and use of antiestrogens are all associated with GSM (Angelou et al., 2020; Scavello et al., 2019; Shifren, 2018). Individuals treated with aromatase inhibitors for breast cancer often have severe GSM symptoms related to extreme estrogen deficiency (Faubion et al., 2017; Shifren, 2018).

Signs and Symptoms: Vaginal dryness and painful intercourse are common symptoms. Other symptoms include vulvar/vaginal itching and burning and loss of libido. Urinary symptoms are less common and include dysuria, urgency, incontinence, and recurrent UTI (Angelou et al., 2020; Faubion et al., 2017; Manda et al., 2021; Mitchell & Waetjen, 2018; Nappi et al., 2019; Scavello et al., 2019). Typical physical examination signs include a loss of pubic hair; decreased subcutaneous fat; pale, dry, nonrugated vaginal walls, and loss of definition of the labia minora and labia majora. The vaginal canal is short with a narrow introitus. Estrogen deficiency can lead to loss of pelvic organ support and subsequent pelvic organ prolapse (Angelou et al., 2020; Faubion et al., 2017; Nappi et al., 2019).

Diagnostic Tests: Patient surveys can be used to evaluate symptomatology and quality of life impacts. Two common surveys are the Vulvovaginal Symptoms Questionnaire and the Day-to-Day Impact of Vaginal Aging (DIVA) Questionnaire (Angelou et al., 2020). In addition to a thorough history, a pelvic examination should be performed to rule out other conditions. There are two physical scoring systems that can be used to evaluate vaginal and vulvar health. A score less than 15 on the vaginal health index or greater than 8 on the vulvar health index indicates objective diagnosis of GSM (Alvisi et al., 2019). If urinary symptoms are present, a urinalysis and culture should be performed.

Differential Diagnosis (Scavello et al., 2019):

- Autoimmune disorders
- Chronic Vaginitis
- Dermatitis
- Diabetes related conditions such as chronic candidiasis or neuropathy
- Eczema
- Foreign bodies
- Lichen planus
- Lichen sclerosus
- Lichen simplex chronicus
- Malignancy
- Pain disorders of the vagina including vulvodynia and chronic pelvic pain
- Trauma

Treatment: Treatment includes maintaining vaginal blood flow, elasticity, lubrication, and muscle tone through vaginal activity with or without a partner that may include sexual stimulation, the use of vaginal dilators, or pelvic floor physical therapy (Angelou et al., 2020; Scavello et al., 2019; Shifren, 2018). Mild to moderate symptoms may be treated with over-the-counter lubricants and/or moisturizers (Alvisi et al., 2019; Angelou et al., 2020; Faubion et al., 2017; Scavello et al., 2019; Shifren, 2018). Regardless of other therapies, lubricants may always be needed for intercourse. Lubricants may be water-based (e.g., Astroglide or KY jelly), silicone-based (e.g., Pjur Eros), or oil-based (e.g., olive oil or coconut oil). Moisturizers (e.g., Luvena or Replens) are longer lasting and are typically applied twice a week. Severe dyspareunia, particularly in those treated for breast cancer, may be relieved with local application of 4% aqueous lidocaine solution with a cotton swab prior to intercourse (Goetsch et al., 2015).

For more severe or persistent symptoms, vaginal estrogen is the most common prescription therapy for GSM. Vaginal estrogen preparations include creams, rings, tablets, and a softgel insert. Serum levels of estrogen remain in the normal postmenopausal range with the use of vaginal estrogen, and a progestin is not required for individuals with a uterus. The exception to this is Femring, which provides systemic estrogen for treatment of vasomotor symptoms in addition to GSM. When Femring is used, a progestin must also be prescribed if a uterus is present (Angelou et al., 2020; Faubion et al., 2017; Nappi et al., 2019; Scavello et al., 2019; Shifren, 2018). Individuals using systemic estrogen for vasomotor symptoms may need supplemental vaginal estrogen to control symptoms of GSM (Faubion et al., 2017). If there is a history of an estrogen-dependent tumor such as breast cancer, vaginal estrogen products should be used with caution, and after a thorough discussion of risks and benefits in consultation with an oncologist (Angelou et al., 2020; Nappi et al., 2019). The U.S. Food and Drug Administration (FDA) requires package inserts for all estrogen products, including vaginal estrogen, to carry a warning that there is a risk of heart attacks, strokes, breast cancer, and blood clots, even though there is minimal systemic absorption of vaginal products (Kagan et al., 2019). It is helpful to give anticipatory guidance to patients about this language in the package insert before prescribing vaginal estrogen.

Other nonestrogen prescription therapies include intravaginal prasterone or DHEA, which is converted in the body to estrogen and testosterone and oral ospemifene, which is an estrogen agonist-antogonist or SERM, and the only oral agent approved for GSM. Neither prasterone nor ospemifene have

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been studied in individuals with breast cancer. All the prescription therapies can be found in Table 15-3.

Vaginal laser therapy and radiofrequency treatments are under investigation for treatment of GSM (Angelou et al., 2020; Faubion et al., 2017; Shifren, 2018). Complementary treatments such as vitamin D, vaginal vitamin E, probiotics, vaginal testosterone, and phytoestrogens such as soy do not have sufficient evidence to recommend them for symptom relief (Angelou et al., 2020).

Follow-Up: Expected response to prescribed therapy is quick, with resolution of symptoms within 2 to 3 months. Many individuals stop using a prescribed treatment prior to this time due to issues related to the vaginal mode of delivery or concerns over safety of treatment. A 3-month follow-up is recommended, and if symptoms are not resolved, adherence to therapy should be assessed (Faubion et al., 2017). If adherence is not an issue, then a re-evaluation for other causes should be considered (Faubion et al., 2017).

Sequelae: Untreated GSM is a progressive condition. The physical changes related to GSM can result in an inability to participate in painless and satisfying sexual activity. Elevated vaginal pH can lead to an increased susceptibility to vaginal infection, and UTI can become chronic.

Prevention/Prophylaxis: The most important prevention is to screen perimenopausal and postmenopausal individuals for GSM and to offer treatment. Recognition of early signs and symptoms of GSM can lead to prevention of symptoms, continued sexual functioning, and improved quality of life.

Referral: Gynecology referral is appropriate for those who do not respond to treatment or have vaginal bleeding. Referral for pelvic floor physical therapy can help maintain blood flow and elasticity of tissues.

Education: All individuals post menopause should be counseled that symptoms of GSM are common and progressive without treatment, and that treatments are available to improve symptoms and quality of life (Faubion et al., 2017). Selection of a treatment is based on goals of therapy and patient preference. Use water-soluble lubricants for patients with atrophic vaginitis. Counsel regarding the benefits of regular sexual activity. Identify age-related difficulty associated with intravaginal application of prescription therapies and address these needs with sensitivity. If a vaginal estrogen is prescribed, inform the individual that the package insert will contain language about risks related to systemic estrogen, even though there is minimal systemic absorption with vaginal estrogen.

TABLE 15-3 Prescription Therapies for Genitourinary Syndrome of Menopause

TREATMENT OPTION	BRAND NAME	DOSE	COMMENTS
Estradiol hemihydrate vaginal tablets	Vagifem and generics	Initial treatment: 1 tablet intravaginally q.h.s. × 14 days followed by maintenance of 1 tablet twice a week	Preloaded on individual applicators. Easy to insert.
17β estradiol cream	Estrace and generics	Initial treatment: 0.5–1.0 g intravaginally q.h.s. followed by maintenance of 0.5–1.0 g one to three times a week	Most common reason for discontinuation is messiness.
Conjugated estrogen cream	Premarin (no generic available)	Initial treatment: 0.5–1.0 g intravaginally q.h.s. followed by maintenance of 0.5–1.0 g one to three times a week	Most common reason for discontinuation is messiness.
17β estradiol vaginal ring	Estring	Change the ring every 90 days	Estring is local estrogen with minimal systemic absorption.
Estradiol acetate vaginal ring—systemic	Femring	Change the ring every 90 days	Femring is a systemic product approved for relief of vasomotor symptoms. It must be used with a progestin if a uterus is present.
17β estradiol vaginal softgel insert	Imvexxy	Initial treatment: 1 insert intravaginally q.h.s. × 14 days followed by maintenance of 1 insert twice a week	Comes in 2 strengths: 4 mcg and 10 mcg. Does not need an applicator.
Prasterone (DHEA) vaginal tablet	Intrarosa	Insert a vaginal tablet q.h.s.	Does not have same package insert warnings as estrogen. Has not been studied in individuals with a history of breast cancer.
Ospemifene oral tablet	Osphena	Oral	Good option if individual unable or unwilling to use a vaginal product. Most common side effect is hot flashes. Has not been studied in individuals with a history of breast cancer.
4% Lidocaine Hydrochloride Topical Solution	Xylocaine and generics	Apply a small amount with a cotton swab to the vaginal introitus prior to intercourse	Effective relief of dyspareunia for individuals who are not able to use estrogen products.

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Clinical Recommendation	Evidence Rating	References
Vaginal estrogen is first-line therapy for genitourinary syndrome of menopause (GSM).	A	American College of Obstetricians and Gynecologists (ACOG), 2014 North American Menopause Society (NAMS), 2017
Nonestrogen water-based or silicone-based vaginal lubricants and moisturizers may alleviate vaginal symptoms	B	ACOG, 2014
Low-dose vaginal estrogen has minimal systemic absorption.	B	NAMS, 2017
Low-dose vaginal estrogen can be considered for those successfully treated for endometrial cancer if nonhormonal options are unsuccessful.	B	NAMS, 2017
For individuals with a history of breast cancer, decisions about low-dose vaginal estrogen should involve the oncologist.	C	NAMS, 2017

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LICHEN SCLEROSUS (VULVAR)

Signal Symptoms: Pruritis, dyspareunia, and pain, although may be asymptomatic (Krapf et al., 2020; Ringel & Iglesia, 2020).

Description: An autoimmune skin disorder affecting the vulva and anogenital tissues. Epithelial thinning and inflammation cause whitened plaques involving the labia minora, labia majora, clitoral region, or anogenital area. If untreated, lichen sclerosus (LS) can result in changes in the architecture of the external genital structures and scarring (Krapf et al., 2020; Ringel & Iglesia, 2020). Decreased sexual interest and activity and pain with sexual activity is common (Krapf et al., 2020).

Etiology: Although LS is considered an autoimmune disease and there are genetic predispositions, the exact etiology is unknown (ACOG, 2020; Fergus et al., 2020; Krapf et al., 2020).

Occurrence: LS occurs in individuals assigned female or male sex at birth. The ratio of female to male is estimated at 3:1 to 10:1 (Fergus et al., 2020). Exact incidence is difficult to assess because many are asymptomatic and LS may be unrecognized by both patients and clinicians (ACOG, 2020). One frequently cited estimate is an incidence of 1.7% of the general population, but this is probably an underestimate (Ringel & Iglesia, 2020). In the setting of long-term care facilities, it is estimated that 1 in 32 individuals may have LS (ACOG, 2020).

Age: Can occur at any age but is more common in older adults. A bimodal distribution of LS occurring most commonly in those before puberty and then after menopause has historically been reported, but newer information suggests that LS is underdiagnosed and underreported in the ages between puberty and menopause (Krapf et al., 2020). The mean age at diagnosis is between ages 52 and 60 (Chamli & Souisi, 2021).

Ethnicity: Not significant.

Contributing Factors: A family history of LS is a contributing factor, as there is a known genetic component to the disease (Fergus et al., 2020). Those with incontinence may develop LS as there is evidence that chronic exposure of the genital tissues to urine is associated with LS (Fergus et al., 2020). Other contributing factors may include genital piercings, higher body mass index, diabetes, hyperlipidemia, tobacco use, hypertension, and coronary artery disease (Fergus et al., 2020).

Signs and Symptoms: When symptoms are present, they commonly include genital itching, burning, and pain. Itching is typically the predominant symptom, and it is worse at night (Chamli & Souissi, 2021). Dyspareunia is common (Krapf et al., 2020). Many individuals experience no symptoms, even with advanced disease (Krapf et al., 2020). On physical examination, the genital epithelium is thin and may be wrinkled with hypopigmented or white patches. The typical presentation is for the whitened areas to be in a "keyhole" pattern around the clitoris and the perineal area (Chamli & Souissi, 2021). In advanced cases, there may be changes to the genital architecture, with narrowing of the vaginal introitus and resorption of the labia (Krapf et al., 2020).

Diagnostic Tests: LS is usually diagnosed by clinical presentation (ACOG, 2020; Chamli & Souissi, 2021; Krapf et al., 2020). Biopsy of the lesion is recommended if the presentation is atypical, not responsive to treatment, or cancer is suspected (ACOG, 2020; Chamli & Souissi, 2021; Fergus et al., 2020). There are no other specific diagnostic tests for LS.

Differential Diagnosis (ACOG, 2020; Chamli & Souissi, 2021):

- Atopic and contact dermatitis
- Crohn's disease
- Eczema
- Genitourinary syndrome of menopause
- Herpes infection

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- Hidradenitis suppurativa
- Infestation of scabies or pediculosis
- Lichen planus
- Lichen simplex chronicus
- Morphea
- Nerve compression or injury
- Neuroma
- Paget disease
- Post-chemotherapy or post-radiation pain
- Postherpetic neuralgia
- Psoriasis
- Tinea cruris
- Trauma
- Vitiligo
- Vulvar precancerous or cancerous lesions
- Vulvovaginal candidiasis

Treatment: Standard treatment for LS is clobetasol 0.05%. Ointment is preferred over cream. Dosing regimens vary, but there is general agreement to apply to the affected area one to two times a day for 4 weeks, followed by a tapering of dose over the next 2 months (ACOG, 2020; Fergus et al., 2020; Krapf et al., 2020; Ringel & Iglesia, 2020). Treatment of asymptomatic LS is recommended to stop progression of the disease (Fergus et al., 2020). If clobetasol is ineffective, treatment with a topical calcineurin inhibitor such as tacrolimus or pimecrolimus can be considered (Fergus et al., 2020; Krapf et al., 2020; Ringel & Iglesia, 2020). Photodynamic therapy, high-frequency ultrasound, and fractional carbon dioxide laser have been studied in the treatment for LS, but more evidence is needed before these are considered first-line therapies (Krapf et al., 2020). Other less common therapies include injection of triamcinolone acetonide into the lesion, with a maximum total dose of 40 mg, and oral treatments such as retinoids, methotrexate, and hydroxyurea (Ringel & Iglesia, 2020). Surgical treatment is reserved for treatment of cancer or release of adhesions and correction of vaginal introital stenosis (ACOG, 2020; Krapf et al., 2020).

Follow-Up: Initial follow-up should occur 3 to 6 months after initiation of treatment. If there is a lack of response to treatment, ability to adhere to the treatment regimen and confirmation of the diagnosis with biopsy should be considered (ACOG, 2020; Ringel & Iglesia, 2020). Long-term follow-up should continue every 6 months, and when remission is achieved, an individualized plan for long-term steroid therapy should be developed (ACOG, 2020; Ringel & Iglesia, 2020). Any new or worsening symptoms should prompt reevaluation (ACOG, 2020).

Sequelae: Untreated LS may lead to scarring, narrowing of the vaginal introitus, resorption of the labia, impaired sexual functioning, and vulvar cancer (Krapf et al., 2020). Risk of progression to vulvar cancer is approximately 5% (ACOG, 2020; Fergus et al., 2020; Ringel & Iglesia, 2020).

Prevention/Prophylaxis: Although there is no known prevention for LS, addressing incontinence and preventing chronic contact of urine with genital tissues is recommended. Early diagnosis and treatment, particularly for those with a family history, will help maintain sexual function and prevent progression.

Referral: Referral to a vulvar dermatoses specialist may be indicated when there is no response to treatment and other causes have been excluded (ACOG, 2020).

Education: Periodic self-inspection of the vulva, particularly for those with a family history, can identify early LS. The rationale for long-term therapy and follow-up should be explained. Discontinuation of therapy is one reason for a lack of response to treatment, and may result in loss of sexual functioning and an increased risk of vulvar cancer (ACOG, 2020; Chamli & Souissi, 2021).

Clinical Recommendation	Evidence Rating	References
Long-term, individualized topical corticosteroid therapy is recommended to prevent progression.	B	American College of Obstetricians and Gynecologists (ACOG), 2020
For individuals with a confirmed diagnosis unresponsive to topical or intralesional corticosteroids, topical calcineurin inhibitors can be considered.	B	ACOG, 2020
Monitoring at 3 months following initial therapy is recommended to assess the response to therapy.	C	ACOG, 2020
In poorly controlled or resistant disease, intralesional corticosteroid injections can be considered.	C	ACOG, 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

OVARIAN CANCER

Signal Symptoms: None; most women are asymptomatic until the disease is in an advanced stage.

Description: Cancer of the ovary is the most lethal of pelvic malignancies in women. Cancerous processes in the ovary and fallopian tube and primary adenocarcinoma of the peritoneum share the same clinical presentation, and all are managed as a single disease process of ovarian cancer (Orr & Edwards, 2018). Many ovarian cancers actually start in the

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fallopian tube (Stewart et al., 2019). Histologically, epithelial ovarian cancer predominates, accounting for approximately 90% to 95% of all tumors (American Cancer Society [ACS], 2021; Lheureux et al., 2019). Germ cell and sex cord stromal histological types account for the other tumors. Within the broader category of epithelial tumors, there are four main subtypes: serous, endometroid, mucinous, and clear cell. The rest are undifferentiated and mixed epithelial carcinomas (Stewart et al., 2019). Serous carcinoma is categorized as high grade (HGSC) or low grade (LGSC), and 70% to 80% of all serous carcinomas are HGSC, which has a poorer prognosis than LGSC (Stewart et al., 2019). The World Health Organization categorizes ovarian tumors as type 1, which present clinically as a large mass, progress slowly, and have a good prognosis. These are typically LGSC, clear cell, mucinous, or transitional cell types (Lisio et al., 2019). Type 2, the majority of tumors, are high-grade lesions with few known risk factors, a rapid spread, and a poor prognosis (ACS, 2021; Lisio et al., 2019).

Etiology: Unknown.

Occurrence: Ovarian cancer only occurs in individuals assigned female sex at birth. It is estimated that in 2021, 21,410 women will be diagnosed with ovarian cancer, and 13,770 will die of the disease (ACS, 2021). Late diagnosis is the primary reason for the poor prognosis. Less than 20% of cancers are detected at an early stage (ACS, 2021; Chandra et al., 2019). For women in the United States, the lifetime risk for developing ovarian cancer is 1.3%, and for those with *BRCA* gene mutations the lifetime risk is 45% (ACS, 2018b; Menon et al., 2018).

Age: The median age at diagnosis is 63, and the peak incidence of epithelial ovarian cancer is for individuals in their 70s (ACS, 2018b; Lisio et al., 2019). Germ cell tumors occur most commonly in adolescents and younger individuals, whereas sex cord stromal tumors occur most often in individuals in their 50s (ACS, 2018b).

Ethnicity: The incidence of ovarian cancer is highest in northern and central Eastern Europe, with lowest rates in Asia and Africa (Lisio et al., 2019). In the United States, ovarian cancer incidence is highest in non-Hispanic White women followed by American Indian or Alaskan Native, Hispanic, Asian and Pacific Islander, with the lowest incidence in non-Hispanic Black women (ACS, 2018a; Lisio et al., 2019). Those of Ashkenazi Jewish descent have an increased risk, primarily because of an increase in *BRCA* gene mutations in that population (Menon et al., 2018). Despite the fact that non-Hispanic Black women in the United States have lower rates of cancer incidence, they have mortality rates second only to non-Hispanic White women. In addition to a higher stage at diagnosis and an increased incidence of comorbidities, Black women are less likely to receive guideline-based treatment and are more likely to have treatment delayed or to not receive treatment at all (ACS, 2018b; Lheureux et al., 2019).

Contributing Factors: Increasing age and family history are the most important risk factors for ovarian cancer (ACS, 2018b, 2021). With a first-degree relative with ovarian cancer, the relative risk (RR) is 4.0, and with a second-degree affected relative, the RR is 2.0 (ACS, 2018b). Risk increases by 70% if there is a first-degree relative with a history of breast cancer (ACS, 2018b). If there is a *BRCA1* or *BRCA2* gene mutation or Lynch syndrome family history, there is an increased risk for breast and ovarian cancer (Lheureux et al., 2019). Approximately 20% of all ovarian cancer is related to a *BRCA* gene mutation (ACS, 2018b). Other risk factors include a personal history of breast cancer, endometriosis, pelvic inflammatory disease, the use of postmenopausal hormone therapy, late menopause, early menarche, nulliparity or having the first child after age 30, obesity, and tall height (ACS, 2021; Lheureux et al., 2019; Lisio et al., 2019; Menon et al., 2018). Rare mucinous tumors are associated with tobacco use (ACS, 2021). Preventive factors include having the first child before age 30 and multiparity, breastfeeding, tubal ligation or salpingectomy, use of an intrauterine device, and use of oral contraceptives (ACS, 2021; Lheureux et al., 2019; Lisio et al., 2019; Menon et al., 2018). There is some evidence that regular use of aspirin or nonsteroidal anti-inflammatory medications might be protective (Lheureux et al., 2019; Menon et al., 2018). There is no reliable evidence that the use of talcum powder is associated with a risk of ovarian cancer (ACS, 2021). Risk reduction for individuals at high risk includes bilateral salpingo-oophorectomy. Salpingectomy with delayed oophorectomy can be considered if childbearing is desired (Menon et al., 2018).

Signs and Symptoms: Ovarian cancer is typically asymptomatic until there is spread outside of the ovary. Once there is dissemination of cancer cells into the peritoneum, the individual may experience a variety of symptoms based on site of implantation including pelvic or abdominal pain or pressure, vaginal discharge or bleeding, gas/bloating, early satiety, constipation, or urinary symptoms such as frequency or urgency. Pain is not usually a symptom of early disease (Orr & Edwards, 2018). Because many of these symptoms are nonspecific and occur with other health conditions, they are frequently overlooked by patient and health-care professional alike (Lheureux et al., 2019). A number of tools have been developed to aid in the earlier detection of ovarian cancer. Some tools use symptom questions alone and some are combined with laboratory testing. To date, no one tool has enough sensitivity or specificity to recommend it for screening, and there is not yet evidence on outcomes related to prediction tools (Funston et al., 2020). Common physical findings include abdominal distention, lower leg edema, and abnormal pelvic examination findings such as an adnexal mass (Orr & Edwards, 2018).

Diagnostic Tests: For individuals with symptoms, a complete history and physical examination, including a pelvic examination and imaging with transvaginal ultrasound, computed tomography (CT), or magnetic resonance imaging (MRI), should be considered. Although a number of models using tumor characteristics on imaging and other factors have been proposed to confirm the diagnosis of ovarian cancer, none have so far shown to be superior to pattern recognition of tumor characteristics and vascular flow by experienced ultrasonographers (Shetty, 2019a). A complete blood count (CBC), cancer antigen 125 (CA-125) and other tumor markers, chest x-ray, and liver function tests (LFTs) are also part of the initial evaluation (Armstrong et al., 2021; Orr & Edwards, 2018).

There are currently no screening tests for individuals at average risk (Lheureux et al., 2019). Routine bimanual pelvic examinations are no longer recommended (American College

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of Obstetricians and Gynecologists [ACOG], 2018; U.S. Preventive Services Task Force [USPSTF], 2017). For individuals at high risk, regular pelvic examinations in combination with a transvaginal ultrasound and CA-125 can be considered, but these tests have not decreased mortality related to ovarian cancer and are associated with a high rate of false positives (ACS, 2021).

Differential Diagnosis (Shetty, 2019b):

- Benign ovarian mass including ovarian and paraovarian cysts
- Broad ligament fibroid
- Distended bladder
- Diverticular abscess
- Fallopian tube abnormalities
- Irritable bowel syndrome
- Pelvic inflammatory disease
- Pelvic kidney
- Peritoneal tuberculosis
- Stool-filled sigmoid colon
- Tubo-ovarian abscess

Treatment: All patients with a diagnosis of ovarian cancer should have an evaluation by a gynecologist oncologist (Orr & Edwards, 2018). Treatment is based on the individual's age, overall health status and comorbidities, and stage and genetic features of the cancer. Unless the cancer is at an advanced stage or the individual is not a surgical candidate, the first treatment is **s**urgical excision, usually a staging laparotomy, with total abdominal hysterectomy and bilateral salpingo-oopherectomy (ACS, 2021; Armstrong et al., 2021; Orr & Edwards, 2018). Neoadjunctive chemotherapy may be used prior to surgery. Early-stage disease may be treated with surgery alone (Orr & Edwards, 2018). For cancers staged II or III, debulking of the tumor is done followed by 3 to 6 months of a platinum- and taxane-based chemotherapy. Chemotherapy may be delivered systemically or into the peritoneum (ACS, 2021; Orr & Edwards, 2018). Targeted therapy with bevacizumab may be used in addition to chemotherapy, especially for recurrent cancer (Lheureux et al., 2019; Orr & Edwards, 2018). Poly (ADP-ribose) polymerase (PARP) inhibitors can be used as maintenance therapy or as an additional treatment for those with *BRCA* gene mutations or who have become resistant to platinum-based chemotherapy (Armstrong et al., 2021; Lheureux et al., 2019).

Follow-Up: Surveillance guidelines include physical and pelvic examinations and CA-125 measurements (if initially elevated) every 2 to 4 months for the first 2 years, every 3 to 6 months for the next 2 years, and annually starting at year 5. If genetic counseling and/or testing was not done previously, it should be done postoperatively. Imaging is scheduled as indicated (Armstrong et al., 2021).

Sequelae: The average 5-year survival rate for all stages is 48% (ACS, 2018a). If the disease is localized, the 5-year survival rate is 93%, but only 16% of new cases are localized to the ovary (ACS, 2021). Although 80% to 90% of ovarian cancers will initially respond to chemotherapy, most will recur over time, and the 5-year survival for metastatic cancer is 29%. Most cancers return within 1 to 4 years (ACS, 2018a; Kossaï et al., 2018; Lheureux et al., 2019). Tumors associated with *BRCA* gene mutations respond more positively to chemotherapy and have a better prognosis than those not associated with *BRCA* gene mutations (Kossaï et al., 2018). Individuals younger than age 65 have twice the survival rate of individuals older than 65 (ACS, 2021).

Prevention/Prophylaxis: In women who are high risk due to genetic mutations (*BRCA1* or *BRCA2*), a risk-reducing bilateral salpingo-oophorectomy (RRSO) may be considered (ACS, 2021), ideally at the age of 35 to 40 years, on completion of childbearing (Armstrong et al., 2021). However, after this surgery is performed, these women are at higher risk for cardiovascular events and osteoporosis due to premature menopause. Combined hormonal contraceptive pills for at least 2 years is a preventive strategy, and high-risk individuals could consider aspirin therapy (Lheureux et al., 2019; Menon et al., 2018).

Referral: Individuals with a significant family history of ovarian or breast cancer should be referred for genetic counseling. All individuals with a diagnosis of ovarian cancer should be referred to a gynecological oncologist. Because of the lethality of the disease, referrals for psychological, social, and spiritual support should be considered as well as referrals for palliative care for advanced disease (Stewart et al., 2019).

Education: Routine screening for women without a family history of ovarian cancer is not currently recommended. Individuals should be encouraged to report the vague persistent symptoms that are associated with ovarian cancer.

Clinical Recommendation	Evidence Rating	References
Individuals with a personal or family history of breast or ovarian cancer or a family history of known or suspected *BRCA* gene mutations should be offered genetic counseling.	B	USPSTF, 2017
Routine pelvic examinations are not recommended for asymptomatic individuals.	C	ACOG, 2018 USPSTF, 2017
The gynecological oncologist is the best provider to perform the initial surgery and determine treatment.	A	Armstrong et al., 2021
For individuals at average risk of ovarian cancer, there is no effective screening method.	A	ACOG, 2018 USPSTF, 2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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PELVIC ORGAN PROLAPSE

Signal Symptoms: Vaginal bulge, pelvic pressure, urinary incontinence or retention, fecal incontinence or retention, sexual dysfunction (American College of Obstetricians and Gynecologists [ACOG], 2019).

Description: Pelvic organ prolapse (POP) is caused by a weakening of the connective tissues of the pelvic floor, resulting in a relaxation of the anterior vaginal wall, the posterior vaginal wall, and/or the ligaments supporting the uterus (Fig. 15-1). This relaxation causes herniation of organs into the vagina: cystocele or urethrocele if the anterior wall is involved, rectocele if the posterior wall is involved, and uterine descensus if uterine ligaments are involved (ACOG, 2019; Weintraub et al., 2020). Relaxation of the apex of the vagina after hysterectomy can cause herniation of bowel into the vagina, called an enterocele (ACOG, 2019). The symptoms of POP are related to negative body image, depression, decreased quality of life, and difficulty achieving activities of daily living (Bugge et al., 2020; Lawson & Sacks, 2018).

Etiology: It is known that there is a genetic component to POP, although no specific cause has been identified (Good & Solomon, 2019; Weintraub et al., 2020). Any condition that results in weakening of the pelvic floor or increased abdominal pressure on the pelvic region can contribute to the development of POP (Good & Solomon, 2019; Weintraub et al., 2020).

Occurrence: POP is most common in those identified female sex at birth. It is estimated that 3% of U.S. women report vaginal symptoms of prolapse; however, because most prolapse is asymptomatic, up to 50% of women have some degree of prolapse identified on examination (ACOG, 2019). It is estimated that 1.5 to 1.8 in 1,000 women per year have surgery for POP (ACOG, 2019). POP in those identified male sex at birth may occur, and primarily involves rectal prolapse. Men are underrepresented in studies on POP, and information on incidence is unknown (Giagio et al., 2021). POP can occur in those with a neovagina after male to female transition surgery, but the incidence is unknown (Manrique et al., 2019; Roslan et al., 2019).

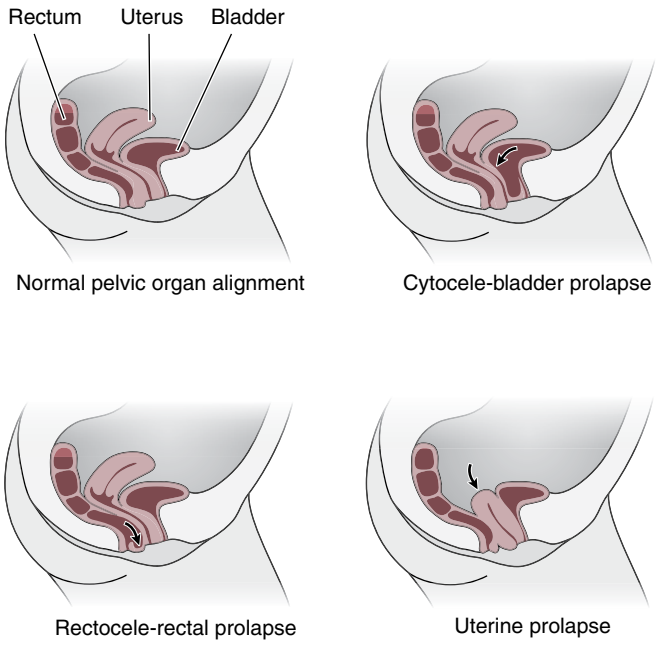

FIGURE 15-1 Types of pelvic organ prolapse. (Adapted from Irion, J. M., and Irion, G. L. (Eds.). *Women's health in physical therapy*. Lippincott Williams & Wilkins, Philadelphia, 2010, p 119.)

Age: POP can occur at any age, but the risk increases with age. Peak incidence is in those ages 70 to 79 (ACOG, 2019; Weintraub et al., 2020).

Ethnicity: Not significant

Contributing Factors: Increasing age is a main contributing factor (Weintraub et al., 2020). Pelvic floor laxity is associated with genetic factors, increased parity, particularly with vaginal births, obesity, chronic constipation, heavy lifting, connective tissue disorders, and menopausal status (ACOG, 2019; Bugge et al., 2020; Good & Solomon, 2019; Weintraub et al., 2020). Evidence on hysterectomy and strenuous exercise as risk factors for POP is mixed (ACOG, 2019; Bø & Nygaard, 2020). There is a risk of recurrence after surgery for POP, which is increased by having a more significant prolapse before surgery, family history of POP, obesity, and having surgery before age 60 (ACOG, 2019; Friedman et al., 2018).

Signs and Symptoms: Symptoms include feeling something bulging from the vagina, pelvic pressure, backache, urinary incontinence or retention, fecal incontinence or retention, dyspareunia, decreased libido, and avoidance of sex due to embarrassment (ACOG, 2019; Bugge et al., 2020; Good & Solomon, 2019; Lawson & Sacks, 2018; Rantell, 2019). On physical examination, the prolapse may be visible on inspection either with or without the aid of separation of the vulvar tissues and the use of a speculum (ACOG, 2019).

Diagnostic Tests: Evaluation includes a complete history, particularly of symptom severity, and a physical examination. Assessing whether POP is affecting urination, defecation, sexual functioning, or activities of daily living in addition to ascertaining if symptoms are worsening is crucial (ACOG, 2019). The physical examination should include an abdominal examination to assess for masses. The pelvic examination should include inspection for the degree of atrophy of external tissues, assessment of pelvic floor muscle tone, and to identify whether any prolapse is visible without the aid of a speculum. The speculum examination is performed with the lower half of a bivalve speculum. The half speculum is placed in the posterior vagina to evaluate for relaxation of the anterior vaginal wall and apex of the vagina and the half speculum is then rotated to retract the anterior vaginal wall to evaluate the posterior vaginal wall and perineal body. It can be helpful to have the patient perform a Valsalva maneuver or cough during the examination to evaluate the extent of prolapse (ACOG, 2019). A complete history and physical examination are usually sufficient for diagnosis of POP. Standard scoring of the extent of prolapse with the International Continence Society Pelvic Organ Prolapse Quantification (POP-Q) tool is recommended, particularly if surgery is anticipated. The POP-Q tool assesses nine points in the vagina, using the hymen as the reference point or zero value. At each of the nine points, structures are evaluated as being above or below the hymen in centimeters

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TABLE 15-4 Stages of Pelvic Organ Prolapse

STAGE	DESCRIPTION OF THE MOST DISTAL PROLAPSE
0	No prolapse. All structures are 3 cm or more above the hymen
I	More than 1 cm above the hymen
II	Between 1 cm above and 1 cm below the hymen
III	Between 1 cm and 2 cm below the hymen
IV	At least 2 cm below the hymen

Source: *ACOG and the American Urogynecologic Society, 2019*

(Good & Solomon, 2019). POP can be staged based on the system in Table 15-4. Urodynamics or other testing may be indicated based on symptoms (ACOG, 2019).

Differential Diagnosis:

- Benign or malignant growth or tumor
- Chronic constipation
- Hemorrhoids
- Stress urinary incontinence
- Urge urinary incontinence

Treatment: Some degree of POP is a common finding on examination, and treatment is indicated only if the individual is symptomatic (ACOG, 2019). The most common initial treatment includes pelvic floor muscle therapy and use of a pessary (Good & Solomon, 2019). Pessaries (Fig. 15-2) are polyvinyl chloride (PVC), latex, or silicon devices inserted into the vagina that provide passive support to the pelvic structures (Bugge et al., 2020; Good & Solomon, 2019; Rantell, 2019). The type and size of pessary is determined by symptoms and pelvic anatomy. The two types of pessaries are support (e.g., ring) and space filling (e.g., gelhorn). Compared to space-filling pessaries, support pessaries are compatible with intercourse and are easier to insert and remove (Bugge et al., 2020; Rantell, 2019). Pessaries need to be removed, cleaned, and reinserted on a regular basis. This may be done by individuals themselves, if possible, on a daily or weekly basis, or by the health-care provider every 3 to 4 months (ACOG, 2019). Two pessaries that must be removed and cleaned daily are the cube and inflatoball pessaries. Failure to remove and clean these daily can result in ulceration and infection of the vagina. These two pessaries are not recommended for those who are not able to perform self-management (Rantell, 2019). Although pessaries have been recommended as first-line treatment for decades, a Cochrane review reported that in four small randomized control trials, pessaries were not effective by themselves, but they may be effective in combination with pelvic floor physical therapy (Bugge et al., 2020). The review recommended more robust research to evaluate pessaries as a treatment option (Bugge et al., 2020). Surgical treatment is indicated for bothersome symptoms when first-line therapies are ineffective or declined (ACOG & The American Urogynecologic Society, 2019). For individuals with significant comorbidities who no longer desire preservation of the vagina or vaginal sexual activity, a minimal surgical procedure to eliminate the vaginal opening (colpocleisis) done under local or regional anesthesia can be a safe and effective treatment option (ACOG & The American Urogynecologic Society, 2019).

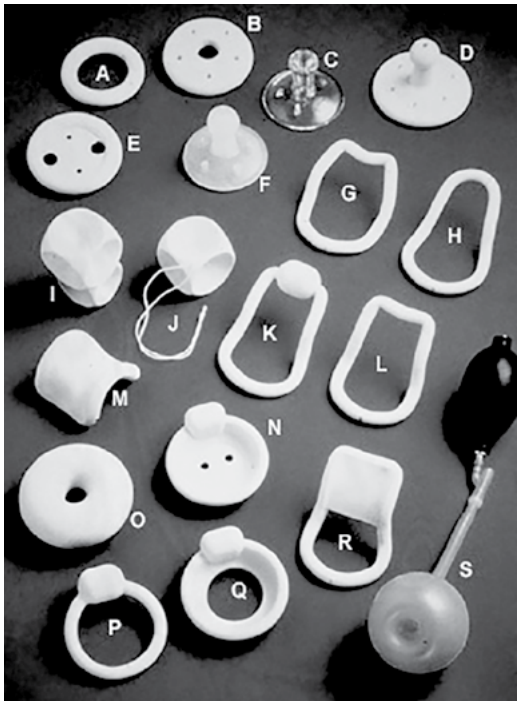

FIGURE 15-2 Types of pessaries. (A) Ring, (B) Shaatz, (C) Gellhorn, (D) Gellhorn, (E) Ring with support, (F) Gellhorn, (G) Risser, (H) Smith, (I) Tandem cube, (J) Cube, (K) Hodge with knob, (L) Hodge, (M) Gehrung, (N) Incontinence dish with support, (O) Donut, (P) Incontinence ring, (Q) Incontinence dish, (R) Hodge with support, (S) Inflatoball (latex).

Follow-Up: If a pessary is in place, and the patient is not maintaining it, then a visit every 3 to 4 months is indicated. If the patient is performing self-maintenance, then a yearly examination is indicated (ACOG & The American Urogynecologic Society, 2019).

Sequelae: Untreated POP often progresses slowly, if at all, so treatment is reserved for POP that is symptomatic (ACOG & The American Urogynecologic Society, 2019). Use of a pessary can result in vaginal erosion, and fistula is a rare complication (ACOG & The American Urogynecologic Society, 2019). If surgery is performed, postoperative sequelae may include bleeding, infection, and temporary urinary dysfunction (ACOG & The American Urogynecologic Society, 2019).

Prevention/Prophylaxis: Performing pelvic floor strengthening exercises, particularly after childbirth, and avoiding constipation can decrease the risk of POP (Good & Solomon, 2019).

Referral: If nonsurgical options are ineffective or not indicated, or if the physical examination findings do not concur with symptomatology, referral to a gynecologist or urogynecologist is indicated (ACOG & The American Urogynecologic Society, 2019). Referral to physical therapy for pelvic floor muscle training is often an initial treatment step.

Education: Educating patients on correct technique for pelvic floor strengthening exercises can help reduce the risk for POP. If there is a risk for chronic constipation, relief measures should be discussed. Assessing for POP and providing patients with resources if they are symptomatic can help patients regain or maintain quality of life (Good & Solomon, 2019; Hage-Fransen et al., 2021).

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Clinical Recommendation	Evidence Rating	References
Treatment of POP is indicated only if symptomatic.	B	ACOG, 2019
Women considering treatment of POP should be offered a vaginal pessary as an alternative to surgery.	B	ACOG, 2019
Obliterative procedures such as colpocleisis should be considered a first-line treatment for those with significant medical comorbidities who do not desire future vaginal intercourse or vaginal preservation.	B	ACOG, 2019
A POP-Q examination is recommended before treatment for the objective evaluation and documentation of the extent of prolapse.	C	ACOG, 2019

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CASE STUDY

A 72-year-old patient (she/her) presents to the outpatient office with a report of a new onset of urinary incontinence with exertion, particularly coughing, and a feeling of lower pelvic pressure. The patient is widowed, and not in a sexual relationship. Her gynecological history includes five normal spontaneous vaginal births, menopause at age 52 with no menopausal issues, and no use of hormone therapy. There is no surgical history, and the patient has an intact uterus and ovaries. Her medical history includes hypertension, which is well controlled with Lisinopril 20 mg orally daily and a history of intermittent bouts of chronic bronchitis treated with antibiotics and benzonatate (Tessalon perles) for cough. The patient presents regularly for care, and her last comprehensive physical examination was 6 months ago.

Vital signs: T 97.6°F, HR 98, RR 22, BP 130/82, BMI 35

Chief Complaint: New-onset urinary incontinence and pelvic pressure

1. What additional subjective information will you be asking the patient?
2. What additional objective findings would you be examining the patient for?
3. What are the differential diagnoses that you are considering?
4. What laboratory tests will help you rule out some of the differential diagnoses?
5. What screening tools will you select to use on this patient?
6. What is your plan of care?
7. What additional patient teaching may be needed?
8. Will you be looking for a consult?

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Ovarian Cancer

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CHAPTER 16

Musculoskeletal Disorders

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ASSESSMENT

To make an accurate assessment of the musculoskeletal system in the older adult, the nurse practitioner needs to be familiar with changes in the musculoskeletal system caused by aging. For example, aging often brings about a decrease in height, resulting from a decrease in the length of the trunk with respect to the length of the extremities. An older person may tilt the head backward to compensate for the bend in the thoracic spine, producing the typical posture of those in this age-group. Because of the loss of subcutaneous fat caused by aging, bony prominences became more noticeable. Some absolute loss of muscle mass occurs, with some muscles diminishing and others atrophying, resulting in sarcopenia (Strasser, 2020). With lean muscle loss there is commonly an increase in body fat, resulting in sarcopenia obesity (Kemp et al., 2018). Without continued use, muscles stiffen, and range of motion (ROM) becomes impaired as an older person ages (Manini et al., 2016).

Often when an older person experiences a limitation in functional ability resulting from pain, weakness, or physical impairment, they seek medical attention. A goal of the nurse practitioner in gathering the subjective information from the older adult is to try to determine whether there is a pattern of symptoms (Browne & Merrill, 2015).

To obtain an accurate history of musculoskeletal problems, ask the patient these questions:

- Is there any pain, swelling, stiffness, change in temperature perception (hot or cold), limitation of movement, weakness, body deformity, or paralysis?
- Are the symptoms constant or intermittent?
- What was the sequence of events that triggered the onset of each symptom and what are the precipitating factors? (Browne & Merrill, 2015)
- Is the muscle, joint, and/or periarticular signs and symptoms related to an accident, illness, or prior trauma?
- What time of day do the symptoms begin and for how long?
- Is there a family history of chronic musculoskeletal conditions?
- Review occupational and hobby history to determine an underlying contributing factor to pain and gross deformities.
- Is there a history of obesity?
- Is there a trigger to the complaint such as lack of mobility, temperature, or position (as in sleeping)? Often the patient complains of one or more of these symptoms; however, the condition may actually be a neurological condition (e.g., Parkinson's disease) or a systemic disorder (e.g., thyroid disease). Additionally, patients may be experiencing a new musculoskeletal condition concomitant with an existing condition, such as a new onset of gout with pre-existing osteoarthritis (OA) of the interphalangeal joints.

In addition, the nurse practitioner should:

- Determine whether the condition has been triggered by medications such as statins, with the known side effect of myalgias (Pedro-Botet et al., 2019), or steroids, which can contribute to bone loss.
- Briefly review dietary history to determine pattern on calcium intake.
- Be alert for other symptoms the patient may describe; for example, constitutional symptoms of fever and malaise may be clustered to form a differential diagnosis (Resnick, 2022).
- Review prior therapy and results, determining what the patient has used in the past to alleviate symptoms to include herbal products such as chondroitin, use of complementary or alternative treatments such as heat or cold, massage, ultrasound, and/or acupuncture or pressure.

Pain or Stiffness

Initially, the nurse practitioner will need to determine whether the presenting symptoms arise from the joint, tendons, muscles, or periarticular structures, such as bursae (Hawker, 2017). Further questioning needs to help distinguish whether the condition is acute or chronic, to include an exacerbation of a former condition that had been deemed in remission or resolved. Is the patient experiencing an inflammatory or noninflammatory condition? It is important to remember that both can coexist in patients. Most importantly, determine how the pain and stiffness is affecting function and quality of life (Browne & Merrill, 2015).

When a patient complains of pain or stiffness with movement, the history of the complaint should be discerned. Ask

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whether the patient has experienced any severe trauma in the past that may be now manifesting itself as an articular degeneration. Because patients who have had a structural deformity or amputation typically place excessive strain on the joints for years, older individuals may experience degeneration of the bone and surrounding musculature. An overextension or a recent increase in activity may lead to muscle soreness, followed by disuse, atrophy, and chronic pain. Adhesive capsulitis or frozen shoulder is a common condition in patients experiencing pain in the shoulder and, in turn, limiting their ROM. Knowing the history of the presenting symptom may help you distinguish between a local inflammation and a systemic problem. Questioning the patient about the time of day when the symptoms of pain and stiffness occur is essential data to support the differential diagnosis. Rheumatic disease, for example, is associated with pain on waking, whereas osteoarthritic pain and stiffness worsen as the day progresses. It is important to remember that within the current cohort of older adults a stoic attitude toward pain may be displayed despite the presence of an acute or chronic musculoskeletal condition.

Weakness and Paralysis

Patients with musculoskeletal problems often complain of weakness and paralysis. Determine whether the disability is local or generalized, constant or intermittent. Local weakness or paralysis may be due to disuse because of pain, trauma, or a neurological problem. Generalized weakness may indicate a systemic disorder or recent deconditioning related to extensive immobility or frailty, as in the case of patients with sarcopenia (Dhillon & Hasni, 2017). Patients with an underlying thyroid disorder may have constant weakness, whereas those with rheumatoid arthritis (RA) may experience weakness intermittently (Resnick, 2022).

Muscular weakness should always be differentiated from subjective fatigue. Generally, proximal weakness results from a myopathy and distal weakness from a neuropathy (Larson & Wilbur, 2020). The patient should be asked about their ability to carry out certain activities of daily living (ADLs), such as:

- Does the patient have difficulty combing their hair?
- Can they lift objects?
- Does the patient have any trouble standing up after sitting in a chair?

Patients with a proximal weakness of the upper extremities may have difficulty grooming the hair or lifting objects. Those with a proximal weakness of a lower extremity may have trouble crossing the legs at the knees or walking. If a patient reports difficulty fastening buttons or turning doorknobs, a neuropathy involving the upper extremity is likely.

Nodularity

Another common complaint in patients with a musculoskeletal disorder is nodularity or deformity. In obtaining the history from a patient with a deformity, the examiner needs to know how long the patient has noticed the deformity:

- Did it occur suddenly?
- Was it the result of trauma?
- Has there been any change in the deformity since its onset, such as a new onset of pain, swelling, or erythema?
- Is there a family history of similar nodularity?

Physical Examination

Focus of the physical examination of the musculoskeletal system includes inspection, palpation, ROM, and joint special maneuvers. Observe for any noted asymmetry, atrophy, wasting, masses, and erythema of the muscles. Examine the skin specifically for any lesions or change in color that may be related to an acute or chronic musculoskeletal condition. Ecchymosis in the area of a joint may be indicative of tendon rupture. Joints and surrounding structures should be examined to determine presence of any deformities, nodularity, subluxation, abnormal angulation, limitation of movement, stability, and malalignment. Palpation may reveal swelling, change in temperature, tenderness, and crepitus (Suneja et al., 2020). Engage the patient in active ROM of joints necessitated by the specific complaint. Specific provocative maneuvers related to pathology occurring in that affected joint(s) is warranted during a focused examination.

GAIT

The initial physical examination of the musculoskeletal system can begin with observing the patient's gait. Overall assessment of gait includes an extensive examination of the lower extremities to include podiatric issues (examining patient's feet). Any gait abnormalities or problems in maintaining balance should be noted. Assessment of gait needs to consider the patient's stance and arm swing (Pirker & Katzenschlager, 2017). Observe for any limping or asymmetrical leg movement or noted deformities. An abnormal stance is referred to as an antalgic gait, often resulting from chronic hip pain and muscle atrophy. Note whether the patient is having difficulty in shifting weight from one leg to the other and instead relies on shoulder movement from side to side. This abnormality in arm swing is referred to as a lurch (Pirker & Katzenschlager, 2017).

Another important aspect of the gait examination is to note the patient's ability to sit in and rise from a chair. If a patient relies on a rocking motion and/or arm strength to stand, consider quadriceps weakness. More sophisticated testing is warranted if the patient demonstrates difficulty in performing this task because they could be at a high risk for falling (Pirker & Katzenschlager, 2017).

POSTURE

Note the patient's posture for any abnormalities of the trunk and spine. Examine the patient while the patient is standing erect to note any changes in the spinal curvature such as scoliosis. In older adults, kyphosis of the thoracic spine is accentuated. While looking at the older person from the side, the examiner may note that the spine appears to form the number 3. If the curve appears more to be a sharp angle, this is called a gibbus. A gibbus deformity of the spine resulting from a vertebral compression fracture may be the first evidence of osteoporosis (Williams, 2009).

RANGE OF MOTION

Patients presenting with a functional limitation should be asked to demonstrate active ROM, which should be performed smoothly and effortlessly. Remember that joint movements include flexion, extension, abduction, adduction, and external rotation. If the patient has limited active ROM, passive ROM should be performed. If the passive range exceeds the active range, the limitation is due to a muscle weakness.

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Patients may resist passive ROM because of fear, a neurological disorder, or a joint abnormality.

JOINT PAIN

When patients complain of joint-related pain, the practitioner needs to determine whether the underlying condition is articular, periarticular, or both. When examining the patient's joints, the joints should be inspected in a relaxed position and then in flexion and in extension. Abnormalities of the position or carrying angle, joint deformity, erythema, swellings, nodulation, and muscle changes should be assessed. In an older patient with muscle changes, the limb or portion of the body will appear thinner, which indicates atrophy. To determine whether bone structure changes have occurred, appearance and symmetry should be observed. Enlargement, excessive curvature, and irregularity may indicate sequelae of childhood rickets, osteoporotic fractures, Paget's disease, OA, tophaceous gout, or bone tumors. Crepitation or a crackling noise may be heard when the joints are put through ROM. Crepitation is produced by the rubbing together of bone or irregular cartilage surfaces (Suneja et al., 2020).

JOINT SWELLING AND NODULARITY

Specific questions about the duration of any swelling, presence of pain, limitation of movement, evidence of erythema, and locking or buckling of the joint are important to assess. Erythema is usually associated with active inflammation and accompanied by swelling. Examples of joint nodulation are the nodules found in the interphalangeal joints in patients with RA and OA. Heberden nodes are nodules of the distal interphalangeal (DIP) joints; Bouchard's nodes are nodules of the proximal joints. Both are found in patients with OA (Suneja et al., 2020). In RA, the metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints and wrist of both hands are commonly involved (Mohammed et al., 2021). Common nodularity/deformity in RA is swan neck deformity, which involves the hyperextension of the PIP joint and flexion of DIP joint, and boutonnière deformity, which is flexion of the PIP joint and hyperextension of the DIP joint (Fox & Chang, 2018).

Rheumatoid nodules are described as firm, nontender nodules often found on the dorsum of the wrist, elbow, or MCP joint (Cabling, 2020). Haygarth's nodes are spindle-shaped enlargements of the middle interphalangeal joints that occur in RA (Suneja et al., 2020). Patients presenting with "sausage-like" digits known as dactylitis may have reactive or psoriatic arthritis (Girolimetto et al., 2021).

Any joint deformity should be palpated to determine whether it fluctuates because of fluid or is firm because of a thickening or enlargement. If there is fluid, the cause may be recent trauma, inflammation, or joint infection. An articular enlargement of RA is usually soft, whereas a joint deformity found in OA is usually firm. Erythema may also be indicative of septic arthritis. If the joint swelling persists for more than 3 days, this may indicate an arthritic condition. Also examine the bursal areas around the joints, palpating for swelling, tenderness, ganglions, and presence of nodules. Tophaceous gout appears as salmon-colored nodules that do not transilluminate, as is possible when examining a superficial inflamed bursa (Williams, 2009). A ganglion is usually a soft cyst-like swelling, often found near joints. Swelling of the bursa is usually tender on palpation. All masses should be measured across their greatest diameter (Suneja et al., 2020).

MUSCLE WEAKNESS

For the patient complaining of muscle weakness, inspect for evidence of muscle atrophy and palpate the muscles during contraction and rest (Larson & Wilbur, 2020). Any fluttering or fasciculations of the muscles should be noted. To determine whether a patient is having true muscle weakness, the patient should perform against the examiner's resistance. One side should be compared with the other and a numerical value for tested muscle strength recorded. Flexor and extensor muscles should be tested for strength (Suneja et al., 2020). Testing of handgrip strength has been found to correlate with lean body mass (Kemp et al., 2018).

BURSITIS, TENDINITIS, AND SOFT TISSUE SYNDROMES

Signal Symptoms: Pain, inflammation, and/or swelling in the structures and tissues surrounding a joint including the bursa, ligaments, tendons and/or muscles

Description: Bursitis is irritation or inflammation of a bursa, a fluid-filled pad that protects soft tissues (such as muscles and tendons) from underlying bony prominences. Tendinitis is irritation or inflammation of the tendon, which is the fibrous connective tissue that attaches muscle to bone. Tenosynovitis is tendinitis that incorporates the tendon sheath lining. Enthesitis is inflammation or pain at the insertion site of tendons, ligaments, fascia, or joint capsules to the bone; it can be mistaken for tendinitis. Myofascial pain is firm knotted muscle pain often of the neck, shoulders, and back. Carpal tunnel syndrome is nerve pain caused by compression of the medial nerve within the wrist. Plantar fasciitis is inflammation and pain of the thickened fibrous aponeurosis that runs from the heel to the toes forming the arch of the foot (Biundo, 2020a; Hubbard et al., 2018; Kushner, 2020).

Etiology: Bursitis is commonly idiopathic or a result of trauma from injury or overuse. Bursitis can also occur with infection most often of the prepatellar and olecranon bursae, which also happens to be the most common locations for hemorrhagic bursitis. Tendinitis is frequently caused by overuse related to tasks such as work, sports/hobbies, and repeated microtrauma. Lateral epicondylitis (tennis elbow) is more common than medial epicondylitis (golfer's elbow) with the former occurring from repetitive forced extension and/or rotation of the wrist/hand and the latter occurring from repetitive clenching of the fingers, such as with golf. Myofascial pain can be the result of poor posture, strain, minor injury, or from degenerative arthritis. Carpal tunnel syndrome can occur from multiple causes including inflammatory arthritis, infection, and overuse/poor positioning. Plantar fasciitis can be caused by pes planus, standing for long periods, running, change in typical shoe height, or heel spurs (Biundo, 2020a; Hubbard et al., 2018; Kushner, 2020).

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Occurrence: Prevalence varies by population and can occur at any time, but these syndromes are most commonly associated with manual labor and athletics (Hubbard et al., 2018). There typically is no clear trend in the incidence of soft tissue syndromes between men and women other than the prevalence related to the underlying cause such as higher incidence of gout in men and inflammatory arthritis in women (Loiacono et al., 2019). Morton's neuroma, however, occurs five times more frequently in women than men (Santiago et al., 2018).

Age: Other than inflammatory arthritis, which affects a younger population; incidence increases with each decade of life after 40 years of age (Loiacono et al., 2019).

Ethnicity: No clear trend related to ethnicity other than incidence within specific populations of underlying cause.

Bursitis and tendinitis can occur secondary to an inflammatory arthritis such as gout or rheumatoid arthritis (RA). Tenosynovitis is often caused by inflammatory arthritis, particularly RA, and can occur with infection. Enthesitis is seen in the spondyloarthropathies, specifically psoriatic arthritis (Biundo, 2020b; Hubbard et al., 2018; Kushner, 2020). Inflammation and risk of tendon rupture, particularly of the Achilles, can occur with fluoroquinolones, more so when administered in conjunction with glucocorticoids and when given to an athletic person (Morales et al., 2019). Metabolic diseases, including diabetes, hyperlipidemia, obesity, and thyroid disease, contribute to tendon and ligament disorders. Carpal tunnel syndrome is commonly affected by metabolic disorders and in younger women, pregnancy (Loiacono et al., 2019).

Signs and Symptoms: Patients presenting with soft tissue syndromes experience pain of varying degrees with movement of the affected area. Acute bursitis is painful especially with motion when the bursa is stretched or compressed. Swelling is common with superficial bursitis such as of the olecranon or prepatellar bursa. Infectious and crystalline bursitis is frequently erythematous, painful, warm and can include pitting edema. Tendinitis pain presents with movement or resistance to movement of the affected tendon. Swelling can occur of the tendon sheath with inflammatory arthritis or infection, and is tender to palpation (Biundo, 2020b; Hubbard et al., 2018).

In assessing a patient, it is important not only to obtain a complete history of present illness, but review past medical history including recent procedures, medications, family history, and social history including occupation and hobbies/athletic activity. Pain associated with inflammatory arthritis will be more pronounced with rest and in the morning and improve with activity. In addition to determining timing and quality of pain, it is important to assess precipitating and alleviating factors.

Signs and symptoms will depend on the location of the area affected. Myofascial pain is associated with the trigger points of the neck, shoulders, and back. Shoulder pain could be subacromial bursitis, supraspinatus tendinitis, or rotator cuff tendinitis and impingement syndrome, which all affect the upper shoulder and the upper third of the arm; or bicipital tendinitis, which also causes shoulder pain but travels down the arm to the elbow and forearm. Elbow pain can include olecranon bursitis, which tends to affect the tip of the elbow; lateral epicondylitis, with pain on the outside of the elbow; or medial epicondylitis, with pain on the inside of the elbow at the respective locations of tendon attachment. Enthesitis of the lateral epicondyle can be difficult to differentiate from epicondylitis; however, enthesitis tends to include a painful nodule at the attachment site (Kaeley et al., 2018). The wrists and hands tend to be affected by de Quervain's tendinitis, which affects the wrist on the side of the thumb and is common after pregnancy; volar flexor tenosynovitis, which affects the volar aspect of the thumb or other fingers, radiates distally, and can lead to trigger finger; Dupuytren's contracture, which is abnormal thickening of skin at the base of the volar aspect of fingers and leads to contracture of the palm of the hand; and carpal tunnel syndrome, which can cause pain, numbness, and weakness of the first three fingers and the medial side of the fourth finger. Discreet swelling commonly of the wrist or hand may be a ganglion cyst; they tend to be painless and idiopathic (Biundo, 2020b; Hubbard et al., 2018).

Lateral hip pain is typically trochanteric bursitis and is noticed particularly with side sleeping or getting up from a deep chair or out of a car. Gluteus medius tendinitis often accompanies trochanteric bursitis, causing pain of the buttocks (typically while climbing stairs). Ischial bursitis causes pain of the buttocks that travels to the posterior thigh and occurs with long sitting on hard surfaces. Knee pain from bursitis is most commonly of the prepatellar bursa and includes swelling of the front of the knee; less often is infrapatellar bursitis from long kneeling with pain just below the knee; pes anserine bursitis occurs of the proximal anterior medial tibia and is noted with knee-to-knee contact with side sleeping, often with osteoarthritis (OA) of the knee, and with jogging. Enthesitis can occur of the medial femoral condyles of the distal femur but again can be difficult to differentiate from other musculoskeletal disorders. Painful, mostly discreet, posterior swelling of the knee may be a Baker's cyst secondary to OA. Ankle and foot soft tissue syndromes include retrocalcaneal bursitis of the posterior heel (often from ill-fitting shoes), calcaneal bursitis of the sole of the heel (often noted with heel spurs), and Achilles' tendinitis with pain, swelling, and ankle stiffness noted when pushing from the ball of the foot. Achilles' enthesitis tends to include a painful nodule at the attachment site. A Morton's neuroma is a painful nerve entrapment neuropathy and nodule most frequently of the third or second plantar intermetatarsal web space (Santiago et al., 2018). Patients may also present with tarsal tunnel syndrome affecting the medial nerve of the ankle, causing pain or burning of the sole of the foot and toes, or plantar fasciitis with pain of the sole of the foot, particularly with walking (Biundo, 2020b; Hubbard et al., 2018).

Diagnostic Tests: Diagnosis of soft tissue syndromes is primarily based on physical examination utilizing inspection, palpation, passive range of motion (ROM), active ROM, and special orthopedic maneuvers. X-rays are not useful with soft tissue syndromes except to identify bone spurs, calcifications, or to rule out another pathology such as a fracture or pseudogout. Ultrasound can be especially useful to assess deep bursae, cysts, tendon tears, and/or inflammation. Power (or color) Doppler can identify neovascularization of a pathological tendon (Loiacono et al., 2019). Magnetic resonance imaging (MRI) can be beneficial to assess inflammation and tendon pathologies as well as rule out other musculoskeletal disorders.

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Laboratory testing should be considered with concern for infection or a crystalline arthropathy, specifically aspiration of a bursa with analysis to include cell count, Gram stain, culture, and microscopy to identify crystals. Blood tests are not typically necessary—a complete blood count (CBC) could help assess for infection, a uric acid is best drawn when a patient is not having a gout flare, and inflammatory markers such as a C-reactive protein (CRP) and an erythrocyte sedimentation rate (ESR) should be reserved for when there is a high suspicion of an inflammatory or infectious process present (Ramakrishnan et al., 2015).

Differential Diagnosis:

- Soft tissue syndromes (bursitis, tendinitis, tenosynovitis, enthesitis, myofascial pain, carpal tunnel syndrome, plantar fasciitis, neuroma)
- Degenerative joint disease
- Infection (cellulitis, infected bursitis, septic joint)
- Inflammatory arthritis (e.g., gout, pseudogout, rheumatoid or psoriatic arthritis)
- Injury (strain, sprain, contusion, tendon rupture, fracture)
- Joint effusion

Treatment: Initial treatment of soft tissue syndromes should include rest and/or short-term immobilization (splint or brace) and use of intermittent heat or cold, respectively for chronic or acute inflammation. As pain and inflammation improve, gentle ROM and exercise should be started as tolerated and gradually increased. This is important to maintain good ROM and avoid contractures, which can develop of the elbow and shoulder in a short period, especially with chronic conditions. Physical therapy (PT) and therapeutic exercise are the cornerstone of treatment for soft tissue syndromes, particularly tendinopathy (Loiacono et al., 2019).

Pharmacological treatment options include addressing infection, inflammation, and the underlying cause. Empiric antibiotics for suspected infection should be initiated until Gram stain and culture results are available; then change accordingly if needed. Crystalline disease should be treated based on current recommendations. NSAIDs can be useful with inflammation and are typically given for 7 to 10 days. With any NSAIDs it is important to consider patient-specific contraindications, including kidney disease, cardiovascular risks, gastrointestinal considerations, and possible adverse medication interactions such as with anticoagulants. The challenge with NSAIDs, particularly with tendinopathies, is that tendons are not well vascularized; thus, there is not good bioavailability where needed. Short-term oral corticosteroids can be useful to reduce inflammation and associated pain without the renal risk; however, there is increased risk of infection and elevation of blood glucose, and they can be contributory to tendon rupture when given with fluoroquinolone antibiotics. Additionally, some studies indicate both NSAIDs and corticosteroids can negatively affect the regenerative processes of tissues (Loiacono et al., 2019).

In the absence of infection, soft tissue corticosteroid injection can be effective when other treatments fail. Indications for corticosteroid injection for soft tissue conditions include bursitis, tendinitis, trigger points, ganglion cyst, nerve entrapment syndromes, and plantar fasciitis. Injections for tendinitis should only be into the tendon sheath and never into the tendon as that can weaken it and increase risk of rupture. As with any injection, there is a risk of infection, and corticosteroid injections can also cause changes in pigmentation, fat atrophy, and elevate blood glucose (Biundo, 2020a).

Alternate treatment options include acupuncture, extracorporeal shock wave therapy, pulsed electromagnetic fields, intratissue percutaneous electrolysis, dry needling, and platelet-enriched plasma; however, studies often are limited and not all show definitive evidence of efficacy. Similarly hyaluronic acid injection studies are limited; however, there appears to be evidence to support anti-inflammatory properties as well as positive effects on collagen synthesis and cell proliferation. Insurance does not always cover these alternative therapies due to lack of evidence and/or efficacy (Loiacono et al., 2019).

Follow-Up: These syndromes are generally acute concerns that will resolve with a combination of nonpharmacological and pharmacological therapies; however, it is important for patients to follow-up if needed. Prescribed medications or antibiotics, arthrocentesis and joint injection, or referral may be necessary.

Sequelae: Soft tissue syndromes left untreated or suboptimally treated can become chronic, leading to degenerative changes and bone spurs/calcifications, and can negatively affect joint ROM. Chronic bursitis leads to bursal adhesions, villi formation, thickening of the bursa wall with proliferation of the synovial lining, and chalky deposits. Tendinopathy typically is a result of degenerative changes, which can include calcium deposits, or repetitive tearing from poor ergonomics and highly repetitive movements (Biundo, 2020a; Loiacono et al., 2019).

Prevention/Prophylaxis: Prevention of soft tissue syndromes requires modifying or avoiding activities that exacerbate the problem. This includes avoiding improper technique and poor positioning in sports and work; and avoiding overuse and repetitive movements for long periods. When soft tissue syndromes are secondary to another condition such as an inflammatory arthritis, it is important to address that to avoid these complications.

Referral: Referral to PT, occupational therapy (OT), or orthopedics may be necessary to further address the current problem or to provide education regarding necessary modifications.

Education: In addition to preventive measures, patients should be educated to maintain a good level of fitness with good strength and flexibility, ease into new exercise routines, use good, properly fitting equipment and shoes, and (when needed) utilize splints, braces, and orthotics. It is important to educate patients to not overwork tendons with overloading and/or repeated stretching because this can initiate the degenerative process by breaking down the collagen fibers (Loiacono et al., 2019). Patients with a history of tendinitis or those on corticosteroids should be educated on the possible adverse effects of fluroquinolones and tendon rupture.

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Clinical Recommendation	Evidence Rating	References
If no infection is present, treat most cases of bursitis and tendinitis with rest, NSAIDs, and intermittent hot or cold. When appropriate, treat with intrabursal corticosteroid injection.	A	Biundo, 2020a
Withdraw bursal fluid to diagnose bacterial or crystal-induced bursitis when the olecranon or prepatellar bursa is affected or when there is redness, tenderness, warmth, and pitting edema.	A	Biundo, 2020a
If septic bursitis is suspected, initial treatment should empirically cover against staphylococcal infection. Treatment regimen can be modified after culture results become available.	A	Biundo, 2020a
Never inject corticosteroids directly into a tendon; doing so can weaken it and increase risk of rupture.	A	Biundo, 2020b
Regular and well-structured exercise has a positive effect on the tendon tissue by strengthening it through the production of new collagen fibers.	A	Loiacono et al., 2019
Eccentric exercises have been shown to promote cross-linking of collagen fibers and facilitate tendon remodeling.	A	Loiacono et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

FRACTURES

Signal Symptoms: Soft tissue swelling, dislocation, altered range of motion (ROM), ecchymosis, local tenderness, pain with any motion.

Description: Fractures are a common cause of disability in older adults. Hip fractures and wrist fractures are among the two most common types of fractures in older adults. Specifically, in patients aged older than 65 years, distal radius fractures are the second most common fractures after hip fractures (Luokkala et al., 2020).

Etiology: Advanced age has been identified as a risk factor for fracture. The World Health Organization predicts that between 2000 and 2050, the proportion of those aged older than 60 will double in numbers from 11% to 22% or 605 million to 2 billion people (Downey et al., 2019). This increase in the older adult population will most certainly see an increase in the numbers of fractures seen in health care.

Occurrence: In the United States, osteoporosis accounts for over 1.5 million fractures annually. By 2050, the costs associated with osteoporotic fractures are expected to exceed $130 billion (Bartl & Bartl, 2019). Hip fractures can be particularly disabling. More than 250,000 hip fractures occur in the United States each year. Estimates show that 30% of people aged 65 years and older fall each year; in that group, 5% of those falls result in fractures. Hip fractures are increasing with excess of 6 million per year predicted in 2050 (Downey et al., 2019).

Age: Our nationwide data indicate the prevalence of hip fractures in older adults is generally on the rise, and the female occupies a higher proportion. Age (especially aged 80 years and older), race (mainly non-Hispanic white), smoking, drinking alcohol, living alone, combined with diabetes and osteoporosis may be closely linked to the occurrence of hip fractures in older adults (Zhang et al., 2021). Patients meeting any of the above criterion need to be screened for potential fall hazards/risks at any point when they enter the health-care system.

Ethnicity: In a sample of Medicare data from 2010 to 2016, Black women with postmenopausal osteoporosis had significantly higher rates of mortality, debility, and destitution after fracture than White women. These Black women had a larger prevalence of femur and hip fractures and a lower prevalence of radius/ulna and clinical vertebral fractures compared with White women (Wright et al., 2020). This racial disparity is important to remember when a Black woman has met criteria for postmenopausal osteoporosis and steps should be taken to prevent falls/fractures.

Contributing Factors: Smokers have an increased risk of fracture and experience more complications with delayed bone healing, even if they have already stopped smoking, because some adverse effects persist for a prolonged period. The patient should also be warned that using e-cigarettes or other tobaccos does not appear to reduce adverse effects on health (Hernigou & Schuind, 2019). Although lifestyle choices can have an effect on bone health, certain genetic health conditions can have equally damaging effects. One study found osteoporosis is more prevalent in people with neurological conditions, such as multiple sclerosis and Parkinson's disease (Kelly et al., 2020). Patients with these neurological conditions should receive appropriate bone health screening.

Signs and Symptoms: Symptoms include soft tissue swelling, ecchymosis, abrasions, edema, skin discoloration, local tenderness, and pain with any motion. Fractures often are a result of injury to the affected area. It is important to palpate the area of maximum tenderness to determine whether more than one bone may be involved (Eiff & Hatch, 2017).

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Neurovascular status should be obtained with any extremity fracture, especially with significant swelling due to the risk of compartment syndrome. Extremity compartment syndrome (ECS) most often develops in the context of severe trauma, especially—nearly 75% of all cases—in long bone fractures, such as tibial and forearm fractures and crush injuries. However, it may also develop from both minor traumas, when treated with tight bandage or constrictive cast, or in nontraumatic cases. ECS represents a surgical emergency: time limit for fasciotomy is within 8 hours from the diagnosis of acute ECS (Coccolini et al., 2020).

Diagnostic Tests: Recommend ordering radiographs of the affected area/injury to rule out and identify the area and type of fracture. Radiographs of the affected area are needed in two and three views (Eiff & Hatch, 2017).

Differential Diagnosis:

- An infectious process/osteomyelitis
- Neoplastic process/multiple myeloma
- Osteoporosis
- Sprain/strain

Treatment: For the pain related to the fracture, narcotic analgesics and/or short-term NSAIDs, if not prohibited, are helpful. Depending on the site of the fracture, casting, walking boot, elastic wrapping, splints, immobilization, traction, or surgical intervention may be used (Eiff & Hatch, 2017). The most common surgical intervention for a fractured hip is the open reduction with internal fixation, especially for fractures of the intertrochanteric or subtrochanteric region. The most common surgical intervention for a distal radius fracture is an open reduction and internal fixation using a volar positioned plate. Nonoperative treatment can be considered the gold standard, but shared decision making between the patient and the treating physician is warranted (Luokkala et al., 2020).

Follow-Up: Adequate nutrition and wound care are important for proper healing. It is common in skilled nursing facilities to start patients on zinc and vitamin C supplements; however, no study is conclusive in this treatment modality. Patients should be questioned about any muscle weakness or paresthesia after the incident. Patients may have return appointments with an orthopedist, physical therapist, or both. The function of the affected area should be evaluated. Determine what impact the injury had on the patient's activities of daily living (ADLs) and instrumental ADLs (IADLs) (Eiff & Hatch, 2017).

Sequelae: To an older adult, a hip fracture can be a life-changing or life-ending event. A large proportion of functionally independent patients are not able to ambulate independently after hip fracture or experience functional loss related to impaired balance and mobility. Morbidity after a hip fracture is not just physical; there is a high incidence of depression and cognitive impairment (both temporary and permanent). The recovery after a fracture is lengthy, and a relatively high number of patients do not manage to achieve preinjury levels of independence or even survive (Reyes et al., 2020). One complication after distal radius fracture is delayed carpal tunnel syndrome. This condition can result from scar tissue invading the carpal tunnel and pressing on the median nerve or from fractures allowed to heal malaligned. Careful follow-up should be performed because delayed carpal tunnel syndrome may occur within 6 months after injury (Watanabe & Ota, 2019). A recent publication describes a 1-year mortality rate post hip fracture of 21% (Downey et al., 2019). Studies have found that 25% of patients die within 1 year of experiencing a hip fracture (Wright et al., 2020).

Prevention/Prophylaxis: Calcium and vitamin D are often recommended by clinicians to boost bone health. One study found vitamin D alone (11 randomized clinical trials with 34,243 participants) showed no significant association with risk of any fracture or of hip fracture. In contrast, daily supplementation with both vitamin D and calcium (6 randomized clinical trials with 49,282 participants) was associated with a 16% reduced risk of hip fracture. (Yao et al., 2019).

Referral: Rehabilitation needs will likely include an orthopedic specialist for complex casting and surgical needs. Physical therapy/occupational therapy (PT/OT) referrals to further evaluate and treat functional physical impairments and to improve ADLs are in order to provide as much independent living as possible. Keep in mind that older patients may be hesitant to resume previous normal activities due to falls. This hesitancy may be justified as one meta-analyses have shown that individuals who have sustained a fracture are at approximately double the risk of sustaining subsequent fractures, as compared to their fracture-free peers (Harvey et al., 2017). This may be resolved by the involvement of a rehabilitation team.

Clinical Recommendation	Evidence Rating	References
Smokers have an increased risk of fracture and experience more complications with delayed bone healing, even if they have already stopped smoking, because some adverse effects persist for a prolonged period.	B	Hernigou & Schuind, 2019
Daily supplementation with both vitamin D and calcium was associated with a 16% reduced risk of hip fracture.	A	Yao et al., 2019
Individuals who have sustained a fracture are at approximately double the risk of sustaining subsequent fractures, as compared to their fracture-free peers.	B	Harvey et al., 2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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GOUT

Signal Symptoms: Monoarticular inflammatory arthritis, podagra (first metatarsophalangeal [MTP] joint), tophi

Description: Gout is the most common inflammatory arthritis in the United States. This chronic disease is caused by hyperuricemia, defined as serum urate or uric acid level >6.8 mg/dL. Gout commonly causes recurrent acute flares and chronic arthritis. The initial gout attack is often podagra—occurring in the first MTP joint (Mandell, 2020). Gout occurs when monosodium urate (MSU) crystals precipitate into the joint space, soft tissues, and periarticular structures, producing an inflammatory response (Golenbiewski & Keenan, 2019). Longstanding disease can result in MSU crystal deposits in larger joints, in cutaneous tissue known as tophi, and the parenchymal of the organs—for example, the kidneys (Mandell, 2020). Clinically, patients can have asymptomatic hyperuricemia or different presentations of gout such as acute gouty arthritis, intercritical periods, or chronic tophoceous gout (Chen-Xu et al., 2019).

Etiology: Urate is the ionized form (salt) of uric acid and is the by-product of purine breakdown in the body (Golenbiewski & Keenan, 2019; Ragab et al., 2017). Uric acid occurs both endogenously by purine metabolism in the liver and exogenously through dietary intake of purine-rich foods. The human body lacks the ability to breakdown uric acid, and the threshold at which serum uric acid (SUA) becomes pathological is 6.8 mg/dL (Maiuolo et al., 2016; Ragab et al., 2017). The higher the SUA and the longer an individual has been hyperuricemic, the greater the chances of developing gout.

Elevated SUA levels can occur in multiple ways, the most common is decreased excretion. The kidneys excrete two-thirds of uric acid and the gastrointestinal (GI) tract one-third. Decreased excretion can occur when there is decreased glomerular function causing decreased renal excretion, use of diuretics, decreased GI tract excretion, the effects of alcohol catabolism on the kidneys, and/or a genetic predisposition. Uric acid levels can be elevated with increased production; however, this scenario is much less likely. Increased SUA due to increased production can occur with hematological conditions such as leukemia and lymphoma, with cytotoxic cancer therapy and radiation therapy where increased cell proliferation and cell death occurs, with obesity due to adipose tissue contributing to production, and as a genetic and/or an enzyme abnormality (Mandell, 2020). Although most purine synthesis occurs within the liver, dietary purine intake can contribute to elevated SUA, particularly in the setting of decreased excretion (Golenbiewski & Keenan, 2019).

Occurrence: Worldwide, gout typically occurs in 1% to 4% of the population, although in some Oceanic countries prevalence is >10% (Golenbiewski & Keenan, 2019). According to the National Health and Nutrition Examination Survey (NHANES), the prevalence of hyperuricemia and gout doubled between the 1960s and the 1990s in the United States and continued to increase into the early 2000s. In recent years the prevalence of gout in the United States is 3.9% or approximately 9.2 million adults (Chen-Xu et al., 2019). Gout is highest among men with a three or four to one male-to-female ratio; however, this discrepancy narrows with age. It is estimated approximately 5.2% of men (5.9 million) and 2.7% of women (3.3 million) have gout (Golenbiewski & Keenan, 2019). There is a higher incidence of gout in postmenopausal women than in premenopausal women (Singh & Gaffo, 2020).

Age: The incidence and prevalence of gout increases with each decade of life. The lowest prevalence is in individuals 20 to 39 years old at 0.7%, and the highest is in individuals 80 years and older at 8.7% (Chen-Xu et al., 2019).

Ethnicity: Some ethnic groups have a higher prevalence of gout, including Blacks, the New Zealand Maori, the Han Chinese, and some Polynesian people. For example, the relative risk of gout in Black men is 1.69 (confidence interval [CI] 95%, 1.02–2.80) compared to White men. Higher incidence of hypertension in Black men is felt to be a contributing factor in higher rates of gout (Singh & Gaffo, 2020).

Contributing Factors: In addition to sex, genetics, and obesity, there is a strong correlation between gout and hypertension, diabetes, kidney disease, heart disease, metabolic syndrome, and hyperlipidemia (Chen-Xu et al., 2019; Singh & Gaffo, 2020). Gout can also be triggered by a medical stressor such as acute dehydration, surgery, infection, or an injury/trauma. Both loop and thiazide diuretics can cause gout attacks as well as urate-lowering therapy (ULT) as it mobilizes urate upon initiation. Purine-rich foods, such as red meats, organ meats, meat gravies and broth, certain seafoods and shellfish, alcohol (particularly beer), and sugary foods and drinks can contribute to elevated SUA (Mandell, 2020).

Signs and Symptoms: Initial gout attacks typically occur nocturnally in the first MTP, with pain peaking within 24 hours and gradually resolving in 1 to 2 weeks (Towiwat et al., 2019). This can sometimes be precipitated by alcohol consumption or a purine-rich meal. Pain is often described as rapidly progressing from severe to excruciating, tender even to very light touch and accompanied by swelling, erythema, and the skin may have a tight shiny appearance. Systemic symptoms of fever/ chills, malaise, and tachycardia are possible. As the disease progresses, flares last longer—up to 3 weeks—and multiple joints can be affected at the same time or sequentially with little to no rest between attacks (Mandell, 2020). Gout can affect the instep, ankle, knee, elbow, and wrist; rarely the cervical spine, shoulder, or hip (Pillinger & Mandell, 2020).

Suboptimally treated patients can develop tophi, firm white-yellow nodules of the interphalangeal and/or MCP joints, wrists, feet, ears, and near the olecranon and Achilles' tendon. Normally painless, tophi can drain chalky white urate crystals and can become inflamed with minimal injury or infected due to ulceration. Tophi contribute to joint erosions and deformity (Mandell, 2020).

Diagnostic Tests: Arthrocentesis with synovial fluid analysis should be completed at initial presentation if gout is suspected; this will also enable ruling out infection. The analysis during a flare should show 2,000 to 100,000 white blood cells (WBCs)/mcL with >80% polymorphonuclear WBCs. Gram stain and culture are important as well because infectious arthritis can

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have similar WBC counts (Mandell, 2020). The gold standard for diagnosis of gout is identification of MSU crystals in synovial fluid using microscopy (Ragab et al., 2017). Joint aspiration is not necessary for recurrent flares unless presentation or symptoms differ (Mandell, 2020).

The diagnosis of gout is supported by an elevated serum uric acid; however, approximately 30% of patients will have a normal SUA during an acute flare. SUA is neither sensitive nor specific enough to solely make the diagnosis, although it is useful to have a baseline level drawn between flares to quantify the hyperuricemia and recheck intermittently or when adjusting urate-lowering medications. Measurement of urinary uric acid is not recommended because it is a poor indicator of therapeutic response (Mandell, 2020). Laboratory testing should include assessing renal function and a complete blood count (CBC) to check for leukocytosis if septic arthritis is a consideration.

Imaging modalities utilized in the diagnosis and treatment of gout include conventional radiography and computerized tomography (CT), dual-energy CT, ultrasound, magnetic resonance imaging (MRI), positron emission tomography (PET), and nuclear scintigraphy (Ragab et al., 2017). Plain x-rays are inexpensive and help to assess the degree of bony erosions and tophi in advanced gout; they may also help to identify chondrocalcinosis, particularly of large joints such as the knees. Bone erosions appear as punched-out lesions of the subchondral bone but must be >5 mm to be visible. Typically, joint space is preserved until late stage of the disease course. Ultrasound is especially useful in identifying subclinical tophi and MSU crystals. Dual-energy CT is unique and clinically relevant because it color codes crystals to differentiate between urate and calcium, which is invaluable with atypical presentation or when arthrocentesis is not possible or inconclusive (Mandell, 2020).

Differential Diagnosis: (Mandell, 2020)

- Chondrocalcinosis/calcium pyrophosphate dihydrate (CPPD)/pseudogout–synovial fluid analysis would reveal calcium pyrophosphate crystals; under microscopy CPPD appear weakly positive birefringent, and MSU appear negative birefringent
- Injury/Trauma—history and imaging
- Inflammatory arthritis (for example, rheumatoid arthritis [RA] or psoriatic arthritis)—serology and distinguishing accompanying symptoms
- Infection/septic arthritis—Gram stain and culture from arthrocentesis
- Cellulitis—similar superficial symptoms without involvement of the joint
- Osteoarthritis—radiographs, narrowing of joint space without hallmark erosions
- Reactive Arthritis—history and serology

Treatment: Treatment of gout involves management of acute flares and treatment of established gout. Acute flares require one or more anti-inflammatory medications (NSAIDs, corticosteroids, and/or colchicine) and are best treated within the first 24 hours of symptoms. Treatment with these medicines should be part of an individualized plan of care weighing the risks and benefits to the patient, taking into consideration other comorbidities, such as renal insufficiency and GI conditions, and requisite laboratory monitoring.

Choice of a NSAID is guided by health-care provider preference, concern for possible adverse effects (such as central nervous system [CNS] intolerance with indomethacin), preferable safety profiles (such as with cyclooxygenase type 2 [COX-2] inhibitors), and to what medicines the patient has previously responded. Any NSAID choice will likely require higher doses, and it is important to sufficiently treat the patient (typically 3–5 days), while at the same time avoiding a rebound attack if discontinued too soon. Careful considerations in this drug choice include chronic kidney disease (CKD), hypertension, heart failure, anticoagulation/thrombocytopenia, and GI conditions (Pillinger & Mandell, 2020). Also, NSAIDs are included in the American Geriatrics Society Beers list of potentially inappropriate medications in older adults.

Corticosteroids offer about the same efficacy as NSAIDs and likewise should be used for the shortest duration possible while avoiding a rebound attack. There are two strategies that appear to be equally efficacious in prescribing corticosteroids (Pillinger & Mandell, 2020). Both use the American College of Rheumatology 2012 guideline recommending an initial dose of 0.5 mg/kg of prednisone or equivalent. Corticosteroids do not require renal impairment dose adjustments; however, they can have significant cardiovascular (CV), GI, CNS, and endocrine effects and can increase risk of infection even when given for short periods. Corticosteroids can be alternatively administered intra-articularly or intramuscularly (FitzGerald et al., 2020; Pillinger & Mandell, 2020).

Colchicine is quite effective in the treatment of gout flares and can be useful as adjuvant therapy at lower doses to prevent attacks. Caution must be exercised with colchicine in patients with CKD as well as in those taking medications that utilize the CYP3A4 pathway, such as clarithromycin, diltiazem, verapamil, statins, and several antifungal and antiretroviral drugs (Pillinger & Mandell, 2020). Updated standards recommend low-dose over high-dose colchicine for acute flares to minimize adverse effects while having similar efficacy (FitzGerald et al., 2020).

While these medicines work to resolve flares, they do not treat the hyperuricemia. Therefore, it is essential to initiate ULT to control gout; to only treat attacks with anti-inflammatory agents allows occult MSU crystal deposition, which can lead to treatment-resistant gout and more systemic disease (Khanna et al., 2020; Pillinger & Mandell, 2020). Typically, ULT is not initiated during an acute flare; conversely, ULT should not be stopped during a flare. Treatment with ULT should be individualized, in part based on renal impairment, GI sensitivity, and cardiovascular risk; some patients may also have a better response depending on the mechanism of action. Allopurinol and febuxostat, xanthine oxidase inhibitors, block urate production and reduce hyperuricemia caused by GI or renal underexcretion or from metabolic overproduction (Pillinger & Mandell, 2020). Allopurinol is the preferred first-line treatment choice; however, careful consideration needs to be given when initiating this medication with Asian and Black patients. It is recommended to check for the genetic marker HLA B*5801 in these populations to avoid serious cutaneous complications, including Stevens-Johnson syndrome. Febuxostat currently has a black box warning for risk of increased cardiac death in cardiovascular patients compared to allopurinol. Probenecid, a uricosuric drug, increases urate excretion. Probenecid is contraindicated for patients who have had renal stones and is less effective with

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renal insufficiency. ULTs are indicated for the treatment of patients with frequent flares (more than 2 flares/year), symptomatic SUA >9.0 mg/dL even with infrequent flares, tophaceous deposits, urolithiasis, and other comorbidities that preclude the use of medications for acute flares, such as CKD or peptic ulcer disease (Mandell, 2020).

Follow-Up: Patients being treated for gout require routine laboratory monitoring particularly for kidney function, liver function, and serum uric acid levels. It is not only important to stay below the saturation threshold of 6.8 mg/dL, but if tophi are present the target level should be <6 mg/dL. If tophaceous deposits contribute to marked disability, it is reasonable to lower the target level to 5 mg/dL to dissolve tophi more rapidly. For patients who do not tolerate higher doses of allopurinol or febuxostat, probenecid can be given in combination for better control or as a monotherapy when the former is contraindicated. Pegloticase is an infusion and reserved for refractory gout; it converts urate into allantoin, which is a water-soluble metabolite of uric acid (Mandell, 2020). Unfortunately, studies indicate health-care providers are not aggressive enough in prescribing urate-lowering therapy and frequently fail to reach proper uric acid levels, thus resulting in poor disease control (Golenbiewski & Keenan, 2019).

Sequelae: Recurrent painful attacks and chronic inflammation affect quality of life, work productivity, and increase health-care utilization (Chen-Xu et al., 2019). Inadequately treated, gout can be a severe, debilitating disease leading to joint destruction and impaired joint function. Progressive renal dysfunction, often in the setting of coexisting hypertension, diabetes and/or nephropathy, further accelerates urate deposits due to decreased excretion. Renal obstruction and infection can be a complication of gout with secondary tubulointerstitial disease. Approximately 10% of kidney stones are from urate precipitates (Mandell, 2020).

Prevention/Prophylaxis: In addition to utilization of ULT, it is important to encourage lifestyle modification in patients with hyperuricemia, including weight loss and reduction in alcohol, fructose, and purine-rich foods. However, it is more important to avoid shaming patients or creating intolerable dietary restrictions because this can contribute to noncompliance and a strict low-purine diet only decreases SUA by about 1 mg/dL (Mandell, 2020; Pillinger & Mandell, 2020). When feasible, switching from a thiazide diuretic to a different antihypertensive is recommended to help reduce the incidence of flares. Although evidence shows low-dose aspirin can contribute to hyperuricemia, generally the benefits of CV risk reduction outweigh this risk. However, moderate to higher doses of aspirin should be avoided. Conversely, both losartan and fenofibrate have shown uricosuric effects; therefore, in patients with relevant comorbidities these medicines can help reduce SUA (FitzGerald et al., 2020; Mandell, 2020).

Referral: A referral to rheumatology may be necessary for arthrocentesis and/or intra-articular injections, complicated cases of gout that are refractory to treatment, or patients who have an unusual presentation of disease. A referral to a dietitian may be beneficial for patients who do not well tolerate ULT or who need further assistance in following a low-purine diet.

Education: Patients should be educated on the first signs of a gout flare and the importance of timely treatment. Abortive therapy initiated within the first 12 to 24 hours is the most effective and can greatly decrease the duration of a flare. This is often accomplished with a dose of colchicine 1.2 mg followed by a dose of 0.6 mg 1 hour later. It is important, for both the provider and the patient, to keep track of flares as often ULT needs to be initiated to avoid future complications. Patients need to be educated that initiation of an ULT or dose increases can cause acute flares; this is to be expected and should be managed with NSAIDs or daily colchicine for up to 6 months (Mandell, 2020).

Clinical Recommendation	Evidence Rating	References
Initiating urate-lowering therapy (ULT) is strongly recommended for patients with gout who have any of the following: ≥1 subcutaneous tophi; evidence of radiographic damage (any modality) attributable to gout; or frequent gout flares (≥2 annually).	A	FitzGerald et al., 2020
Initiating ULT is conditionally recommended for patients who have previously experienced >1 flare but have infrequent flares (<2/year).	B	FitzGerald et al., 2020
Initiating ULT is conditionally recommended for patients with moderate to severe CKD (stage ≥3), SUA concentration >9 mg/dL, or urolithiasis.	C	FitzGerald et al., 2020
Allopurinol as the preferred first-line treatment choice, over all other ULT, is strongly recommended for all patients, including those with moderate-to-severe CKD (stage ≥3).	A	FitzGerald et al., 2020
The choice of either allopurinol or febuxostat over probenecid is strongly recommended for patients with moderate-to-severe CKD (stage ≥3).	A	FitzGerald et al., 2020
Starting treatment with low-dose allopurinol (≤100 mg/day and lower in patients with CKD [stage ≥3]) and febuxostat (≤40 mg/day) with subsequent dose titration over starting at a higher dose is strongly recommended.	A	FitzGerald et al., 2020
Administering concomitant anti-inflammatory prophylaxis therapy (e.g., colchicine, NSAIDs, corticosteroids) over no anti-inflammatory prophylaxis therapy is strongly recommended.		

Continued

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Clinical Recommendation	Evidence Rating	References
Continuing concomitant anti-inflammatory prophylaxis therapy for 3–6 months over <3 months, with ongoing evaluation and continued prophylaxis as needed if the patient continues to experience gout flares, is strongly recommended	A	FitzGerald et al., 2020
A treat-to-target management strategy that includes ULT dose titration and subsequent dosing guided by SUA measurements to achieve a target SUA, over a fixed-dose ULT strategy, is strongly recommended for all patients receiving ULT.	A	FitzGerald et al., 2020
Achieving and maintaining an SUA target of <6 mg/dL over the use of no target is strongly recommended for all patients receiving ULT	A	FitzGerald et al., 2020
Continuing ULT indefinitely over stopping ULT is conditionally recommended.	C	FitzGerald et al., 2020
Switching to an alternative oral ULT agent, if available and consistent with other recommendations, is conditionally recommended for patients taking febuxostat with a history of cardiovascular disease (CVD) or a new CVD-related event.	C	FitzGerald et al., 2020
Switching to pegloticase over continuing current ULT is strongly recommended for patients with gout for whom xanthine oxidase inhibitor treatment, uricosurics, and other interventions have failed to achieve the SUA target, and who continue to have frequent gout flares (≥2 flares/year) or who have unresolving subcutaneous tophi.	A	FitzGerald et al., 2020
Limiting alcohol, purine, and high-fructose corn syrup intake is conditionally recommended for patients with gout, regardless of disease activity.	B	FitzGerald et al., 2020
Weight loss is conditionally recommended for those patients with gout who are overweight/obese, regardless of disease activity.	B	FitzGerald et al., 2020

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INFLAMMATORY ARTHRITIS (SPONDYLOARTHROPATHY)

Signal Symptoms: Inflammatory arthritic conditions may manifest with rashes, ulcerations, joint nodularity, fatigue, swelling, erythema, joint stiffness, limited range of motion (Pujalte & Albano-Aluquin, 2015).

Description: Spondyloarthropathy encompasses a spectrum of inflammatory arthritic disorders, including ankylosing spondylitis, non-radiographic axial spondyloarthropathy, reactive arthritis, psoriatic arthritis, and enteropathic arthritis associated with Crohn's or ulcerative colitis. All of these types of arthritis can have similar features and often overlap in signs and symptoms. This section addresses psoriatic arthritis, ankylosing spondylitis and non-radiographic axial spondyloarthropathy. The presentation of late-onset psoriatic arthritis and ankylosing spondylitis is highlighted.

PSORIATIC ARTHRITIS

Description: Psoriatic arthritis is a heterogenous disease that can affect the skin, nails, and peripheral and axil joints (Raychaudhuri et al., 2017). The condition may begin as an asymmetric oligoarticular type of psoriatic arthritis that involves different joints on each side of the body; later though most patients will have polyarticular arthritis (Tiwari & Brent, 2021). Ninety-five percent of patients will have peripheral joint disease as evidenced by synovitis and/or tenosynovitis. Enthesitis (where extensors tendons insert to bone) and dactylitis (tendon sheath swelling in the digit giving it a sausage type appearance) are common findings. About 5% of patients will have axial involvement. There is a predominant distal interphalangeal (DIP) joint involvement in the hands, which can help differentiate it from rheumatoid arthritis (RA), as well as axial involvement, which is not typically seen in RA. Psoriatic arthritis can affect up to 30% of all patients with psoriasis (Ogdie & Gelfand, 2015). Typically, a diagnosis of psoriasis will precede the arthritis by 8 to 10 years (70%). In a small subset of patients, the inflammatory arthritis will occur first (Napolitano et al., 2016).

Etiology: Both genetic and environmental factors play a role in the development of psoriatic arthritis, although the exact etiology is unknown. Just as with RA, it is a cytokine-mediated disease. Evidence suggests that trauma and infection may play a role (Ogdie & Gelfand, 2015).

Occurrence: The prevalence of psoriatic arthritis is 1.9% to 2.7% per 100 in the United States (Tiwari & Brent, 2021). Women and men are equally affected (Caso et al., 2019).

Ethnicity: Whites are affected two times more often than other ethnicities.

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Age: Psoriatic arthritis generally has its onset around the fourth to fifth decade, and the age of onset shows a peak age around 50 years, whereas late-onset psoriatic arthritis begins in patients aged 60 and older (Caso et al., 2019).

Contributing Factors: Family history and genetic predisposition tend to be contributing factors to the development of psoriatic arthritis in younger adults (Caso et al., 2019). There have been some studies implying in older adults with late-onset psoriatic arthritis that obesity contribute to the development of psoriatic arthritis; however, it may be more related to the misdiagnosis of psoriatic arthritis as osteoarthritis (OA). Smoking has been shown to contribute to the development of psoriatic arthritis in older adults (Caso et al., 2019). Environmental factors have been suggested with the development of psoriatic arthritis, especially situations that lead to trauma or mechanical stressor (Ogdie & Gelfand, 2015; Tiwari & Brent, 2021). Patients with severe psoriasis and those with psoriatic nails tend to be at a higher risk of developing psoriatic arthritis than patients who do not have severe disease (Ogdie & Gelfand, 2015).

Signs and Symptoms: When questioning the patient about signs of symptoms of an inflammatory arthritis, inquire about the onset and the progression of joint involvement, any constitutional symptoms, exposure to environmental factors, past traumas, and impact if any of functional ability. Note presence of swelling, erythema, and nodularity, counting the number of joints affected (Pujalte & Albano-Aluquin, 2015). The articular and periarticular presentation of psoriatic arthritis includes a peripheral arthritis that maybe oligoarticular then progresses to polyarticular. Specific joint signs include enthesitis and dactylitis. There may be axial joint involvement, including the sacroiliac joint (Tiwari & Brent, 2021); however, studies have shown that there tends to be less of this type of involvement. Joints may be swollen and tender to the touch. Additionally, the patient may have psoriatic skin manifestation, onycholysis, and pitting of the nails. Uveitis may occur bilaterally as a chronic eye condition (Tiwari & Brent, 2021). In older adults with psoriatic arthritis, the progression of the disease tends to have a more acute onset with more severe effect on joints than in younger patients. One study showed that erosions that occurred in the hand and feet tend to be more extensive in older adults than in younger patients with psoriatic arthritis (Punzi et al., 1999). In one study comparing younger and older patients diagnosed with psoriatic arthritis, the older patients were found to be predominately female, have higher body mass index (BMI) and more severe joint damage (Polachek et al., 2019).

Differential Diagnosis: Other inflammatory anthric conditions can mimic psoriatic arthritis.

- Diffuse idiopathic skeletal hyperostosis (DISH): Patients generally do not have spinal symptoms and can be diagnosed via x-ray.
- Polymyalgia rheumatica (PMR): A response to NSAIDs occurs in patients presenting with psoriatic arthritis, whereas steroids are used in the treatment of PMR.
- RA: Generally, the negative rheumatoid factor (RF), the DIP involvement, and the axial involvement are not characteristic of RA.
- Reactive arthritis: Onset is triggered by an infection.
- Ankylosis spondylitis: No cutaneous manifestations and symmetric sacroiliitis

(Angelopoulou, et al., 2020; Caso et al. 2019; Napolitano et al., 2016; Tiwari & Brent, 2021).

Diagnostic Tests: There are no specific laboratory tests for psoriatic arthritis. Erythrocyte sedimentation rates and C-reactive protein (CRP) may be elevated as with other inflammatory arthropathies. Normal rates for a patient's age do not discount the diagnosis (Tiwari & Brent, 2021). For patients with late-onset psoriatic arthritis, elevated synovial concentration of proinflammatory cytokines have been found (Caso et al., 2019). For patients with suspected psoriatic arthritis, if ordered to rule out RA, generally the RF is negative. Anemia can also occur. HLA-B27 will be positive in 25% of patients. Ultrasound and/or magnetic resonance imaging (MRI) can help to identify enthesitis and dactylitis. X-rays can show erosions and ankylosis of the DIP and proximal interphalangeal (PIP) joints as well as a pencil-in-cup deformity at the DIPs. Osteolysis of the bones can occur in more aggressive disease (arthritis mutilans). Sacroiliitis can be present on x-ray and/or MRI (Tiwari & Brent, 2021).

Treatment: The approach is to focus on a target considering the disease severity (Tiwari & Brent, 2021). For patients with psoriatic arthritis the treatment goals should focus on clinical remission, preserving or improving the patients' quality of life, and inhibiting structural damage that can result from joint erosion (Napolitano et al., 2016). Patients with very mild oligoarticular disease might be managed with intra-articular steroids and NSAIDs. For older adults, the transition to using disease-modulating antirheumatic drugs (DMARDs) would be considered if there is extensive skin involvement and/or more than three joints involved. Methotrexate and leflunomide can be used (Noviani et al., 2020). They both may have mild improvement in skin and peripheral involvement, including synovitis and dactylitis. They have not been shown to halt axial disease or nail disease. Anti-tumor necrosis factor (TNF) agents (adalimumab, etanercept, certolizumab pegol, golimumab, and infliximab) with or without methotrexate are effective medications for arthritis, dactylitis, enthesitis, spondylitis, and skin disease (Frampton, 2107; Raychaudhuri, et al., 2017). Similar efficacy has been shown with both the IL-17 agents (secukinumab and ixekisumab) and IL-23 agents (guselkumab). A phosphodiesterase type-4 inhibitor (apremilast) can be used but has less efficacy than the other biologics. Janus kinase (JAK) inhibitors can be used. Currently tofacitinib is approved for psoriatic arthritis but not arthritis. Additional more selective JAK-inhibitors are being studied. Abatacept, an agent that blocks CD80 and CD86 pathways of T-cell costimulation, can also be used to treat psoriatic arthritis, but it is not approved in psoriasis. Careful monitoring and periodic adjustments may need to be made to medications for older adults (Caso et al., 2019). All of these medications increase the risk of infection and patients must be current with vaccinations (Caso et al., 2019; Raychaudhuri et al., 2107).

Follow-Up: Monitor the patient to determine management of symptoms, disease progression, impact on quality of life and function. Consider the development of comorbidities and monitor and refer as indicated.

Sequelae: As the disease progresses, severe joint deformity can manifest such as arthritis mutilans (Napolitano et al., 2016). Comorbidities associated with psoriasis include cardiovascular disease (CVD) (Queiro et al., 2019b), depression, diabetes, metabolic syndrome, and malignancy (Caso et al., 2019;

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Takeshita et al., 2017). Hepatic and pulmonary disorders can also occur (Ogdie et al., 2018). Studies have shown that hypertension is common in older adults who developed psoriasis (Alonso et al., 2016; Queiro et al., 2019a). The risk of fractures is increased for patients with psoriasis and psoriatic arthritis (Ogdie et al., 2107).

Prevention//Prophylaxis: There are no preventive measures for developing psoriasis. Maintaining a normal BMI, limiting alcohol, and smoking cessation maybe beneficial form having the disease progress (Ogdie & Gelfand, 2015).

Referral: Patients with psoriatic arthritis benefit from an interprofessional approach to care depending on the extent of the condition and how it has impacted their functional ability and quality of life. Referral to a rheumatologist is recommended for management of the complex cases not responding to treatment. Depending on comorbidities, referral to dermatology and cardiology referrals may be needed as the disease progresses (Tiwari & Brent, 2021). Patients may benefit from occupational therapy (OT) referral for adaptive equipment and to physical therapy (PT) to assist with treatment modalities aimed at maintaining and/or restoring joint function.

Education: Patients should be encouraged to limit or refrain from alcohol and smoking. A healthy diet and physical activity should be recommended to all patients. Depending on treatment prescribed, patients on immunosuppressive medications need to understand the side effects of these medications, the need to avoid infections, and the importance of keeping immunizations up to date (Tiwari & Brent, 2021).

AXIAL SPONDYLOARTHRITIS (NON-RADIOGRAPHIC AND ANKYLOSING SPONDYLITIS)

Description: Axial spondyloarthritis (axSpA)—both non-radiographic axSpA and ankylosing spondylitis—is a chronic, systemic inflammatory disease affecting the sacroiliac joints, spine, and occasionally the peripheral joints. In more advanced disease, sacroiliitis is present on plain film x-ray of the sacroiliac joints, and this is characteristic of ankylosing spondylitis. This is a later finding and can take several years before it presents, if at all. Patients with inflammatory back symptoms (discussed later) who do not have x-ray evidence of sacroiliitis may have sacroiliitis seen on magnetic resonance imaging (MRI); these patients are described as having non-radiographic axSpA. Some of these patients will never go on to develop sacroiliitis on x-ray, although their disease burden is similar to axSpA (Wenker & Quint, 2021).

Etiology: Genetics and environmental factors play a role. A close association has been shown to exist between the human leukocyte antigen (HLA) B27 and axSpA (Toussirot & Wendling, 2005).

Occurrence: Overall prevalence of ankylosing spondylitis in general U.S. population is 0.30% to 0.50%. In younger patients, axSpA is more common in men. In late-onset axSpA, the ratio of men to women is about equal (Toussirot & Wendling, 2005).

Age: Symptoms usually begin in late adolescence/early adulthood through the third decade of life. Although very rare, late-onset ankylosis spondylitis occurring after age 50 is overlooked for other rheumatic conditions such as rheumatoid arthritis (RA) and polymyalgia rheumatica (PMR) (Toussirot & Wendling, 2005). One study showed an estimate to be about 2 out of 100,000 people versus 7 out of 100,00 people for cases in those younger than 55 years of age (Carbone et al., 1992).

Contributing Factors: Strongest predictions for developing ankylosing spondylitis is the genetic predisposition for individuals who are HLA-B27 positive, and the rate of occurrence for ankylosing spondylitis increases in HLA-B27 positive individuals who have a family history. Ankylosing spondylitis also been linked to environmental factors. There is a strong association between the axial spondyloarthritis, including ankylosing spondylitis, and gut inflammation, namely involving *Klebsiella pneumonia* bacteria (Rashid et al., 2015). This linkage extends to high starch consumption because gut microbes such as *Klebsiella* are saccharolytic (involved in the process of fermentation of carbohydrates and starch), suggesting that high starch consumption is a risk factor to develop ankylosing spondylitis (Oh et al., 2012).

Signs and Symptoms: Patients present with insidious back pain longer than 3-month duration. Often the pain continues through the night, with patients waking with morning stiffness. Patients may also report limited spinal mobility and postural anomalies. Pain may extend to the buttock and hips. Patients may experience limited chest expansion ability (Moll & Wright, 1974). Axial as well as peripheral arthritis is common in late-onset axSpA (Wenker & Quint, 2021). Pain improves with exercise/movement, which is a way to help differentiate it from mechanical back pain. In late-onset spondyloarthropathy, older adults tend to present with increased levels of cervical spine manifestations and peripheral arthritis (Montilla et al., 2012; Toussirot & Wendling, 2005).

Differential Diagnosis: Rule out any mechanical low back pain in all patients with axSpA (Wenker & Quint, 2021). In older adults presenting with late-onset spondyloarthropathy, the differential diagnosis includes RA, PMR, and seronegative symmetric synovitis with pitting edema (Montilla et al., 2012; Toussirot & Wendling, 2005). Negative rheumatoid factor (RF) and response to NSAIDs often occurs in patients with axSpA and not in PMR. Seronegative symmetric synovitis generally only affects the wrists and hands. Ankylosing spondylitis often effects the lower limbs with asymmetric pitting edema, and the patient is positive for HLA-B27 (Toussirot & Wendling, 2005).

Diagnostic Tests: HLA-B27 may be ordered to support the diagnosis of axSpA, as evidence of antigen is found in 85% to 95% of people with ankylosing spondylitis, although some estimates are lower (Sieper & Poddubnyy, 2016). Acute-phase reactants such as the erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) can be elevated. Platelet count can also be elevated in patients with inflammatory arthritis such as ankylosing spondylitis. X-rays of the sacroiliac joints can be diagnostic, showing bilateral sacroiliitis. In patients with non-radiographic axSpA, x-rays will be negative, but an MRI of the pelvis with T1 sequences will show sacroiliitis. Syndesmophytes can be seen in more advanced disease as well as spinal fusion present on x-ray (van Tubergen et al., 2012).

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Treatment: The course for ankylosing spondylitis can be variable; however, the first 10 years of disease may predict the subsequent course of the disease. Exercise is especially important in these patients and should always be recommended in addition to medications. Patients with high markers of inflammation, lack of response to NSAIDs, and early hip involvement predict a poor prognosis (Ward et al., 2019). As with other inflammatory diseases, early detection and initiating treatment is key. NSAIDs are first-line therapy and can improve symptoms. The 2019 Update of the American College of Rheumatology/Spondylitis Association of America/Spondylarthritis Research and Treatment Network Recommendations for the Treatment of Ankylosing Spondylitis and Non-radiographic Axial Spondyloarthritis have updated recommendations for treatment. If patients are not responding to treatment with NSAIDs, then the next line of treatments are to begin a tumor necrosis factor (TNF) inhibitor (TNFi), which are recommended over secukinumab or ixekizumab as the first biologic used in patients with axSpA. If a patient is not responding to a TNFi, it is recommended then to add one of the human monoclonal antibodies to interleukin-17A (secukinumab or ixekizumab) for patients who did not have a response to a TNFi rather than adding a second TNFi. It is not advised to prescribe low-dose methotrexate with TNFi, and sulfasalazine or methotrexate is only recommended in patients experiencing persistent peripheral arthritis or when TNFis are contraindicated (Ward et al., 2019).

Follow-Up: Monitoring the patients to determine management of symptoms, disease progression, impact on quality of life and function. Consider the development of comorbidities and monitor and refer as indicated.

Sequelae: In patients with late-onset axSpA, there is an increased risk of cardiovascular disease due to the inflammatory nature of this condition (Wenker & Quint, 2021). In addition, patients with axSpA tend to have poor sleep due to sleep apnea and complain of fatigue (Wang et al., 2020). Ankylosing spondylitis is part of a spectrum of spondyloarthropathy diseases, so patients are at risk for developing other inflammatory conditions, such as inflammatory bowel disease, uveitis, and psoriasis. Additionally, older patients with axSpA are at increased risk for developing fragility fractures (Wenker & Quint, 2021).

Prevention/Prophylaxis: There is no primary prevention known for axSpA. Smoking cessation is advised given that limited chest expansion often occurs in these patients (Dülger et al., 2019; Zhu et al., 2019). Exercise may be beneficial to patients with axSpA (Regal et al., 2016; Zhu et al., 2019).

Referral: Patients with complicated axSpA should be referred to a rheumatologist. Additionally, if patients have comorbid inflammatory conditions, such as inflammatory bowel disease or anterior uveitis, referral to specialist is warranted. As cardiac manifestations are the most common comorbidity in older patients with axSpA, monitoring for signs of cardiac conditions such as heart block or valvular disease and referral to cardiology early on in cases of late-onset axSpA are recommended. Patients would also benefit from physical therapy (PT) referral to enhance physical activity and range of motion (ROM) (Wenker & Quint, 2021).

Education: Patients can benefit from knowing that this is a progressive condition that benefits from both pharmacological as well as nonpharmacological interventions such as exercise and participating in PT and water therapy. Given that patients have limited chest expansion ability, they are at increased risk for pulmonary infection; thus, keeping immunizations current is highly recommended and smoking cessation is recommended (Wenker & Quint, 2021).

Clinical Recommendation	Evidence Rating	References
In a study comparing younger patients diagnosed with psoriatic arthritis compared with patients diagnosed with late-onset psoriatic arthritis, the majority of the patients were female and had higher body mass index, more joint damage, and less HLA-C*06.	B	Polachek et al., 2019
In a study comparing patients with psoriatic arthritis compared to patients without inflammatory arthritis, patients with psoriatic arthritis had higher frequencies of multiple comorbidities such as hypertension, diabetes, cardiovascular disease, and obesity.	A	Queiro et al., 2019b
In adults with active non-radiographic persistent axial spondyloarthritis (axSpA) despite treatment with NSAIDs, treatment with tumor necrosing factor medications is recommended.	A	Ward et al., 2019
Physical therapy is recommended for patients with axSpA.	B	Ward et al., 2019
Treatment with NSAIDs is recommended for first-line treatment of axSpA.	C	Ward et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

OSTEOARTHRITIS

Signal Symptoms: Joint pain and stiffness that improves with rest; worsens with activity and weight-bearing. Often affects the hands, hips, knees, and low back causing functional limitations.

Description: Osteoarthritis (OA), or degenerative joint disease, is the most common form of arthritis and a significant cause of pain and disability in older adults. It is a progressive, heterogeneous joint disease driven by a combination of inflammatory

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and biomechanical processes with the progressive loss and destruction of articular cartilage leading to joint space narrowing, degeneration of ligaments, subchondral bone thickening, synovitis, hypertrophy of the joint capsule, and formation of osteophytes (Chen et al., 2017; Van Spil et al., 2019).

Etiology: No longer considered simply "wear and tear" arthritis, OA is a heterogeneous disease without a singular pathogenic mechanism of OA; considerable patient-specific variability exists. Predisposing risk factors include age, sex, past injury/trauma, and genetics (He et al., 2020). Emerging research seeks to understand this heterogeneity by focusing on gene expression and biomarkers in order to subtype OA into phenotypes/endotypes such as senescent, inflammatory, metabolic, genetic, and estrogen deficiency (Van Spil et al., 2019; Werdyani et al., 2021). Studies have shown that 39% to 78% of OA can be attributed to genetic factors (He et al., 2020).

Occurrence: The exact incidence and prevalence of OA vary based on the definition of OA, which can include radiographic, symptomatic, and doctor-diagnosed (Vina & Kwoh, 2018). According to the Centers for Disease Control and Prevention (CDC), 32.5 million adults in the United States are affected by OA, with half of these of working age (18 to 64 years of age) (CDC, 2020). The total number is expected to increase to 78 million by 2040 (He et al., 2020). In 2017, the worldwide prevalence of OA was estimated to be 303 million people, with the most common joints causing disability being the knees (60.9%), hands (23.5%), and hips (5.5%) (Global Health Metrics, 2019; Kloppenburg & Berenbaum, 2020). Musculoskeletal diseases, including OA, are the second leading cause of years lived with disability and the numbers are increasing due to aging and obesity (Loeser, 2017; Sebbag et al., 2019). Women reported a higher prevalence of provider-diagnosed arthritis compared to men (23.5% vs. 18.1%) (Barbour et al., 2017). Women are more likely to develop hand (specifically after menopause), foot, and knee OA, whereas men have a higher rate of shoulder and cervical spine OA (Vina & Kwoh, 2018).

Age: OA is not age dependent; however, the average person begins experiencing symptoms around 55 years of age and will live with the disease for approximately 26 years (Van Spil et al., 2019). In adults aged 65 or older, 22.2 million (49.6%) have OA compared to 8 million (7%) young adults (18 to 44 years) and approximately 24.2 million (29.3%) middle-aged adults (45 to 64 years) (Barbour et al., 2017).

Ethnicity: Non-Hispanic Whites (25.3 million) have the highest proportion of OA whereas Hispanics have the lowest, (78% vs. 7%) (Hochberg & Cisternas, 2019); however, Mexican Americans seem to have similar prevalence of knee OA compared to White Americans (Callahan et al., 2021). Compared to other ethnicities, African Americans are more likely to develop symptomatic knee and hip OA (Vina & Kwoh, 2018). Studies have shown an 80% to 90% decreased prevalence of hip OA within the Chinese population compared to Whites; however, the Third National Health and Nutrition Examination Survey indicated a 45% increased prevalence of knee OA in Chinese women compared to White women, with no difference in their male counterparts (Callahan et al., 2021).

Contributing Factors: In addition to risk factors of age, sex, and hormone profile, past injury/trauma/surgery, and genetics, OA is affected by obesity, chronic overload/overuse, inflammation, and metabolic syndrome (He et al., 2020). Modifiable risk factors include excess body weight, injuries/trauma, and occupations/hobbies that require repetitive overuse/overload (CDC, 2020). Higher rates of OA have been reported in individuals who have a high school education or less compared to those who have completed college or higher (Barbour et al., 2017). Increased bone mineral density has been linked to increased rates of hip, knee, and hand OA (Vina & Kwoh, 2019). Adults with obesity, diabetes, and heart disease were 1.5, 1.7, and 1.9 times more likely to have arthritis, respectively, compared to their counterparts without these comorbidities (Barbour et al., 2017).

Signs and Symptoms: Individuals seek medical attention for the concern of morning stiffness (<30 minutes) and/or pain with movement or mechanical loading of the affected joint often in the context of activities of daily living. Additional symptoms include muscle weakness, functional limitations, gait alternations/adaptations, fear of movement, joint instability, and/or sleep problems. Pain associated with OA may be described as sensitive to touch and pressure, dull and aching, throbbing, or sharp and stabbing (Rice et al., 2019). Early OA tends to be intermittent and with predicted activities; however, it can occur suddenly with subsequent joint instability—giving way or locking up such as with the knee. As OA advances, the pain can become more constant and can occur at night (Fu et al., 2018). OA may include mild warmth, minimal erythema, and varying degrees of swelling and tenderness to palpation; however, in general a big, red, hot, painful joint is more consistent with infection or an inflammatory arthritis, particularly a crystalline arthropathy.

Women are more prone to hand OA, particularly just after menopause; 67% of women compared to 55% of men show evidence of radiograph OA; however, most are asymptomatic. When symptomatic, common concerns are decreased dexterity and/or grip strength. Hand OA has the hallmark features of nontender bony Bouchard's nodes (nodules of the proximal interphalangeal [PIP] joints) and/or Heberden nodes (nodules of distal interphalangeal [DIP] joints). The carpometacarpal (CMC) joint is a very common area of OA known as "the squaring of the thumb" and can have crepitus upon examination. Erosive hand OA affects these same joints but tends to be more painful and cause joint destruction with erosions and ankylosis thereby decreasing function (Perrotta et al., 2019).

Hip and knee OA are a major cause of disability with decreased physical function and activity, both in working adults and older adults. In addition to reported pain and gait disturbances with hip OA, decreased external and internal rotation of the hip can easily be elicited on examination. Knee OA is worse with increased load bearing (e.g., walking down stairs). Crepitus from knee OA is easily palpated during examination. Medial knee tenderness is more common than lateral pain because medial knee joint space narrowing is more common. A knee effusion can occur with OA as well as trauma, inflammatory arthropathies, and infections (He et al., 2020).

Additional common areas of OA include the foot, specifically the first metatarsal; the cervical and lumbar spine; and the shoulders. All of these areas may be affected by pain with use and decreased function and range of motion (Vina & Kwoh, 2018). Cervical OA can cause a range of symptoms

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including headaches, referred pain to shoulders and scapula, and radiculopathy down the arm(s). Lumbosacral OA involves pain across the lower back with radiation to the buttock and thigh. Nerve root compression is likely with radiculopathy below the knee and possible motor, sensory, and reflex deficits (Lindsey & Dydyk, 2021).

Diagnostic Tests: X-rays and clinical examination are the mainstays for OA diagnosis. Radiographically, OA presents with joint space narrowing, osteophytes (bone spurs), subchondral sclerosis, cyst formation, and abnormalities of bone contour (He et al., 2020). X-rays are best ordered weight-bearing when applicable and in two- or three-view. Other types of imaging, such as ultrasound and magnetic resonance imaging (MRI), may be used to detect soft tissue damage/irritation of cartilage, ligaments, synovium, and/or tendons or to better assess radicular symptoms (Kloppenburg & Berenbaum, 2020). Arthrocentesis should be considered for joint effusions. The specimen should be sent for synovial fluid analysis that includes cell count, crystal analysis, and culture. The synovial fluid in OA is usually clear, colorless-yellow, and viscous, and has less than 2,000 white blood cells per μL (He et al., 2020). Laboratory studies, including complete blood count (CBC), comprehensive metabolic panel (CMP), and vitamin D level, should be obtained before initiating long-term drug therapy; if prolonged morning stiffness (>60 minutes) or inflammation is suspected, uric acid, C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and rheumatoid factor (RF) may be ordered (Perrotta et al., 2019). Although still novel, in the future biomarkers could further delineate phenotypes to help direct treatment (Van Spil et al., 2019).

Differential Diagnosis: (Kontzias, 2020)

- Trauma: fracture, dislocation, soft tissue injury (bursitis; torn ligament, tendon, muscle)
- Inflammatory arthritis (rheumatoid arthritis [RA], polymyalgia rheumatica [PMR], systemic lupus erythematosus [SLE], spondyloarthropathy)
- Crystalline disease (gout, chondrocalcinosis/calcium pyrophosphate dihydrate [CPPD]/pseudogout)
- Infection/septic arthritis
- Cancer (metastatic disease, multiple myeloma, bone tumor)
- Other spinal conditions (spinal stenosis, disc herniation)
- Referred pain
- Avascular necrosis, particularly in patients with history of oral corticosteroid use
- Paget's disease

The presence of systematic symptoms in the setting of joint pain or divergent onset of symptoms warrants further work-up. Red flags as part of a spinal OA work-up include loss of bowel or bladder continence, saddle anesthesia, numbness, and/or fever/chills (Lindsey & Dydyk, 2021).

Treatment: The lack of any therapy that slows disease progression is a major limitation in the treatment of OA. Current pharmacological and nonpharmacological modalities seek to alleviate pain and focus on improving symptoms and function (Loeser, 2017). Management of OA is multifactorial utilizing oral, topical, and intra-articular medications as well as physical, surgical, behavioral, educational, and psychosocial interventions (Kolasinski et al., 2020).

Oral NSAIDs and acetaminophen are mainstay pharmacological treatment choices for OA. NSAIDs can be particularly efficacious at reducing inflammation and pain associated with OA; however, caution is advised due to risk of renal and cardiovascular side effects and gastrointestinal (GI) toxicity/bleeding. NSAIDs are best prescribed at the lowest effective dose on an as-needed basis instead of scheduled and with routine monitoring. As a selective NSAID, cyclooxygenase type 2 (COX-2) inhibitors offer the anti-inflammatory benefits with a better GI risk profile; however, these medications carry a higher cardiovascular risk and still require routine laboratory studies. Topical NSAIDs are not quite as effective, but they offer a better safety profile. Over-the-counter (OTC) topical preparations include lidocaine 4% and capsaicin, both of which offer variable patient responses. Acetaminophen can be effective against OA pain at higher therapeutic doses, but it is important to avoid alcohol and other medications that contain acetaminophen due to possible liver toxicity. Duloxetine, tramadol, and opioids are only conditionally recommended by the American College of Rheumatology, although duloxetine can help patients in multiple ways with pain and mood. Neither oral corticosteroids nor disease-modulating antirheumatic drugs (DMARDs), such as methotrexate and hydroxychloroquine, is recommended. Nutritional supplements such as glucosamine and chondroitin are not currently recommended due to a lack of unbiased evidence-proven efficacy (Kolasinski et al., 2020; Sen & Hurley, 2021).

Intra-articular joint injections can offer localized relief without extensive systemic effects. Corticosteroid injections work well in the setting of acute OA pain, and they are relatively low cost and low risk. As OA progresses, patients tend to experience a variable response, a risk of infection is possible with any injection, and (as with any corticosteroid) blood glucose can briefly elevate. There is ongoing controversy of repeated corticosteroid injections possibly accelerating OA progression and bone destruction (Kloppenburg & Berenbaum, 2020). Hyaluronic acid injections are a gel-like viscosupplementation primarily for knee OA. They are considerably more expensive and not always covered by insurance because of mixed evidence of efficacy compared to placebo. Any joint with suspected infection should never be injected, only arthrocentesis should be performed; and a joint with surgical hardware should not be punctured with a needle (Sen & Hurley, 2021). Emerging therapies for knee OA include the recently fast-tracked by the U.S. Food and Drug Administration (FDA), highly purified, injectable trans-capsaicin CNTX-4975. Studies are ongoing with CNTX-4975 to improve procedure protocol due to associated pain (Kloppenburg & Berenbaum, 2020). Regenerative medicine, including mesenchymal stem cell therapy and platelet rich plasma injections, so far have shown little to no benefit (Kloppenburg & Berenbaum, 2020).

Exercise and physical therapy (PT)/rehabilitation are first-line treatments for OA. Evidence-based OA treatment guidelines recommend both aerobic and resistance exercises for knee, hip, and hand OA as well as self-management programs. PT/occupational therapy (OT) can assist patients with splints, braces, and assistive devices. Weight loss is strongly recommended when appropriate. Tai chi is more strongly recommended than yoga; both help to maintain joint function and flexibility and reduce risk of falls in older adults (Kolasinski et al., 2020; Rice et al., 2019). Arthroscopic surgery including meniscus or anterior cruciate ligament repair,

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and joint débridement and/or irrigation may be appropriate for some patients to help reduce pain and improve function (Loeser, 2017; Rice et al., 2019). For end-stage hip or knee OA, a joint replacement may be an effective treatment option. However, joint replacements have a life span of approximately 15 to 25 years, they sometimes fail, and there is the risk of complications (Kloppenburg & Berenbaum, 2020).

No matter what treatment options are chosen, it is important to individualize the plan of care to the patient needs/preferences and work to address indirect aspects of OA that affect quality of life, including poor sleep, depression, central sensitization, and impaired coping skills. Current research aims to classify OA phenotypes to identify patients at higher risk of disease progression. This would then allow targeted treatment including prevention strategies for individuals with particular disease mechanisms and risk factors (Deveza et al., 2019).

Follow-Up: Patients should follow up with their health-care provider no longer than 4 weeks after initiation of treatment for OA. This will allow the patient adequate time to schedule and start an exercise program or PT and have an idea of how it is helping. If either of these are too difficult due to joint function and/or pain, water therapy should be considered. This timeline will also allow the patient to try any new pharmacological treatment options and to have laboratory values rechecked including a CMP and CBC. It is important to periodically repeat these laboratory tests to monitor renal and liver function and assess negative gastrointestinal (GI) effects in addition to the patient's reported symptoms.

Sequelae: As a progressive disease, OA will continue to worsen leading to pain, joint deformity and/or functional impairment. To date, only a total joint replacement will effectively fully treat OA; however, complications as high as fourfold in the year following surgery have been reported (Charlesworth et al., 2019).

Prevention/Prophylaxis: Maintaining optimal weight and consistent low-to-moderate levels of activity throughout one's lifetime are the best methods for prevention of OA and for helping mitigate the effects of OA. For individuals genetically predisposed to OA, it is advisable to avoid trauma/joint injuries and repetitive/overuse activities including occupations and hobbies.

Referral: Patients need referrals to PT/OT and in some instances water therapy. They may need a referral to orthopedics if they are not responding to standard nonsurgical treatments. Referral to rheumatology may be necessary for unusual presentation of the disease.

Education: In addition to weight management and exercise/rehabilitation, it is important to educate patients on effective physical and mental coping strategies to better help manage OA pain and impaired function, such as assistive devices and home modifications and self-management and cognitive behavioral therapy strategies. A healthy lifestyle that includes proper rest and nutrition can be beneficial; lower rates of clinical and radiographic knee OA have been observed when a Mediterranean diet is adhered to as well as high dietary fiber and sufficient vitamin D (Vina & Kwoh, 2019).

Clinical Recommendation	Evidence Rating	References
Encourage exercise that includes a combination of low-impact aerobic and resistance training tailored to the impairments, functional requirements, and preferences; use water therapy when land physical therapy is not tolerated.	A	Rice et al., 2019 Kolasinski et al., 2020
Tai chi is strongly recommended for knee and/or hip osteoarthritis (OA).	A	Kolasinski et al., 2020
Yoga and balance exercises are conditionally recommended for knee and/or hip OA.	B	Kolasinski et al., 2020
Weight loss: combination of strategies, including regular weight monitoring, increased physical activity, social support, meal plans, limiting portion size, reducing fat and sugar intake, time-restricted feeding, and addressing behavioral triggers to eating.	A	Rice et al., 2019 Kolasinski et al., 2020
Encourage active self-management and positive behavioral changes such as regular exercise, weight loss, good sleep hygiene and activity pacing.	A	Rice et al., 2019 Kolasinski et al., 2020
Cognitive behavioral therapy has small positive effects on OA pain and fatigue and moderate to large positive effects on self-efficacy and pain coping.	B/A	Rice et al., 2019 Kolasinski et al., 2020
Oral NSAIDs are strongly recommended for knee, hip, and/or hand OA.	A	Kolasinski et al., 2020
Topical NSAIDs are strongly recommended for knee OA and conditionally recommended for hand OA.	A/B	Kolasinski et al., 2020
Topical capsaicin is conditionally recommended for knee OA (and conditionally recommended *against* for hand OA due to possibly of then touching one's eyes/face).	B	Kolasinski et al., 2020
Acetaminophen, duloxetine, and tramadol are conditionally recommended for knee, hip, and/or hand OA.	B	Kolasinski et al., 2020
Glucosamine and chondroitin sulfate are recommended.	B	Charlesworth et al., 2019 Kolasinski et al., 2020

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Clinical Recommendation	Evidence Rating	References
Intra-articular glucocorticoid injections are strongly recommended for knee and/or hip OA and conditionally recommended for hand OA.	A	Kolasinski et al., 2020
Ultrasound guidance for intra-articular glucocorticoid injection is strongly recommended for injection into hip joints.	A	Kolasinski et al., 2020
Intra-articular hyaluronic acid injection for knee OA.	B	Charlesworth et al., 2019 Kolasinski et al., 2020
Cane use is strongly recommended for patients with knee and/or hip OA in whom disease in one or more joints is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant use of an assistive device.	A	Kolasinski et al., 2020
Tibiofemoral knee braces are strongly recommended for patients with knee OA in whom disease in one or both knees is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant use of an assistive device, and who are able to tolerate the associated inconvenience and burden associated with bracing.	A	Kolasinski et al., 2020
Patellofemoral braces are conditionally recommended for patients with patellofemoral knee OA in whom disease in one or both knees is causing a sufficiently large impact on ambulation, joint stability, or pain to warrant use of an assistive device.	B	Kolasinski et al., 2020
Hand orthoses are strongly recommended for first CMC joint OA.	A	Kolasinski et al., 2020
Hand orthoses are conditionally recommended for OA in other joints of the hand.	B	Kolasinski et al., 2020
Thermal modalities (use of local hot or cold) may provide short-term positive effects on pain.	B	Rice et al., 2019
Joint replacement for end-stage hip or knee OA.	C	Kloppenburg & Berenbaum, 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

POLYMYALGIA RHEUMATICA AND GIANT CELL ARTERITIS

Signal Symptoms: New onset of stiffness and aching in neck, shoulders, pelvic girdle; unable to get out of bed in the morning without extreme difficulty; difficulty in lifting arms over one's head for polymyalgia rheumatica. Onset of a new headache, visual loss, jaw claudication, scalp tenderness in patients with giant cell arteritis (GCA).

Description: Polymyalgia rheumatica (PMR) is a clinical inflammatory syndrome characterized by fatigue, aching, pain, and stiffness, primarily in the neck, shoulders, hips, and pelvic girdle, occurring primarily in older adults. Older adults may relate the presentation of aches and pains to old age and delay seeking treatment. Initially, patients may report unilateral stiffness and aching, although muscle aching with guarded range of motion (ROM) will affect eventually both sides of the body (Milchert & Brzosko, 2017; Muller et al., 2016). Musculoskeletal symptoms have been linked to nonerosive articular and extra-articular synovitis (Camellino et al., 2019). Systemic manifestations include low-grade fever, anorexia, depression, weight loss, and malaise (Camellino et al., 2019; Mahmood et al., 2020).

Synovial proliferations are found in patients with PMR. Patients are often found to have an elevated erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) level (Lally & Spiera, 2018). If both of these inflammatory markers are not elevated, the diagnosis of PMR cannot be discarded (Camellino et al., 2019; Lally & Spiera, 2018). There is a close association with patients presenting with PMR developing GCA, a common vascular condition in older adults; approximately 40% to 60% of patients who are diagnosed with GCA have clinical presentation of PMR (Lally & Spiera, 2018; Sharma et al., 2020). GCA is a chronic inflammatory condition (primary vasculitis) that involves large and medium-sized arteries (Nordborg et al., 2000; Sharma et al., 2020).

The percentage of patients with PMR who eventually develop GCA is around 10% to 20%, but varied percentages have been reported (Masson et al., 2017). Assessing for signs and symptoms of vasculitis early is important to avoid the complications of GCA, namely, irreversible blindness (Vodopivec & Rizzo, 2018). Patients need to be alerted to the symptoms of GSA because they are additive to PMR.

Etiology: The etiology of PMR and GCA is unknown. A relationship between the presence of the human leukocyte antigen (HLA) DR4 haplotype and presentation of PMR and GCA has been suggested (Camellino et al., 2019; Dinkin & Johnson, 2021; Nordborg et al., 2000).

Occurrence: For the United States, the highest incidence of PMR and GCA is found in northern states that have

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populations with similar ethnic backgrounds to northern European countries with rates of incidence found to be 20/1,000,000 adults (Acharya & Musa, 2021; Sharma et al., 2020). Throughout the world, the highest incidence of PMR and GCA is found in populations with northern European ancestry (Sharma et al., 2020). PMR and GCA are more common in women than men (Sharma et al., 2020).

Age: PMR and GCA occur predominantly in adults older than 50 years old, with an average age of peak incidence in the eighth decade of life (Lally & Spiera, 2018).

Ethnicity: PMR and GCA is six times more common in Whites than in Blacks, Alaskan Natives, Asians, and Hispanics (González-Gay & Pina, 2015). Patients who are descendants from northern European countries have the highest rate of PMR and GCA, whereas the lowest prevalence has been noted in the Japanese (Berti & Dejaco, 2018).

Contributing Factors: Advanced age and a possible genetic predisposition are thought to contribute to the development of PMR and GCA. Infectious conditions such as mycoplasma pneumonia, Epstein-Barr, and parvovirus suggested a connection with developing PMR and GCA (Acharya & Musa, 2021; Dinkin & Johnson, 2021). Patients with a history of myocardial infarction, peripheral vascular disease, and stroke have been shown to tend to develop PMR and GCA (Camellino et al., 2019). Risk factors for GCA also include history of smoking (Dinkin & Johnson, 2021).

Signs and Symptoms: Often, the onset of PMR occurs in patients who report good health prior to symptom presentation. Reports of impairment in function due to pain such as the ability to get up out of bed in the morning, raise arms to groom hair, getting up from chairs or the toilet. Patients complain of fatigue and generalized malaise and may attribute the symptoms to influenza or the exacerbation of existing arthritic conditions, such as osteoarthritis (OA) (Buttgereit et al., 2016). Additionally, patients usually have bilateral, proximal aching and stiffness in the neck, shoulders, upper arms (Acharya & Musa, 2021; Camellino et al., 2019), hips, thighs, and lower back, with patients reporting aching and pain in the shoulder girdle (Lally & Spiera, 2018). Stiffness occurs in the morning and may last more than 30 minutes to 1 hour; however, on exertion, fatigue and aching may return (Matteson & Dejaco, 2017). Pain at nighttime may impair sleep, limiting mobility and/or positional changes (e.g., inability to turn over in bed at night) (Acharya & Musa, 2021).

When the patient is questioned, there may be no report of actual peripheral joint pain. Musculoskeletal pain and related symptoms may be present about 1 month before the diagnosis is made; however, sudden onset of PMR can occur in older adults (Acharya & Musa, 2021). Fever, anorexia, weight loss, apathy, night sweating, fear, anxiety, and depression are also constitutional symptoms of PMR (Buttgereit et al., 2016; Milchert & Brzosko, 2017). Muscle weakness usually is not elicited on physical examination. It is important to note that pain often inhibits accurate assessment of muscle strength because patients can neither raise the thigh to resistance nor laterally abduct upper arms to resistance due to pain. Tenderness may be detected on palpation to the muscle groups mentioned earlier (Acharya & Musa, 2021). Examine for contracture of the shoulder or adhesive capsulitis resulting from extended limitation of movement due to persistent pain over time. Patients may report a decreased ability to grasp small objects. Check for signs of carpal tunnel syndrome, such as paresthesia of the thumb and index and middle fingers due to flexor tenosynovitis (Acharya & Musa, 2021). An unusual presentation of PMR is RS3PE, which involves distal extremity swelling with pitting edema present over the dorsum of hands, wrists, ankles, and tops of feet (Higashida-Konishi et al., 2021; Salvarani et al 2002). Examine for evidence of claudication in the lower extremities and/or pitting edema, which can be signs of GCA (Tracey & Su, 2020). Diagnostic studies may reveal anemia. Checking for signs of pallor is important.

Because GCA is associated with PMR, the work-up should include questions to evaluate for this vasculitis, such as complaints of occipital or temporal headaches, visual disturbances (amaurosis fugax [transient vision loss] or transient diplopia), high fever, jaw and tongue pain, sore throat, hoarseness, ear pain, painful scalp, and limb claudication as a result of vascular occlusion (Hayreh, 2021; Tracey & Su, 2020). Assess for tender temporal arteries and visual acuity (Dinkin & Johnson, 2021). Funduscopic examination may reveal retinal hemorrhages, cotton-wool patches, and edema of the optic disc (Salvarani et al., 2002). Neurological findings are also common in patients with GCA due to occlusion of internal carotid or vertebral arteries; neuropathies, transient ischemic attacks, and stroke have been known to occur in patients with extensive GCA (Dinkin & Johnson; 2021; Soriano et al., 2017). Consider, too, that patients with GCA may develop thoracic aortic aneurysm or even dissection; thus, attention to potential for these presenting conditions is warranted, especially for those who have history of hypertension (Tracey & Su, 2020).

Diagnostic Tests: An elevated ESR of more than 30 to 40 mm/hr and CRP level greater than 6 mg/dL are common findings in PMR (Mahmood et al., 2020). Obtain complete blood count (CBC) with indices to determine presence of normochromic, normocytic anemia, and thrombocytosis, which are common in patients with PMR (Milchert & Brzosko, 2017). The use of ultrasound in establishing diagnosis of PMR may find evidence of subdeltoid bursitis, tenosynovitis, hip synovitis, glenohumeral joint bursitis, and trochanteric bursitis (Buttgereit et al., 2016; Camellino et al., 2020). For patients with GCA, the ESR generally is found to be greater than 50 mg/hr, often elevated to 100 mm/hr or greater (Dinkin & Johnson, 2021). Patients with symptoms of GCA need to be referred for temporal artery biopsy (van der Geest et al., 2020). There have been cases of patients who had a positive temporal artery biopsy for GCA with normal CRP (Parikh et al., 2006). Ultrasound of the temporal artery is also being used to diagnose GCA (Rubenstein et al., 2020).

For patients with symptoms of claudication, imaging studies can be beneficial in determining presence of lower extremity vasculitis (Rubenstein et al., 2020). Liver enzyme tests often show elevated alkaline phosphate in patients with PMR and GCA (Milchert & Brzosko, 2017).

Considering the need for long-term corticosteroids, diagnostic studies should also include urea and electrolytes, thyroid-stimulating hormone (TSH) and dipstick urinalysis, and bone density testing if no recent results are available for the patient when the diagnosis is established and treatment with corticosteroids begins (Tracey & Su, 2020).

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Differential Diagnosis:

PMR:

- Late-onset rheumatoid arthritis (RA) (specifically, the absence of rheumatoid factor (RF) and normal anti-citrullinated protein antibody (anti-CCP) can rule out initial diagnosis of late-onset RA.
- Polymyositis (patients who have demonstrated proximal weakness characteristic of polymyositis would have a positive muscle biopsy)
- Fibromyalgia (generally fibromyalgia begins in younger adulthood and the ESR is normal)
- Hypothyroidism (thyroid hormone is not elevated as a result of PMR)
- Hyperparathyroidism (parathyroid hormone level is not elevated as a result of PMR)
- OA (radiographic changes would demonstrate evidence of OA and not PMR)
- Bursitis and tendinitis (constitutional symptoms generally are not evident in patients with bursitis and tendinitis)
- Rotator cuff injuries
- Carcinomatosis
- Chondrocalcinosis
- Depression
- Systemic lupus erythematosus (antinuclear antibody [ANA] would not be significantly elevated in patients with PMR; slight ANA elevation can be expected in older adults absent of disease)
- Multiple myeloma (patients with multiple myeloma do not respond to corticosteroids and noted absence of Bence Jones' protein in urine or serum or urine electrophoresis)
- Infective endocarditis
- Vasculitis
- Parkinson's disease (ESR is not elevated in patients with Parkinson's disease, and corticosteroid therapy would not produce a clinical response to the stiffness experienced)
- Calcium pyrophosphate dihydrate crystal deposition disease (arthrocentesis of affected joints would be negative for this condition and arthrocentesis would show crystals that typically present positive birefringence)
- Late-onset ankylosing spondylitis (radiographic findings of syndesmophytes)
- Diffuse idiopathic skeletal hyperostosis (DISH)
- Inflammatory amyloidosis
- Paraneoplastic syndrome from lung cancer (corticosteroid would not produce a clinical response and radiographic imaging would be negative)

GCA:

- Acute angle-closure glaucoma in emergency medicine
- Granulomatosis with polyangiitis
- Herpes zoster
- Iritis and uveitis
- Migraine headache
- Non-arteritic ischemic optic neuropathy
- Persistent idiopathic facial pain
- Retinal artery occlusion (RAO)
- Retinal vein occlusion (RVO)
- Transient ischemic attack

(Acharya & Musa, 2021; Camellino et al., 2019; Mahmood et al., 2020; Milchert, & Brzosko, 2017; Seetharaman, 2020)

In patients with symptoms typical of PMR and a normal ESR, also consider drug-induced myalgias from lipid-lowering agents, beta blockers, and dipyridamole (Camellino et al., 2019; Snyder, 1991).

Treatment: If the patient presents with signs and symptoms only of PMR, start low-dose prednisone 12.5 to 25 mg daily, to be tapered to a dose of 10 mg daily within 4 to 8 weeks and, thereafter, the daily dose should be decreased by 1.0 to 1.25 mg daily every 4 weeks (Camellino et al., 2020). Lower starting doses (7.5–10 mg) may be considered in patients of "smaller body habitus, milder symptoms, uncontrolled diabetes or risk for significant drug adverse reactions" (Mahmood, 2020, p. 552). Symptoms should begin to resolve after 24 hours. However, immediate relief from corticosteroids may not be indicative of PMR because multiple conditions that mimic PMR would also show sign and symptom improvement after prednisone is initiated (Matteson & Dejaco, 2017). Prednisone is tapered off slowly, continuing over months, when the symptoms have resolved and the ESR and CRP levels returns to normal level or near normal level from the patient's baseline (because ESR can be elevated normally because of increased age) (Alende-Castro et al., 2019). Patients presenting with visual disturbances, jaw claudication, or other symptoms of GCA need a higher dose of oral corticosteroids with a gradual tapering depending on symptoms and laboratory values. For GCA, the suggested initial dose of prednisone is 40 to 60 mg daily, a gradual tapering depending on symptoms and laboratory values. Tapered dose within 2 to 3 months should be reduced to 15 to 20 mg daily, and, after 1 year, to ≤5 mg daily (Camellino et al., 2020). Treatment may last 1 to 2 years (Mahmood et al., 2020).

Follow-Up: Assess the patient for proximal pain, morning stiffness, resolution of constitutional symptoms, and adverse reaction to corticosteroids. For patients with PMR, the ESR and/or CRP need monitoring until the levels decrease and previously reported symptoms are alleviated. The CBC can be repeated to determine whether the anemia has resolved. Generally, a return to normalization of ESR and CRP resolves within 2 to 4 weeks of treatment of corticosteroids in patients with PMR and GCA (González-Gay & Pina, 2015). Initially, the patients may need to return every couple of weeks to determine the clinical response to therapy. This is followed by approximately an every-3-month surveillance to determine response to treatment and any adverse reactions to the long-term corticosteroids. Additional monitoring of urea and electrolytes and glucose should continue every 3 months while on corticosteroids (Mundell et al., 2017).

Follow up on the results of the dual-energy x-ray absorptiometry scan. Prophylactic therapy to prevent osteoporosis with bisphosphonates and calcium and vitamin D supplementation of 800 to 1,000 IU daily is needed in patients taking glucocorticoids >7.5 mg for more than 3 months (Acharya & Musa, 2021; Camellino et al., 2019). Patients also presenting with GCA need to be monitored in the same way, with repeated eye examinations as warranted, including examination for cataracts resulting from corticosteroid therapy (Petri et al., 2015). Because patients with GCA are at risk for developing aortic aneurysm, follow-up abdominal examination for aortic aneurysm is needed. This complication is of great concern, especially with patients who are at high risk for developing aortic aneurysms, such as patients who

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smoke, are hypertensive, and have arteriosclerotic heart disease (Tracey & Su, 2020).

Sequelae: Patients diagnosed with PMR only should be alerted to the signs of GCA because patients with untreated GCA are at risk for blindness (Vodopivec & Rizzo, 2018). Additional complications from GCA include pericardial effusion, tongue necrosis and interstitial lung disease (ILD) (Dinkin & Johnson, 2021). Patients should be informed that they must complete all of the prescribed medication to avoid a relapse. Despite the initial symptom relief, extended treatment with corticosteroids is the mainstay of treatment. Patients often relapse following an initial case of PMR; up to 50% of patients have a recurrence of PMR (Lally & Spiera, 2018). Studies have shown that women, those with elevated ESR rates, and those with peripheral arthritis were at high risk for relapse (Camellino et al., 2020; Matteson & Dejaco, 2017). There has also been indication that a percentage of patients with PMR eventually develop late-onset RA (Kermani & Warrington, 2013).

Patients with PMR may be at risk for developing vascular disorders, especially cardiovascular disorders (Camellino et al., 2019); thus, these patients should be screened carefully. The incidence of cataracts has been found to increase in patients with PMR (Camellino et al., 2019). Practitioners will need to continue to monitor patients for any new symptoms following treatment for PMR. When examining a national database of patients with PMR, Muller and colleagues (2016) found a trend of new cancer diagnoses in patients with PMR, without pre-existing cancer, 6 months after initial diagnosis. In one systematic review, it was found that the rate of hematogenous cancer was significantly higher in patients with a diagnosis of PMR (Partington et al., 2018).

Prevention/Prophylaxis: No preventive measures exist for PMR, but because the disease can recur, patients should be advised to contact their health-care providers when any of the prevailing signs and symptoms reappear. Patients on long-term corticosteroids should be up to date on immunizations for influenza and pneumonia (Tanrıöver et al., 2016). Prophylaxis for *Pneumocystis carinii* pneumonia is recommended for patients on >20 mg prednisone for extended periods of time.

Referral: For patients with signs of visual disturbance, funduscopic changes, or both, referral to an ophthalmologist is warranted if the patient can be evaluated immediately. If not, these patients should be referred to an emergency department for immediate evaluation for probable temporal artery biopsy (Vodopivec & Rizzo, 2018). Consultation with a rheumatologist is warranted for patients who have GCA and for patients with PMR alone that have spinal involvement, who do not respond initially to corticosteroid treatment, are unable to take corticosteroids, and are candidates for a disease-modifying agent, or have prolonged duration of PMR of 6 to 12 months (Caylor & Perkins 2013).

Education: Patients should be taught the possible side effects of taking long-term glucocorticoids, such as insomnia, elevation of blood pressure and blood glucose level, hot flashes, edema, and exacerbation of heart failure. Patients and their caregivers need to be informed not to abruptly cease taking the glucocorticoids. In addition to being at risk for osteoporosis, the likelihood for developing infections, fractures, diabetes, peptic ulcers, cataracts, depression, and weight gain increases with steroid use. Patients should be instructed to include an adequate amount of dietary calcium and vitamin D in their diets (Acharya & Musa, 2021; Mahmood et al., 2020). Given the risk of vascular disorders, patients who smoke should be highly encouraged to begin smoking cessation. Patients who do not have GCA should be alerted to potential symptoms, such as visual disturbance, headache, temporal and scalp tenderness, jaw pain (especially while chewing), and limb pain given the development of late GCA after a PMR diagnosis (Liozon et al., 2018).

Clinical Recommendation	Evidence Rating	References
Highest incidence of polymyalgia rheumatica (PMR) occurs in people who live in Scandinavian Countries and in the northern United States in people with northern European ancestry.	A	Sharma et al., 2020
For patients taking 20 mg of prednisone a day for treatment of PMR, there was a lower percentage of relapse than patients who were prescribed 10 mg of prednisone a day.	A	Buttgereit et al., 2016
The ultrasound halo sign was found to have high sensitivity and specificity for diagnosing giant cell arteritis.	A	Sebastian et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

RHEUMATOID ARTHRITIS

Signal Symptoms: Symmetrical inflammatory arthritis; Joint pain and swelling, particularly of the metacarpophalangeals (MCPs) and proximal interphalangeals (PIPs), wrists, and metatarsophalangeals (MTPs); morning stiffness lasting longer than 60 minutes.

Description: Rheumatoid arthritis (RA) is the most common inflammatory arthritis. This chronic systemic autoimmune disease is characterized by joint pain, swelling, and morning stiffness, particularly of the hands and feet. If untreated or suboptimally treated, RA leads to joint deformity and loss of

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mobility (Terrie, 2021). RA is characterized by cytokine-mediated (tumor necrosis factor [TNF] and interleukins) persistent synovitis and formation of pannus, which is invasive synovial tissue that leads to destruction of the cartilage, subchondral bone, and soft tissues of the affected joint, including tendons and ligaments. Inflammatory infiltrates in the subchondral bone are an integral part of the pathogenesis of RA and can cause inflammatory cysts and later bone erosions (Ostrowska et al., 2018).

RA usually has an insidious onset but progresses rapidly over the first year. This rapid progression can continue for the next 5 to 6 years. Within 10 years of onset of symptoms, approximately 80% of individuals will develop permanent joint deformities (Kontzias, 2020). Early progression is associated with worse outcomes; therefore, it is important to diagnose and treat early with the goal of achieving remission or low disease activity and minimizing exacerbations (Bullock et al., 2018). In addition to decreased physical function, RA contributes to anxiety, depression, economic hardship, and overall decreased quality of life (Fiest et al., 2017). At least 10% of RA patients will experience severe disability despite proper treatment (Kontzias, 2020).

Extra-articular involvement can be significant with RA—affecting the lungs, heart, skin, and/or eyes. RA-related interstitial lung disease (ILD) is associated with high rates of morbidity and mortality, the median survival is 5 to 8 years after ILD becomes symptomatic. Cardiovascular disease increases the mortality rate to 1.5 to 3 times higher for patients with RA compared to the general population. Neurological manifestations are typically complications of articular inflammation that invades or compresses nerves including of the spinal cord (Kim & Suh, 2020). RA can also cause vasculitis, rheumatoid nodules, eye conditions (episcleritis, scleritis, and/or keratoconjunctivitis sicca), and indirectly glucocorticoid-induced osteoporosis and increased rates of infection. Patients with RA have a decreased life expectancy of 3 to 10 years (Kim & Suh, 2020; Kontzias, 2020).

Etiology: The exact cause of RA is unknown. Several contributing factors have been identified, including environmental, hormonal, immunological, and infectious components and genetics. It is estimated that genetic factors account for half of all RA cases. The strongest correlations have been noted with family history of RA, smoking/exposure to tobacco smoke, obesity, and/or female sex (Terrie, 2021).

Occurrence: An estimated 1.3 to 1.5 million individuals in the United States have RA (Fiest et al., 2017; Terrie, 2021). RA is prevalent in 0.5% to 1% of the population (Terrie, 2021). It is estimated that onset of RA in older adulthood accounts for 10% to approximately 30% of all cases of RA (Targońska-Stępniak et al., 2021). Compared to men, women are two to three times more likely to develop RA, with the greatest incidence of RA occurring in women 65 years and older. Women comprise 75% of RA diagnoses (Terrie, 2021).

Age: The onset of RA is typically between the ages of 35 years and 60 years. RA can affect the pediatric population, referred to as juvenile RA (Bullock et al., 2018; Terrie, 2021). Elderly onset rheumatoid arthritis (EORA) generally begins after age 65 (Kobak & Bes, 2018; Serhal et al., 2020).

Ethnicity: RA is highest among Whites with the highest age-standardized prevalence in high-income North America, Western Europe, and the Caribbean and the lowest in Southeast Asia, Oceania, and western sub-Saharan Africa (Safiri et al., 2019).

Contributing Factors: Socioeconomics, lifestyle, and psychological stressors very likely impact the development of RA and affect patient outcomes (Terrie, 2021). It is theorized that for some, RA develops when a genetically susceptible person has an autoimmune reaction triggered by external stimulus such as smoking, trauma, or infection (Paul et al., 2017). Obesity is considered a contributing factor because increased secretion of adipokines cause a chronic subclinical inflammatory state. Smoking and obesity account for RA incidence of 14% and 14.7%, respectively (Ye et al., 2021).

Signs and Symptoms: RA often begins with subtle symptoms, but it can present as a viral syndrome with low-grade fever, malaise, weakness, and poor appetite (Terrie, 2021). Onset of disease is symmetrical and targets MCPs, PIPs, wrists, MTPs and ankles. RA can also affect the knees, elbows, and cervical spine—rarely affecting the distal interphalangeals (DIPs) until late disease (Tanaka, 2020).

In addition to hand pain, common initial patient concerns include decreased grip strength and painful walking, both of which improve with activity. Morning stiffness classically lasts longer than 60 minutes and improves with activity. Patients often do not want to stop moving because rest causes "gel" phenomenon or gelling—the stiffness and pain return with prolonged inactivity (Kontzias, 2020).

Generalized fatigue is a common symptom both initially and during exacerbations (Terrie, 2021). Almost half of RA patients will experience dry eyes and/or dry mouth, approximately 35% will develop rheumatoid nodules on the extensor surface of the forearm (Cabling, 2020), 25% experience compressive neuropathy of the hands and feet, and close to 10% develop RA-associated ILD (Tanaka, 2020).

For patients with EORA, the signs and symptoms often present more acutely. There is an increase in the type of constitutional symptoms, such as weight loss, myalgias, and polymyalgia rheumatics (PMR)-like symptoms (Serhal et al., 2020). The larger joints, such as the shoulders and wrists, are more frequently involved than in younger patients with a new onset (Kobak & Bes, 2018; Serhal et al., 2020).

Examination of the patient should include all joints of upper and lower extremities for swelling, tenderness, and limitation of movement; and of the cervical spine to assess decreased range of motion (ROM) and pain, which could indicate atlantoaxial subluxation. Atlantoaxial subluxation (instability between C1 and C2 vertebrae) occurs in 65% of patients with RA; when severe, it increases the risk of spinal cord compression. Joints should be assessed for flexion contractures, which can develop rapidly particularly of the elbows. Patients often hold joints in a flexion position to minimize pain. Advanced and suboptimally treated disease can lead to ulnar deviation along with boutonnière and swan-neck deformities of the fingers and fusion (ankylosing) of the wrists and ankles (Kontzias, 2020).

Diagnostic Tests: Laboratory tests including rheumatoid factor (RF) (positive) and acute phase reactants: C-reactive protein (CRP) (elevated) and erythrocyte sedimentation rate (ESR) (elevated) are associated with RA and inflammation; however, the most sensitive and specific test for RA, at 90% or

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higher, is the anti-cyclic citrullinated peptide (anti-CCP). High levels of RF and anti-CCP indicate a more aggressive phenotype. It is possible to have a false-positive RF, such as with hepatitis C or systemic lupus erythematosus (SLE), or even a seronegative RA with both tests being negative, although this is less likely. The frequency of RF positivity has been found to be lower in patients with EORA (Kobak & Bes, 2018). Additional laboratory findings that act as acute phase reactants due to inflammation include elevated white blood cell (WBC) count, low hemoglobin, elevated ferritin, and/or low albumin.

Imaging is important both for diagnosing and monitoring RA progression. Ultrasound can be especially beneficial with early disease activity because radiographic findings will not appear until damage has already occurred (with the exception of soft tissue swelling). With established disease, common x-ray findings include joint space narrowing that indicates cartilage absorption, subluxation that indicates soft tissue involvement, and bone erosions that indicate bone destruction (Tanaka, 2020). Inflammatory infiltrates in the subchondral bone, which can lead to inflammatory cysts and later erosions, can be seen on magnetic resonance imaging (MRI) as bone marrow edema in early RA and are an indicator of rapid disease progression (Ostrowska et al., 2018).

Differential Diagnosis: Differential diagnoses for RA include the following (Kontzias, 2020):

- Crystal arthropathy: gout or chondrocalcinosis—joint aspiration would reveal monosodium urate crystals or calcium pyrophosphate crystals
- Osteoarthritis (OA)—radiographs, history, and negative serology
- SLE or mixed connective tissue disease—serology and distinguishing accompanying symptoms
- Spondyloarthropathy: psoriatic arthritis, reactive arthritis, ankylosing spondylitis—not typically symmetrical, peripheral joints (MCPs, MTPs); imaging and serology
- PMR—joints affected, laboratory test results, and rapid onset/rapid response to glucocorticoids
- Polymyositis—muscle enzymes and muscle biopsy
- Sarcoidosis—presentation (monoarticular or oligoarticular) and other physical findings
- Fibromyalgia—pain without stiffness, nonarticular, negative laboratory results
- Other arthritides: trauma—history and imaging; septic—typically one affected joint and Gram stain and culture from arthrocentesis; infectious (hepatitis B and C, HIV, and Lyme disease)—serology; malignancy-related—imaging

Treatment: Early diagnosis is key because the first 12 weeks after initial symptoms are the optimal treatment window to achieve less joint destruction, no functional impairment, and induce remission (Guo et al., 2018). Methotrexate (MTX), a conventional synthetic disease-modifying antirheumatic drug (cs-DMARD), is the recommended initial treatment unless contraindicated. If there is a contraindication for MTX, leflunomide or sulfasalazine should be initiated. If there is no improvement in 3 months or remission in 6 months even with appropriate dose adjustment, then either a JAK inhibitor or a biologic DMARD (bDMARD) should be added. Hydroxychloroquine (HCQ) is conditionally recommended for low disease activity or as part of triple therapy (Fraenkel et al., 2021). Azathioprine and cyclosporine are infrequently used unless for treatment of extra-articular complications. Low-dose glucocorticoids are recommended for short-term adjunctive therapy to alleviate pain and swelling at diagnosis and during exacerbations (Tanaka, 2020). Caution should be exercised, particularly with MTX and NSAIDs because of gastrointestinal (GI) cardiovascular risk. Aspirin is not recommended (Kontzias, 2020).

Biologic treatments include tumor necrosis factor (TNF)-alpha inhibitors: adalimumab, etanercept, infliximab (and biosimilars), golimumab, certolizumab pegol; Janus kinase (JAK) inhibitors: tofacitinib, baricitinib, upadacitinib; IL-6 inhibitors: sarilumab, tocilizumab; T-cell costimulatory molecule modulator: abatacept, which carries less risk of opportunistic infections; and B-cell depleter: rituximab, which is used for refractory patients. The interleukin (IL)-1 receptor inhibitor anakinra is not frequently used (Kontzias, 2020). With any immunosuppressive medication, patients need to be tested for hepatitis and tuberculosis. Additionally, a good history is important to determine any past infections that could cause complications such as histoplasmosis and past family medical history for multiple sclerosis or other demyelinating disease as TNF inhibitors place patients with this history at increased risk of developing multiple sclerosis (MS) (Bullock et al., 2018).

Biologics can predispose patients to increased risk of infection and the rare risk of lymphoma. TNF inhibitors should be used with caution in older adults with heart failure because they can worsen heart failure. Treatment should also include supportive measures such as exercise/weight management, rest, intermittent heat or cold, physical therapy/occupational therapy (PT/OT), splinting, surgery for severe joint damage, smoking cessation, and proper nutrition (the Mediterranean diet is recommended) (Kontzias, 2020; Ye et al., 2017).

Follow-Up: Patients should have regular appointments for joint assessment, for medication management, and for disease progression monitoring, in addition to urgent visits for exacerbations. Additionally, patients taking cs-DMARDs, particularly MTX, require routine monitoring of liver function, renal function, and blood counts. JAK inhibitors and IL-6 inhibitors require follow-up lipid panel testing after initiation as levels can increase. Of note, IL-6 inhibitors also suppress acute phase reactants inconsequential of disease control as IL-6 regulates acute phase protein synthesis. HCQ requires yearly eye examinations to monitor for retinal toxicity (Guo et al., 2018). All health-care providers of rheumatology patients should assess and address the psychosocial impact of disease, functional status, and ability to carry out activities of daily living (ADLs).

Sequelae: Many older adults with long-standing disease often have permanent joint deformities, such as ulnar deviation and joint fusion, even in the context of no active disease. Newer therapies and prompt diagnosis and treatment have helped decrease these complications. Cardiovascular disease risk reduction is important given the increased risk due to systemic inflammation. Patients need to be monitored for lung involvement due to increased mortality once symptomatic. Cervical radiographs may be needed before general anesthesia/intubation to assess risk of cervical myelopathy (Kontzias, 2020).

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Prevention/Prophylaxis: RA cannot be prevented, but the complications of it can be mitigated with prompt treatment. Individuals with a family medical history of RA can possibly reduce their risk by maintaining optimal body weight and not smoking (Ye et al., 2017).

Referral: Patients experiencing arthralgia that is not easily explained, not monoarticular, or not obviously OA, need further work-up that includes laboratory testing, imaging, and a referral to rheumatology. PT and OT are of great benefit for strengthening and exercise programs, addressing splinting and orthotic needs, and other providing adaptive equipment/modifications that provide independence in ADLs and improve physical function.

Education: Patient education should focus on the need for appropriate treatment and the evidence-based safety profile of available medications including biologics, which many patients fear. Patients should be educated on the importance of vaccinations and the proper timing of administration. Live vaccinations should be avoided while on treatment. Immunosuppressive medications should be held when there is active infection. Because many patients feel good on corticosteroids, they are sometimes reluctant to wean off them and consider other treatment options. Therefore, education should also include the known adverse effects of long-term moderate-high dose corticosteroids including increased risk of diabetes, osteoporosis, infection, osteonecrosis, Cushing, and cardiovascular, ophthalmological, and GI effects (Yasir et al., 2021). Inform patients and ensure they understand that pain management, particularly with narcotics, does not treat inflammation and systemic effects of RA and should be used judiciously. Education should help patients manage extra-articular manifestations such as dry eye, dry mouth, fatigue, and neuropathy.

Clinical Recommendation	Evidence Rating	References
Start disease-modulating antirheumatic drugs (DMARDs) soon after diagnosis.	A	Mian et al., 2019
Disease activity should be monitored regularly using composite indices such as DAS28.	A	Mian et al., 2019
Methotrexate should be used first line, and short-term corticosteroids are a useful supplement.	A	Fraenkel et al., 2021
Patients receiving methotrexate, always administered as once weekly, should also take folic acid 1 mg daily.	A	Bullock et al., 2018
Biologic therapies should be used when there is persistently active disease and csDMARDs are not effective	A	Mian et al., 2019
Remission or low disease activity is the preferred target.	A	Mian et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

SJÖGREN'S SYNDROME

Signal Symptoms: Dry eye, fatigue (most frequent symptom), systematic vasculitis, lung or neurological involvement that may be severe and life threatening. A rare complication is the development of B-cell lymphoma (Cornec et al., 2015).

Description: Sjögren's syndrome is an autoimmune disorder characterized by mononuclear cell infiltration in the exocrine glands, which can lead to dry eye (xerophthalmia), dry mouth (xerostomia) and (dysphagia). Dr. Henrik Sjögren coined the term *sicca condition* to describe the disease he studied in his lifetime as an ophthalmologist (Baer & Walitt, 2018). Sicca refers to a dry eye disease from tears not providing adequate moisture. However, it is now known that Sjögren's syndrome is a systemic rheumatic disease with autoimmune-induced inflammation of the lacrimal and salivary glands and mononuclear cell infiltration and destruction of the lacrimal and salivary glands, which result in impaired tear and saliva production. It can manifest in focal lesions, including focal or motor deficits, stroke, or cerebellar syndromes (Altun et al., 2021).

The autoimmune distinction is important because therapies directed at the immune system might be beneficial to those with Sjögren's syndrome (Baer & Walitt, 2018). Due to the syndrome's autoimmune nature, systemic manifestations can include cryoglobulinemic purpura, nonerosive symmetrical arthritis, interstitial lung disease (ILD), Raynaud's phenomenon, pericarditis, autoimmune hemolytic anemia, and renal disease, including glomerulonephritis to tubulointerstitial nephritis. Renal involvement is a systemic complication of primary Sjögren's syndrome. In some cases, a renal biopsy is necessary for definitive diagnosis of kidney involvement (Ramponi et al., 2020).

Etiology: Although the etiology is unknown, Sjögren's syndrome is known to be an autoimmune disorder. There is a decrease in tears and saliva occurring when the glands that produce these fluids are damaged by inflammation. Researchers believe that genes affect the risk of developing Sjögren's syndrome, but that development of the condition may be triggered by environmental or viral/bacterial stressors (Sam & George, 2020). There are two prevailing theories on the origin of the dry eye symptom. In one theory, the origin of dry eye may be due to neuropathic dry eye. The nerve dysfunction, either from nerves on the ocular surface (cornea

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or conjunctiva) or more centrally from higher order neurons. The cause of Sjögren's syndrome may be evaporative dry eye in which the tears dry too quickly, a dysfunction of the Meibomian glands.

Occurrence: The prevalence of primary Sjögren's syndrome ranges from 0.1% to 1% in the general population. When Sjögren's syndrome affects patients suffering from another connective tissue disease, such as systemic lupus erythematosus (SLE) or rheumatoid arthritis (RA), it is considered secondary. Secondary Sjögren's syndrome is present in up to 17% of patients with RA (Cornec et al., 2015). Sjögren's syndrome is the second most common systemic rheumatic disease (Baer & Walitt, 2018).

Age: Generally, the onset of Sjögren's syndrome occurs after 40 years of age. The condition predominantly affects women (9:1 ratio) in their middle age—both in premenopausal and postmenopausal women, but it can also affect different populations (Cornec et al., 2015; Ramponi et al., 2020). Within the research per Ramírez (2017), associated comorbidities vary by sex. Women are more prevalent with concomitant hypothyroidism. Men with primary Sjögren's syndrome were more frequently diagnosed with more severe, long-term form of the syndrome involving ILD, lymphadenopathy, and lymphoma.

Ethnicity: The syndrome affects between 1 and 23 persons per 10,000 inhabitants in European countries (Ramos-Casals et al., 2020). The average ethnicity affected is White and of European descent.

Contributing Factors: Multiple environmental factors may play a role in the pathogenesis of Sjögren's syndrome, including infectious, hormonal, and stress-related factors. Genetics may also have a role (Bautista-Vargus et al., 2020).

Signs and Symptoms: Clinical features include dry mouth, dry eyes, or dryness in the throat, nose, lips, or skin. The glands in the neck and face may swell up. Women may also experience vaginal dryness. Joint swelling and stiffness also occur. Symptoms of heartburn may occur from the stomach to the chest. Rare inflammation to liver, lungs, and kidneys may also occur. Those afflicted may have tiredness, numbness, and tingling in parts of their body (Sam & George, 2020).

Diagnostic Tests: In 2014, the American European Consensus group and American College of Rheumatology designated classification criteria for Sjögren's syndrome (Cornec et al., 2015). Blood studies include immunoglobin testing for Sjögren's syndrome and testing for elevated antinuclear antibodies (ANA), anti-RO/SSA and anti-La/SSB antibodies, or rheumatoid factor (RF), but these elevations are not always present. One study showed only 2% had positive immune serology when undergoing comprehensive ANA testing (Hadas, 2020). Patients with Sjögren's syndrome had lower lymphocyte, hemoglobin, and C3 levels but higher prevalence of RF, ANA, anti-rO/SSA and anti-La/SSB and higher immunoglobulin G (IgG) and median fluorescence intensity (MFI) levels compared to those with dry eye syndrome and controls. The novel multiplex serology method correctly identified anti SSA/B autoantibodies by ELISA among Sjögren's syndrome, patients with dry eye syndrome, and controls. Other laboratories include cryoglobulin testing, protein electrophoresis, hepatitis C and HIV (if at risk), and thyroid tests.

Sjögren's syndrome can involve salivary gland swelling in one-half of patients, and lymphoma may develop in 5% to 10% of patients (Sam & George, 2020). A salivary gland biopsy around the face or under the surface of the inner lip also may be used to make diagnosis. The minor salivary gland biopsy is invasive and has a moderate diagnostic performance. Ultrasound-guided core needle biopsy has good safety and results comparable to open biopsy of minor salivary gland of the lip. It can, however, cause permanent sensory loss of the lips (Borner et al., 2021). Less invasive methods, such as imaging, biomarkers, and skin biopsy are on the horizon (Bautista-Vargus et al., 2020). New testing includes ocular surface staining scores or salivary gland ultrasonography (Jousse-Joulin & Coiffier, 2020). Noninvasive tools include elastography, ultrasonography technique, magnetic resonance imaging (MRI), MR sialography, and fluorodeoxyglucose-positron emission tomography. Salivary gland ultrasonography should be the first choice in primary Sjögren's syndrome because of accessibility. It is noted that major salivary gland ultrasonography should be included in future classification criteria for primary Sjögren's syndrome. It is simple, noninvasive and less expensive.

Per the 2002 American-European Consensus group (AECG), assessing for Sjögren's syndrome should include a history/review of systems, examination, laboratories, ophthalmological examination, sialometry (measure of saliva flow), and imaging (Cornec et al., 2015). The 2002 AECG and the 2012 American College of Rheumatology (ACR) criteria can assist with diagnosis (Cornec et al., 2015). Schirmer test, tear breakup time, and ocular surface staining are used to evaluate for keratoconjunctivitis sicca. Schirmer test utilizes filter paper strips and measures moisture in both eyes simultaneously. Ocular surface staining with vital dyes allows slit-lamp visualization of devitalized conjunctival cells and corneal epithelial defects. Lissamine green is most used to stain the conjunctiva, and fluorescein is used in the cornea. It is more sensitive than the Schirmer test for detecting dry eye. Of note, the Schirmer test result is less accurate in older adults because the degree of wetting declines with age (Baer & Walitt, 2018; Cornec et al., 2015). Tear breakup time is used to assess the stability of the tear film. An abnormal result occurs with meibomian gland dysfunction (Baer & Walitt, 2018).

In 2016, the ACR and the European Alliance of Associations for Rheumatology (EULAR) Sjögren's syndrome classification criteria updated elements while maintaining a patient has either anti-RO/SSA antibodies or a positive minor salivary gland biopsy. Although there is not one specific diagnostic test for Sjögren's syndrome, criteria for diagnosis include if an individual having one symptom of ocular or oral dryness (positive response to at least one of five standardized questions), salivary gland enlargement, or a characteristic extraglandular manifestation of Sjögren's syndrome as defined by a positive domain in EULAR Sjögren's syndrome disease index. Drawbacks include antibody testing because antibodies to anti-Ro/SSA and ant-La/SSB are not specific to just Sjögren's syndrome; they can be positive in other rheumatic conditions (Shiboski et al., 2017).

Differential Diagnosis:

- Sicca syndrome
- Sarcoidosis
- Granulomatosis with polyangiitis or vasculitis

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- IgG4-related disease
- Chronic hepatitis C virus
- HIV
- Graft-versus-host disease
- Head and neck radiation therapy (Cornec et al., 2015)

Treatment: There is no curative treatment for Sjögren's syndrome currently. There are topical medications used in symptom management. Systemic immunomodulatory and immunosuppressive agents may be needed to manage various extraglandular manifestations. A multidisciplinary approach is needed (Ramos-Casals et al., 2020).

For dry eye symptoms, artificial tears/lubricant ointment are for immediate and long-term use. Topical ocular NSAIDs/corticosteroids may be prescribed by an ophthalmologist for a period of 2 to 4 weeks (Ramos-Casals et al., 2020). Many topical treatments studied are inconclusive. Hydroxychloroquine, immunosuppressive agents, or rituximab show inconclusive or negative results in studies. Regular eye examinations are recommended.

Dry mouth management includes drinking water, chewing gum, or saliva substitutes. Muscarinic agonists can substantially increase saliva production and to a lesser extent, tear flow. Care must be taken when these medications are prescribed to older adults. These drugs are contraindicated in patients with uncontrolled asthma and angle-closure glaucoma. Regular dental care is recommended as is fluoride (Baer & Walitt, 2018; Ramos-Casals et al., 2020; Vivino et al., 2016).

Joint pain management includes analgesics, topical NSAIDs, and hydroxychloroquine. The 2019 EULAR recommendations and a 2019 Cochrane review concluded that effects of topical ciclosporin on both symptoms and signs are inconsistent (Vehof et al., 2020). Those with systemic symptoms may require treatment with corticosteroids or immunosuppressive agents such as methotrexate, azathioprine, mycophenolate, or cyclophosphamide. Conventional disease-modulating antirheumatic drugs (DMARDs) and the newer biologic therapies, including tumor necrosis factor (TNF)-inhibiting drugs (etanercept, adalimumab, and infliximab) may be considered. Rituximab and other biologics are being evaluated for Sjögren's syndrome that affects the entire body (Ramos-Casals et al., 2020; Vivino et al., 2016).

Nasal dryness symptom management includes humidifiers and nasal saline irrigation. Heartburn remedies include proton pump inhibitors and H_2-receptor blockers to lessen acid reflux symptoms. Vaginal moisturizers and lubricants are initial treatment options for vaginal dryness (Baer & Walitt, 2018; Sam & George, 2020).

Follow-Up: Follow-up with specialists is required if comorbidities are present or organ damage exists. Regular eye examinations, dental cleanings, and further testing by specialists may be needed.

Sequelae: Most patients with Sjögren's syndrome have limited symptoms such as dry eye and mouth. Their general health and life expectancy are largely unaffected. Increased mortality may be related to conditions associated with SLE, lymphoma, RA, or primary biliary cirrhosis (Cornec et al., 2015).

Prevention/Prophylaxis: There are currently no prevention/prophylaxis measures known or practiced. Routine eye examinations are needed to detect further damage.

Referral: Refer to an ophthalmologist and a rheumatologist for specific testing and treatments. Coordinate with the primary care provider for symptoms such as fatigue. Referrals to support groups for new and ongoing diagnoses include the International Sjögren's Network, Sjogren's Syndrome Foundation in the United States (sjogrens.org) and the Arthritis Foundation.

Education: Inform patients on how to manage their symptoms. Advise patients that certain medications (both prescription and over-the-counter) may aggravate symptoms. Drugs that induce ocular or oral dryness include anticholinergics, histamine receptor antagonists, antidepressants, diuretics, antispasmodics, antihypertensives, and sedatives (Baer & Walitt, 2018).

Clinical Recommendation	Evidence Rating	References
Fluoride should be used in patients with a dry mouth to prevent caries.	A	Vivino et al., 2016
Musculoskeletal pain can be managed with disease-modulating antirheumatic drugs and then corticosteroids (short and long term).	C	Vivino et al., 2016
Exercise is recommended for the management of fatigue.	C	Vivino et al., 2016

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SYSTEMIC LUPUS ERYTHEMATOSUS

Signal Symptoms: Livedo reticularis (mottled purplish discoloration), malar rash (butterfly rash), mucocutaneous lesions, arthralgias, myalgias, pleurisy, myocardial dysfunction, hypertension, cognitive dysfunction, idiopathic thrombocytopenic purpura, lupus nephritis.

Description: Systemic lupus erythematosus (SLE) is one of the most complex autoimmune diseases and has multiple clinical presentations. The disease is characterized by multisystem involvement and has a chronic relapsing nature. The course of the disease is variable, alternating between periods of stable

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disease (remission) and/or flares with high disease activity. There are currently three different classification criteria to aid in the diagnosis of SLE (Pan et al., 2020): *1997 Update of the 1982 American College of Rheumatology Revised Criteria for Classification of Systemic Lupus Erythematosus* (American College of Rheumatology, 1997); Systemic Lupus International Collaborating Clinics—SLICC Criteria (Markowitz & D'agati, 2007); and the 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus (Aringer et al., 2019).

Etiology: The pathogenesis of SLE is not quite well understood. It is characterized by the production of autoantibodies and the deposition of immune complexes, affecting a wide range of organs. Genetic factors, environmental factors, and hormonal factors are believed to contribute to the occurrence of SLE. Breakdown of self-tolerance plays a critical role in the occurrence and development of SLE. Innate and adaptive immune responses against self-antigen induce the production of autoantibodies and the deposition of immune complexes in tissues leads to the activation of complement, accumulation of neutrophils and monocytes, and self-reactive lymphocytes (Pan et al., 2020).

Occurrence: The incidence of SLE in the United States ranges from 2.0 to 7.6 cases per 100,000 persons per year. Prevalence ranges from 14.6 to 68 cases per 100,000 persons. SLE affects more women than men, with a ratio of 9:1 and a higher incidence among women of childbearing age. Men tend to have severe manifestations at the time of diagnosis.

Age: Lupus will mostly affect young men and women between the ages of 15 to 45. For older adults presenting with SLE for the first time, late onset is considered after age 50, which accounts for 10% to 20% of all lupus cases. There is usually less organ damage, but with insidious onset of disease (Aljohani et al., 2017).

Ethnicity: SLE Disproportionately affects Black women with a three to four times higher prevalence than Whites. There is a higher incidence of SLE among the Afro-Caribbean, Asian, American Indian, and Hispanic descent populations as compared to the White population. Black, Asian, and Hispanic individuals with SLE tend to develop more severe disease, exhibit a greater number of manifestations, and rapidly accumulate damage from lupus. Even after considering socioeconomic factors, race/ethnicity remains a key determinant of poor outcomes (Lewis & Jawad, 2017; Stefanidou et al., 2013; Stojan & Petri, 2018).

Contributing Factors: Recent studies have shown that genetic, epigenetic, immunoregulatory, ethnic, hormonal, family history of autoimmune disease, and environmental factors are associated with the development of the disease (Trentin et al., 2021). Given the high rate of polypharmacy in older adults, review all medications to determine whether there is drug-induced SLE suspected (Séguin et al., 2021). Rule out the following medications: Anti-tumor necrosis factor (TNF) drugs (adalimumab, certolizumab pegol, etanercept, and golimumab), hydralazine, anticonvulsants, isoniazid, thorazine, procainamide, penicillamine, and minocycline.

Signs and Symptoms: Common signs and symptoms of SLE include fatigue, weight loss, and fever without infection. Most patients also report arthralgias and myalgia (Lam et al., 2016). In addition to constitutional symptoms, prevalent signs and symptoms in specific organ systems include musculoskeletal, skin, renal, neuropsychiatric, hematological, cardiac, pulmonary, gastrointestinal (GI), or reticuloendothelial (Lam et al., 2016). Overall, late-onset SLE has lower systemic manifestations (Chanprapaph et al., 2021). In late-onset SLE, cutaneous manifestations are less common except for sicca symptoms, which are caused by lymphocytic infiltration of exocrine glands—most notably the salivary and lacrimal glands—causing xerophthalmia (dry eyes) and xerostomia (dry mouth), pericarditis, and lung involvement. (Lewis & Jawad, 2017; Medlin et al., 2016; Medlin et al., 2018; Stojan & Petri, 2018).

The pulmonary manifestations found in late-onset SLE include interstitial lung disease (ILD) and serositis (inflammation of the serous tissues that protect organs) as compared to findings in a younger population (Medlin et al., 2018). Late-onset SLE has lower lupus-associated autoantibody involvement (Chanprapaph et al., 2021).

Diagnostic Tests: The diagnosis of lupus is based on detailed history, clinical presentation, and laboratory analysis. The new European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus classification system, although *not* diagnostic, delineates additive weighted criteria that guide clinicians toward the diagnosis of SLE (Aringer, 2019). The criteria (Fig. 16-1) indicates that an elevated antinuclear antibody (ANA) titer of ≥1:80 on Hep-2 cells is the established entry point in the decision making (Aringer et al., 2019). Positive laboratory work-up only, without presenting symptoms, does not support the diagnosis of SLE and does not require treatment. Although the diagnosis of SLE relies on both physical signs and laboratory data to confirm, the patient's prognosis and monitoring of treatments relies on regular diagnostic testing.

Complex laboratory work-up to SLE may include ANA. Note, however, that while present in 96% of patients with SLE, it has extremely poor specificity, with many false positives. It can be present in 10% of healthy individuals and may be positive in other autoimmune conditions, such as hypothyroidism. ANA alone is not a definitive test for SLE. If patient's symptoms are highly suspicious for SLE, referral to rheumatology is appropriate. Rheumatology may order the following tests:

- Anti-double-stranded DNA antibodies (anti-dsDNA)—present in 50% of patients with SLE Complement level 3 and 4 (C3 and C4)—abnormally low when active disease; it represents complement consumption, but it is not specific to SLE and can be seen in other complement deficiencies. Normal levels can indicate low disease activity. Chronic low C3 Can be associated with lupus nephritis.
- Antibodies to cytoplasmic components
  - Anti-Ro/SSA—mostly associated with primary Sjögren's syndrome but can be found in 20% to 30% of SLE patients; associated with subacute cutaneous lupus and photosensitivity.
  - Anti-La/SSB
- Anti-Smith antibodies—are present in 20% of SLE patients; interfere with ability to transcribe RNA to DNA.
- Antibodies to ribonucleoprotein (RNP)—interfere with RNA to bind to cytoplasm cells; present in mix connective

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Entry criterion

Antinuclear antibodies (ANA) at a titer of ≥ 1:80 on HEp-e cells or an equivalent positive test (ever)

If absent, do not classify as SLE
If present, apply additive criteria

Additive criteria

Do not count a criterion if there is a more likely explanation than SLE.
Occurrence of a criterion on at least one occasion is sufficient.
SLE classification requires at least one clinical criterion and ≥ 10 points.
Criteria need not occur simultaneously.
Within each domain, only the highest weighted criterion is counted toward the total score.

Clinical domain and criteria	Weight
Constitutional	
Fever	2
Hematologic	
Leukopenia	3
Thrombocytopenia	4
Autoimmune hemolysis	4
Neuropsychiatric	
Delirium	2
Psychosis	3
Seizure	5
Mucocutaneous	
Non-scarring alopecia	2
Oral ulcers	2
Subacute cutaneous OR discoid lupus	4
Acute cutaneous lupus	6
Serosal	
Pleural or pericardial effusion	5
Acute pericarditis	6
Musculoskeletal	
Joint involvement	6
Renal	
Proteinuria > 0.5g/24h	4
Renal biopsy Class II or V lupus nephritis	8
Renal biopsy Class III or IV lupus nephritis	10

Immunology domains and criteria	Weight
Antiphospholipid antibodies	
Anti-cardiolipin antibodies OR Anti-β2GP1 antibodies OR Lupus anticoagulant	2
Complement proteins	
Low C3 or low C4	3
Low C3 AND low C4	4
SLE-specific antibodies	
Anti-dsDNA antibody* OR Anti-Smith antibody	6

Total score:

Classify as Systemic Lupus Erythematosus with a score of 10 or more if entry criterion fulfilled.

FIGURE 16-1 Classification Criteria for Systemic Lupus Erythematosus. (Reprinted from Aringer, M., et al. (2019). 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for systemic lupus erythematosus. *Arthritis & Rheumatology, 71*(9), 400–1412 with permission.)

tissue disease; patients usually present with Raynaud's phenomenon, pulmonary hypertension, and puffy hands.
- Erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)—indicates level of inflammation; does not always relate to disease activity.
- Anti-histone—present in drug-induced SLE and rheumatoid arthritis (RA)

Patients with suspected SLE should also have a complete blood count (CBC) to identify lymphopenia, thrombocytopenia, and anemia; comprehensive metabolic panel (CMP) to evaluate hepatic and renal function; and urine analysis with microscopy to check for protein and the protein and creatinine ratio, which can identify hematuria, pyuria, and proteinuria (Ali, 2018). When following a patient with SLE, consider ordering CBC/CMP/ESR/CRP, C3 levels, C4 levels, anti-double-stranded DNA (anti-dsDNA) levels, and urine with microscopy to monitor the effectiveness of treatment and the progression of the illness (Wallace, 2014; West, 2019).

Differential Diagnosis: Because of its varied presentations and multisystem involvement, the differential diagnosis for SLE is broad, and can include the following (Ali, 2018; Lam et al., 2016; Wallace, 2014):

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- Malignancies
- Infectious processes (cytomegalovirus, Epstein-Barr virus, HIV, and hepatitis)
- RA
- Scleroderma
- Fibromyalgia
- Thrombotic thrombocytopenic purpura
- Multiple sclerosis (MS)
- Myositis/dermatomyositis
- Vasculitis
- Hashimoto's thyroiditis
- Psoriatic arthritis
- Sarcoidosis
- Chronic fatigue syndrome
- Adult-onset Still's disease

Treatment: The treatment for SLE is as complex as the disease, with multiple medications being required for different manifestations. Management of SLE in older adults should be under the care of rheumatology. Table 16-1 delineates select medication treatment for SLE depending on the organ system(s) involved and progression of the disease.

Follow-Up: In older patients with SLE, follow-up needs to focus on potential sequelae. Patients with SLE/lupus nephritis are at increased risk for infections. They should be encouraged via shared decision making to receive inactivated vaccines, such as the pneumococcal polysaccharide vaccine (PPV-23), the pneumococcal conjugate vaccine (Prevnar 13), and annual influenza vaccine following Centers for Disease Control and Prevention (CDC) recommendations for patients who are immunosuppressed. If not already diagnosed with underlying heart disease, patients with SLE have a 7.5-fold increase in coronary artery disease. The combined coronary artery disease-promoting effects of SLE and chronic kidney disease lead to an even higher cardiovascular risk. Routine care for patients with SLE should include screening for cardiovascular risk factors, counseling for lifestyle modification such as smoking cessation, encouraging physical activity and weight loss, and screening for symptoms suggestive of heart disease. Another concern is the development of osteoporosis because of the long-term use of glucocorticoids. According to the 2017 American College of Rheumatology guidelines; more than 10% of patients who receive long-term glucocorticoid treatment are diagnosed with a fracture, and 30% to 40% have radiographic evidence of vertebral fractures. The highest rate of bone loss occurs within the first 3 to 6 months of glucocorticoid treatment, and a slower decline continues with persistent use (Buckley et al., 2017). Consider periodic screening for depression and anxiety, which can impact quality of life for patients with SLE (Figueiredo-Braga et al., 2018). Screening, diagnosis, and referral to mental health providers should be part of normal health assessment by the primary care provider (Lam et al., 2016).

Sequelae: A study done by Petri and Magder (2018) demonstrated that even patients who achieve low disease activity have organ damage, including musculoskeletal, central nervous system (CNS), and renal damage; osteoporotic fractures; and myocardial infarction.

Prevention/Prophylaxis: There is no prevention or prophylaxis for the development of SLE. Disease flare prevention and rapid treatment of flares are key to decreased progression of SLE. Patients should be educated on recognizing well-known triggers for flares, including sun exposure and infections, and advised to contact their providers as soon as a flare begins.

TABLE 16-1 Medications for SLE Management

MEDICATION	USES	SIDE EFFECTS
Topical steroids (e.g., hydrocortisone, triamcinolone, fluocinolone)	• Can be used short term to treat lupus rashes and skin lesions	• Burning or stinging sensation when applied • Thinning of skin with extensive use
NSAIDs	• Can be used to help treat arthralgias, polyarthritis, and myalgias. • Must add a proton pump inhibitor. • The clinician should watch blood count and creatinine. • Avoid use if kidney involvement is present. • Never for long-term use.	• Development of peptic ulcer disease, acute renal failure, and stroke/myocardial infarction with long-term use
Antimalarial drugs (mainstem of SLE treatment) Hydroxychloroquine (HCQ; most prescribed): 6.5 mg/kg up to a maximum of 400 mg daily. Has less ocular and GI reactions than chloroquine.	• Modulates the immune system, reducing flares by as much as 50%. • May prevent activation of plasmacytoid dendritic cells. • Benefits of hydroxychloroquine include maintaining remission, protecting against vascular and thrombotic events. • Is safe to use during pregnancy and while breastfeeding. • Protects against ultraviolet light and may improve skin lesions. • Can improve muscle and joint pain, pericarditis, pleuritis, fatigue, and fever. • Patients should get an eye examination by an ophthalmologist prior to initiation and annually after 5 years of regular HCQ use.	• Prevalence of retinal toxicity was <2% during the first 10 years of use; however, it increased to ~20% after 20 years of routine HCQ use. • Nausea and diarrhea—most common side effects • Skin rashes—bluish color • Cardiomyopathy (rare)

Continued

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TABLE 16-1 Medications for SLE Management—Continued

MEDICATION	USES	SIDE EFFECTS
Glucocorticoids (oral, IV, and topical forms) Acthar gel (repository corticotropin injection)—activates adrenal gland to produce glucocorticoids; has the same effect and side effects as glucocorticoids	• Dose dependent on severity and complication. • Should be avoided as long-term treatment. • High-dose therapy should be reserved for organ threatening presentation, such as SLE, nephritis, hemolytic anemia.	• Decreased bone density • Infections • Sodium retention • Edema • Hypertension • Glucose intolerance • Hypokalemia • Insomnia • Euphoria, depression, and mania • Osteonecrosis • Moon face and buffalo hump • Glaucoma, cataracts
Methotrexate	• Antimetabolite and cytotoxic agent • Reduces antigen-dependent T-cell proliferation and suppresses inflammation. • Dose varies in patients with SLE from 10 to 25 mg weekly with folic acid or folinic acid supplementation. • Mostly used to treat joint pain; can be used to treat some skin manifestations of SLE.	• Anemia, neutropenia • Stomatitis and oral ulcers (can be prevented or alleviated by folate) • Nodulosis, hepatic fibrosis, pulmonary fibrosis, lethargy, fatigue, and renal insufficiency • Contraindicated in pregnancy. It is considered a teratogenic agent. Should be given under cover of two forms of contraception. • Hair loss
Mycophenolate mofetil	• Inhibits B and T cell proliferation. • Used for organ-threatening disease such as lupus nephritis. Patients are typically started at 500 mg/day, with maintenance target of 2–3 g/day. • No consistent data on the tapering schedule during maintenance phase.	• Serious infections and gastrointestinal manifestations. Contraindicated in pregnancy due to increased risk of birth defects and miscarriages. Should be given under cover of two forms of contraception. Stop at least 12 weeks before planned pregnancy.
Cyclophosphamide	• Potent immunosuppressive and alkylating agent that depletes B + T cells. • Used to treat severe manifestations of autoimmune/inflammatory diseases. • Has a well-established efficacy in lupus nephritis and is given in lower doses than typically prescribed for cancer chemotherapy. • Due to a high rate of clinical relapse, it sometimes requires a repeated course of treatment.	• Nausea, vomiting, hair loss (reversible) • Increase risk of common and opportunistic infections. • Teratogenicity, sterility, and secondary hematological malignancy • Toxicity to the urinary bladder, including hemorrhagic cystitis and bladder cancer
Belimumab	• Blocks the activity of B lymphocytes. • Available in both subcutaneous and IV formulations. • Currently approved to be used in the treatment of lupus nephritis in addition to standard treatment. • Moderate efficacy in serologically active patients with skin and joint involvement.	• Infections • Headaches • Depression
Voclosporin	• A next-generation calcineurin inhibitor approved in 2019 to be used in combination therapy for the treatment of lupus nephritis. Structurally like cyclosporine A but has increase potency and faster elimination. • Does not require drug levels to be checked.	• Opportunistic infections • Gastrointestinal disorders • Kidney dysfunction • Hyperkalemia • Diabetes • Increased blood pressure

Sources: *Fanouriakis & Bertsias, 2019; Fanouriakis et al., 2019; Fava & Petri, 2019; Golder & Tsang-A-Sjoe, 2020; Guerreiro Castro & Isenberg, 2017; Samotij & Reich, 2019; Rovin et al., 2021.*

Referral: Patients with SLE should be referred to a rheumatologist as soon as the diagnosis is suspected. Other specialists such as nephrology and neurology should be considered depending on the presentation and progression of the disease.

Education: Recent studies have linked worse outcomes to low health literacy in patients with SLE. In order to increase understanding and compliance, patient education is paramount for patients and their families. All aspects of the disease, including manifestation, treatments and flare prevention should be initiated as soon as the diagnosis is made. Referral to patient education Web sites and foundation will help the patient cope with the recent diagnosis and the complications of such a complex disease. (Katz et al., 2021).

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Clinical Recommendation	Evidence Rating	References
Hydroxychloroquine is recommended for all patients with SLE unless contraindicated, at a dose not exceeding 5 mg/kg.	C	Fanouriakis et al., 2019
Glucocorticoids can be used at doses and route of administration that depend on the type and severity of organ involvement.	C	Fanouriakis et al., 2019
Pulses of IV methylprednisolone (usually 250–1000 mg per day, for 1–3 days) provide immediate therapeutic effect and enable the use of lower starting dose of oral glucocorticoids.	C	Fanouriakis et al., 2019
For chronic maintenance treatment, glucocorticoids should be minimized to less than 7.5 mg/day (prednisone equivalent) and, when possible, withdrawn.	C	Fanouriakis et al., 2019
First-line treatment of skin disease in SLE includes topical agents (calcineurin inhibitors), antimalarials (HCQ, quinacrine), and/or systemic glucocorticoids.	C	Fanouriakis et al., 2019
In nonresponsive cases or cases requiring high-dose GC, methotrexate, retinoids, dapsone, or mycophenolate can be added.	C	Fanouriakis et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

VASCULITIS

Signal Symptoms: Blood vessel inflammation often with palpable purpura, livedo reticularis, urticaria, ulcers and/or nodules with acute symptoms of fever, fatigue, weakness, weight loss, and/or arthralgia (Sangolli & Lakshmi, 2019).

Description: Vasculitis can be either primary or secondary. Vasculitis can cause inflammation of any size blood vessel—venules, arterioles, capillaries, veins, and/or arteries. This inflammation often leads to ischemia, necrosis, and possible organ inflammation. Clinical manifestations depend on which blood vessels are involved. Small vessel vasculitis (SVV) includes granulomatosis with polyangiitis (GPA, formerly known as Wegener's granulomatosis), which affects the upper and lower respiratory tract and kidneys; eosinophilic granulomatosis with polyangiitis (known as Churg-Strauss' syndrome), which affects the respiratory tract; microscopic polyangiitis (MPA); Henoch-Schönlein's purpura (HSP), which is an immunoglobulin A (IgA) vasculitis notably affecting the skin (most common in children); cryoglobulinemia; and leukocytoclastic vasculitis affecting the skin. Medium vessel vasculitis (MVV) includes thromboangiitis obliterans (also known as Buerger's disease), polyarteritis nodosa, and Kawasaki's disease, which primarily affects children. Large vessel vasculitis (LVV) is composed of Takayasu's arteritis, affecting the aorta and its major branches; and giant cell arteritis (GCA, also known as temporal arteritis), commonly affecting the temporal artery, although it can also affect the aorta and its major branches (Langford, 2003; Sangolli & Lakshmi, 2019; Villa-Forte, 2020). Vasculitides are also classified using the Chapel Hill nomenclature to indicate antineutrophil cytoplasmic antibody (ANCA)-associated such as GPA and MPA, immune complex such as Cryoglobulinemic vasculitis (CV) and HSP, variable vessel such as Behçet's disease, single organ such as cutaneous or central nervous system (CNS), and those associated with systemic disease (Okazaki et al., 2017).

Etiology: Primary vasculitis occurs in the absence of any associated disease or any precipitating cause with the initial event being the vessel wall inflammation. In primary vasculitis, an autoimmune mechanism is believed to be the key contributor. Secondary vasculitis may appear with a pre-existing inflammatory disorder or with cancer; it can also be triggered by a drug, toxin, or infection. (Sangolli & Lakshmi, 2019; Villa-Forte, 2020).

Occurrence: Vasculitis is relatively rare, affecting approximately 38 to 40 individuals per million. GCA is the most common form of vasculitis with a pooled prevalence of 51/100,000 among adults older than 50 years of age (Li et al., 2021). Within cutaneous vasculitis cases, infection accounts for 22%, drugs 20%, autoimmune/connective tissue disorders 12%, HSP 10%, and less than 5% each in primary vasculitis, systemic inflammatory disease, or malignancy (Sangolli & Lakshmi, 2019). Takayasu's arteritis and GCA are more common in women, whereas HSP, polyarteritis nodosa, Behçet's disease, and thromboangiitis obliterans affect more men (Langford, 2003). Death due to vasculitis, in general, is more common in women than men (Rodriguez-Pla & Rossello-Urgell, 2021).

Age: Vasculitis is more common in adults than in children. The mean age of onset is 47 years old in adults and 7 years old in children. GCA is rarely seen in individuals younger than 50 years of age (Li et al., 2021; Sangolli & Lakshmi, 2019).

Ethnicity: GCA affects individuals with a Scandinavian background the most and individuals with Asian ancestry the least (Li et al., 2021). Behçet's disease classically affects individuals with ancestry from Eastern Asia, the Middle East, or the Mediterranean (Okazaki et al., 2017).

Contributing Factors: There is no known etiology for primary vasculitis, but it is believed that immune regulatory mechanisms, genetics, and environmental factors increase susceptibility to developing vasculitis (Sangolli & Lakshmi, 2019). Contributing factors to secondary vasculitis include systemic

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autoimmune diseases such as systemic lupus erythematosus (SLE), rheumatoid vasculitis, sarcoid vasculitis, or relapsing polychondritis vasculitis (Okazaki et al., 2017). There is a very strong correlation with use of tobacco products and/or cannabis and thromboangiitis obliterans (Olin, 2018).

Signs and Symptoms: Clinical manifestations of vasculitis are directly related to the impaired blood vessel function and eventual vessel wall breakdown. Inflammation causes an insufficient blood supply leading to a localized tissue reaction, which can lead to organ dysfunction. Regardless of the type of vasculitis, patients may also present with systemic symptoms, including fever, malaise, fatigue, weakness, arthralgia, poor appetite, or weight loss. Because of these symptoms it is essential to rule out malignancy, specifically solid tumors, in older adults (Sangolli & Lakshmi, 2019).

Cutaneous manifestations are observed with all three vessel sizes vasculitides. With small vessel vasculitis, the most common findings are urticaria, palpable purpura (often of the legs), targetoid lesions, or vesiculobullous lesions. In medium vessel disease, livedo reticularis, ulcers, pitted scars, subcutaneous nodules, or gangrene can occur. Oral and/or genital ulcers, as well as skin lesions and joint pain can be seen with Behçet's disease. Nerve damage, which initially presents as hypoesthesia or hyperesthesia, can be seen with medium vessel disease in addition to myalgia, lymphadenopathy, new-onset hypertension or coronary artery aneurysms (Sangolli & Lakshmi, 2019; Villa-Forte, 2020).

GCA presents as unilateral temporal headache, jaw claudication, exquisite scalp tenderness, and is often accompanied by acute systemic symptoms including fatigue and unintended weight loss. Approximately 20% of patients with GCA will have a history of polymyalgia rheumatica (PMR) (Li et al., 2021). Large vessel cutaneous symptoms tend to occur secondary to the underlying disease but can include severe, emergent symptoms such as CNS symptoms of stroke or unequal pulse and/or blood pressures in extremities, limb claudication, or limb/digit ischemia (Sangolli & Lakshmi, 2019; Villa-Forte, 2020). Other organ-threatening or life-threatening manifestations of vasculitis include hematuria, proteinuria, and casts associated with rapidly progressive glomerulonephritis (SVV); bloody, foamy sputum associated with pulmonary alveolar hemorrhage; abdominal pain associated with mesenteric ischemia (MVV); and any cardiac involvement (Chung et al., 2021; Sangolli & Lakshmi, 2019).

Diagnostic Tests: Clinical assessment cannot be underestimated in the evaluation of vasculitis; this will direct the differential diagnosis and thus what testing is necessary. Initial laboratory studies should include a complete blood count (CBC), comprehensive metabolic panel (CMP), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), hepatitis panel, and a urinalysis. Additional testing, such as antineutrophil cytoplasmic antibodies (ANCA) and cryoglobulins, would be considered based on clinical findings and normally completed by rheumatology. Tissue biopsy is standard in the diagnosis of vasculitis, the earlier in the disease process the better, although appropriate imaging with expertise in reading the imaging results can be less invasive and more cost-effective (Dejaco et al., 2018; Sangolli & Lakshmi, 2019).

Imaging in vasculitis depends in part on the size of the vessel disease suspected but is especially useful with LVV. Ultrasound and magnetic resonance imaging (MRI) (high resolution) are the preferred choice for GCA and Takayasu's arteritis because these tests highlight the characteristic vessel wall abnormalities. Computed tomography (CT), CT angiography, and positron emission tomography (PET) scans may be used as an alternative in the evaluation of the aorta and extracranial arteries; they are not recommended for evaluation of cranial arteries (Dejaco et al., 2018).

Differential Diagnosis: The differential diagnoses for vasculitis include conditions that mimic the disease and thus need to be excluded first as well as primary diseases that can cause secondary vasculitis (Sangolli & Lakshmi, 2019).

- Infection/infectious disease including infective endocarditis, hepatitis, HIV, tuberculosis, syphilis, rickettsial infection
- Drug toxicity/toxin exposure including hydralazine, montelukast, propylthiouracil, hormonal contraceptives, tobacco/cannabis, cocaine
- Malignancy/lymphoma
- Thrombotic/thromboembolic conditions, including antiphospholipid syndrome and sickle cell disease; history should include obstetric history of recurrent spontaneous abortions
- Systemic disease including amyloidosis, rheumatoid arthritis (RA), SLE, sarcoidosis

Treatment: Treatment for vasculitis typically includes corticosteroids during the acute phase and lower doses for maintenance therapy when necessary. Best practice for an accurate diagnosis is to obtain testing and/or imaging before initiation of corticosteroids given the significant response within the first week of treatment. Depending on the nature of the vasculitis, some are acute and self-limiting, lasting less than 6 months, whereas others will remain a lifelong condition. Treatment of secondary vasculitis should focus on addressing the primary cause.

Most treatments for vasculitis include immunosuppressants and disease-modulating antirheumatic drugs (DMARDs) such as hydroxychloroquine, methotrexate, cyclophosphamide, mycophenolate mofetil, or azathioprine. Colchicine is the mainstay for treatment of Behçet's disease. Dapsone is the usual treatment for cutaneous vasculitis, but patients must first be tested for G6PD before starting this medication. Antivirals are the standard for hepatitis C cryoglobulinemia. Biologic therapies include tumor necrosis factor (TNF) inhibitors (adalimumab, etanercept, infliximab), abatacept, tocilizumab, or rituximab (Sangolli & Lakshmi, 2019).

Follow-Up: Patients will need to follow up regularly with rheumatology (at least every 3 months) and for laboratory studies every 2 to 3 months—most often a CMP and CBC. Patients with stable vasculitis may be able to stretch visits and labs out to every 6 months. Patients taking hydroxychloroquine will require yearly retinal eye examinations.

Sequelae: In addition to possible complications of glomerulonephritis, pulmonary alveolar hemorrhage, limb/digit, or mesenteric ischemia, with GCA there is concern for severe, permanent blindness if left untreated or suboptimally controlled. This blindness is monocular, on the side with temporal arteritis, rarely affecting both eyes at the same time. In MVV, mononeuritis multiplex progression can lead to wrist or foot drop or paralysis. Patients can also have complications of immunosuppressive therapy, which should be monitored both through labs as well as a thorough review of systems to identify any new problems (Sangolli & Lakshmi, 2019).

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Prevention/Prophylaxis: There is no prevention for primary vasculitis, but it is important to adhere to treatment to minimize disease activity. Precautionary measures to reduce the risk of secondary vasculitis requires good control of underlying conditions and avoidance of triggers, including toxins, drug allergies, and tobacco.

Referral: After initial work-up or in cases of suspected vasculitis, the patient should be referred to rheumatology for evaluation and management.

Education: General measures include medication compliance, routine lab testing, regular follow-ups, and avoidance of smoking/tobacco use. Patients need to be aware that any new symptoms and any medication changes require notifying their health-care provider immediately; severe, acute symptoms should be directed to the emergency department. Corticosteroids, immunosuppressants, and biologics predispose patients to increased risk of infection and corticosteroids increase risk of osteoporosis, so it is important to educate patients on these effects and treat appropriately. Patients need to update any new provider, and specifically before any procedures such as dental work, that they are taking immunosuppressants and/or biologics. Patients taking these medications should not receive live vaccines; timing of other vaccinations may depend on timing of immunosuppressive medications, so this should be discussed with the prescribing provider. Patients of childbearing age should be counseled on use of appropriate birth control and preconception planning (Sangolli & Lakshmi, 2019).

Clinical Recommendation	Evidence Rating	References
Early imaging in patients with suspected large vessel vasculitis (LVV), particularly giant cell arteritis (GCA), is strongly recommended with the expectation that it will not delay initiation of treatment.	A	Dejaco et al., 2018
Ultrasound should be the primary imaging test in patients with suspected GCA presenting predominantly with cranial symptoms because of easy access, evidence of good test performance, low cost, and the absence of radiation or other procedural risks. The "halo" sign of temporal arteries is the most relevant ultrasound finding in GCA.	A	Dejaco et al., 2018
Ultrasound and/or magnetic resonance imaging (MRI) are first choices for evaluating cranial arteries, GCA, and Takayasu's arteritis.	A	Dejaco et al., 2018
Positron emission tomography, MRI, and/or computed tomography may be used for detection of mural inflammation and/or luminal changes in extracranial arteries to support the diagnosis of LVV, GCA, or Takayasu's arteritis.	A	Dejaco et al., 2018
Temporal artery biopsy is the gold standard test for the diagnosis of GCA.	C	Dejaco et al., 2018
GCA can be diagnosed with high clinical suspicion and a positive imaging test; diagnosis does not require additional tests (further imaging or biopsy).	A	Dejaco et al., 2018

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CASE STUDY

Ruby, an 86-year-old, thin, osteoporotic woman, gets up onto a stepstool to reach something on the top shelf of her cabinet. She loses her balance and falls onto her left side. She finds that she cannot sit up without pain. Her daughter later finds her and calls an ambulance to take her to the emergency department. Per radiograph, left femoral fracture is present. Surgery is scheduled for open reduction with internal fixation (ORIF). Blood clot prevention injections and pain medications are prescribed. Next, the patient is monitored for postoperative anemia and infection. After discharge, Ruby has rehabilitation for inpatient and then nursing home temporary care for 30 days. She is discharged to her daughter's home with home health and assistive equipment.

Today's visit:

Chief complaint: "I am still recovering from my fall last month and now am staying at my daughter's but want to go home."

Objective: Blood pressure (BP) 100/60 mm Hg, pulse 87, respiratory rate 20 breaths/min

1. What additional subjective data are you seeking?
2. What additional subjective data will you be assessing for?
3. Are there any national guidelines you want to consult for the postoperative and rehabilitation care of this patient with an ORIF related to osteopenia of the left femur?
4. What tests will you want to order as part of this follow-up visit?
5. Are there any new differential diagnoses you need to consider?
6. What is your plan of care?
7. What additional patient teaching may be needed?
8. Are there additional community resources to consider?
9. Will you be looking to add any referrals for this patient?

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CHAPTER 17

Central and Peripheral Nervous System Disorders

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ASSESSMENT

The neurological assessment of the older adult begins with the initial encounter with the patient, taking into consideration the overall appearance, hygiene, facial expression, gait, and posture (Seraji-Bzorgzad et al., 2019). Whether it is the masked facial expression of Parkinson's disease (PD), the facial dystonia of progressive supranuclear palsy (PSP), or the ptosis of myasthenia gravis (MG), certain neurodegenerative conditions are often visually initially recognizable and should be considered in the differential diagnosis when patients present with acute and progressive neurological signs and symptoms.

Early in the neurological examination is an assessment of cognition to ensure accuracy of the patient's comprehensive history or chief complaint. Consider, however, the need to obtain historical information from collateral sources (Seraji-Bzorgzad et al., 2019). The interview should begin with an assessment of level of consciousness, speech pattern, mood and affect, concentration ability, short-term memory, and orientation. This information can usually be obtained during the course of a standard interview. "The key to appreciating a memory impairment or subtle dementing illness is to perceive incongruities among the patient's appearance, dress, language or behavior" (Williams, 2009, p 236). There are several short screening tools that can be administered to the patient to assess cognition:

- The Mini-Cog is a short dementia assessment that combines three-word recall with clock-drawing capability. Patients are given a total score reflecting accuracy in clock drawing and recollection of the given three words. A score of 0 to 2 is a positive screen for dementia (Borson, 2000).
- The St. Louis University Mental Status Examination (SLUMS), a 12-item assessment, has been shown to detect mild neurocognitive disorders. A patient's level of high school is considered when interpreting the score. A score of 19 or below in any patient is indicative of dementia (Tariq et al., 2006). If any questions regarding the mental status arise, family members may be asked for additional information to investigate the patient's cognitive abilities further.
- The Montreal Cognitive Assessment (MoCA Version 7.1) is a tool designed to measure the status of a patient's attention, concentration, executive function, memory, and orientation. It has been tested on patients with a variety of neurodegenerative conditions, as well as those with a history of substance abuse (Berstein et al., 2011.). The score can be adjusted for patients with a lower level of education. (Milani et al., 2018). A score of 26 or higher out of a possible score of 30 is considered normal cognition (Nasreddine et al., 2005).

With neurological conditions, in addition to asking questions about the initial/current presentation (onset, duration, sequential progression of signs and symptoms), question that patient about the time of day, acute versus progressive, have any of the signs and symptoms temporarily subsided (as in remission) (Armitage, 2015). The focused interview for a neurological complaint should include asking about the following signs and symptoms in older adults:

- Loss of consciousness or presyncope, including a full description of any episodes and their precipitating factors
- Any speech or language disturbances as in the ability to recall words, correct selection of words, or constant repeating of phrases
- Change in vision, including diplopia, ptosis, loss of vision
- Change in hearing, including tinnitus or acute hearing loss
- Change in the sense of smell or taste and possible precipitating factors (such as COVID-19)
- Any mood swings, new onset of headaches, and change in level of awareness or reversal or alteration in judgment or memory
- Pertinent family history of any acute neurological or neurodegenerative disease or unknown conditions with specific symptomatology
- Information about previous occupations and hobbies that may have involved trauma or chemical exposure for each patient

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- All medications (including over-the-counter [OTC] medications)
- Diet and sleep patterns
- A careful assessment of social history, including alcohol use and any current or previous substance abuse
- Any episodes of seizures, "spells," shaking palsy, dizziness, falls, weakness or paralysis, tremors, involuntary movements, pain, numbness, paresthesia, gait problems, or restlessness of the legs

The positive findings determined in the history of present illness and review of systems will guide the episodic neurological examination. A complete neurological examination, however, begins with testing of the cranial nerve function.

Cranial Nerve Function

CRANIAL NERVE I (OLFACTORY)

As anosmia (loss of the sense of smell) and hyposmia (diminished sense of smell) are symptoms present in older adults who have a number of both acute and chronic conditions as well as part of normal aging (atrophy of the olfactory bulb), cranial nerve I should be routinely tested. Loss of the sense of smell in one nostril would be an abnormal finding (Besdine, 2019). Make sure to test one nostril at a time using familiar scents such as coffee. Olfactory Sniffin' Sticks Test could be used for comprehensive evaluation (Bagnasco et al., 2021; Rebholz et al., 2020). This sense may be lessened or absent because of COVID-19, allergic rhinitis, influenza, common cold, head trauma, smoking, use of cocaine, or normal aging. It may also be congenitally absent (Gladstone & Black, 2002a). A distorted sense of smell in both nostrils of familiar odors has been found in patients early in the progression of neurodegenerative conditions such as Alzheimer's disease (AD). Other neurogenerative conditions that patients experience anosmia or hyposmia include PD, amyotrophic lateral sclerosis (ALS), and Huntington's disease. Patients with hyposmia or anosmia are at risk for safety issues (such as eating rancid foods or the inability to detect smoke, gas, or other noxious chemicals) and malnutrition (Rebholz et al., 2020).

CRANIAL NERVE II (OPTIC)

When examining the eyes of an older person, you may note that upward gaze and, to a lesser extent, downward gaze can be slightly limited. Eye movements, when tracking an examiner's finger during evaluation of visual fields, may appear jerky and slightly irregular or have subtle changes (Seraji-Bzorgzad et al., 2019). Assess pupillary reactions to light and visual fields. Presbyopia, the loss of accommodation, is a normal aging change. Older adults experience difficulty with depth perception, decreased color discrimination affected by yellowing of the lens (ability to discern between blue and green colors) (Salvi et al., 2006), slowed adjustment to low light, and reduced contrast sensitivity (Besdine, 2019). Older patients should be encouraged to continue ophthalmical examinations; the goal should remain for vision to be corrected as needed to 20/20. Funduscopic examination will reveal disc or small vessel abnormalities (Salvi et al., 2006).

CRANIAL NERVES III, IV, AND VI (OCULOMOTOR, TROCHLEAR, AND ABDUCENS)

These nerves may be examined together by testing extraocular movements and convergence. Inspect for ptosis. While weakening of the levator muscle's ability to attach to the lid can be contributed to aging, there are several conditions that cause acquired ptosis, such as MG, diabetes, stroke, brain tumor, and Bell's palsy. Generally, pupils are smaller in an older adult, a condition known as senile miosis. A hallmark of PSP is supranuclear vertical gaze palsy; however, limitation of vertical gaze and convergence are common age-related changes noted on testing of cranial nerves (Seraji-Bzorgzad et al., 2019).

CRANIAL NERVE V (TRIGEMINAL)

The motor function of this nerve can be assessed by palpating the temporal and masseter muscles. If the patient has no teeth, this test may be difficult to interpret. The sensory function of this nerve should be tested with sharp and dull stimuli in all three branches: ophthalmic, maxillary, and mandibular (Edvinsson et al., 2020). If any abnormalities are noted, light touch and temperature sensation should also be assessed. The corneal reflex should be assessed using a wisp of cotton. Patients who wear contact lenses may have diminished corneal reflexes. Older adults may naturally have decreased lacrimal secretions; certain medications, such as anticholinergics, may exacerbate this condition (Gladstone & Black, 2002a).

CRANIAL NERVE VII (FACIAL)

Observe the patient's face at rest and continue to observe throughout the examination for any asymmetry. Motor function may be tested by asking the patient to smile, frown, raise both eyebrows, close eyes tightly and resist the examiner's attempts to open them, and puff out both cheeks. A peripheral injury to this nerve, such as Bell's palsy, may affect both the upper and the lower face, whereas a central lesion mainly affects the lower face (Suneja et al., 2020).

CRANIAL NERVE VIII (ACOUSTIC)

Assess auditory acuity using the whisper test. If hearing loss is present, test for lateralization using the Weber test and for air versus bone conduction using the Rinne's test. The ear canals should be checked for cerumen impaction or ruptured tympanic membrane, which are leading causes of conductive hearing loss and could contribute to overall hearing loss. Presbycusis, a normal aging change, results in older adults losing the ability to hear at higher tones (Michels et al., 2019).

CRANIAL NERVES IX AND X (GLOSSOPHARYNGEAL AND VAGUS)

Observe the quality of the patient's voice. Hoarseness may indicate vocal cord paralysis; a nasal quality may indicate paralysis of the palate. Difficulty in swallowing could indicate palatal or pharyngeal weakness. Inspect movement of the palate and pharynx when the patient swallows. (Armitage, 2015). Test the gag reflex by stimulating the back of the throat on each side (Suneja et al., 2020). Older adults experience a decrease in taste perception of saltiness, sweetness, sourness, and bitterness (Malaty & Malaty, 2013).

CRANIAL NERVE XI (SPINAL ACCESSORY)

Observe for atrophy or fasciculations in the trapezius muscles. Test motor strength bilaterally with a shoulder shrug (Armitage, 2015).

CRANIAL NERVE XII (HYPOGLOSSAL)

Inspect for fasciculations of the tongue at rest. Look for asymmetry of movement, atrophy, or deviation from midline. Atrophy or fasciculations suggest peripheral lesion. If there

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is an upper motor neuron lesion, the protruded tongue will diverge toward the side of the lesion, and fasciculations of the tongue will be present; however, no fasciculations or atrophy appears in upper motor neuron disease. The tongue will deviate away from the side of the lesion (Armitage, 2015; Suneja et al., 2020).

Motor Function

Assessment of motor function should focus on inspection of body position and involuntary movements (tremors, tics, or fasciculations). Note that the incidence of benign essential tremor increases with aging. Inspect the patient's muscle bulk, comparing sizes and contours of muscles. Pay particular attention to the hands, shoulders, and thighs. Atrophy of the hand muscles may occur with normal aging. Muscular atrophy may also result from diseases of the peripheral nervous system, motor neuron disease, rheumatoid arthritis, muscle disuse, and malnutrition.

Motor assessment also includes inspection of muscle tone, best assessed by the patient's resistance to passive stretch. Inspect tone in all extremities during flexion and extension. Increased tone that is worst at extremes of the range is known as spasticity; resistance that persists throughout and in both directions is known as lead-pipe rigidity. Decreased resistance suggests peripheral nervous system disease, cerebellar disease, or the acute stage of spinal cord injury. If a passive resistant movement in any direction is noted, consider dementia reflecting bilateral frontal lobe dysfunction; this irregular movement is referred to as partonia or greenalite (Gladstone & Black, 2002b). In patients with cogwheel rigidity, ratchet-like jerking movements can be detected by the examiner on passive flexion and extension of the muscle. Initially a unilateral, asymmetric tremor presents in patients with PD who develop tremor; if it is a drug-induced PD, the tremor is often symmetric (Seraji-Bzorgzad et al., 2019).

Assess muscle strength against resistance in all major muscle groups and grade on a scale from 0 to 5, with 5 being active movement against full resistance. Test the biceps and triceps; grip strength; finger abductions; opposition of the thumb; trunk strength; flexion, extension, abduction, and adduction at the hip; flexion and extension at the knee; and dorsiflexion and plantarflexion of the foot during passive range-of-motion (ROM) exercises (Larson & Wilbur, 2020). If you note weakness, assess strength against gravity alone or with gravity eliminated. Many clinicians make further distinctions by using plus or minus signs toward the stronger end of the scale (Williams, 2009). Determine whether there are patterns of objective weakness that are asymmetrical, distal, and/or proximal only (Larson & Wilbur, 2020).

It is first important to rule out whether any weakness is subjective, which is actually found to be fatigue rather than the loss or alteration of normal strength. Patients, however, may experience both fatigue and true weakness. Differentiate between constant versus intermittent weakness, and establish the patterns of weakness:

- Weak arm and leg (same side): hemiparesis or hemiplegia
- Weak legs, normal arms: paraparesis
- All four limbs weak: tetraparesis
- One limb weak: monoparesis
- Proximal muscle weakness (often from a myopathy)
- Distal muscle weakness (often from a neuropathy) (Larson & Wilbur, 2020)

Determining subjectively the patient's limitations in activities of daily living (ADLs) can further help the practitioner establish the severity of the weakness. Ask questions pertaining to function of the upper extremities, such as the ability to lift one's arms over the head for grooming or dressing (proximal upper extremity weakness) versus the ability to use utensils or turn a door handle (distal upper extremity weakness). For lower extremity, proximal weakness questions can be asked about the ability to climb stairs or cross one's legs.

It is critical to accurately assess the presentation of weakness in older adults because it is a common complaint. When evaluating a patient presenting with generalized weakness, the practitioner must consider the presence of sarcopenia coexisting with frailty (Larson & Wilbur, 2020).

An overall test of weakness and mobility is the Get Up and Go Test. It includes a number of tasks, such as standing from a sitting position, walking, turning, stopping, and sitting down, all of which are important tasks needed for a person to be independently mobile. These tasks also help determine whether the patient is having proximal weakness of the lower extremities (von Haehling et al., 2010).

Test coordination using rapid alternating movements of the hands, fingers, and feet and point-to-point movements. In some neurodegenerative conditions such as PD, movements may be slow and irregular with imprecise timing. The inability to perform repetitive movements in a rapid rhythmic method is called dysdiadochokinesia (Gladstone & Black, 2002c).

Patients with appendicular ataxia may have difficulty with finger-to-nose testing. The examiner may note undershooting (hypometria) and overshooting (hypermetria) of a target (dysmetria), as well as the decomposition of a movement or the inability to complete a movement (Suneja et al., 2020).

Gait function should be tested. Assess tandem gait, walking on toes and heels, hopping in place, and shallow knee bends on each side. All components of gait should be assessed; they include initiation of walking; step length, height, symmetry, continuity, and cadence (rhythm); velocity (speed of walking); stride width; progression; turn ability; walking posture; and need for any assistive devices. It is important to consider sensation, musculoskeletal and motor control, and attention, which are components needed for independent, coordinated walking (Jerome et al., 2015; Nnodim et al., 2020). Romberg's test is to evaluate position sense and is performed with the patient's feet together and eyes closed for 20 to 30 seconds without support. Only minimal swaying should occur in patients with a normal finding (Besdine, 2019). This test may be combined with the pronator drift test, in which the patient stands with eyes closed and both arms straight forward, palms up. Normally, this position may be held for 20 to 30 seconds. After instructing the patient to maintain this position, tap the patient's arms briskly downward. The arms should return smoothly to the horizontal position; a downward drift indicates muscle weakness. Allow extra time for the older patient to perform gait and coordination maneuvers (Seraji-Bzorgzad et al., 2019).

Sensory Function

Assessment of sensory function helps to establish a lesion of the sensory cortex, the level of a spinal cord lesion, or the location of a peripheral lesion. Sensory function is tested using pain and temperature (spinothalamic tract), position and vibration (posterior column), and touch (posterior horn).

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When you locate an area of hypersensitivity or sensory loss, map out its boundaries in detail. Unilateral sensory loss suggests a lesion in the spinal cord or higher pathways; a symmetrical sensory loss suggests a neuropathy such as that experienced by persons with diabetes. Touch and vibratory sensations may diminish because of normal aging (Seraji-Bzorgzad et al., 2019). Discriminative sensations test the ability of the sensory cortex to analyze and interpret stimuli. These techniques include stereognosis, number identification, two-point discrimination, point localization, and extinction (Suneja et al., 2020).

Reflexes

During assessment of the reflexes, the patient should be relaxed, with limbs positioned symmetrically. Palpate the tendon to locate position and make sure the tendon is slightly stretched. Strike the tendon briskly and note the speed, force, and amplitude of response. Grade on a scale from 0 to 4 pluses, with the normal response at 2 pluses. The older adult may have diminished or absent reflexes, usually affecting lower extremities (Achilles' tendon most notably) (Besdine, 2019).

If the response is asymmetrical, check the force and location of the strike. Nurse practitioners who elicit reflexes on patients with multi-infarct dementia may, however, note brisk asymmetrical reflexes as a sign of focal corticospinal tract dysfunction (Gladstone & Black, 2002d). If the response is symmetrically diminished, the examiner may use reinforcement, in which isometric contraction of other muscles may increase reflex activity. Ask the patient to clench the teeth when testing upper extremities and to lock hands together and pull hands against each other when testing lower extremities (Gladstone & Black, 2002a).

Assess all reflexes: biceps (C5, C6), triceps (C6, C7), brachioradialis (C5, C6), patellar (L2, L3, L4), and ankle (S1). Assess the abdominal reflex by stroking each side of the abdomen both above (T8, T9, T10) and below (T10, T11, T12) the umbilicus (Gladstone & Black, 2002d; Suneja et al., 2020). Evaluate the plantar response by stimulating the lateral aspect of the sole of the foot from the heel to the ball of the foot, curving medially across the ball. Look for flexion of the toes as a normal response. If dorsiflexion of the big toe and fanning of the other toes is noted, this constitutes a positive Babinski response, indicating a central nervous system (CNS) lesion. This response may also be noted in certain unconscious states (e.g., drug or alcohol intoxication, postictal state) (Suneja et al., 2020).

The clinical significance of positive findings when testing primitive reflexes such as palmomental, glabellar, and grasp remains controversial. Numerous studies have shown that primitive reflexes are common findings in the general aging population without any CNS disorder (Snow, 2020). If a patient when tested has several primitive reflexes versus just one, the likelihood of underlying neurological condition increases (Gladstone & Black, 2002d; Seraji-Bzorgzad et al., 2019).

Abnormal or Involuntary Movements

With the incidence of neurodegenerative conditions increasing with older adulthood, the practitioner needs to assess for any involuntary movements such as fasciculations, spasms, chorea, tremors, tics, and athetosis (Seraji-Bzorgzad et al., 2019). Abnormal movements could also be a side effect of psychotropic medications that can cause extrapyramidal symptoms (Gladstone & Black, 2002a). Make sure to document completely all findings of the neurological examination, especially if additional diagnostic testing is indicated. The identification of subtle nervous system abnormalities has been shown to be associated with the risk of stroke and even death in healthy older adults (Inzitari et al., 2008).

BELL'S PALSY

Signal Symptoms: Unilateral isolated acute facial weakness.

Description: Bell's palsy is characterized by an acute onset (72 hours or fewer), unilateral facial weakness. It is an isolated peripheral neuropathy affecting the seventh cranial nerve (facial nerve) on one side of the face. Taste may be diminished on the ipsilateral tongue, and hyperacusis may occur in the ipsilateral ear. The facial palsy is self-limited and typically improves over several weeks to months, with complete recovery by 1 year in up to 85% of patients. Risk factors for incomplete recovery include age older than 55 years, hypertension, pain (except for ear pain), complete facial paralysis, and reduced lacrimation.

Etiology: The cause of Bell's palsy is unknown, though it is hypothesized to be a herpes viral infection (Gilden, 2004).

Occurrence: Bell's palsy develops in 11 to 40 per 100,000 people annually worldwide (De Diego et al., 1999) and affects men and women equally.

Age: Average age at onset is 40 years, with a higher incidence in people over 70 years of age.

Ethnicity: Bell's palsy affects all ethnicities.

Contributing Factors: Diabetes, pregnancy, severe preeclampsia, obesity, upper respiratory ailments, and hypertension have been reported as risk factors for Bell's palsy (Baugh et al., 2013).

Signs and Symptoms: Patients with Bell's palsy develop unilateral weakness of the face over 1 to 2 days. The facial weakness is in a lower motor neuron pattern (Table 17-1), causing difficulty showing teeth, puffing cheeks, pursing lips, whistling, flaring the nostril, raising the forehead, and closing the eye. Patients may experience loss of taste on one side because the facial nerve innervates the taste for the anterior two-thirds of the tongue, and sometimes this is the initial symptom. The lacrimal and minor salivary glands may be affected, though most patients don't report dry eye or mouth. Facial pain (particularly postauricular) is common. There may be an abnormal sensitivity to sound (hyperacusis) due to dysfunction of the stapedius muscle.

Physical examination is notable for unilateral weakness affecting the upper and lower face muscles, including the frontalis and orbicularis oculi. Although many patients with Bell's palsy report facial "numbness," formal testing should demonstrate intact sensation. Taste may be diminished and

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TABLE 17-1 Features of Lower Motor Neuron Versus Upper Motor Neuron Facial Weakness

	LOWER MOTOR NEURON	UPPER MOTOR NEURON
Location of lesion	• Facial nerve • Facial nerve nucleus or fascicle in the pons (usually accompanied by other neurological signs)	Central nervous system lesion in the corticobulbar tract (motor cortex, corona radiata, internal capsule, brainstem)
Pattern of weakness	Upper and lower facial muscles affected	Upper face spared (i.e., eye closure and forehead elevation)
Ipsilateral taste and lacrimation	May be affected	Unaffected
Ipsilateral hyperacusis	May be present	Absent
Features of smile on examination	Genuine and forced smiles are affected equally.	Genuine smile is stronger than forced smile.
Ipsilateral arm weakness	Absent	Usually present

can be tested using a cotton swab dipped in lemon or sugar water applied to the anterior tongue on the affected side. The rest of the neurological and head and neck examination is normal, including a thorough cranial nerve and strength examination and inspection of the palate and auditory canal for vesicular herpes zoster lesions (Reich, 2017).

Diagnostic Tests: The diagnosis of Bell's palsy is clinical, based on patient history and examination. If the presentation is typical (i.e., a spontaneous, acute, unilateral, isolated peripheral facial palsy), and there are no red flag features in the history or examination (including a detailed neurological and head and neck examination) to indicate an alternate diagnosis, then no diagnostic tests are needed. Electrodiagnostic studies such as electromyography (EMG) and electroneuronography are not recommended for routine use in patients with Bell's palsy, though these studies can be offered to patients with complete facial paralysis for prognostic purposes (Baugh et al., 2013; Guntinas-Lichius et al., 2020).

Any atypical features in the history or examination require further work-up to exclude other etiologies causing facial weakness. Magnetic resonance imaging (MRI) of the brain with contrast in a patient with Bell's palsy may show enhancement of the facial nerve. MRI can also evaluate for alternate diagnoses such as tumor, stroke, multiple sclerosis (MS), and stroke. If concerning features such as severe headache or multiple cranial neuropathies are present, lumbar puncture should be considered to evaluate for meningitis. Serum laboratory studies can be sent to evaluate for infections and inflammatory disorders that can cause facial nerval palsies, particularly if the facial nerve palsy is recurrent or bilateral (Reich, 2017).

Differential Diagnosis: The differential diagnosis of facial weakness is broad, including:

- Tumors compressing the facial nerve or along the corticobulbar tract in the brain
- Infections, particularly acute HIV, mononucleosis, varicella zoster, Lyme disease, syphilis, and otitis media
- Guillain-Barré syndrome (GBS) (usually accompanied by limb weakness and areflexia)
- Meningitis (including infectious, inflammatory, neoplastic); may cause multiple cranial nerve palsies and symptoms of meningeal irritation (headache, light sensitivity, neck stiffness, pain with eye movements)
- Trauma
- Stroke; can cause unilateral facial weakness, though it is typically in an upper motor neuron pattern and accompanied by additional features
- Inflammatory conditions (such as sarcoidosis and Sjögren's syndrome); can cause facial nerve palsies, often bilaterally (Reich, 2017)

Reactivated varicella zoster virus causing a facial nerve palsy is referred to as Ramsay Hunt's syndrome. This condition commonly causes a rash in the external auditory canal or on the palate and can also affect cranial nerve VIII, leading to concurrent hearing loss and vertigo.

Treatment: The majority of patients with Bell's palsy will recover without treatment. Steroids, when started within the first 72 hours of symptom onset, increase the probability of recovery of facial weakness and should be offered (Baugh et al., 2013; Gronseth et al., 2012). The addition of an antiviral medication to steroids may have a modest effect on the likelihood of recovery and can be considered, although results of studies are mixed (Baugh et al., 2013; Sullivan et al., 2016). Antiviral medications should not be used as monotherapy for the treatment of Bell's palsy (Cao et al., 2021; Gagyor et al., 2019).

Because Bell's palsy causes weakness of eye closure, it is important to protect the eye from injury, particularly during sleep. Loss of the ability to blink and close the eyelid can lead to corneal drying, abrasion, and ulceration. The patient should keep the eye moist and protected by using artificial tears frequently during the day and an artificial tear ointment and/or taping the eyelid closed at night (MacIntosh & Fay, 2019).

Follow-Up: The patient should be reexamined after treatment to assess for symptom improvement.

Prevention/Prophylaxis: There is no prevention for Bell's palsy.

Referral: If the patient's symptoms do not recover by 3 months or worsen beyond the acute setting, or if other neurological signs are evident, the patient should be referred to a neurologist or other facial nerve specialist. The patient should be referred to an ophthalmologist if they experience any signs of corneal irritation or injury.

Education: Patients should be counseled that Bell's palsy is usually a self-limited and benign condition. Education about the importance of meticulous eye care is important to prevent corneal injury.

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Clinical Recommendation	Evidence Rating	References
The diagnosis of Bell's palsy is based on history and examination and does not require routine laboratory testing or diagnostic imaging.	C	Baugh et al., 2013
Steroids increase the probability of facial weakness recovery and should be started within 72 hours of symptom onset.	A	Baugh et al., 2013 Gronseth et al., 2012
Among patients receiving oral corticosteroids for Bell's palsy, the addition of antiviral therapy may help increase the likelihood of recovery and reduce the late sequelae of Bell's palsy, although results are mixed.	B	Sullivan et al., 2016 Gagyor et al., 2019
Eye protection measures should be initiated for patients with Bell's palsy experiencing impaired eye closure.	C	Baugh et al., 2013 MacIntosh & Fay, 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

BRAIN TUMOR

Signal Symptoms: Headaches, with or without nausea and vomiting; seizures; changes in mental function or personality; motor or language deficits; visual problems.

Description: A brain tumor is a malignant or benign neoplasm of the brain or its supportive structures, which may arise from glial cells, blood vessels, connective tissue, meninges, or pituitary or pineal glands. Brain tumors may be considered low grade or slow growing or high grade, which tend to grow quickly and invade the surrounding tissues. Primary brain tumors include gliomas, meningiomas, medulloblastomas, gangliogliomas, and schwannomas. Non-Hodgkin's lymphomas may also originate in the central nervous system (CNS) and are called primary CNS lymphomas (American Cancer Society [ACS], 2021a).

Etiology: The etiology of brain tumors is largely unknown. CNS tumors have been associated with rare genetic conditions, including Li-Fraumeni's syndrome, neurofibromatosis 1 and 2, and Von Hippel-Lindau's disease (ACS, 2021b).

Occurrence: Each year, more than 24,000 cases of brain and CNS cancer are diagnosed. More than 18,000 deaths are attributable to brain and CNS cancers. The 5-year survival rate is 32.6% (National Cancer Institute [NCI], 2021; National Comprehensive Cancer Network [NCCN], 2021). Brain tumors are more common in males than females (NCI, 2021).

Age: Median age of diagnosis is 66 years (NCI, 2021).

Ethnicity: Whites have a higher incidence compared to Blacks, Asian/Pacific Islanders, and American Indian/Alaskan Natives (NCI, 2021).

Contributing Factors: High-dose ionizing radiation given for other cancers is a risk factor. Patients with neurofibromatosis types 1 and 2, Von Hippel-Lindau's syndrome, Li-Fraumeni's syndrome, and Turcot's syndrome are also at increased risk (ACS, 2021b). CNS lymphoma is associated with an immunocompromised immune system (ACS, 2021b).

Signs and Symptoms: Signs and symptoms are produced by tumor infiltration of nervous tissue, displacement of brain structures by tumor mass, or increased intracranial pressure (ICP). Symptoms may be physical—including headaches, fatigue, or focal signs—or behavioral—including hallucinations, anxiety, depression, memory problems, and decreased attention and concentration (Comelli et al., 2017). Headaches occur more than half of the time and are often associated with seizures, visual disturbances, and persistent nausea with vomiting (Wong & Wu, 2021). Generalized headache can be associated with increased ICP.

Memory loss and other cognitive changes may be subtle. Patients may report having decreased energy, fatigue, increased desire to sleep, and lack of interest in normal activities (Wong & Wu, 2021).

Seizures may affect 50% to 80% of patients with brain tumors. New-onset focal seizures in individuals older than 40 years are suspicious for brain tumor until proven otherwise. Syncope due to an increase in ICP can mimic a seizure with a few tonic-clonic jerks. Papilledema may be present in increased ICP, though less commonly in older adults (Wong & Wu, 2021).

Focal neurological changes are related to the area of the brain invaded by tumor. Frontal and parietal lobe tumors may cause changes in memory, behavior, and cognitive function. Memory, hearing, vision, and emotions are affected most often by temporal lobe tumors. Symptoms of temporal lobe tumors may mimic symptoms of affective or psychotic thought disorders. Visual changes can occur with occipital lobe tumors, in addition to speech, motor, and sensory changes for left-sided occipital masses and an inability to grasp abstract concepts for right-sided occipital masses. Lesions in the cerebellum affect balance and coordination. Pituitary tumors may present with the symptoms of hypothyroidism, hypercortisolism, diabetes insipidus, or visual changes (Wong & Wu, 2021).

Diagnostic Tests: The following tests are recommended for a person with suspected brain tumor:

- Complete blood count (CBC) to assess for anemia or infection
- Thyroid-stimulating hormone (TSH) because hypothyroidism or hyperthyroidism can be associated with mental status changes or hypothyroidism with pituitary tumors
- Venereal disease research laboratory (VDRL) if neurosyphilis is a possibility

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- Chemistries to assess for electrolyte and chemical imbalances
- Gadolinium-enhanced magnetic resonance imaging (MRI) of the brain is the preferred radiological examination for either brain tumor or suspected bleeding in the brain. Computed tomography (CT) scan with contrast enhancement is acceptable in special circumstances, such as when a patient is uncooperative or when MRI is unavailable. Magnetic resonance spectroscopy (MRS) is used in specialized circumstances.
- Positron emission tomography (PET) scan is not used to diagnose tumors of the CNS but may have an ancillary role to examine for metastasis or after treatment.
- Electroencephalogram (EEG) is useful for evaluating possible seizure activity.
- Lumbar puncture should not be performed before MRI or CT scan because of the potential for fatal brain herniation to result. Lumbar puncture can yield pressure readings and cerebrospinal fluid (CSF) for cytology, protein, glucose, and tumor markers.
- Testing blood for tumor markers, α-fetoprotein, or β–human chorionic gonadotropin is useful for the diagnosis of some brain tumors.
- Histological examination of a biopsy specimen of brain tissue may be preferred when feasible (Wong & Wu, 2021).

A careful history of symptoms is invaluable. Complete physical examination should include skin survey for stigmata of neurocutaneous syndromes or melanoma, lymph node examination, abdominal examination for hepatomegaly or splenomegaly, and rectal examination with guaiac stool testing. Breast and pelvic examinations in women and cardiopulmonary examination are recommended. The neurological evaluation should include a mental status evaluation, testing for cognitive deficits or memory loss, and assessment for personality changes. Family members may be able to provide clues about subtle personality changes. Ophthalmical examination is essential to assess for papilledema, although this may not be present in patients 55 years old and older. Test also for asymmetry of strength, sensation, visual fields, reflex activity, cranial nerve function, and radicular signs.

Differential Diagnosis:

- Stroke: There is acute onset of headache with persistent focal neurological deficits. CT scan or MRI is diagnostic.
- Aneurysm: In acute rupture, there is a sudden intense headache, often with signs of meningeal irritation. MRI is preferred for diagnosis.
- Arteriovenous malformation: There is a chronic unilateral throbbing headache with no prodromal or associated symptoms. CT scan or MRI may be diagnostic.
- Meningitis: Headache usually is associated with fever and nuchal rigidity. Cerebrospinal fluid is obtained through a lumbar puncture for diagnosis.
- Abscess: Abscess is often associated with fever or other signs of infection.
- Syphilis: Neurosyphilis may occur at any time during infection and up to 35 years later. Symptoms vary according to the area infected. Diagnosis is based on CSF abnormalities and a reactive serological test for syphilis.
- HIV: Various neurological manifestations can be caused by the virus or opportunistic infections; the incidence of CNS lymphoma is increasing in these patients.
- Subdural hematoma: Persistent headache occurs after trauma, with poorly defined intellectual impairment. This may be ruled out by noncontrast CT scan or MRI.
- Postconcussion syndrome: A dull, constant headache occurs within 24 hours of trauma. The patient may complain of loss of concentration, giddiness, irritability, and anxiety.
- Trauma: History of injury to the head or neck is present.
- Temporal arteritis: This is usually characterized by a slow-onset headache that is worse at night, temporal in more than one-half of patients, often with jaw claudication and temporal artery tenderness as well as an elevated erythrocyte sedimentation rate (ESR).
- Normal pressure hydrocephalus (NPH): This condition often presents with dementia, gait disturbances, and incontinence of bladder or bowel.
- Multi-infarct dementia: This may present with impaired cognition and symptoms of upper motor neuron disease in patients with a history of hypertension, atrial fibrillation, diabetes, carotid artery disease, or smoking.
- Alzheimer's disease: This presents with progressive dementia, memory disturbances, and behavioral changes, which are usually gradual over years.
- Chemical poisoning: History of exposure to chemicals, such as carbon monoxide, pesticides, or industrial materials, is present.
- Migraine: Migraine is characterized by an often-unilateral headache with a pulsating quality, associated with nausea and vomiting, photophobia, or phonophobia; prodromal or aura symptoms may be present (Wong & Wu, 2021).

Treatment: Treatment of brain tumor includes surgery, radiation, chemotherapy, glucocorticoids, anticonvulsants, immunotherapy, and gene therapy (NCCN, 2021).

Follow-Up: Prognosis depends on the tumor type, patient age, functional neurological status, extent of resection, tumor location, and extent of metastasis at diagnosis. Tumor grade, patient age, functional status, and complete surgical resection are the important prognostic factors for survival in people with malignant gliomas (NCCN, 2021). During the first year after treatment, the patient should have a focused history and physical examination, including a neurological and funduscopic examination every 3 months. MRI of the brain is recommended 2 to 6 weeks after radiation, then every 2 to 4 months for 2 to 3 years, and then less frequently (NCCN, 2021). Patients receiving palliative care should be seen as necessary for pain and symptom control; hospice care is recommended for these patients.

Sequelae: Various neurological deficits, personality changes, seizure disorders, and chronic head pain can result from brain tumor. Paraplegia, hemiplegia, and quadriplegia are also consequences of brain tumor. Bradycardia, hypertension, and respiratory arrest can occur with increased ICP. Brain herniation is a life-threatening emergent complication.

Prevention/Prophylaxis: Instruct patients to avoid radiation exposure.

Referral: Refer patients to a neurosurgeon, oncologist, radiation oncologist, and hospice, as appropriate.

Education: Genetic counseling is warranted in hereditary syndromes of brain tumor.

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Clinical Recommendation	Evidence Rating	References
Gadolinium-enhanced MRI of the brain is the recommended diagnostic examination for suspected brain tumor.	A	National Comprehensive Cancer Network (NCCN), 2021 Wong & Wu, 2021
Patients with persistent headache that is different from their usual pattern with protracted nausea, vomiting, seizures, neurological symptoms, or positional worsening should be evaluated for brain tumor.	A	Wong & Wu, 2021
Hospice should be offered if life expectancy is less than 6 months, and in patients who are not candidates for surgery or chemotherapy, have deteriorating neurological status, and have poor or worsening functional status.	C	NCCN, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

MYASTHENIA GRAVIS

Signal Symptoms: Diplopia, ptosis, dysphagia, dysphonia, nasal tone, jaw fatigue, neck fatigue, respiratory difficulty. Less frequently: weakness in the hands, difficulty raising hands above head, weakness of legs.

Description: The diagnosis of myasthenia gravis (MG) relies on a history of fatigable muscle weakness (Lazaridis & Tzartos, 2020; Rousseff, 2021). Patients suffer from intermittent, fatigable muscle weakness that worsens with prolonged muscle exertion and improves with rest (Behin & Le Panse, 2018). Gilhus et al. (2019) report involvement of muscle groups is either generalized or localized. Generalized MG comprises 85% of patients while 15% experience only ocular symptoms. More often innervated cranial nerves are affected leading to asymmetric weakness of extraocular muscles which results in diplopia and ptosis. Speech, swallowing, and facial muscles are also frequently affected. During a myasthenic crisis, bulbar (cranial nerves IX, X, XI, and XII) and respiratory muscle involvement is grossly impaired and can be life threatening.

Etiology: Myasthenia gravis is an uncommon neuromuscular disease caused by an immune-mediated decrease in viable nicotinic acetylcholine receptors (AChRs) (Rousseff, 2021). In this autoimmune process, portions of the neuromuscular junction (NMJ) on the postsynaptic membrane of striated skeletal muscles are attacked (Behin & Le Panse, 2018). The reduction of electrical impulses over the NMJ results in a failure of the muscle fiber to generate an action potential, and ultimately, in muscle weakness (Gilhus et al., 2019). Most patients can be diagnosed by specific autoantibodies: AChR, muscle-specific kinase (MuSK), low-density lipoprotein-related protein 4 (LRP4), and double-seropositive MG (Behin & Le Panse, 2018, Rousseff, 2021). Autoantibodies or anti-muscle-specific kinase (anti-MuSK) proteins are found at the neuromuscular junction (Lazaridis & Tzartos, 2020). Anti-MuSK proteins are generated by the immune system and assail muscle-specific kinases (Lazaridis & Tzartos, 2020). Research indicates anti-MuSK antibodies impede the transmission of signals linking muscles and nerves (Lazaridis & Tzartos, 2020). The LRP-4 facilitates signaling to MuSK and is present in roughly 20% of MuSK-MG. The LRP-4 was determined to be a causative agent in the past 10 years, and it is not clearly diagnostic like acetylcholine-receptor binding antibody (AChR-Ab) or muscle-specific kinase antibody (MuSK-Ab) (Rousseff, 2021). Patients who are treatment resistant require further investigation for double-seropositive MG. Double-seropositive patients may exhibit fewer typical features than those of AChR patients and require a comprehensive approach to diagnosis and management (Rousseff, 2021).

Thymoma is found in approximately 15% of patients, frequently in those with AChR antibodies (Gilhus et al., 2019). Abnormalities in the thymus and the link to MG are well known; however, the direct correlation remains unclear (Lisak & Richman, 2020). The thymus is part of the lymphoid system where B and T cells form antibodies. As the central immunity regulation organ, it is logical to suspect aberrations effect tolerance that initiates an immune facilitated attack on AChR (Lisak & Richman, 2020). The presence of a thymoma significantly increases the patient's chance of having severe disease, refractory MG, more severe electromyography (EMG) findings, and overall poorer outcomes (Mantegazza & Antozzi, 2018). Whether the pathogenesis of MG is primary or secondary to abnormal thymus function remains unknown. Imaging of the thymus is recommended in patients where MG is suspected (Mantegazza & Antozzi, 2018).

Occurrence: In the United States, the Myasthenia Gravis Foundation of America (2021) reports there is an annual incidence of roughly 14 to 20 per 100,000. Prevalence of the disorder is difficult to assess because many patients likely remain undiagnosed (Narayanaswami et al., 2021). The Myasthenia Gravis Foundation of America reports somewhere around 36,000 to 60,000 people are living with MG nationally.

Age: Myasthenia gravis is present among all cultures and demonstrates no geographic predilection (Narayanaswami et al., 2021). Females have higher rates in the second and third decades of life, whereas male occurrence are highest in

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the seventh or eighth decade (Larson & Wilbur, 2020). Myasthenia gravis can occur at any age; however, onset typically occurs after age 50 (Larson & Wilbur, 2020).

Ethnicity: Studies have shown that myasthenia gravis can occur in people of all race and ethnic backgrounds and has been found to be slightly more prevalent in patients of African ancestry. Additionally it is more prevalent in people living in countries located near the equator (Dresser et al., 2021).

Contributing Factors: Jowkar (2018) reports contributing factors to aggravating MG include worsening of existing chronic illness, pregnancy, menstrual cycle, mental health issues, surgical procedures, infection, warm climates, and decreasing immunosuppression.

Signs and Symptoms: Examiners should obtain a thorough history including the onset, duration, and progression of symptoms. Onset is typically insidious with a slow and progressive development (Larson & Wilbur, 2020). Patients will present with or report a history of one or more of the following: diplopia, ptosis, dysarthria, dysphagia, masticatory weakness, nasal toned speech, neck fatigue, and, in severe cases, respiratory difficulty (Rousseff, 2021). Ptosis is a symptom of an underlying failure of the oculomotor nerve of the levator palpebrae superioris and is found exclusively in 15% to 20 % of MG patients (Gilhus et al., 2019). Ptosis occurs in patients of any age and has numerous etiologies (Jabbehdari & Golnik, 2018). To examine for ptosis, the patient looks up for one minute. Initiation or worsening of ptosis occurs during this test (Larson & Wilbur, 2020). Tight closure of the eyelids may force fatigue of the orbicularis oculi muscles in which the sclera is seen (Larson & Wilbur, 2020). To examine for diplopia, the patient stares at an object laterally for 30 to 60 seconds (Larson & Wilbur, 2020).

Larson and Wilbur (2020) report extremity weakness typically is more severe proximally than distally. To examine muscle fatigue, formal strength assessment using a muscle grading tool is essential to aid in the diagnosis. Note whether repetition of movement of the extremity induces fatiguability. Careful attention is paid to the distribution of weakness, whether proximal or distal and asymmetrical versus symmetrical. Visually assess any signs of muscle atrophy, fasciculations, or involuntary movements. A comprehensive examination also includes cranial nerve testing. To examine upper extremity weakness, the patient abducts the arms for two minutes while the examiner watches for slow fatiguing of the deltoid muscles. To evaluate leg strength, the supine patient raises one leg at a time, off the examining table, and holds for 90 seconds. Failure to hold the leg for the full 90 seconds indicates weakness. When assessing respiratory function, ask the patient to count to 20 on a single breath. The number the patient is able to reach multiplied by 100 provides a rough estimate of vital capacity (Larson & Wilbur, 2020).

Diagnostic Tests:

Serum Antibody Tests: All patients presenting with common clinical features of MG should first receive serum testing for AChR-Ab (Lazaridis & Tzartos, 2020). Eighty-five percent of patients are noted to have AChR-Ab (Lazaridis & Tzartos, 2020). Patients with singularly ocular involvement represent 50% with AChR-Ab (Lazaridis & Tzartos, 2020). Identifying autoantibodies to acetylcholine-receptor binding, which are specific to MG, is key to confirming a diagnosis. An anti-MuSK antibody test identifies circulating autoantibodies and helps to confirm the type of MG or exclude a diagnosis of MG (Lazaridis & Tzartos, 2020).

Blood Work: Patients with suspected ocular MG may have hyperthyroidism and should receive additional testing via thyroid function tests to eliminate any association with hyperthyroidism or other metabolic states (Larson & Wilbur, 2020).

Electrodiagnostic Testing: A neuromuscular specialist applies a stimulating electrode probe to select muscles. Electrical impulses are sent to the muscles and nerve activity is recorded. This test is only part of the diagnostic picture, as patients with severe MG may have normal results (Gilus et al., 2019). For those with MuSK MG, repetitive nerve stimulation testing is only about 50% sensitive but higher in those with AChR MG at roughly 80%. Nerve stimulation is more specific for MG than single-fiber EMG (Gilus et al., 2019).

Computed Tomography (CT) of the Chest: CT is ordered after the confirmation of MG. This procedure examines the presence of thymoma. Thymomas occur in 10% to 15% of patients (Gilus et al., 2019).

Differential Diagnosis:

- Amyotrophic lateral sclerosis (ALS): Commonly causes muscle fasciculations and spares ocular movements. An EMG and laboratory tests aid in confirming of the diagnosis (Larson & Wilbur, 2020).
- Aponeurotic ptosis: Most common form of eyelid drooping and is found commonly in older adults. An ophthalmologist or neurologist confirms diagnosis (Latting et al., 2017).
- Brainstem glioma: A form of brain cancer where a patient may complain of diplopia, weakness, gait instability, dysphagia, and headache. Imaging confirms the diagnosis. (Ney, 2018).
- Graves' disease: An autoimmune disorder in which patients present with several symptoms, including muscle weakness and fatigue. Laboratory work results include an abnormally low thyroid-stimulating hormone (TSH) level (Subekti & Pramono, 2018).
- Guillain-Barré syndrome (GBS): The most frequently seen cause of neuromuscular weakness. Patients display ascending, progressive, symmetrical weakness of the feet and legs with a reduction or loss in tendon reflexes. Patients may or may not have peripheral sensory changes. Cerebrospinal fluid tests and nerve conduction studies with EMG are advantageous to diagnosis (Liu et al., 2018).
- Lambert-Eaton's myasthenic syndrome: Characterized by proximal weakness; autonomic dysfunction and areflexia are findings in this paraneoplastic neuromuscular junction disorder. Symptoms result from antibodies that work to diminish release of acetylcholine. More than half of patients with Lambert-Eaton's have small cell lung carcinoma. Antibody testing and electrophysiological studies assist in confirming the diagnosis (Kesner et al., 2018).
- Multiple sclerosis (MS): Inflammatory disease of the central nervous system (CNS); patients may experience diplopia or unilateral vision loss as a result of optic neuritis.

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Ataxia, fatigue, weakness of limbs (due to transverse myelitis), and paresthesias of the hands and feet are also frequent findings. Bowel or bladder dysfunction may be present. Imaging to examine for brain or spinal lesions as well as cerebrospinal fluid (CSF) studies validate or refute the diagnosis (Reich et al., 2018).

- Neurosarcoidosis: A form of sarcoidosis in which facial nerves are affected. Cranial neuropathy comprises 50% to 70% of cases. A clinical examination and imaging are helpful in determining the diagnosis (Voortman et al., 2019).
- Polymyositis: Patients typically complain of acute difficulty with climbing stairs, walking, raising arms above the head. Pain is also frequently reported. Work-up includes blood work with complete blood count (CBC) demonstrating leukocytosis, positive rheumatoid factor, and elevated erythrocyte sedimentation rate or C-reactive protein (CRP) levels (Schmidt, 2018).
- Tolosa-Hunt's syndrome: Patients possess ipsilateral oculomotor paralysis with unilateral orbital pain. Patients respond quickly to steroids (Bugeme et al., 2020).

Treatment: The care plan should be aggressive with the goal for significant improvement or resolution of symptoms (Gilhus et al., 2019). The subgroup of MG dictates treatment with consideration given to appropriateness of thymectomy, acetylcholinesterase inhibitors, immunotherapy, intravenous immunoglobulin, and plasma exchange.

Medications: Anticholinesterase inhibitors—Farmakidis et al. (2018) report the most commonly used acetylcholinesterase inhibitor is pyridostigmine. Acetylcholinesterase inhibitors act on the neuromuscular junction by improving interactions between the acetylcholine and the acetylcholine receptor. Pyridostigmine works most effectively when taken approximately every 4 hours. Starting dose is 60 mg and may be titrated up 60 to 120 mg every 4 hours and increased to a daily maximum dose of 1,500 mg for regular release or 1,080 mg for extended release. Side effects most commonly seen are loose stools, flatulence, and abdominal cramping. Patients with AChR autoantibody MG respond at higher rates to anticholinesterase inhibitors than do MuSK+ patients. Response in ocular MG patients is limited. During a myasthenia crisis, anticholinesterase inhibitors can complicate respiratory management due to increasing secretions.

Immunotherapy—Corticosteroid treatment is selected for patients who demonstrate inadequate response to pyridostigmine alone (Gilus et al., 2019). Because immunotherapy drugs prednisone and prednisolone act quickly to affect the symptoms of MG, they are the preferred first-line medications (Gilus et al., 2019). Patients with severe MG need higher doses and response typically occurs in 2 to 4 weeks (Gilus et al., 2019). A common dosing regimen will begin with prednisone 20 mg daily with incremental 5 mg increases every 3 to 5 days until symptoms subside (Gilus et al., 2019). Patients may be tapered in 4 weeks or kept on a maintenance dosage (Gilus et al., 2019). Favorable outcomes are seen with maintenance of low-dose steroids in all MG patient groups (Gilus et al., 2019). Bulbar patients receiving high-dose corticosteroids should be watched closely during the first week of treatment (Gilus et al., 2019). Patients with ocular MG experience good outcomes with lower doses of corticosteroids, which are considered first-line treatment (Alhaidar et al., 2022). Patients in respiratory crisis benefit from high-dose, daily treatments of corticosteroids in conjunction with IV immunoglobulin (IVIg) or plasma exchange treatment (PLEX) (Gilus et al., 2019). High-dose steroids have adverse side effects, including weight gain, increased appetite, impaired glucose tolerance, mood lability, osteoporosis, increased risk of infections, and skin atrophy. Because of known side effects, steroids are often added at a lower dose to a treatment regimen that includes immunosuppression drugs (Behin & Le Panse, 2018). Other frequently used immune-suppressing drugs include azathioprine, mycophenolate, methotrexate, tacrolimus, and cyclosporine (Gilus et al., 2019). Suppression takes on many mechanisms of action. Immunotherapy drugs work by curbing antigen production and diminishing circulating T cells (corticosteroids), hindering T and B cell production via cell cycle reduction (azathioprine, methotrexate, and mycophenolate), and obstructing T cell activation (cyclosporine, tacrolimus) (Menon et al., 2020). Patients on immunosuppressive therapies typically require less pyridostigmine and experience stabilization of disease with remission of symptoms (Gilus et al., 2019). Immunotherapy has seen decades of use with demonstrated efficacy for MG (Menon et al., 2020). These medications also have enumerable side effects, including increased incidence of susceptibility to cancer and vulnerability to life-threatening infections (Menon et al., 2020).

Rituximab—This monoclonal antibody targets the transmembrane protein CD20 found on the surface of B lymphocytes (Farmakidis et al., 2018; Gilhus et al., 2019). Rituximab works by impeding antibody creation and suppressing humoral immunity by decreasing circulating CD20+B cells (Gilhus et al., 2019). It is indicated for patients with MuSK Ab+ who fail to see results with initial immunotherapy or those with refractory MG (Gilhus et al., 2019). A typical regimen for infusion is 375 mg/m^2 given weekly for 4 weeks or two administrations of 1 g infusions, separated by 2 weeks. Patients may need additional infusion therapy every 4 to 6 months. Side effects include headache, fever, nausea, weakness, diarrhea, and infections from lowered immunity (Farmakidis et al., 2018; Gilhus et al., 2019).

Eculizumab—This drug was approved by the U.S. Food and Drug Administration (FDA) in 2017 and is a human monoclonal antibody that works on the complement cascade (Farmakidis et al., 2018). Patients with generalized MG who are AChR-Ab positive and have moderate to severe disease are candidates; however, current recommendations cite its use only when other immunotherapies have failed to see a response (Farmakidis et al., 2018; Narayanaswami et al., 2021). Eculizumab is administered through an intravenous infusion. Dosing starts at 900 mg per week for the first 4 weeks and is increased to 1,200 mg the fifth week and for subsequent dosages (Farmakidis et al., 2018). Patients must receive a meningococcal vaccine before starting therapy (Farmakidis et al., 2018).

IVIgs—Administered intravenously, IVIg works by preventing antigen cell interaction with T cells and neutralizing cytokines and antibodies (Gilhus et al., 2019). Typically, IVIg is utilized in conjunction with high-dose steroids in respiratory crisis (Gilhus et al., 2019; Menon et al., 2020). It may also be given prior to initiating immunotherapies in an attempt to bring symptoms under control. Both IVIg and PLEX are fast-acting treatments that result in immediate response (Gilhus et al. 2019).

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Plasmapheresis (Plasma Exchange, PLEX)—Plasmapheresis is conducted through a central or peripheral line and works by removing plasma-soluble autoantibodies and cytokines (Farmakidis et al., 2018). To date, there is no definitive study that demonstrates that PLEX improves MG patient outcomes; however, evidence suggests it can be beneficial (Farmakidis et al., 2018). Short-term plasmapheresis is useful during a respiratory crisis or an impending crisis (Farmakidis et al., 2018). It may also be tried in patients who fail to respond to immunosuppressant therapies with moderate disease (Farmakidis et al., 2018). Improvement is seen for most patients by the third treatment with the effects lasting weeks (Farmakidis et al., 2018).

Thymectomy: This procedure involves removing the thymus and tumor. Histological studies guide appropriate chemotherapy, radiation, and observation (Farmakidis et al., 2018). Older adults with small, slow-growing thymomas should have regular surveillance scans with magnetic resonance imaging (MRI) or CT and typically do not require surgery (Gilus et al., 2019).

Follow-Up: Patients are typically maintained on pyridostigmine. Those who fail to show response should be questioned about their dosing intervals. Lack of clinical improvement may be due to adherence issues (difficulty taking it every 4 hours), underdosing, or overdosing. The patient should be asked about noted instances of shortness of breath because this can indicate impending respiratory compromise. Questions regarding lifestyle are also important to ask because MG can by triggered by lifestyle events such as emotional stress (Jowkar, 2018).

Sequelae: Most patients who respond to treatment can obtain a semblance of normal function and quality of life. Full strength and use of muscles is usually good with adequate treatment; lifelong damage of muscles is rare (Gilhus et al., 2021). Dysphagia can result in nutritional deficits, and patients should be evaluated for worsening difficulties with intake. In severe cases, the nerves that innervate the diaphragm are compromised and respiratory distress is life threatening (Gilhus et al., 2019).

Prevention/Prophylaxis: No recommendations exist for prevention of MG; however, some medications that may worsen MG should be avoided. (This is not an exhaustive list.)

- Antibiotics—Patients should refrain from using antibiotics unless there is a clear indication. Penicillins or cephalosporins are preferred when possible.
- Anti-seizure—Patients can experience worsening symptoms with phenytoin, phenobarbital and gabapentin and should be monitored closely.
- Arrhythmia drugs—Quinidine, procainamide, and disopyramide may exacerbate MG.
- Arthritis medications—Penicillamine and antimalarials (chloroquine, hydroxychloroquine, quinine) can further exacerbate weakness.
- Hypertension—Calcium channel blockers and beta blockers may worsen weakness.
- Magnesium—All forms should be avoided except for multivitamins, which generally have acceptable levels of magnesium.
- Narcotics/sedatives/hypnotics—These medications decrease respiratory drive, which may already be compromised in patients with MG patients. Use with caution. Patients undergoing surgery with the use of anesthesia should consult with their neurology provider prior to the procedure (Narayanaswami et al., 2021; Sheikh et al., 2021).

Referral: Referral to a neurologist is appropriate for patients who do not respond to medication therapy and/or who need EMG testing. Patients with bulbar symptoms may need to be seen by a speech therapist for evaluation of dysphagia or dysphonia. Patients with ocular MG or those with vision involvement may also benefit from consulting a neuro-ophthalmologist (Jabbehdari & Golnik, 2018). Generalized weakness is common in MG, and an evaluation with a customized care plan from physical therapy to optimize activities of daily living may be of benefit (Farrugia & Goodfellow, 2020). Patients who develop dysfunctional breathing may need a referral to respiratory therapy for further evaluation (Farrugia & Goodfellow, 2020).

Education: Older patients will likely have comorbidities that may exacerbate MG, and counseling is directed toward minimizing these factors. Patients should be educated on signs and symptoms of worsening respiratory distress because this condition is a medical emergency. A comprehensive treatment plan includes physical activity with exercise. Refer patients to seek additional information through the Myasthenia Gravis Foundation of America at https://myasthenia.org/.

Clinical Recommendation	Evidence Rating	References
Patients with generalized myasthenia gravis (MG) who are acetylcholine-receptor binding antibody positive and have moderate to severe disease are candidates for eculizumab; however, current recommendations cite its use only when other immunotherapies have failed to see a response. Prior to starting therapy with eculizumab, patients must receive a meningococcal vaccine.	A	Farmakidis et al., 2018
Treatment with plasma exchange during respiratory crisis is beneficial.	A	Farmakidis et al., 2018
Older adults with small, slow-growing thymomas should have regular surveillance scans with magnetic resonance imaging or computed tomography and typically do not require surgery.	A	Gilhus et al., 2019

Continued

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Clinical Recommendation	Evidence Rating	References
Rituximab is indicated for patients who are positive for anti-muscle-specific kinase antibodies who fail to see results with initial immunotherapy or for those with refractory MG.	A	Gilhus et al., 2019
Patients with suspected ocular MG may have hyperthyroidism and should receive additional testing via thyroid function tests to eliminate any association with hyperthyroidism or other metabolic states.	A	Larson & Wilbur, 2020
All patients presenting with common clinical features of MG should first receive serum testing for acetylcholine receptor antibody.	A	Lazaridis & Tzartos, 2020
Imaging of the thymus is recommended in patients where MG is suspected.	A	Mantegazza & Antozzi, 2018
Patients undergoing surgery with the use of anesthesia should proceed with caution due to potential adverse effects of suppressing respiratory drive.	A	Narayanaswami et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PARKINSON'S DISEASE

Signal Symptoms: Bradykinesia, rest tremor, rigidity, akinesia, impaired postural reflexes.

Description: Parkinson's disease (PD) is the second most common chronic progressive neurodegenerative disorder. PD occurs as the result of the loss of dopamine-producing cells in the substantia nigra, located in the basal ganglia. The formation of Lewy bodies from alpha-synuclein cytoplasmic inclusions in the remaining dopaminergic neurons are the pathological features of PD. This causes degeneration of the dopamine pathway in the brain and is responsible for the development of motor symptoms in PD (Cerri et al., 2019). Motor symptoms include resting tremor, rigidity, akinesia, bradykinesia, and impaired postural reflexes (resulting in postural instability). Subtle motor impairments may precede the development of overt clinical signs and symptoms by many years.

Etiology: The cause of primary or idiopathic PD is unknown. It is thought to be a confluence of genetic factors, environmental risks, mitochondrial dysfunction, oxidative stress, and possibly chronic inflammation (Tysnes & Storstein, 2017). Secondary PD (Parkinson's syndrome) may be caused by head injury, toxins, heavy metals, herbicides, pesticides, dopamine-depleting drugs, encephalitis, hypoparathyroidism, and Wilson's disease. Parkinsonism includes known variants of PD, including multisystem atrophy (MSA), progressive supranuclear palsy (PSP), corticobasal degeneration (CBD), Lewy body dementia (LBD), vascular parkinsonism, and neuroleptic-induced parkinsonism.

Occurrence: It is estimated that PD affects 4 million people worldwide and 1 million in the United States. In the United States, 60,000 people are being diagnosed each year. (Halli-Tierney et al., 2020). The incidence of PD in men is higher than in women at a ratio of 2:1. The disease tends to progress faster in women and is associated with higher mortality when compared with men (Cerri et al., 2019).

Age: The incidence of PD increases with age. It affects 3% of those older than the age of 65 and up to 5% of those older than 85 (Cerri et al., 2019). It is rarely seen before the age of 40.

Ethnicity: PD can be found in all cultures and ethnic backgrounds. According to a nationwide Medicare database, there is a lower prevalence among the Asian and African American populations and a higher prevalence in European American and Latino populations in the United States (Marras et al., 2018).

Contributing Factors: Stress is not a direct causative factor in PD, but it may contribute to worsening symptoms. A major life stressor is often reported with the diagnosis of PD (another medical or surgical concern, a move, retirement, loss of a job, a fire, or loss of a child). Carbon monoxide exposure, MPTP (an illicit drug), and a combination of genetic and environmental factors contribute to the diagnosis of PD. In certain families, genetic factors do result in an increased risk of developing PD.

Signs and Symptoms: Though not everyone with PD will develop tremors, PD does commonly present initially as a unilateral rest tremor in the upper extremities that disappears with movement. This is often referred to as a pill-rolling tremor, which describes the appearance of rolling a pill between the thumb and forefinger. Tremor can also affect the legs, lips, chin, and tongue. Patients may also describe an internal tremor that may not be visible but rather felt inside. Rigidity is another primary feature of PD and is defined as increased resistance to passive range of motion of a joint, such as the elbow or wrist. Bradykinesia is defined as slowness of movements, small movements, and a decrease in automatic movements. It is one of the cardinal symptoms of PD and manifests in many ways, including decreased speed or amplitude in finger taps, hand grasps, and hesitation or arrest of movements (freezing). Patients develop decreased facial expression in which there is a decrease in eye blinking (masked facies) and mouth movements. Patients take small, shuffling steps and have decreased arm swing during ambulation. Other gait changes include stooped posture in which the trunk leans forward and the back is kyphotic. This stooped posture causes the trunk to be in front of the patients' normal center of gravity. This leads to a festinating

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gait, in which the patient takes small and fast steps in an attempt to catch up to the top half of their body to recover their balance. This commonly leads to postural instability and falls. Patients also experience an associated softening of the voice (hypophonia) and drooling (sialorrhea) due to decreased spontaneous swallowing. Handwriting size is smaller (micrographia).

In addition to the above motor symptoms in PD, there are non-motor symptoms that can be equally debilitating and often undertreated. Therefore, it is essential to assess for and treat these symptoms. Mood changes are widespread in PD and range from depression, anxiety, and apathy to pseudobulbar affect, irritability, and labile moods. Depression and anxiety affect some 35% of patients with PD. Dementia affects 30% to 40% of patients with PD and may be associated with hallucinations, illusions, or delusions (Parkinson's psychosis) (Hayes, 2019). Slowed cognitive processing and impairment of executive functions and impairment of visuospatial memory are common in PD (i.e., the ability to plan, organize, pay attention, remember details, strategize, and manage time and space). Orthostatic hypotension is also common in PD and causes safety concerns because it increases the risk of falls. Rapid eye movement (REM) sleep behavior disorder causes patients to act out their dreams at night (i.e., kicking, yelling, punching, hitting). In severe cases, patients can injure their bed partner or themselves. Constipation, impotence, and urinary urgency/incontinence are also common issues.

The neurological examination will reveal most PD motor symptoms, and noting the patient's movement, coordination, and gait is crucial. The examiner will observe the patient while in the seated position with hands at rest for signs of tremor, noting the frequency and amplitude of the tremor. To assess rigidity, the examiner will passively move the head/neck, arms, and legs and feel for any resistance or difficulty achieving full range of motion (ROM) or cogwheeling. Bradykinesia is assessed by observing the patient tapping their fingers, opening and closing their hands, alternating pronation and supination of the hands, and toe tapping, noting any differences in speed, amplitude, or arrest of the movements. Observe facial expression and voice changes (Tarakad & Jankovic, 2017). Postural stability is assessed using the pull test. The examiner stands behind the patient and informs the patient that they will be pulled with two hands on the shoulders backward; then the patient is pulled, and the recovery is documented. Note whether the postural reflexes are impaired or absent. During gait assessment, observe for small shuffle steps, kyphotic or stooped posture, and reduced or absent arm swing. Also assess for en bloc turning, where a patient takes multiple small steps to turn around instead of turning on a pivot (Hayes, 2019). Tandem walking (heel-to-toe in a straight line) can also help assess balance.

Strength generally does not deteriorate despite the rigidity. Tendon reflexes are almost always normal. Orthostatic vitals should be obtained to assess for orthostatic hypotension. Early in the diagnostic phase, the patient's cognitive status needs to be assessed to provide a baseline, given the prevalence of dementia developing in patients with PD. This can be done using the Montreal Cognitive Assessment (MoCA). Smell is commonly impaired (hyposmia) early in PD; therefore, evaluating cranial nerve I (olfactory nerve) could be helpful. Check the patient's ocular movements; impairment of upward or downward gaze is common in progressive supranuclear palsy but not in idiopathic PD.

Diagnostic Tests: Diagnosis of PD is made clinically based on history and physical examination findings and requires the presence of two cardinal signs—bradykinesia with either rigidity or rest tremor, or both. Improvement of motor symptoms with levodopa supports the diagnosis. The most definitive diagnostic test for PD is the pathological features noted in the brain during autopsy (Tarakad & Jankovic, 2017). Magnetic resonance imaging (MRI) may be ordered to rule out suspected brain lesions or abnormalities, such as NPH or atypical conditions such as vascular parkinsonism or corticobasal syndrome. In cases when the diagnosis is unclear, a DaTSCAN (ioflupane [123I]) injection, also known as phenyltropane, can be ordered to indicate the presence of PD. The radiotracer is injected into the blood and circulates to the brain, attaching itself to dopamine transporter molecules on dopamine neurons, which then can be detected using special imaging equipment. In PD, there will be less signal seen on the scan indicating a loss of dopamine neurons (Armstrong & Okun, 2020). Also, olfactory dysfunction, REM sleep behavior disorder, autonomic dysfunction (constipation), and depression are strongly linked to PD and commonly occur years before a diagnosis of PD. The loss of smell and REM sleep behavior disorder especially help to support the diagnosis.

Differential Diagnosis:

- Drug-induced parkinsonism: Confirmed by improvement with the withdrawal of dopamine blocking medication such as neuroleptics and metoclopramide
- Essential (benign familial) tremor: Tremor is an action tremor 6 to 8 Hz compared with PD tremor, which is at rest and has a 3 to 6 Hz frequency.
- Corticobasal degeneration: Unilateral rigidity and coarse tremor, apraxia, and myoclonus of affected limb; poor response to levodopa
- PSP: Supranuclear gaze abnormality, gait instability, and falls, with axial-predominant rigidity. Tremor is usually absent.
- LBD: Dementia, hallucinations, delusions, and fluctuations in lucidity that worsen rapidly with progression (Hayes, 2019)
- Multisystem atrophy (MSA): Early and prominent autonomic dysfunction and poor response to dopamine
- MSA-parkinsonian subtype (MSA-P) (formerly called striatal nigral degeneration): Autonomic dysfunction and dystonia are present.
- MSA-cerebellar subtype (MSA-C) (formerly called olivopontocerebellar atrophy): Distinguished by inherited parkinsonism, progressive ataxia, dementia, difficulty with balance, and dysarthria (Jellinger, 2018)
- Huntington's disease: This disorder is genetic in origin and characterized by chorea, clumsiness, and cognitive decline.
- Creutzfeldt-Jakob's disease: A rapidly progressive syndrome of mental deterioration, lead-pipe rigidity, myoclonus, aphasia, apraxia, and hallucinations
- Normal pressure hydrocephalus (NPH): Gait apraxia, urinary incontinence, and dementia are present.

Treatment: There are various medications for both motor and non-motor symptoms and surgical options available to treat PD. Patients with mild disease and no interference with ADLs may not require treatment (Tarakad & Jankovic, 2017).

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Medications for Motor Symptoms:

- Carbidopa/levodopa (Sinemet): Used for bothersome symptoms or in older adults. Replenishes depleted dopamine in the brain by increasing the dopamine precursor levodopa to stimulate dopamine receptors. Start carbidopa/levodopa 25/100 (carbidopa 25 mg, levodopa 100 mg) one tablet tid. Titrate slowly to symptomatic relief.
- Dopamine agonists: Less potent than carbidopa/levodopa. Used for mild symptoms. Watch for compulsive behaviors, fatigue, and daytime somnolence.
  - Ropinirole (Requip): Start 0.25 mg tid, increase gradually. Max: 24 mg/day
  - Pramipexole (Mirapex): Start 0.125 mg tid, increase weekly. Max: 4.5 mg/day
  - Rotigotine (Neupro patch): Start 2 mg/day, increase weekly. Max: 8 mg/day
- Amantadine: Is thought to augment dopamine release from presynaptic nerve terminals or to inhibit dopamine reuptake and antagonized *N*-methyl-D-aspartate (NMDA) receptors. Reduces dyskinesia and improves tremor and other motor symptoms. Start 100 mg daily, increase weekly. Max: 100 mg tid
- Entacapone (Comtan): Given with each dose of levodopa to extend the effectiveness of levodopa. Stalevo is the combination of carbidopa, levodopa, and entacapone. Stalevo dosages reflect the amount of levodopa (50, 75, 100, 125, 150, and 200) in each pill combined with carbidopa and Comtan 200 mg.
- Selegiline (Deprenyl, Eldepryl): Monoamine oxidase-B inhibitor that inhibits the enzyme responsible for inactivating dopamine. Adding selegiline 5 mg/day (increasing to 10 mg/day within 1 week) can improve the wearing-off effect of levodopa (doses to be given before lunch).
- Rasagiline (Azilect): Monoamine oxidase-B inhibitor that can be used alone or with Sinemet. Start 0.5 mg/day, increase to 1 mg/day.
- Rytary: Extended-release carbidopa/levodopa; used for people who experience wearing-off symptoms
- Duodopa: Levodopa/carbidopa gel continuously administered using a pump and percutaneous endoscopic jejunostomy tube. Indicated in late PD because it offers the possibility of more on time when the patient can function.
- Rescue medications: Indicated for abrupt wearing off of medications or "freezing" episodes where the patient is unable to move (Tarakad & Jankovic, 2017).
  - Apomorphine (Apokyn): Subcutaneous injectable (2 to 4 mg)
  - Apomorphine (Kynmobi): Sublingual film for "off" episodes
  - Levodopa inhalation powder (Inbrija): Orally inhaled levodopa (42 mg)

Medications for Non-motor Symptoms:

- Dementia: Rivastigmine patch, donepezil, memantine
- Parkinson psychosis: Pimvaserin, quetiapine
- Orthostatic hypotension: Droxidopa (Northera), midodrine, fludrocortisone
- Constipation: MiraLAX and Senokot
- Orthostasis and constipation may also be treated with adequate water intake.

Surgical Management

- Deep brain stimulation (DBS): A surgical procedure that implants microelectrodes in the brain and a battery device implanted in the chest that generates impulses that stimulates the brain through the microelectrodes. The two most common targets utilized for PD are the subthalamic nucleus and globus pallidus interna. Settings are programmed in the clinic and can be adjusted over time as the disease progresses.
- High-frequency ultrasound: Consists of directing beams of ultrasonic energy precisely and accurately on targets deep in the brain without damaging surrounding normal tissue.

Nonpharmacologics

- Physical therapy: Most effective treatment for balance issues in PD
- Speech therapy: Used for hypophonia, dysarthria, dysphagia
- Exercise: Research indicates improvement in motor and non-motor symptoms and quality of life in patients with PD who consistently exercise an average of 40 to 60 minutes, 3 times/week, for 4 to 12 weeks (Wu et al., 2017).

Follow-Up: Typically, every 3 to 6 months to assess for disease progression and effectiveness of treatment for both motor and non-motor symptoms.

Sequelae: PD results in chronic and progressive immobility. As the disease advances, the patient is at risk of injury from falls due to postural instability. The hazards of immobility (Olson et al., 1990) can prove deadly, including megacolon from constipation, aspiration pneumonia, pulmonary embolism, decreased appetite from inactivity (anorexia), urinary tract infections, and sepsis resulting from disruption in skin integrity. With medical therapies, surgery, and regular exercise, a patient with PD can have a relatively normal life expectancy.

Prevention/Prophylaxis: No pharmacological treatments are available to slow or prevent disease progression in PD. Some research indicates high intensity exercise significantly slows the worsening of motor symptoms in PD (Armstrong & Okun, 2020).

Referral: Refer patients with unusual presentation or bothersome complications and those who do not respond to the initial medication regimen to a neurologist or movement disorder neurologist. Early referral to physical therapy (PT), occupational therapy (OT), and speech therapy is recommended.

Education: Provide patients and family members with written information about PD, including information about local support groups. The following are helpful resources:

- National Institute of Neurological Disorders and Stroke (https://www.ninds.nih.gov/)
- Parkinson's Foundation (https://www.parkinson.org/Living-with-Parkinsons/Resources-and-Support or contact the helpline at 1-800-4PD-INFO [473-4636])

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Clinical Recommendation	Evidence Rating	References
Olfaction dysfunction is a "preclinical" sign of Parkinson's disease (PD).	A	Halli-Tierney et al., 2020
Depression affects 30%–40% of patients with PD.	A	Hayes, 2019
Beyond the benefits on physical health, exercise gives patients a more active role in the management of their PD.	A	Wu et al., 2017
A new method to investigate postural instability in PD uses computer-controlled motors to deliver precise pulls to the shoulders of subjects while standing.	A	Di Giulio et al., 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PERIODIC LIMB MOVEMENT DISORDER

Signal Symptoms: Tightening, bending, or flexing of one or both legs at the hip, knee, ankle, or toes.

Description: Periodic limb movement disorder (PLMD) is disrupted sleep caused by periodic limb movements of sleep (PLMS), which are rhythmic movements (tightening, bending, or flexing) of one or both legs at the hip, knee, ankle, or toes every 5 to 90 seconds. To be considered PLMD, this movement must occur at least 15 times a night, disrupt sleep, and not be caused by any other sleep disorder (Stefani & Hogl, 2019). Each movement lasts approximately 2 seconds, although they can last longer, and they occur in light non-rapid eye movement (REM) stages of sleep during the first half of the night.

Etiology: Although the exact cause is unknown, PLMD has been associated with low iron levels, vitamin deficiencies, restless legs syndrome (RLS), diabetes, and kidney disease.

Occurrence: The exact prevalence is unknown because it is difficult to isolate PLMD from other sleep disorders, but one study did show 28.6% of subjects had more than 15 PLMS an hour (Haba-Rubio et al., 2016), and another study showed a prevalence in their subjects was 21.1% (Doan et al., 2018). Older studies estimate a prevalence between 3% and 11%.

Age: It can occur in both children and adults but is more common as people age.

Ethnicity: Data regarding ethnicity is limited. However, in a study of individuals with both RLS and PLMS, it was found that the combination of these was present more in White and Hispanic individuals as compared to Black and Chinese American individuals (Doan et al., 2018).

Contributing Factors: PLMS/PLMD is often associated with other sleep disorders such as RLS, REM sleep behavior disorder, sleep apnea, and narcolepsy. It has been associated with diabetes, kidney disease, attention deficit disorder, iron deficiency, and withdrawal from benzodiazepines and may be aggravated by caffeine, alcohol, antidepressants, neuroleptics, and antiemetics (Sleep Foundation, 2021).

Signs and Symptoms: A rhythmic movement (tightening, bending, or flexing) of one or both legs at the hip, knee, ankle, or toe every 5 to 90 seconds. The disruption of sleep this causes can result in excessive daytime sleepiness or fatigue for both the individual experiencing the movements and the bed partner whose sleep is also disturbed. The focused interview for PLMD should include the following:

- Ask about the urge to move or unpleasant sensations and if they are partially or totally relieved by movement such as walking or stretching (to differentiate from RLS) or if they have been told they yell out, kick, or hit in their sleep (to differentiate from REM sleep behavior disorder).
- Ask if they have noticed any activities or other contributing factors that make their symptoms worse.
- Ask about sleep patterns. Does the patient keep their partner awake?
- Ask if they are tired during the day from an interrupted night of sleeping?

Diagnostic Tests: PLMS are identified on a sleep study known as a polysomnogram (PSG), which is considered the gold standard for diagnosis (Kurtis et al., 2018). Laboratory work such as ferritin, iron studies, folate, vitamin B_{12}, magnesium, thyroid function tests, and a basic metabolic panel can also be ordered to identify deficiencies and metabolic concerns.

Differential Diagnosis: Differential diagnoses for PLMD include but are not limited to:

- Restless legs syndrome (also in this chapter)
- REM sleep behavior disorder (physically and verbally acting out dreams during REM stages of sleep)
- Sleep-related breathing disorder
- Hypnagogic foot tremor
- Myoclonus

Treatment: There are limited studies on the treatment of PLMS/PLMD, and isolated PLMD may not require treatment. When PLMS occurs in association with another sleep disorder, the treatment typically focuses on other disorders such as RLS. A meta-analysis done by Meng-Ni and associates (2018) did show that the patch, rotigotine (Neupro), is efficacious in treating PLMS as are the dopamine agonists, ropinirole (Requip) and pramipexole (Mirapex). Alpha-2-delta ligands can be used if needed. Deficiencies such as

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iron deficiency should be treated. Good sleep hygiene should be reviewed, and stress-reduction measures should be instituted.

Follow-Up: Ask about sleep, exercise, and relationships. Sleep disturbances can cause hypertension (check blood pressure at each visit) and stress in relationships.

Sequelae: True PLMD results in disruptive sleep. Sleep deprivation can cause relationship problems, hypertension, and daytime sleepiness that can compromise safety. PLMS/PLMD has also been associated with cardiovascular events (Winkelman et al., 2017).

Prevention/Prophylaxis: There is no specific prevention of PLMD, although treating other sleep disorders and preventing deficiencies and other medical comorbidities may help.

Referral: If PLMD is suspected, refer to a sleep center for a PSG sleep study. If difficult to treat, a referral should be made to a sleep specialist, who will address other sleep issues such as sleep apnea, if present, or a movement disorders neurologist.

Clinical Recommendation	Evidence Rating	References
Diagnostic criteria should be used to diagnose periodic limb movement disorder. Periodic limb movements of sleep (PLMS) must occur at least 15 times a night, disrupt sleep, and not be caused by any other sleep disorder.	A	Stefani & Hogl, 2019
A polysomnogram should be ordered as the gold standard to confirm PLMS.	A	Kurtis et al., 2018
Rotigotine (Neupro) is efficacious in treating PLMS, as are the dopamine agonists ropinirole (Requip) and pramipexole (Mirapex).	A	Meng-Ni et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PERIPHERAL NEUROPATHY

Signal Symptoms: Paresthesia, allodynia, sensory impairment, altered gait.

Description: Peripheral neuropathy (also known as polyneuropathy [Jin, 2021]) is a common neurological syndrome involving the peripheral nerves of the dorsal, ventral spinal nerve roots, dorsal root ganglia, brachial, lumbosacral plexus, cranial nerves, sensory, motor, autonomic, or mixed nerves (Castelli et al., 2020), producing variable signs and symptoms. The pathology and severity of the disease differ due to an array of medical disorders. Although the specific mechanisms affecting peripheral nerves are unknown, peripheral nerves respond in three ways: Wallerian degeneration, axonal degeneration, and segmental demyelination (Jin, 2021). In axonal degeneration (dying-back phenomenon), the axon degenerates at the distal end of the axon causing a symmetrical degeneration in a distal to proximal gradient as it progresses. Early sensory alteration includes numbness, pain, or burning sensation in a stocking and glove pattern of the lower extremities. Later stages involve proximal numbness, distal weakness, or atrophy. Other symptoms may be an electric shock sensation, allodynia, hyperalgesia, and hyperesthesia (Castelli et al., 2020; Choi & Di Maria, 2021; Jin, 2021). Segmental demyelination refers to focal degeneration of the myelin sheath with preservation of the axon. This is least common compared to axonal degeneration. It has a rapid course as in Guillain-Barré syndrome (GBS), focal mononeuropathies, generalized sensorimotor or motor neuropathies, hereditary neuropathies, immune-mediated diseases (Choi & Di Maria, 2021; Jin, 2021).

Etiology: The etiology of peripheral neuropathy is poorly understood (Kaeley et al., 2019). Peripheral neuropathy can be caused by multiple factors affecting the sensory, motor, or autonomic fibers, leading to a host of signs and symptoms that may be acute (as seen with trauma or nerve infarction), subacute (existing over a period of months, as seen when the causative agent may be related to drugs, toxins, or metabolic diseases), or insidious/chronic (as occurring with chronic inflammatory demyelinating neuropathies) (Motiwala, 2021). Common causes of peripheral neuropathy are attributed to nerve entrapment, vasculitis, amyloidosis (Kaeyle et al., 2019), nutritional deficiencies (vitamin B_{12} deficiencies), metabolic diseases (diabetes mellitus), inflammatory processes, hereditary processes, autoimmune diseases (rheumatoid arthritis), toxins and drugs (chemotherapy agents), systemic diseases (hypothyroidism, uremia), infections (HIV), and malignancies (Castelli et al., 2020; Choi & Di Maria 2021). Vitamin D deficiency is associated with paresthesia and parasympathetic dysfunction and is highly prevalent in diabetic populations (Iqbal et al., 2018).

Occurrence: The prevalence of peripheral neuropathy in the general population is approximately 1% to 7% with higher rate among those older than age 50 (Castelli et al., 2020; Lipsitz et al., 2018). Peripheral neuropathy affects 25% to 50% of individuals with diabetes, and is dependent upon age, number of years with diabetes, and the degree of diabetic control (Castelli et al., 2020; Hicks et al., 2021).

Peripheral neuropathy exists in approximately 70% of persons with chronic diseases (Lipsitz al., 2018). Diffuse symmetrical distal sensorimotor neuropathy is the most common manifestation in diabetic peripheral neuropathy and is thought to affect about 34% of persons with diabetes (Hicks et al., 2021). About 39% of the population with rheumatoid

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arthritis have sensorimotor axonal neuropathy and pure sensory type peripheral neuropathy (Kaeley et al., 2019).

Approximately 25% to 46% of peripheral neuropathy is idiopathic (Castelli et al., 2020).

Age: The incidence of peripheral neuropathy increases with age at an estimate of 8% per 100,000 in persons older than 55 (Castelli et al.; 2020; Choi & Di Maria, 2021; Motiwala, 2021; Zhou, 2021).

Ethnicity: There is no specific ethnic group. The high prevalence of peripheral neuropathy increases due to the increasing diagnosis of diabetes mellitus (England & Asbury, 2004).

Contributing Factors: Although there are many causes, diabetes is the most frequent cause, accounting for 30% to 45% of patients with polyneuropathy (Lipsitz et al., 2018; Rutkove, 2021).

Signs and Symptoms: The presentation of peripheral neuropathy can be nonspecific and vary depending upon the pattern of neuropathy. Many symptoms reported may exist in other neurological diseases. Peripheral neuropathies vary in severity. The earliest symptoms are sensory related: numbness, burning, paraesthesia, or dysesthesia in the feet or toes. These are chronic and slowly progressive, and medical attention is not sought until months to years after the onset of symptoms when they have worsened (Motiwala, 2021).

The signs on examination include decrease in pin or vibration sense and reduced deep tendon reflexes. Weakness is an uncommon complaint and rarely found on examination except in advanced cases (Jin, 2021).

Autonomic symptoms may include postural dizziness and syncope; erectile dysfunction; bladder involvement; alteration in bowel pattern (diarrhea or constipation); dryness of mouth, eyes, and skin; skin discoloration; callus; and trophic changes related to the joints and enlarged joints such as Charcot's joints (Motiwala, 2021; Rutkove, 2021). Positive symptoms caused from uninhibited or abnormal spontaneous nerve activity may result in pain, muscle cramps or twitching. Negative symptoms indicate nerve reduction activity and lead to a loss of sensation, weakness, ataxia, and atrophy. For example, distal sensory loss may be a contributing factor to delayed wound healing and loss of balance in darkened surroundings or after closing the eyes. Neuropathic pain is often more common and observed at rest and bedtime (Motiwala, 2021).

A diagnosis can be made or suspected by history taking (Zhou, 2021). A detailed history of symptoms is important in helping to narrow the differential diagnosis. It includes symptom onset and timing; whether acute, subacute, or chronic; location; and distribution pattern (focal, multifocal, and symmetrical patterns). Aggravating and remitting factors give clues to exogenous causes, and a systems review should evaluate for autonomics and vasomotor symptoms. A nutritional assessment identifies nutritional deficiencies (such as vitamins B and D deficiencies or anemia). The occupational and military history gives clues for potential exposure to neurotoxic agents, environmental toxins, chemical exposures, or pesticides. History of chronic alcohol use, family history, and immunizations also provide clues (Castelli et al., 2020).

The review of systems includes a history of the overall functional ability to perform activities of daily living (ADLs) (Castelli et al., 2020) and factors such as clumsiness, any falls or injuries, gait disturbances (slapping, stomping, antalgic gait, ataxia), difficulty getting out of low chairs and climbing stairs, recurrent tripping while stepping off curbs (partial foot drop), difficulty with eating, nausea, vomiting, anorexia, problems with bowel and bladder functions (e.g., constipation, diarrhea, incontinence), any sensory changes such as numbness, dysesthesias, or pain, and any incidence of burn injuries due to decreased ability to detect temperature changes/hot or cold.

To confirm a suspected diagnosis of neuropathy that is based on a patient's history, a comprehensive physical examination should be performed to rule out other causes of weaknesses or sensory loss such as radiculopathy or central disorders. Normal changes of aging in older adults older than 65 include a decline in vibration sense and ankle reflexes. These findings in otherwise healthy older adults may obscure the distinction from polyneuropathy. Components of the physical examination include a motor and sensory examination, reflexes, gait, and relevant cerebellar and cranial nerve examinations (Motiwala, 2021).

Motor Examination: Observe for muscle atrophy of distal muscles; atrophy of small muscles of the feet and prominence of intermetatarsal spaces in the feet, loss of prominence of extensor digitorum brevis muscle bulk over lateral aspect of dorsum of foot, loss of plantar muscle fullness; and in the upper extremities, muscle mass loss in the first web space over the dorsal aspect of hand and flattening of thenar and hypothenar muscle prominence. Passive movement of the joints will reveal a reduced resistance and floppiness when the tone is reduced in significant neuropathy. Check for muscle weakness, which may be symmetrical or asymmetrical; observe whether the weakness follows a dermatome or a nerve distribution. In length-dependent neuropathies, weakness first involves distal muscles in early stages—as seen in inflammatory neuropathies (chronic inflammatory demyelinating polyneuropathy). Functional testing identifies functional disabilities along with subtle weakness often overlooked during strength testing. Arising from a seated position without support of the chair or performing knee bends will reveal the proximal lower extremity strength. Walking on heels may identify mild ankle dorsiflexor muscle weakness, and walking on the toes may detect subtle ankle plantar flexor muscle weakness (Jin, 2021; Motiwala, 2021).

Sensory Examination: Begin the sensory examination distally and compare distal segments with proximal segments, one side with the other side, and lower extremities with upper extremities.

Check for stocking and glove pattern sensory loss, sensory ataxia, positive Romberg's sign, reduced or absent reflexes, and pseudoathetosis. Sensory impairment precedes motor weakness in common neuropathies. With no sensory complaint, a cotton wisp, pin, or tuning fork to the feet will suffice. Large fibers carry the sensation of fine, light touch, vibration, and proprioception, whereas small fibers carry impulses from receptors and are responsible for crude touch, pain, and temperature. In most peripheral neuropathies, the sensory findings are prominent distally in lower extremities and then spread proximally as the condition progresses. Fingers become involved after the symptoms spread toward the knees and lower extremities. Sensation can be present but may show a slight reduction in intensity. Loss of vibratory

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sense or reduction of it suggest neuropathy. If vibration sense is absent distally, more proximal boney prominences should be assessed until normal sensation is detected. Significant proprioceptive loss may be indicated in the presence of abnormal movements in the fingers of the outstretched hand when the eyes are closed (called pseudoathetosis). If the distribution differs from the typical distal or length-dependent pattern, other diagnoses should be explored. Sensory loss in a dermatomal pattern should alert you to radiculopathy. If sensory loss conforms to a large peripheral nerve, a diagnosis of mononeuropathy should be explored (such as C6 radiculopathy, peroneal neuropathy, or L5 radiculopathy [Jin, 2021; Motiwala, 2021]).

Reflexes are affected distally in a length-dependent fashion, and ankle reflexes will be diminished or absent. A significant asymmetry of reflexes is unusual and indicates an associated condition. Coexisting conditions such as radiculopathy would cause asymmetrical loss of reflexes or conditions such as cervical spondylotic myelopathy that can preserve deep tendon reflexes even in the midst of neuropathy (Rutkove, 2021).

Examination of gait and balance is observed by tandem gait, proximal lower extremity strength and ambulation. A positive Romberg's sign is often associated with abnormal gait. Abnormal gait (ataxia, steppage gait, stomping, antalgic) is a cause of multiple falls in older adults (Motiwala, 2021).

Bilateral facial weakness is commonly seen in Guillain-Barré. Pupillary abnormalities may be associated with diabetic neuropathy. Dysarthria and nystagmus may be associated with cerebellar disorders and not neuropathy. The cerebellar examination guides in distinguishing sensory ataxia from cerebellar ataxia. In addition, look for skin rashes as in vasculitis, connective tissue disorders, skeletal muscle involvement as in pes cavus, and scoliosis as in hereditary neuropathy (Castelli et al., 2020; Gjerum & Midttun, 2017; Motiwala, 2021).

Diagnostic Tests: The etiology of neuropathy is not always clear based on history and examination alone. Approximately 20% to 30% of patients with peripheral neuropathy do not have a determinable cause. Selective use of laboratory tests in patients with polyneuropathy should be based on history and clinical features as well as electrodiagnostic tests (Castelli et al., 2020; Rutkove, 2021; Zhou, 2021). Rather than testing for every possible cause of neuropathy, the American Academy of Neurology recommends tests with the highest yield. Routine laboratory studies include basic metabolic function panel with fasting glucose, complete blood cell count, liver function panel, vitamin B_{12}, vitamin B_1, serum protein immunofixation electrophoresis, thyroid function testing, antinuclear antigen, and Sjögren's syndrome antibodies A and B (anti-R, anti-La) (Jin, 2021).

Consider in some patients depending on risk and clinical findings: 2h glucose tolerance test, methylmalonic acid, homocysteine level, vitamin E, vitamin B_6, copper, zinc, HIV, Lyme disease, hepatitis B and hepatitis C, cryoglobulin, rheumatoid factor, erythrocyte sedimentation rate, C-reactive protein, antigliadin antibodies, anti-transglutaminase antibodies, serum light chains, urine immunofixations, electrophoresis, and light chains (Castelli et al., 2020; Jin, 2021; Zhou, 2021).

Electromyogram and nerve conduction studies are the most useful diagnostic tests for initial work-up in evaluating patients with suspected peripheral neuropathy and should be done first (Castelli et al., 2020; Jin, 2021; Rutkove, 2021). These tests validate the presence of a neuropathy, specify what type of nerve fibers are involved (sensory, motor, or a combination), and help in establishing the differential diagnosis (Choi & Di Maria, 2021; Jin, 2021). A nerve conduction study may be normal in patients with small fiber neuropathy because the test evaluates large fiber function. When a large fiber neuropathy is found by a nerve conduction study or electromyography (EMG), a diagnosis of peripheral neuropathy is established, and a skin biopsy is unnecessary (Zhou, 2021). EMG distinguishes myopathies from neuropathies (Choi & Di Maria, 2021).

Skin biopsy is the gold standard for diagnosing peripheral neuropathy/small fiber neuropathy with a high diagnostic efficiency. It is useful in confirming distal sensory polyneuropathy in patients older than 75, when there are absent sural sensory responses that are attributed to aging changes (Rutkove, 2021; Zhou, 2021).

Quantitative sensory testing has been validated for evaluating symptoms of sensory neuropathy but has significant limitation in that it cannot differentiate whether impaired response to sensory stimuli is due to peripheral nerve disease or a central nervous system (CNS) disease. It is not recommended as a stand-alone test (Zhou, 2021).

Although not widely available, autonomic testing evaluates postganglionic sympathetic unmyelinated sudomotor axon nerve function and is helpful in evaluating autonomic symptoms. It may be ordered if there are sweating abnormalities (Zhou, 2021). Genetic testing should be considered if a positive family history exists (Castelli et al., 2020; Zhou, 2021).

Differential Diagnosis: Neurological disorders involve some form of disturbance of sensation, motor function, and balance. The presence of these symptoms is nonspecific to peripheral neuropathy because they can cause dysfunction in other parts of the nervous system. Determining the part of the nervous system is helpful for diagnostic accuracy. Atypical neuropathies are acute, non–length-dependent patterns of symptoms and have a more prominent motor component. Many atypical neuropathies are accompanied by other systemic symptoms (Jin, 2021).

- Cerebrovascular accident, neoplasm, multiple sclerosis (MS) (Jin, 2021)
- Myelopathy (degenerative and joint disease of the cervical spine) (Jin, 2021)
- Radiculopathy (degenerative disc disease of the cervical and lumbar spine) (Jin, 2021)
- Amyotrophic lateral sclerosis (ALS) (Jin, 2021)
- Sjögren's syndrome, cisplatin chemotherapy, paraneoplastic syndrome, vitamin B_6 toxicity
- Neuromuscular disorders (myasthenia gravis [MG]) (Jin, 2021)
- Muscle myopathy (dermatomyositis, steroid myopathy) (Rutkove, 2021)
- Chronic inflammatory demyelinating polyneuropathy (Rutkove, 2021)
- Nerve entrapment (Faktorovich et al., 2021)
- Syringomyelia/dorsal column disorders (Faktorovich et al., 2021)
- Upper motor neuron disorders (spasticity/hyperreflexia) (Motiwala, 2021)

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Treatment: Peripheral neuropathy is an irreversible disease. Treatment is mostly supportive and directed at preventing disease progression and controlling complications (Hicks & Selvin, 2019). Management of peripheral neuropathy involves treating the identifiable underlying cause, optimizing daily function, preventing injury (Hicks & Selvin, 2019; Zhou, 2021), and managing neuropathic pain. Pain management may be difficult and challenging in older adults because of safety and tolerability of medications. Tailor treatment based on comorbidities, drug tolerability, and potential drug-to-drug interactions. Rarely is there complete relief of neuropathic pain. Pharmacological interventions (Table 17-2) provide approximately 30% to 50%

TABLE 17-2 Pharmacological Agents for Neuropathic Pain

DRUG	DESCRIPTION
Tricyclic antidepressants (TCAs) • Amitriptyline • Desipramine • Nortriptyline	• May be used as the first- or second-line • Have a higher risk profile, especially in the older adult population • Are thought indirectly modulate the opioid system in the brain via serotonergic and norepinephrine neuromodulation, among other properties (Iqbal et al., 2018) • Are effective for constant and lancinating, paroxysmal pain. • Require up titration to effective doses over a period of 6–8 weeks before efficacy is observed • Baseline electrocardiogram recommended before administration • Caution should be taken in older adults and in patients who have ischemic heart disease, narrow-angle glaucoma, or prostatism **Amitriptyline** • Has the greatest efficacy among TCAs. • Is initiated at a low dose (10–25 mg) daily • Maintenance dose: 25–100 mg once daily (Iqbal et al., 2018). • At higher doses, sedation, confusion, anticholinergic effects, and orthostatic hypotension are common, especially in older adults.
Antidepressants • Venlafaxine • Duloxetine	**Venlafaxine** • Initial dose 37.5 mg daily. • Maintenance dose 75–225 mg daily. • Side effects: nausea, dizziness, anticholinergic effects • Is not FDA approved for treatment of painful diabetic peripheral neuropathy (DPN) and must be slowly weaned to reduce the potential for adverse side effects **Duloxetine** • At 40 mg and 60 mg shows efficacy in treating painful DPN • Initial dose: 20–30 mg daily • Maintenance dose: 60–120 mg/day; has a moderate effect in reducing pain by about 30% • Side effects: nausea, constipation, sweating, asthenia, and dry mouth • Monitor: hyponatremia sodium levels and blood pressure
Anticonvulsants • Gabapentin • Pregabalin	• Often given to suppress shooting or stabbing pain **Gabapentin** • Initial dose 100–300 mg tid • Titrate dose up by 300 mg increments every 3–5 days until adequate pain relief is achieved. • The median effective dose ranges from 900 to 1600 mg, although some patients may require doses of 3600 mg/day. **Pregabalin** • Effective ranges: 150–600 mg/day • Initial dose: 25–75 mg tid • Maintenance dose: 300–600 mg daily
Opioids (nonnarcotic centrally acting analgesia) • Tramadol • Tapentadol	• Dose: 200–400 mg/day • Well-tolerated but transient nausea and constipation occur in about 20% of patients • Use with caution in patients with impaired hepatic or renal function and in patients taking other psychoactive medications. • May be used for breakthrough pain in combination with other neuropathic agents (Iqbal et al., 2018).
Topical agents • Capsaicin • 5% lidocaine patch	• Dose: 0.025%–0.075% applied to affected area tid–qid • May be useful in patients with painful, burning feet • Presumably produces pain relief through the depletion of substance P in unmyelinated nociceptive fibers • Intense burning sensation of the skin occurs after initial application before improvement is seen. • Allow at least 4 weeks to determine efficacy. • Even after 4 weeks the beneficial effect may be marginal. • Some patients may have relief from burning feet and allodynia by topical application of 5% lidocaine patch.

Sources: *Finnerup et al. (2010); Iqbal et al. (2018); Mahmoud & Tampi (2011).*

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reduction in pain intensity; greater than 50% pain relief is considered a good outcome (Harati & Bosh, 2008; Iqbal et al., 2018; Motiwala, 2021; Zhou, 2021).

Several oral medications help to alleviate neuropathic pain. Gabapentin, pregabalin, and antidepressants (amitriptyline, nortriptyline, venlafaxine, duloxetine, bupropion) appear to be moderately effective and are recommended as first-line options in managing neuropathic pain (Castelli et al., 2020). Duloxetine and pregabalin remain first-line therapy for neuropathic pain in diabetic peripheral neuropathy in five major guidelines published by the American Association of Clinical Endocrinologists, American Academy of Neurology, European Federation of Neurological Societies, National Institute of Clinical Excellence (United Kingdom), and the American Diabetes Association, and their use has been approved by the U.S. Food and Drug Administration (FDA) (Iqbal et al., 2018).

Topical medications include lidocaine and capsaicin as adjuncts to oral medications (Castelli et al., 2021). Tramadol drugs or NSAIDs may be necessary for breakthrough pain (Rutkove, 2021). Opioids are reserved as a last-line option and should not be used routinely because of limited effectiveness, long-term safety concerns and abuse potential (Castelli et al., 2021; Hicks & Selvin, 2019).

Tricyclic antidepressants have been shown to reduce neuropathic pain but have not been given approval by the FDA because of serious side effects and risks (Hicks & Selvin, 2019). Duloxetine has been associated with a reduction in opioid use compared with other modalities and lower health care cost (Hicks & Selvin, 2019).

A pilot study on the effectiveness of topical cannabidiol (CBD) oil in supportive relief of peripheral neuropathy of the lower extremities conducted by Xu et al. (2020) demonstrated that transdermal application of CBD oil 250 mg applied four times a day improved pain and sensation in patients with peripheral neuropathy (Xu et al., 2020).

Follow-Up: Because peripheral neuropathy is a persistent disease process, follow-up is based on the underlying disease processes involved (Motiwala, 2021).

Sequelae: Peripheral neuropathy causes a range of complications and has a debilitating impact on quality of life. Common difficulties in daily activities include sleep disturbances, difficulty walking (a tendency to trip easily), climbing stairs, and performing daily chores involving gripping objects (Win et al., 2019). It is a major contributing factor for balance problems and falls leading to a significant loss of functional decline and mobility. In the United States, approximately 30% of adults aged 65 and older fall each year. Both large and small fiber dysfunction contribute to the inability to recognize position sense or to ascertain where the feet are on the floor thereby increasing the risk of falls (Lipsitz et al., 2018; Zhou, 2021). Orthostatic hypotension is another contributing factor of falls (Gjerum & Midttun, 2017).

Atrophic change in an enervated immobile extremity combined with recurrent painless trauma predisposes the skin to ulceration and poor wound healing. Severe infections such as osteomyelitis or osteolysis may eventually result in limb amputation. Approximately 25% of persons having diabetes may develop foot ulcers during their lifetime, which progress to infection and may require amputation. This unfortunate sequence of events can be avoidable with proper care (Abdissa et al., 2020; Hicks & Selvin, 2019; Zhou, 2021).

Because of the physical and mental component of quality of life, anxiety and depression have been reported in 43% of the population with peripheral neuropathy and 45% to 53% of patients employed average about 5.5 missed workdays per month (Hicks & Selvin, 2019).

Prevention/Prophylaxis: There are several health-promoting activities patients can do prophylactically:

- Avoid repetitive motions, cramped positions, constant exposure to offending toxins, and excessive alcohol consumption.
- Meticulous foot care, ankle braces, foot orthosis, and proper shoes help to reduce the risk of falls and injury, the development of ulcers, or the worsening of slow-healing wounds due to sensory impairment.
- Assistive walking devices used due to substantial leg weakness will help to ensure safety and reduction of falls and injury.
- Avoid inactivity. Exercise can increase microvascular circulation, for release of neurotrophic factors, attenuation of oxidative stress and for physiological well-being of the body (Abdissa et al., 2020).
- Hand or wrist splints will be helpful if the hands or wrists are involved.

Wearing padded socks and supportive shoes provides foot protection and facilitates wound healing. Foot care and emollient creams moisturize dry skin. Regularly inspect skin for prevention and early detection of ulcer (Rutkove, 2021; Zhou, 2021).

Referral: Referral to a neurologist should be considered when initial laboratory testing, history, and physical examination findings are unrevealing; for acute, subacute, severe, or progressive symptoms to prevent a delay in treatment; for polyradiculoneuropathy or multifocal neuropathy deviating from the usual presentations that match anatomic distribution; and pure motor or autonomic signs in the absence of sensory changes (Castelli et al., 2020; Choi & Di Maria, 2021; Jin, 2021; Motiwala, 2021). Referral to podiatry is beneficial for appropriate shoes for extra depth and special orthotics with positive finding of proprioception sensory impairment or gait disturbances and for ankle-foot orthoses for foot drop (Choi & Di Maria, 2021). Occupational therapy may assist with appropriate assistive ambulation devices, splints, and braces (Rutkove, 2021). Psychological support is beneficial for those experiencing anxiety and depression (Zhou, 2021). Physical therapy referral is beneficial. Older adults with peripheral neuropathy of the lower extremities typically have balance and gait disturbances because of sensory ataxia. Physical therapy can help with gait and transfers (sit to stand) (Iqbal et al., 2018; Lipsitz, 2018).

Education: Discuss the typical course of the disease and its impact on daily life, foot care and surveillance, the importance of healthy eating and weight loss, and fall precautions. Lifestyle modifications include testing bath water with a body part without numbness before submerging the feet and avoiding sitting too close to fireplaces, if present. Instruct patients to avoid crossing the legs at the knee to avoid prolonged pressure or constriction and further nerve damage. Advise patients of the need for regular follow-up visits, even if no symptoms are present (Zhou, 2021).

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Clinical Recommendation	Evidence Rating	References
Initial evaluation for suspected peripheral neuropathy includes complete blood count, comprehensive metabolic panel, fasting blood glucose, thyroid-stimulating hormone, vitamin B_{12}, and serum protein electrophoresis with immunofixation.	C	Castelli et al., 2020
Referral for electrodiagnostic studies should be done if symptoms worsen (acute onset, asymmetrical, predominant motor or autonomic symptoms, rapidly progressive course, or if initial work-up is normal and symptoms persist).	C	Castelli et al., 2020
Imaging is not routinely ordered to help in diagnosing peripheral neuropathy. Magnetic resonance imaging may be helpful in localizing an atypical neuropathy (polyradiculopathy, plexopathy, or radiculoplexus neuropathy).	C	Castelli et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

RESTLESS LEGS SYNDROME

Signal Symptoms: Urge to move legs when at rest.

Description: Restless legs syndrome (RLS) is a common neurological and sleep disorder characterized by an intense urge to move the legs (or sometimes the arms). It may be associated with discomfort and the inability to resist the urge to move their legs. The sensations causing the urge may be described as aching, burning, creeping, crawling, cramping, gnawing, pulling, painful, throbbing, tingling, restless, or itchy, though sometimes individuals state they are unable to describe the feeling. Movement of affected limbs provides relief, but discomfort recurs unless the movement continues. RLS symptoms have circadian rhythmicity, starting or worsening at night. Symptoms are elicited by sitting or lying down.

Etiology: RLS may be idiopathic or primary or may be secondary due to a medical condition. There is a known genetics component because it can be found in families with approximately 25% of family members of those with RLS also experiencing symptoms (Sundaresan et al., 2019).

Occurrence: According to the Restless Legs Syndrome Foundation (2021), 7% to 8% of the population has RLS, with 2% to 3% having symptoms severe enough to require treatment. RLS occurs twice as much in women as in men.

Age: RLS can occur in people of all ages, including children. Primary RLS typically has an onset before age 45 (often familial) but is more common in older adults (Didato et al., 2020).

Ethnicity: RLS has a prevalence of 5% to 10% in the White population and is less common in Asian and Black populations.

Contributing Factors: Inheritability is estimated at 54% to 64.9% (Seeman, 2020). Many medications, such as antidepressants, antipsychotics, antiemetics, antihypertensives, and neuroleptics, as well as herbal and over-the-counter (OTC) cold and allergy medications, can aggravate RLS symptoms. Alcohol, caffeine, and nicotine are other substances that may aggravate RLS. Iron-deficiency anemia, vitamin B_{12} deficiency, folate deficiency, and renal disease can all contribute to symptoms. Depression and anxiety and attention-deficit disorder have been associated with RLS, although the former two may be more related to their treatment (Seeman, 2020).

Signs and Symptoms: Symptoms are worse at night while at rest but can occur during the day. An urge to move the legs (or other body parts) is usually accompanied or caused by uncomfortable and unpleasant sensations in the legs. The focused interview for RLS should include the following:

- Ask about the urge to move or unpleasant sensations and if they are partially or completely relieved by movement such as walking or stretching.
- Ask if the urge to move or unpleasant sensations are worse or only occur in the evening or night or during the day.
- Ask about any activities or contributing factors that make their symptoms worse.
- Ask about sleep patterns. Does the patient keep their partner awake?
- Is the patient tired during the day from an interrupted night of sleeping?

Diagnostic Tests: Typically, the diagnosis of RLS is based on subjective complaints meeting the criteria of the International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale. Box 17-1 lists the essential diagnostic criteria. Blood work to identify contributing causes should be ordered (ferritin and iron studies for anemia, B_{12} level, and a metabolic panel for diabetes or kidney disease). If iron deficiency is found, the underlying cause should be sought.

Differential Diagnosis: Common disorders to rule out are listed, but many disorders may masquerade as RLS, such as:

- Akathisia (including hypotensive and neuroleptic-induced)
- Vascular or neurogenic claudication
- Neuropathy/radiculopathy
- Chronic pain syndrome associated with (lumbar, cervical) positional discomfort
- Nocturnal leg cramps
- Hypnic jerks

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BOX 17-1

Essential Diagnostic Criteria for Restless Legs Syndrome

An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs (sometimes the urge to move is present without the uncomfortable sensations, and sometimes the arms or other body parts are involved in addition to the legs).
The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity, such as lying or sitting.
The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
The urge to move or unpleasant sensations are worse in the evening or night than during the day, or only occur in the evening or night (when symptoms are very severe, the worsening at night may not be noticeable, but must have been previously present).

SUPPORTIVE CRITERIA

Positive family history
Positive response to dopaminergic drugs
Periodic leg movement during wakefulness or sleep as assessed with polysomnography or leg activity

ASSOCIATED FEATURES

Natural clinical course of the disorder: RLS can begin at any age, but most patients seen in clinical practice are middle-aged or older. Most patients have a progressive clinical course, but a static clinical course is sometimes seen. Remissions of a month or more are sometimes reported.
Sleep disorders are a frequent but unspecific symptom of RLS.
Medical evaluation/physical examination: The neurological examination is usually normal. Probable causes for secondary RLS should be excluded. A low serum ferritin (<45–50 mcg/L) may be found in RLS patients (Connor et al., 2017).

- Depression with somatic syndrome
- Volitional movements
- Lower limb arthritis
- Fibromyalgia
- Chronic venous insufficiency (Sundaresan et al., 2019)

Diabetic neuropathy is damage to the peripheral nerves due to diabetes and is most common in the legs and feet. Symptoms include numbness, tingling, hypersensitivity, muscle weakness, and sharp pain.

Leg cramps are sudden, painful, and involuntary contractions of the muscles of the legs; these may have no real cause but can be bothersome. If leg cramping is disturbing sleep, assess and consider these causes as possibilities: diuretics, Addison's disease, Parkinson's disease (PD), muscle overextension and overexercise, diabetes, hypoglycemia, hemodialysis, calcium channel blockers, peripheral artery disease, nerve compression, diabetes, and dehydration.

Periodic limb movements are repetitive, rhythmic flexing or jerking of the legs only occurring during sleep. It is a sleep disorder and can disturb sleep and result in daytime sleepiness. It may be associated with RLS but is different.

Radiculopathy, a type of neuropathy, occurs from compression on nerves in the spine, resulting in pain, tingling, numbness, and weakness. "Sciatica" pain radiating to the legs is an example. Pain can occur from a herniated disk, bone spur, osteoarthritis, tumor, infection, scoliosis, and stenosis.

Akathisia is an inner restlessness causing the patient to make frequent position changes and movements. This is often caused by neuroleptics (Kwatra et al., 2018).

Treatment: Although RLS is a chronic condition, the symptoms may be intermittent. When severe or disruptive to sleep, treatment is recommended. The patient should make lifestyle changes to remove aggravating factors and to reduce or abstain from alcohol or nicotine. Conservative measures such as good sleep hygiene, hot or cold packs, relaxation techniques, and exercise (though excessive exercise can worsen symptoms) should be recommended. Repetitive transcranial magnetic stimulation, compression devices, counterstrain manipulation, infrared therapy, and standard acupuncture may reduce restless legs syndrome severity (Harrison et al., 2019). Low levels of B_{12}, ferritin (less than 75 µg/L), transferrin saturation (less than 20%), and folate should be treated. Medications the patient is taking should be evaluated to see whether they may be contributing to RLS symptoms and if they are still needed or can be changed to a similar medication that does not worsen RLS.

For medical treatment of chronic, persistent RLS causing distress and when nonmedical therapies do not relieve the symptoms, the following medications may be considered:

- Iron (if indicated), 325 mg ferrous sulfate once daily (should be separated from levodopa by 2 hours if the patient also has PD and is prescribed medication containing levodopa). Ferritin and iron saturation should be monitored every 3 to 6 months to avoid iron overload, and treatment can be discontinued when adequate levels are reached (ferritin >75 µg/L and transferrin saturation >20%).
- Alpha-2-delta calcium channel ligands are the initial drugs of choice (Kwatra et al., 2018).
  - Gabapentin (Neurontin): Starting dose is 100 to 300 mg 2 hours before bedtime.
  - Gabapentin enacarbil (Horizant): 600 mg once daily at 5:00 p.m.
  - Pregabalin (Lyrica): Starting dose is 50 to 75 mg 2 hours before bedtime.
- Dopamine agonists
  - Pramipexole (Mirapex): Starting dose is 0.125 mg 2 hours before bedtime.
  - Ropinirole (Requip): Starting dose is 0.25 mg 2 hours before bedtime.
  - Rotigotine (Neupro) patch: Starting dose is 1 mg/24 hours.

Oxycodone/naloxone is also considered efficacious (Winkelmann et al., 2018), but opioids should be avoided and only used as a last resort for refractory RLS. Tramadol and methadone may also be considered (Gossard et al., 2021) but with caution.

Follow-Up: Evaluate the success of treatment and for augmentation every 6 to 12 months or more frequently if needed.

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Augmentation often occurs with RLS treatment, meaning symptoms can be more intense and can occur earlier and earlier in the day, requiring more medication. The alpha-2-delta calcium channel ligands are less likely to cause augmentation than dopaminergic medications.

Ask about sleep, exercise, and relationships because sleep disturbances can cause hypertension and tension in relationships. Check blood pressure at each visit.

Sequelae: RLS can cause difficulty falling asleep or staying asleep. Sleep deprivation can cause relationship problems, hypertension, and daytime sleepiness and can affect safety.

Prevention/Prophylaxis: There is no prevention for RLS, but recommend daily exercise and a healthy diet, review the tenets of sleep hygiene, and monitor and treat relevant deficiencies and disorders.

Referral: Refer to a sleep or movement disorders specialist if it is an unusual case or if the patient is nonresponsive to initial treatment.

Education: Provide patients and families with written information about RLS, including support groups in the community if available. They can also learn more about RLS, including updates in treatments and clinical trials, at www.rls.org.

Clinical Recommendation	Evidence Rating	References
Diagnosis of restless legs syndrome (RLS) is subjective and can be made based on the criteria of the International Restless Legs Syndrome Study Group (IRLSSG) Rating Scale.	C	Kurtis et al., 2018
Repetitive transcranial magnetic stimulation, compression devices, counterstrain manipulation, infrared therapy, and standard acupuncture may reduce restless legs syndrome severity.	A	Harrison et al., 2019
Alpha-2-delta calcium channel ligands are the initial drugs of choice for RLS.	A	Kwatra et al., 2018
Iron supplementation should be used to treat ferritin levels less than 75 µg/L.	A	Kwatra et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

SEIZURE DISORDERS

Signal Symptoms: Brief periods of confusion, loss of consciousness, staring with little or no motor activity, bizarre behavior, memory changes, falls, cognitive changes, sleep disorders, twitching, and involuntary movements.

Description: *Seizure* is a transient occurrence of signs and symptoms attributable to abnormal, excessive, or synchronous neuronal activity in the brain and can result from many causes (American Association of Neuroscience Nurses [AANN], 2016; Fisher et al., 2014). *Epilepsy* is a disease of the brain defined by at least two unprovoked (or reflex) seizures separated by at least 24 hours; one unprovoked (or reflex) seizure and the probability of further seizures similar to the general recurrence risk of at least 60% after two unprovoked seizures occurring over the next 10 years; or the diagnosis of an epilepsy syndrome (Thijs et al., 2019). In 2017, the International League Against Epilepsy simplified the seizure classification so that a basic version could be used by general practitioners and a more descriptive version could be used by specialists (Pack, 2019). Specifically, now the seizure classification starts with whether the initial manifestation of the seizure is focal or generalized. Focal seizures (formally called partial seizures) originate within a neuronal network limited to one hemisphere and may be discretely localized or more widely distributed. Generalized seizures originate at some point within the brain and rapidly engage bilateral distributed networks. Seizures of unknown onset are classified as such if the onset is missed or unclear (Pack, 2019). Acute symptomatic seizures are those occurring in close temporal relationship to the acute central nervous system (CNS) insult, which could consist of a metabolic, a toxic, a structural, or an infectious origin or an inflammation process. (Beghi et al., 2015). Epilepsy is considered resolved for people who had an age-dependent syndrome but have passed the applicable age and are seizure-free or, in other cases of epilepsy, for those who have been seizure-free for the past 10 years and have not taken antiepileptic drugs for the past 5 years (Thijs et al., 2019).

In the older adult, precipitating factors could be a nervous system infection, acute traumatic brain injury, and fluctuations in blood sugar or electrolyte levels. It is also important to distinguish nonepileptic episodic events, which may resemble epileptic seizures but are distinguished by differences in symptomatology as well as the lack of abnormal epileptiform activity indicated on an electroencephalogram (EEG) (Hopp, 2019). The focus of this section is on new-onset seizures and epilepsy in older adults. Underdiagnosis of seizures is common in the older adult.

Etiology: Epilepsy is mainly due to mechanical stimulation of a stroke lesion, nerve cell degeneration around the lesion, and glial scar formation (Liu et al., 2016). Understanding the epidemiology of epilepsy in older adults is important because of the association with poorer quality of life. There are unique challenges in terms of diagnosis and treatment within this group because of differences in clinical presentations and etiology compared with younger patients, presence of comorbidities and cognitive difficulties, and physiological

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changes that affect pharmacological management (Acharya & Acharya, 2014). Recognizing that persons older than age 65 years are a heterogeneous group, recommendations have been made to divide patients into three groups based on age: 65 to 74 years (young-old); 75 to 84 years (middle-old); and older than 85 years (old-old). These groups are further subdivided based on health status: patients with only epilepsy, patients with epilepsy and multiple medical comorbidities, and the frail older adults. In addition, consideration should be given to persons living independently and those living in nursing homes.

Cerebrovascular disease accounts for 20% to 50% of seizures in older adults. Likewise, 10% of patients with stroke are at risk of developing seizures within 5 years. Hemorrhagic strokes are more likely to be associated with seizures than infarcts. In contrast, patients with transient ischemic attacks (TIAs) have a relatively low incidence of seizures. Additional causes of epilepsy in older adults include cryptogenic or stroke-related seizure, followed by dementia and tumors. (Lee, 2019). Neurodegenerative disease accounts for 10% to 20% of epilepsy that is due to dementia and neurodegenerative disease associated with cognitive impairment. Patients with Alzheimer's disease (AD) have a 10 times higher risk of epilepsy, which increases as the disease progresses. Recognition of seizures in this population may be difficult; however, older adults do respond well to antiepileptic drugs (AEDs) (Acharya & Acharya, 2014). Trauma, particularly head trauma, accounts for up to 20% of epilepsy in the older adult. Being age 65 years or older has been identified as a risk factor for developing epilepsy after a head injury. Brain tumors are responsible for approximately 10% to 30% of seizures in the older adult and are more likely with low-grade, slow-growing tumors (Acharya & Acharya, 2014). However, underlying etiologies can be found in only 50% (Liu et al., 2016; National Institute of Neurological Disorders and Stroke [NINDS], 2019).

Occurrence: The incidence and prevalence of seizure disorders is highest in the older adult; therefore, older adult patients are the fastest growing demographic within patients with epilepsy. Estimated incidence and prevalence rates of epilepsy among older adults in the United States are 2.41/1,000 and 10.8/1,000, respectively (Lee, 2019). The prevalence rate has been found to be higher among nursing home residents than community-dwelling older adults. Incidence rates are slightly higher for women than men and increase with age. Prevalence and incidence rates may be underestimated due to the difficulty in identifying seizures and diagnosing epilepsy. Status epilepticus is two to five times more common in older adults than in young adults with an annual incidence of 86 per 100,000 in individuals older than 60 years (Lee, 2019). These rates indicate an under-recognized public health issue.

Age: There is a bimodal presentation of seizures over the life span, with the second initial presentation beginning around age 50 (Thijs et al., 2019).

Ethnicity: Overall, epilepsy is more common in people of Hispanic background than in non-Hispanics. African Americans, however, are more likely to develop epilepsy over the lifetime with the higher rate for stroke and hypertension among African Americans as a possible contributing factor to seizure disorders as one ages (Epilepsy Foundation, 2019).

Contributing Factors: As noted, stroke and other cerebrovascular diseases are the most important risk factor for new-onset seizures. Neurodegenerative disease, brain tumor, and brain trauma are known risk factors for developing new-onset seizures in older adults. Additional precipitating factors could be nervous system infection, fluctuations in blood sugar or electrolyte levels, metabolic or toxic factors (e.g., drugs or excessive amounts of alcohol), depression, and coexisting conditions such as diabetes and hypertension (Chi Vu et al., 2018).

Multiple drugs have been shown to either cause seizures or potentially lower seizure thresholds. These include psychotropic drugs, theophylline, narcotics, tramadol (Ultram), antimicrobials, chemotherapeutic agents (methotrexate, chlorambucil), general anesthetics (ketamine, enflurane), local anesthetics, stimulants, antiarrhythmics (verapamil, mexiletine, procainamide, propranolol), diphenhydramine, baclofen, and chlorpromazine (Krupa et al., 2019).

Signs and Symptoms: Under the International League Against Epilepsy's 2017 system, seizures are first classified by onset as either focal (originate within networks in a hemisphere), generalized (originate in a point and quickly spread to involve bilateral networks), or unknown. Level of awareness subdivides focal seizures in those with retained awareness and impaired awareness. Focal seizures are further categorized by the earliest and most prominent motor or non-motor manifestation. All classifiers are optional and depend on the available level of detail. Generalized seizures are divided into motor and non-motor (absence) seizures. Seizures of unknown onset might have features that can still be classified (Thijs et al., 2019). Rather than using labels (e.g., simple partial, myoclonic), the labels have been removed and more descriptive terminology is used. The term *semiology* is used to describe the sensory/motor/behavioral presentations. An important point is that new-onset (or first-ever) seizure age is not an independent predictor of seizure recurrence, and older patients are more likely than younger ones to sustain a seizure-related injury. Treatment for older patients should be based on risk factors for recurrence rather than age (Lawn et al., 2013).

Diagnosing new-onset seizures in older adults is challenging due to the presentation and comorbidities. As noted, the most common seizures in the older adult are focal in onset. Confusion and memory problems are common presenting symptoms, and the postictal phase may be prolonged. A reliable history and an eye-witnessed event are the most important diagnostic factors, especially in new-onset seizures (Thijs et al., 2019). Obtain information concerning family history of seizures, any head injuries or other history of trauma (observe bruises, cuts, burns), and any past history of seizures. Information concerning whether the individual has lived outside of the United States (particularly in unincorporated areas with poor sanitation) can raise suspicion of neurocysticercosis. This parasitic infection results from ingestion of eggs from the adult tapeworm and is the most common parasitic infection of the brain with epilepsy as the most common presentation. With the immigration of people from Latin America to the United States, this disease is a growing problem (Sharma et al., 2015).

Obtain a complete description of the seizure, including any aura (a warning of the seizure), along with a complete description of the patient's behavior during the seizure and

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in the postictal period. If the seizure was observed, note whether there was evidence of pallor, cyanosis, abnormal movements, tongue biting, urinary incontinence, impaired continence, or postictal symptoms such as confusion, headache, and drowsiness. As noted previously, new-onset seizures are associated with dementia and cerebrovascular disease in older adults; therefore, it is imperative to include cognitive function screening. An estimate of the time for each phase of the seizure is helpful. How the patient felt before and after the seizure can offer insight into the potential nature of the cause of the event. A thorough neurological examination is performed, with particular attention paid to any focal or localizing symptoms. If the individual is currently taking AEDs, screen for any symptoms of toxicity, including nystagmus, ataxia, and slurred or slowed speech.

Diagnostic Tests: A detailed history is imperative from the patient and, if possible, an eyewitness. The diagnostic approach is similar to that of a younger person. To begin, ascertain if the symptoms were epileptic seizures or nonepileptic in nature (see Differential Diagnosis). Older adult patients may not have prominent automatisms, as in focal seizures. Postictal confusion can last from hours to days. In the initial work-up of a new-onset seizure in an older adult, multiple diagnostic tests are needed. Blood tests include blood glucose because extreme hypoglycemia or hyperglycemia can cause provoked generalized tonic-clonic seizures (GTCS); complete blood count (CBC) (an elevated white blood count can indicate a systemic or CNS infection, which can lead to a provoked GTCS); and electrolyte panel (hyponatremia, hypernatremia, or uremia can lead to a provoked GTCS). Erythrocyte sedimentation rate (ESR), renal function tests, liver function tests, and calcium tests should be done. Baseline tests allow decisions to be made about potential medications. A thyroid screen (i.e., thyroid-stimulating hormone [TSH]) is done because hypothyroid neuropathy may be confused with focal seizure activity.

A toxicology screen may be indicated because illicit substances may cause an unprovoked GTCS. A rapid plasma reagin (RPR) may be done to rule out the possibility of syphilis, which, in tertiary form, may present as a seizure disorder. A lumbar puncture may be performed if there is concern for a primary CNS infection. A basic electrocardiogram (ECG) can confirm syncope in association with a cardiac arrhythmia. In the event that there is an abnormal ECG, an echocardiogram may be required. Tilt-table testing can be useful to detect baroreceptor and vasopressor dysfunction or sympathetic failure due to autonomic neuropathy in older people. EEG and brain magnetic resonance imaging (MRI) are the most important tests for unprovoked seizures (Thijs et al., 2019), although a routine EEG may be of limited use in older adults due to low sensitivity and specificity. An ambulatory prolonged EEG may be indicated. The MRI is the preferred test because it is more accurate than a computed tomography (CT) scan. A brain MRI with and without contrast should be done to rule out old scar tissue, mesial temporal sclerosis, or other structural reasons for the seizures. Neuroimaging with contrast increases the ability to identify tumors, inflammatory disease, and abscesses. An EEG is indicated after any unprovoked seizure event to support the diagnosis of idiopathic generalized or focal-onset epilepsy. A normal result does not prove the patient does not have a potential for seizures; multiple EEG studies may be indicated.

Differential Diagnosis: The most common differential diagnoses for seizures include:

- Neurological: TIA, transient global amnesia, confusional migraine, RLS
- Cardiovascular: syncope, orthostatic hypotension, cardiac arrhythmias, carotid sinus syndrome
- Drug intoxication
- Infections
- Endocrine/metabolic disturbances (e.g., hypoglycemia, hyperglycemia, hyponatremia, hypokalemia)
- Sleep disturbances: obstructive sleep apnea, hypnic jerks
- Dementia
- Psychological: nonepileptic, psychogenic seizures
- Drug induced: alcohol withdrawal (peak incidence of first seizures occurs late in life); use of one or more drugs in high doses with coexisting illness (antihistamines, antidepressants, antipsychotics, hypoglycemic drugs) (Acharya & Acharya, 2014; Chi Vu et al., 2018)

Treatment: Patients with provoked seizures need to be treated for the underlying cause and usually do not need AEDs. With unprovoked seizures, the decision to treat depends on whether the patient has a single seizure or recurrent seizures (epilepsy). Unlike management in younger adults, AEDs may be appropriate after a single seizure in the older adult because of the high rate of recurrence. It is generally easier to achieve seizure-free status in older patients compared with younger age-groups (Chi Vu et al., 2018). The goal of management should be the maintenance of a normal lifestyle, with complete control of seizures with minimal side effects. Seizures in the older adult tend to respond better to AEDs than those in young individuals and can often be appropriately controlled with monotherapy. Pharmacotherapy continues to be the mainstay of treatment for seizures; however, AED management can be complicated because of the coexistence of other diseases (e.g., dementia, polypharmacy), and the likelihood of dose-related and adverse side effects. These medications should be introduced slowly, titrating up depending on symptoms (Thijs et al., 2019).

Concern when prescribing AEDs for older adults include changes in pharmacokinetic parameters, polytherapy, and susceptibility to adverse effects (Lee, 2019). AEDs are commonly prescribed to the older adult and to about 10% of nursing home residents for a variety of reasons, including migraine prophylaxis, psychiatric disorders, pain management, and seizures. AEDs are the fifth most common cause of drug side effects in the older adult and, therefore, need to be carefully prescribed and monitored. The pharmacokinetics and pharmacodynamics of AEDs are distinct in older adult patients. Physiological changes relevant to pharmacotherapy in the older adult include decreased gastrointestinal motility, decreased serum albumin, increased body fat to lean mass ratio, decreased total body water, decreased liver mass and blood flow, decreased cytochrome P450 enzyme activity, decreased renal flow and weight, and decreased glomerular filtration rate, among others. The dose of medications may need to be reduced in patients with decreasing glomerular filtration rates 30 to 59 mL/min (Lee, 2019). For example,

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reduction in serum albumin levels leads to reduction in protein binding and increase in free fraction of the drug. This is an issue for high protein bound drugs such as phenytoin, carbamazepine, and valproic acid because of the increased risk of toxicity.

Older adults have a narrower therapeutic window than younger adults. Many AEDs are metabolized by the liver, especially the P450 enzyme, which is decreased. The potential for drug interactions is a major consideration in selecting an AED. Older AEDs (e.g., phenytoin, phenobarbital, carbamazepine) are enzyme-inducers, which increases the likelihood of interactions with other medications. Newer medications such as lamotrigine and levetiracetam are better choices for older adults on multiple medications. Calcium and vitamin D supplements should be considered because of the risk of osteoporosis with AED use. Pharmacodynamic changes include alterations in receptor distribution and density, receptor affinity and function, neurotransmitter release, and autonomic and homeostatic function. Toxicity from medications is poorly recognized in the older adult and can be attributed to multiple causes. Older adults with multiple chronic illnesses are more likely to be taking medications that interfere with AEDs.

Benzodiazepines (diazepam, lorazepam) are most commonly used for rescue or only in the acute setting. Although these are generally considered CNS depressants, the older adult may experience idiosyncratic effects such as restlessness, hyperactivity, and psychosis. Phenobarbital has been used in the treatment of seizures since the 1950s. Some older adult patients may have been on the medication for many years and will continue to require consistent monitoring. Phenobarbital is not recommended for a patient with new-onset seizures.

The newer AEDs offer some advantages for older adult, including a better side-effect profile. However, they are more expensive, and the name brands may not be covered by various insurance programs. Lacosamide is indicated as monotherapy and as adjunctive therapy for focal seizures. It blocks sodium channels and converts to inactive metabolites in the liver (Abou-Khalil, 2019). Oxcarbazepine is a second generation carbamazepine but with fewer side effects. This drug is only 38% protein bound and can be introduced more quickly in the older adult than carbamazepine. A concern for prescribing oxcarbazepine is possible hyponatremia, especially in older adults taking diuretics (Abou-Khalil, 2019). Lamotrigine is well absorbed orally by the older adult. Although the medication is eliminated by hepatic metabolism and then excreted renally, the drug is safely used in the older adult with renal failure. Side effects are minimal, and several studies have shown that it is well tolerated by the older adult. Lamotrigine has some mood-stabilizing effects, which may also help in treatment of the older adult. Levetiracetam is not metabolized by the P450 system and is entirely renally excreted. Dosage in renal failure may need adjustment. Gabapentin is also completely excreted unchanged in the urine. This drug is generally well tolerated in the older adult and is less likely to be involved in drug interactions; however, high dosages are often required for effective seizure control.

Topiramate has demonstrated good efficacy in older adult patients but may interact with digoxin and warfarin. Selection of topiramate, however, should not be considered for first-line treatment in older adults with cognitive impairment because of adverse effects (Abou-Khalil, 2019; Sommer & Fenn, 2010). Pregabalin has oral bioavailability exceeding 90%, is not bound to plasma proteins, and readily crosses the blood-brain barrier. The dosage must be titrated slowly to avoid adverse cognitive effects. Felbamate is primarily metabolized by the liver and has a number of drug interactions. Used carefully, this can be a good choice in pharmacoresistant seizures. Tiagabine is also metabolized by the liver and has a drug interaction profile similar to carbamazepine. Zonisamide is 40% bound to protein and its major elimination pathway is hepatic, but it can be safely used in the older adult. Long-term use of Depakote is not recommended in older adults because adverse side effects include reversible parkinsonism, tardive dyskinesia, gait disorder, dementia, and brain atrophy (Abou-Khalil, 2019).

Caution should be exercised in the use of generic medications because these have been shown not to have the same efficacy as brand-name medications. A patient who is stable on generic medications can become toxic or have breakthrough seizures if switched to brand-name medications. Similarly, the patient who is stable on brand-name medications and is switched to generic may experience a significant decrease in serum levels, leading to breakthrough seizures.

Seizure surgery can be considered in the older adult if the seizures are medically intractable, and the seizures are related to a focal structural lesion. A study by Punia and colleagues (2018) found that resective epilepsy surgery (RES) is often underutilized for people 65 and older. A cohort of older adults who underwent RES had comparable outcomes to a younger group of patients despite having more comorbidities and diagnosed for a longer duration of time (Punia et al., 2018).

Vagus nerve stimulation (VNS) has also been used in patients with refractory epilepsy. VNS is provided by a surgically implanted device programmed to deliver a brief electric stimulation on a schedule. The efficacy of this treatment has been established in general populations, but the data on the older adult are sparse.

Follow-Up: Seizure management is a significant challenge, and the patient and any caretakers should be seen frequently. A seizure calendar/journal is maintained by the patient and should be reviewed on each visit. Precipitating factors for an increase in seizures, such as stress, sleep deprivation, or viral illness, should be noted. Questions concerning potential medication side effects are asked on each visit. For some medications, periodic levels are monitored and adjusted to ensure therapeutic levels. The incidence of depression in adults with epilepsy has been reported as high as 50%. Causes of the depression include lifestyle changes, loss of confidence and independence, as well as biochemical alterations in the brain due to the seizures. The potential loss of freedom following a seizure is heightened by driving restrictions, which are based on the laws of the individual state and range from 6 months to at least 1 year seizure free.

Sequelae: Sudden unexpected death in epilepsy (SUDEP) is defined specifically as the sudden, unexpected, witnessed, or unwitnessed, nontraumatic, and nondrowning death in patients with epilepsy with or without evidence for a seizure, and excluding documented status epilepticus, in which postmortem examination does not reveal a structural or toxicological cause for death. Individuals with epilepsy have a mortality rate two to three times greater than that of the population at large (Thijs et al., 2019). SUDEP accounts for 8% to 17% of these deaths and is more likely to occur in

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those with frequent seizures. Patients and their families need to be warned of the potential for SUDEP and the importance of controlling the variables that can lead to SUDEP, such as abrupt cessation of AEDs.

Convulsive status epilepticus incidence is almost twice that of the general population. Associated mortality rate is also higher in older patients, 38% in those older than 60 years and more than 50% in those older than 80 years. Nonconvulsive status epilepticus (NCSE) is equally common in the older adult, but much more difficult to diagnose because it can present with general symptoms such as confusion, psychosis, lethargy, or coma, or a more focal cognitive disturbance with aphasia. These symptoms are very general and may not be associated with any observable seizure activity. Due to the nonspecific nature of the symptoms, the presence of seizures on the EEG is the most important diagnostic step. Incidence rate of all types of status epilepticus in the older adult is 54.2 per 100,000 people.

Prevention/Prophylaxis: Prevention of potential causative factors such as stroke, meningitis, and active management of disease processes such as AD and dementia is an important part of prevention of seizures. Care in preventing falls may also decrease the incidence of head injuries leading to seizures. Prophylactic use of AEDs following head injury and stroke remains controversial but may be indicated.

Referral: For new-onset seizures, referral to a neurologist/epileptologist or to a comprehensive epilepsy center would be in the best interest of the patient. If traditional medications become difficult to manage, the patient should be referred to a neurologist.

Education: Comprehensive education should be provided to patients and their families/caregivers. This education includes seizure recognition and first aid, treatment plans and side effects, safety practices to prevent injury during seizures, and lifestyle considerations appropriate for age (e.g., driving, work, sleep, coping skills, stress management). Community resources, as well as evidence-based Web-based resources, should be discussed (e.g., Epilepsy Foundation, NINDS). Educating patients and their families about SUDEP, ascertaining seizure precipitants, and promoting compliance with treatment are important strategies. Very specific information should be provided to patients who are nonadherent with medications or appear to be in denial of the diagnosis. Patients should maintain a seizure calendar that chronicles seizures and all precipitants. Strategies to ensure compliance with daily medication include the use of medication boxes and telephone alarms. Patients should inform the provider of any changes in other medications to avoid potential interactions. Inform patients and family members that abrupt cessation of medications is very dangerous and that all AEDs should be carefully weaned.

Clinical Recommendation	Evidence Rating	References
The main cause for new-onset epilepsy in older adults was found to be stroke. The second cause was dementia.	C	Chi Vu et al., 2018
Resective epilepsy surgery is a treatment option for epilepsy in older patients, particularly for drug-resistant or difficult-to-treat seizures that are due to drug interactions for coexisting conditions.	C	Chi Vu et al., 2018 Punia et al., 2018
Cerebrovascular disease and depression were found to be significantly associated with new-onset epilepsy.	C	Chi Vu et al., 2018
If there is doubt about the diagnosis of epilepsy after starting medication, stopping it is a reasonable option.	C	Chi Vu et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

STROKE

Signal Symptoms: Sudden weakness or numbness on one side of the body, language impairment, trouble seeing in one or both eyes, alteration in balance and/or coordination, severe headache without known cause.

Description: Stroke is a rapidly evolving cerebrovascular syndrome of sudden onset, with symptoms suggestive of a nonepileptic focal neurological deficit. There are two major types of strokes: ischemic, indicating blockage of an artery, and hemorrhagic, usually resulting from a leak or rupture in an artery wall. Acute stroke is a medical emergency.

Etiology: Approximately 87% of all strokes are ischemic (Virani et al., 2020) and develop when an artery in the brain is obstructed by a clot that eithers forms in the brain or travels from somewhere else. Ischemic strokes are classified into casual subtypes: cardioembolic, small vessel occlusion (lacunar stroke), large vessel atherothrombotic, other unusual, determined etiology, and undetermined etiology. Cardioembolic strokes occur when a blood clot forms elsewhere in the body, travels to the brain through the circulatory system, and becomes lodged in a cerebral artery. Cardioembolic strokes are generally associated with atrial fibrillation, valvular disorders, heart failure, and other states associated with thrombus formation. Large vessel strokes occur when a major artery in the brain is blocked, presumably by a blood clot that forms as a result of an inflammatory response to an unstable

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atherosclerotic plaque. Lacunar infarcts occur in the small arteries that branch from main cerebral arteries. Unusual etiologies of stroke include nonatherosclerotic vasculopathies, hypercoagulable states, or hematological disorders. An exhaustive work-up, an incomplete work-up, and more than one possible source can lead to a label of undetermined etiology (Kleindorfer et al., 2021).

Hemorrhagic stroke usually results from either a nonstructural or structural cause, where a weakened area of an artery in or around the brain ruptures. The most common nonstructural hemorrhage is caused by pathophysiological changes that occur in small arteries from long-standing hypertension, often triggered by an accelerated hypertensive episode. Structural etiologies include ruptured aneurysms and arteriovenous malformations. Incidence is varied by race and mechanism. Approximately 10% of all events are intracerebral hemorrhage (ICH) and 3% are subarachnoid hemorrhage (Virani et al., 2020). *Hemorrhagic transformation* is a term that refers to bleeding into infarcted tissue and is thought to be associated with reperfusion. It occurs within days or weeks from stroke onset.

A transient ischemic attack (TIA) is an episode of focal neurological impairment of presumed ischemic origin, typically lasting only a few minutes with no permanent deficits. The episode of neurological dysfunction is caused by focal brain, spinal cord, or retinal ischemia without acute infarction (Kleindorfer et al., 2021). Absence of tissue findings makes TIA a tissue-based definition rather than a time-defined definition. Transient hypotension, in conjunction with significant carotid stenosis, may also cause a TIA. The significance of TIA lies in the heightened short-term risk of stroke, with a 3% to 10% risk at 2 days and a 9% to 17% risk of stroke within 90 days of a TIA. Over the following 10 years, there is a 4% per year risk of stroke, myocardial infarction (MI), or vascular death (Virani et al., 2020).

Occurrence: Stroke is the leading neurological cause of death and disability in the United States, with an estimated 795,000 people each year suffering a new or recurrent stroke (Virani et al., 2020). The stroke incidence rate is higher for men compared with women at younger ages, but not at older ages. Lifetime risk for women is higher than men, with rates one in five for women and approximately one in six for men ages 55 to 75 years. Prevalence of TIA increases with age. True prevalence is difficult to ascertain, as many fail to report neurological symptoms to their health-care provider (Virani et al., 2020).

Age: Approximately 7.0 million Americans 20 years old and older have had a stroke. The prevalence of silent cerebral infarction rises from 6% to 28% with increasing age. With an aging population, by 2030 prevalence is expected to increase 20.5% in those 18 years old and older, adding 3.4 million more people with stroke (Virani et al., 2020).

Ethnicity: Native Americans, Alaskan Natives, Hispanics, and Blacks have more TIAs and are at higher risk for stroke and stroke mortality than Whites. Blacks carry the highest risk and Hispanics carry a moderate risk, whereas Whites carry the lowest risk (Virani et al., 2020).

Contributing Factors: Risk factors for stroke include advanced age, family history of stroke, hypertension, diabetes, smoking, prior history of TIA or stroke, hyperlipidemia, cardiovascular disease, carotid stenosis, atrial fibrillation, obesity, sedentary lifestyle, alcohol abuse, and some infections (endocarditis, bacterial meningitis). Less common risk factors include sleep apnea, drug abuse, migraine, hypercoagulable disorders, hormone replacement therapy or oral contraceptive use, sickle cell anemia, and other inflammatory processes (Kleindorfer et al., 2021).

Signs and Symptoms: Determination of time last known well is critical. TIA is a precursor to stroke in 15% of all cases. Patients having a TIA or ischemic stroke may report sudden onset of the following symptoms: weakness, numbness, or paralysis in the face, hand, arm, or leg (usually unilateral); difficulty speaking or understanding verbal communication; blurred, doubled, or decreased monocular or binocular vision; loss of balance or coordination; and severe headache. Cortical symptoms, including aphasia, gaze deviation, hemianopia, and neglect are correlated with large vessel occlusions (LVO) (Powers et al., 2019).

Patients with a hemorrhagic stroke may report any of these symptoms, along with nausea and vomiting, altered mental status, sensitivity to light, and neck stiffness. Physical signs may include one or more of the following: decreased visual acuity or field cut, diplopia, slurred speech, aphasia, and hemiparesis or sensory changes of the face, arm, or leg. A decrease in coordination or unsteady gait can occur. Elevated blood pressure is common along with acute confusion (Hemphill et al., 2015).

Any other focal signs on neurological examination should be assessed carefully. Physical examination should include repeated measures of vital signs and examination of the head and neck for signs of trauma and infection, checks of the peripheral and carotid pulses, auscultation of the neck for bruits, and a complete neurological examination for focal abnormalities. The consequent impairment depends on the location and extent of the stroke (Hemphill et al., 2015). Recommended is the National Institutes of Health Stroke Scale (NIHSS), a validated tool that standardizes approach to the neurological examination (Powers et al., 2019).

Diagnostic Tests: All patients with symptoms consistent with stroke should be transported via emergency medical services (EMS) to the nearest certified stroke facility for rapid assessment and early treatment. For patients with a suspected LVO, noninvasive imaging with computed tomography (CT) angiography and/or magnetic resonance angiography should be done emergently up to 24 hours. Perfusion CT and magnetic resonance imaging (MRI) are recommended for patients eligible for reperfusion between 6 and 24 hours. Even for patients whose symptoms have resolved, immediate diagnostic tests should include a noncontrast CT scan or MRI of the head to evaluate for presence of hemorrhage, electrocardiogram (ECG), and laboratory assessment (oxygen saturation, complete blood count [CBC], prothrombin time/activated partial thromboplastin time [PT/aPTT], troponin, lipids, and complete blood chemistry) (Powers et al., 2019).

A head CT scan is almost 100% sensitive for ICH. Ischemic events may not be visible on CT scan for 24 to 48 hours and may be noted anywhere in the cerebral cortex, cerebellum, or brainstem. MRI is helpful in early diagnosis of ischemic or hemorrhagic strokes but may not be available in all centers. If a hemorrhagic stroke is confirmed, consider referral to a neurosurgeon. Further diagnostic testing includes carotid

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duplex studies, CT angiography and/or magnetic resonance angiography, if not done emergently, to look for intracranial and extracranial vascular occlusion in the head or neck, as well as cardiac monitoring and an echocardiogram (Powers et al., 2019). Treatment choices will depend on results of initial assessments and time elapsed between onset of symptoms and confirmed diagnosis (Hemphill et al., 2015; Powers et al., 2019). The purpose of acute hospitalization is to establish stroke etiology in order to prevent subsequent events.

Differential Diagnosis:

- Seizure with Todd's paralysis: loss of consciousness, seizure activity, incontinence, postictal state
- Migraine aura: more common in women, history of similar event, preceding aura, with or without headache, photophobia
- Syncope/dizziness/vertigo: common types include neurocardiogenic (vasovagal), situational, orthostatic, and syncope related to cardiac ischemia or arrhythmia. Associated with sweating, pallor, and nausea. May have dim vision, decreased alertness, and transient loss of consciousness.
- Transient global amnesia: poor recall of recent events with impaired ability to retain new memories without other cognitive or focal neurological impairment
- Toxic-metabolic disorders: hypoglycemia, hyperglycemia, hyponatremia, drug or alcohol intoxication, ruled out based on history and laboratory findings
- Multiple sclerosis (MS): paroxysmal transient attacks of ataxia and dysarthria
- Brain tumor: gradual progression of symptoms, other primary malignancy, seizure at onset, ruled out based on brain imaging studies
- Systemic infections: acute illness with recrudescence of previous stroke symptoms
- Conversion disorder: inconsistent clinical examination, nonfocal symptoms, neurological findings in a nonvascular distribution, increased risk in those with recent stress or trauma or with history of mental health condition

Treatment: Emergency transport to the nearest designated stroke center should be initiated for patients with suspected stroke, regardless of the severity of neurological deficits, and be evaluated as high priority triage. Patients should be given nothing by mouth (NPO) with IV fluids (isotonic sodium chloride) started to maintain euvolemic status in most patients. Patients with fever (greater than 38°C [100.4°F]) should be treated with antipyretics and an aggressive search for the source of fever initiated. Hypoglycemia and hyperglycemia should be identified and treated promptly. Both can produce symptoms that mimic ischemic stroke, and both may worsen neuronal injury. The goal for hypoglycemia treatment is to achieve normoglycemia. Hyperglycemia during the first 24 hours is associated with poor outcomes, thus glucose level goals of 140 to 180 mg/dL with avoidance of hypoglycemia is advised. Supplemental oxygen is recommended to attain oxygen saturation greater than 94% (Powers et al., 2019).

For eligible patients who present within 4.5 hours of the onset of symptoms and a hemorrhagic event is ruled out, recombinant tissue-type plasminogen activator (alteplase, also known as t-PA), an IV thrombolytic agent, has been established to decrease long-term disability. The most important factor in successful treatment is early administration. Additionally, for patients who have an LVO, intra-arterial treatment with mechanical thrombectomy within 24 hours of symptom onset has been found to be safe and effective, demonstrating improved outcomes and reduced mortality. Other investigational methods of reperfusion, including intra-arterial thrombolysis remain unproven. Endovascular and research availability depends on location; treatment should only be performed at an experienced stroke center. The American Stroke Association guidelines support that cities, counties, regions, and states develop a stroke system of care that will enable patient access to optimal care (Powers et al., 2019).

Early administration of aspirin within 24 to 48 hours following stroke has shown benefit and is recommended in ischemic events but is generally delayed until 24 hours after alteplase administration. Urgent anticoagulation to prevent recurrent stroke, avoid neurological worsening, or improve outcomes is not recommended (Powers et al., 2019).

Hypertension is common in acute stroke and may spontaneously decline within 90 minutes of stroke onset. Aggressive use of antihypertensives may reduce perfusion pressure and prolong or worsen ischemia. Rapid reduction of blood pressure regardless of the degree of hypertension may be harmful. The consensus recommendation is to lower the blood pressure by 15% during the first 24 hours if the systolic pressure is greater than 220 mm Hg or diastolic blood pressure is greater than 120 mm Hg. Note: a systolic pressure greater than 185 mm Hg or a diastolic pressure greater than 110 mm Hg is a contraindication for thrombolytic therapy. Therefore, the management of blood pressure in acute ischemic stroke will depend on whether the patient is a candidate for thrombolytic therapy. There is no evidence to determine which antihypertensive should be used; an individualized approach is best (Powers et al., 2019).

Hemorrhagic events should be initially managed in an intensive care or stroke unit. For patients taking anticoagulation medications, reversal may be indicated. If patients present with systolic pressures 150 to 220 mm Hg, aggressive reduction is considered safe down to 140 mm Hg. Prophylactic antiepileptics are not recommended. Ideally, neurosurgical care should be available, though the usefulness of surgery for most patients is not well established. Patients should be monitored at frequent intervals for signs of cerebral edema, and control of other comorbid diseases are also indicated (Hemphill et al., 2015).

Follow-Up: Indications for follow-up depend on the type and extent of the stroke. Rehabilitation should begin during the acute phase as soon as the patient can tolerate, with all patients undergoing a formal rehabilitation needs assessment prior to discharge. Post-acute goals support the pursuit of the highest level of functioning possible. A stroke-specific rehabilitation environment is preferred, if available. Rehabilitation targets should be designed around (1) functional outcomes, (2) lifestyle interventions, (3) enhancement of cardiorespiratory fitness, (4) prevention of complications and deconditioning, and (5) social reintegration. Education regarding stroke, rehabilitation, recovery, and what to expect is critical for the survivor, family, and caregivers. Whenever possible, the stroke survivor, family, and caregivers should be involved in decision making regarding treatment and care planning. Use of standardized assessment instruments will be helpful in

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establishing baseline, setting goals, and tracking progress. Standardized stroke assessment instruments are found in Box 17-2 (Powers et al., 2019; Winstein et al., 2016).

Whenever possible after a stroke, patients should have regular contact with a care team with expertise in stroke rehabilitation to assess for changes in level of function, control medical comorbidities, manage pain, assess for depression/anxiety, address complex rehabilitation issues, and implement prevention strategies for secondary stroke prevention (Winstein et al., 2016). Community- or home-based rehabilitation services are recommended following discharge from either acute hospitalization or inpatient rehabilitation, when feasible, and should include a team approach with nursing, medical interventions, and specialized equipment as needed. Given today's electronic climate, it is reasonable to consider other methods for follow-up at home, especially for those in rural environments, including the use of discharge phone calls, telehealth, and Web-based or smart-phone enabled support (Winstein et al., 2016).

Sequelae: Stroke survivors are at high risk for complications related to immobility, such as skin breakdown and contractures, loss of muscle strength, and pulmonary compromise. Risk assessments should routinely be performed for other common complications including malnutrition, bowel and bladder incontinence, deep vein thrombosis, pain, falls, seizures, and osteoporosis. Assessment of cognition and memory, communication abilities, sensorimotor impairment, and psychosocial status should be undertaken regularly in the subacute and chronic phases of stroke recovery. Speech and swallowing difficulties also may persist after a stroke. Depression and anxiety are also common. Stroke survivors should be screened for depression both during the acute phase and regularly thereafter, with treatment as indicated (Winstein et al., 2016). Monitoring of the caregiver burden and access to available community resources is also imperative. Finally, all stroke survivors are at risk for recurrent stroke and other cardiovascular events (Kleindorfer et al., 2021). Appropriate strategies should be implemented for prevention/prophylaxis.

BOX 17-2

Standardized, Validated Instruments for Assessment of Stroke Survivors

- Global disability (Rankin scale)
- Measures of disability/ADLs (Barthel Index; Functional Independence Measure [FIM™])
- Instrumental activities of daily living (PGC Instrumental Activities of Daily Living; Frenchay Activities Index)
- Mental status (Folstein Mini-Mental State Examination; Neurobehavioral Cognition Status Exam [NCSE])
- Speech and language (Boston Diagnostic Aphasia Examination; Porch Index of Communicative Ability [PICA]; Western Aphasia Battery)
- Paresis/strength (Motricity Index, muscle strength, grip pinch dynamometry)
- Tone (Modified Ashworth scale)
- Sensorimotor impairment (Fugl-Meyer, Chedoke McMaster Stroke Assessment, impairment inventory)
- Upper extremity function (Action Research Arm Test, Box and Block Test, Chedoke Arm and Hand Activity index, Wolf Motor Function Test)
- Balance (Berg Balance Scale, Functional Reach Test)
- Mobility (walking speed, Timed Up and Go, 6-minute walk test, functional ambulation category, observational gait analysis)
- Self-reported impairments, limitations, and restrictions (Stroke Impact scale, motor activity log, Activities-Specific Balance Confidence Scale)
- Technology for monitoring activity and participation (accelerometers, step activity monitors, pedometers)
- Depression (Beck Depression Inventory [BDI]; Center for Epidemiologic Studies Depression [CES-D]; Geriatric Depression Scale [GDS])

Sources: Winstein et al. (2016).

Prevention/Prophylaxis: Strategies to prevent stroke are similar to strategies used to prevent other cardiovascular diseases: control of hypertension, diabetes, dyslipidemia, sleep apnea, and cardiac disease through lifestyle and pharmacotherapeutic agents. Encourage patients to eat healthy, increase physical activity levels, lose weight (if indicated), avoid heavy alcohol intake, and stop smoking. Secondary stroke prevention with antithrombotics, including antiplatelet or anticoagulant agents, is recommended for virtually all patients without contraindications. For those with noncardioembolic ischemic TIA or minor stroke or identified carotid disease, short-term treatment with dual antiplatelets is recommended (Kleindorfer et al., 2021; Powers et al., 2019). Anticoagulation therapy is recommended in survivors of stroke with known arrhythmias or hypercoagulable states. Atrial fibrillation is the most common stroke causing arrythmia for which four direct-acting oral anticoagulants are available that are preferable to warfarin because they are as effective and may be safer (have lower risk profiles), they do not require routine blood tests, and they do not require dietary adjustment in patients with embolic stroke. In patients with a cryptogenic stroke of unknown embolic etiology with ongoing screening, almost 30% will be diagnosed with atrial fibrillation, which will alter treatment course. Carotid endarterectomy (CEA) or carotid angioplasty and stenting (CAS) may be considered for stenosis greater than 50% (Kleindorfer et al., 2019).

Referral: Referrals depend on the type and severity of impairment from the stroke and the influence of any comorbid illnesses. Referrals to physiatry (rehabilitation medicine), neurology, interventional neuroradiology, vascular surgery, psychiatry, and cardiology for consultation are common.

Education: Stroke education should address stroke prevention, treatment, and recovery. For stroke survivors, emphasize the cause of the stroke, control of individual risk factors to prevent future events, and importance of early identification with EMS activation and treatment of recurrent stroke. A Mediterranean-type diet is recommended. A home exercise program to maintain or improve functional levels should be introduced and strongly encouraged. Programs with balance training components have been shown to reduce falls (Winstein et al., 2016). The individually tailored exercise program will also enhance cardiorespiratory fitness and

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reduce risk of recurrent stroke, as well as improve cognition and memory. Information to access stroke support groups for patients and caregivers should be provided. Emphasis should be placed on the importance of periodic follow-up with the primary care provider for recovery monitoring, surveillance for complications, ongoing management of risk factors, and secondary prevention. The American Stroke Association offers help and support to stroke survivors and caregivers. Contact them via the Stroke Family Warmline at Stroke.org/speakwithus and at 1-888-4STROKE (1-888-478-7653). Up-to-date, stroke-specific guidelines and scientific statements for professionals are available online at the American Heart Association, https://professional.heart.org/en/guidelines-and-statements.

Clinical Recommendation	Evidence Rating	References
Rapid transport to the closest facility that can administer alteplase.	A	Powers et al., 2019
A stroke rating scale, preferably the National Institutes of Health Stroke Scale (NIHSS), is recommended for initial assessment.	B	Powers et al., 2019
Suspected stroke should receive emergent brain imaging on arrival prior to any treatment (noncontrast computed tomography).	A	Powers et al., 2019
IV alteplase is recommended within 4.5 hours of ischemic stroke for those who meet eligibility.	A	Powers et al., 2019
For eligible alteplase patients, benefit is time dependent and should be initiated as quickly as possible.	A	Powers et al., 2019
Patients with signs of large vessel occlusions should receive emergent noninvasive vessel imaging (CT angiography, magnetic resonance angiography).	A	Powers et al., 2019
Endovascular therapy recommended up to 0–24 hours if: a) age ≥18 years b) imaging confirms large vessel occlusion b) NIHSS score 6 c) ASPECTS score of ≥6 d) prestroke modified Rankin Scale score 0–1 e) core volume <70 mL f) mismatch ratio >1.8 g) mismatch volume >15	A, B	Powers et al., 2019
Stroke unit care (comprehensive specialized stroke care) that incorporates rehabilitation is recommended.	A	Powers et al., 2019
Dysphagia screening prior to eating, drinking, or taking oral medications is recommended in all stroke patients.	B	Powers et al., 2019
Patients with large infarctions are at high risk for edema and increased intracranial pressure. Measures to decrease risk and close monitoring during the first few days are recommended.	C	Powers et al., 2019
Craniectomy is recommended in cerebellar infarcts with brainstem compression. Ventriculostomy placement is recommended for hydrocephalus.	A	Powers et al., 2019
Administration of aspirin is recommended within 24–48 hours of ischemic stroke onset.	A	Powers et al., 2019
For mild ischemic stroke (NIHSS ≤3), treat with dual antiplatelets for 21 days then one alone.	A	Powers et al., 2019
For patients with noncardioembolic ischemic stroke or transient ischemic attack (TIA), antiplatelet agents rather than oral anticoagulation are recommended to reduce the risk of recurrent stroke and other cardiovascular events.	A	Powers et al., 2019
For patients with cardioembolic strokes of unknown etiology, use of anticoagulation is not recommended.	A	Kleindorfer et al., 2021
Provide deep vein prophylaxis with intermittent pneumatic compression in immobile stroke patients.	B	Powers et al., 2019
Routine laboratory tests (complete blood count, troponin, chemistry, coagulation studies, Hb A1c, and lipid panel) are reasonable in the evaluation of suspected stroke/TIA.	A	Kleindorfer et al., 2021

Continued

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Clinical Recommendation	Evidence Rating	References
Baseline electrocardiogram is recommended to screen for atrial fibrillation or other cardiac arrhythmias.	A	Kleindorfer et al., 2021
For patients with TIA/ischemic stroke within the past 6 months and ipsilateral carotid artery stenosis:		Kleindorfer et al., 2021
■ Severe (70%–99%), carotid endarterectomy (CEA) is recommended if morbidity and mortality risk is <6%.	A	
■ Moderate (50%–69%), CEA recommended based on patient-specific factors (age, sex, comorbidities) and risk <6%.	B	
■ Mild (<50%) carotid stenosis, no indication for CEA or stent.	A	
In patients with carotid stenosis and TIA/ischemic stroke, intensive medical therapy with antiplatelets and control of lipids and hypertension is recommended.	A	Kleindorfer et al., 2021
In patients with nonvalvular atrial fibrillation and TIA/ischemic stroke, oral anticoagulation is recommended.	A	Kleindorfer et al., 2021
In patients with left ventricular thrombus and TIA/ischemic stroke, warfarin is recommended for ≥3 months.	B	Kleindorfer et al., 2021
In patients with left atrial/appendage thrombus and cardiomyopathy and TIA/ischemic stroke, warfarin is recommended for at least 3 months.	B	Kleindorfer et al., 2021
In patients with mechanical heart valves and TIA/ischemic stroke, warfarin is recommended with an International Normalized Ratio target of 3.0.	B	Kleindorfer et al., 2021
Short-term dual antiplatelets are recommended for early arriving minor stroke (<24 hours), high-risk TIA, or symptomatic intracranial stenosis.	B	Kleindorfer et al., 2021
Long-term dual antiplatelet therapy is not recommended.	A	Kleindorfer et al., 2021
Treatment with a statin is indicated for eligible patients; goal is LDL-C <70 mg/dL.	A	Powers et al., 2019 Kleindorfer et al., 2021
Smoking cessation/nicotine replacement therapy is recommended.	A	Powers et al., 2019
Limit alcohol intake to maximum or 2 drinks a day for men and 1 drink a day for women.	A	Kleindorfer et al., 2021
Office blood pressure goal is <130/80 mm Hg for most patients.	A	Kleindorfer et al., 2021
Diabetes control with goal Hb A1c ≤7%.	A	Kleindorfer et al., 2021
In patients 18–60 years old with patent foramen ovale and cryptogenic stroke, closure should be considered with cardiology.	B	Kleindorfer et al., 2021
In intracerebral hemorrhage (ICH), 1–4 days after bleeding has stopped, it is okay to use low molecular weight heparin or low-dose unfractionated heparin for venous thromboembolism prevention.	A	Hemphill et al., 2015
Patients with cerebellar ICH who are deteriorating or have brainstem compression and/or hydrocephalus should undergo surgical decompression as soon as possible.	B	Hemphill et al., 2015
Appropriate management of medical comorbidities (hypoglycemia and hyperglycemia, hyperthermia, hypoxia, arrhythmias, etc.) during the acute, subacute, and chronic phases of stroke recovery can significantly improve outcomes.	A	Kleindorfer et al., 2021
Long-term cardiac monitoring is reasonable to detect atrial fibrillation.	B	Kleindorfer et al., 2021
Targeted injection of botulinum toxin into upper limbs is used to improve range of motion and lower limbs to reduce spasticity.	A	Winstein et al., 2016
A balance training program is recommended for those with poor balance and fall risk.	A	Winstein et al., 2016
Intensive, repetitive, mobility training is recommended for all stroke survivors with gait limitations.	A	Winstein et al., 2016
Patients with functional limitations in ADLs and mobility should be considered for community- or home-based rehabilitation post-discharge.	A	Winstein et al., 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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TRIGEMINAL NEURALGIA

Signal Symptoms: Paroxysms of shooting pain affecting one dermatome of the face.

Description: Also known as *tic douloureux,* trigeminal neuralgia is a painful disorder of the trigeminal nerve (cranial nerve V) that causes unilateral, brief, and recurrent paroxysms of shock-like electric pain that are sudden in onset and termination and are limited to the dermatome of one (or two contiguous) branches of the trigeminal nerve. In addition, there may be a less severe persistent pain in the same nerve distribution. Characteristically, the pain is triggered by normally innocuous tactile stimuli to the face or mouth, such as wind blowing across the face, chewing, and shaving (Headache Classification Committee of the International Headache Society [IHS], 2018). Trigeminal neuralgia is a chronic condition, though patients may experience periods of remission.

Etiology: Classical trigeminal neuralgia is caused by intracranial vascular compression of the trigeminal nerve root, most often by the superior cerebellar artery. Secondary trigeminal neuralgia is due to an underlying neurological or medical condition such as a cerebellopontine angle tumor or multiple sclerosis with demyelination of the axons of the fifth cranial nerve. Idiopathic trigeminal neuralgia has no identifiable cause (Cruccu et al., 2020).

Occurrence: Trigeminal neuralgia affects 12.6 to 28.9 per 100,000 people annually (van Hecke et al., 2014) and is more common in women than men.

Age: The incidence of trigeminal neuralgia increases with age.

Ethnicity: All ethnicities are affected, but trigeminal neuralgia may be less common among Jewish populations (Rothman & Monson, 1973).

Contributing Factors: Hypertension, migraine, and multiple sclerosis (MS) are risk factors for developing trigeminal neuralgia.

Signs and Symptoms: Trigeminal neuralgia is a clinical diagnosis (Bendtsen et al., 2020). Patients with trigeminal neuralgia have unilateral orofacial pain restricted to the territory of one or more divisions of the trigeminal nerve (Fig. 17-1). The maxillary and mandibular divisions are more commonly affected. The pain is paroxysmal in nature and brief in duration (from <1 second to 2 minutes, but usually a few seconds). The pain is described as a "shock" or an "electric sensation" and occurs from 1 to >50 times daily. Pain can be triggered by innocuous stimuli on the face or mouth in the vast majority of patients (Headache Classification Committee of the IHS, 2018). This triggered paroxysmal pain is specific for trigeminal neuralgia and may be pathognomonic for the disease (Cruccu et al., 2020). The pain is typically severe and can be disabling. Patients may refrain from activities that trigger the pain such as eating, shaving, and going outside when in the cold or wind. Patients may develop situational depression and even suicidal ideation due to the pain of trigeminal neuralgia.

Neurological examination is normal in patients with classical or idiopathic trigeminal neuralgia, except for mild hypoesthesia in the affected facial dermatome reported in some patients. The typical paroxysmal pain can be elicited on examination using provocative maneuvers, such as touching or moving the face; this solidifies the diagnosis of clinically established trigeminal neuralgia. These paroxysms of pain may be accompanied by brisk muscle contractions due to involuntary facial movement in response to pain (Cruccu et al., 2016).

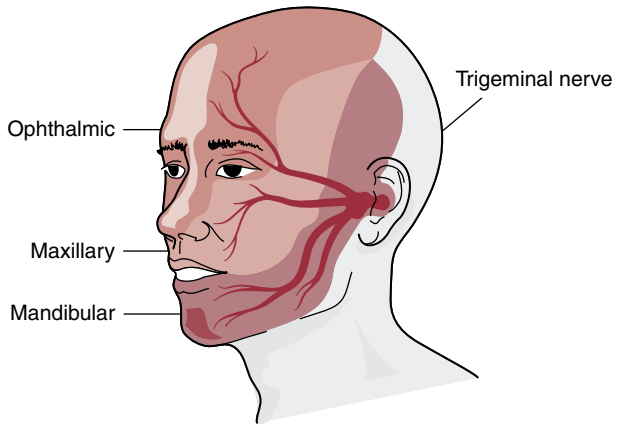

FIGURE 17-1 Dermatomes of the three trigeminal nerve branches: ophthalmic (V1), maxillary (V2), and mandibular (V3).

Diagnostic Tests: Brain magnetic resonance imaging (MRI) is recommended to evaluate for the underlying etiology of the trigeminal neuralgia (Bendtsen et al., 2019). Neurovascular compression is seen in classical trigeminal neuralgia and a structural lesion affecting the trigeminal nerve is seen in secondary trigeminal neuralgia. Patients with idiopathic trigeminal neuralgia have normal brain imaging.

Differential Diagnosis: There are many potential causes of orofacial pain, and the differential diagnosis is broad (Headache Classification Committee of the IHS, 2018). Other primary headache and facial pain disorders include:

- Glossopharyngeal neuralgia: paroxysmal stabbing pain affecting the ear, throat, base of the tongue, or beneath the angle of the jaw
- Optic neuritis: pain behind the affected eye with associated vision changes due to demyelination of the optic nerve
- Ischemic ocular motor nerve palsy: headache and binocular diplopia due to ischemic injury of cranial nerve III, IV, or VI
- Persistent idiopathic facial pain (previously known as atypical facial pain): persistent facial and/or oral pain with a normal examination and no identifiable cause
- Short-lasting unilateral neuralgiform headache attacks: These trigeminal autonomic cephalalgias are a group of primary headache disorders that cause stabbing pain in the trigeminal nerve distribution on one side at a time (though can change sides) with associated autonomic features (conjunctival injection, lacrimation, nasal congestion, rhinorrhea, eyelid edema, ptosis, miosis, or facial sweating).
- Primary stabbing headache: stabbing pain on the scalp

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Secondary causes of orofacial pain include:

- Painful trigeminal neuropathy: facial pain in an area of sensory loss, caused by damage to the trigeminal nerve (such as acute herpes zoster, post-herpetic neuralgia, tumor, or trauma)
- Dental pain
- Temporomandibular disorder
- Giant cell arteritis (also known as temporal arteritis): chronic vasculitis that often causes pain in the temporal area, with associated tenderness to palpation and jaw claudication. Left untreated, patients can suffer permanent blindness or other neurological complications.
- Facial pain due to carotid or vertebral artery dissection

Treatment: Carbamazepine or oxcarbazepine are recommended as first-line agents for trigeminal neuralgia. Oxcarbazepine is generally better tolerated than carbamazepine. If ineffective, second-line or add-on treatments include gabapentin, pregabalin, lamotrigine, phenytoin, baclofen, or botulinum toxin injections (Bendtsen et al., 2020).

In refractory cases, surgical management can be considered. For classical trigeminal neuralgia, microvascular decompression is the procedure of choice. Ablation procedures can be considered when there is no neurovascular compression (Bendtsen et al., 2020).

Follow-Up: Patients should be monitored for symptom control and medication side effects. Carbamazepine and oxcarbazepine have many potential side effects, including sedation, nausea, dizziness, diplopia, hyponatremia, rash, and hematological complications. Patients should also be monitored for psychiatric comorbidities; depression, including suicidal ideation, has been described as a sequela of unrelenting trigeminal neuralgia pain. Patients should have routine follow-up with their dentist because oral hygiene may be poor in patients whose pain is triggered by brushing teeth (Bendtsen et al., 2020).

Prevention/Prophylaxis: There is no prevention for trigeminal neuralgia.

Referral: If the patient's symptoms do not improve with medications, if atypical features are present, or if other neurological signs are evident, the patient should be referred to a neurologist. If the symptoms are refractory to medical management, referral for neurosurgical consultation should be considered. Psychology referral should be considered for patients experiencing anxiety and depression and to learn pain coping skills (Bendtsen et al., 2020).

Education: Patients should be counseled about avoiding triggers, possible medication side effects, and available neurosurgical procedures.

Clinical Recommendation	Evidence Rating	References
Trigeminal neuralgia is a clinical diagnosis.	C	Cruccu et al., 2016 Headache Classification Committee of the IHS, 2018 Scholz et al., 2019
Brain magnetic resonance imaging should be performed to evaluate for an underlying structural etiology upon diagnosis of trigeminal neuralgia.	B	Bendtsen et al., 2019
First-line medications for the treatment of trigeminal neuralgia are carbamazepine or oxcarbazepine.	A	Bendtsen et al., 2019
Surgical treatments can be curative; the best results are seen with microvascular decompression surgery for classical trigeminal neuralgia (62%–89% achieve pain freedom).	B	Bendtsen et al., 2019
Medical management is recommended prior to offering surgery for trigeminal neuralgia.	C	Bendtsen et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

Sue is a 68-year-old healthy woman with no significant medical history. She is in the office today with complaint of intractable nausea and vomiting for the past 5 weeks with an 11-pound weight loss. On review of systems, she also has noted a dull, persistent headache, difficulty with concentration, and some blurred vision. She states these other problems are likely due to this gastrointestinal "bug" that will not go away. She denies similar symptoms in the past. Her mother died of complications of diabetes at 42 years old, her father died of a heart attack in his late 50s, one brother died in a car accident in his late teens, and the other died of complications of diabetes in his late teens. She is a nurse, married, with two adult children who are in good health. She drinks a beer or glass of wine on most days, sometimes two. She has never used tobacco products or illegal drugs.

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What are the differential diagnoses that you are considering?

Continued

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CASE STUDY—cont'd

4. What laboratory tests will help you rule out some of the differential diagnoses?
5. What radiological examinations would you order?
6. What is your treatment and specific information on the prescription you will give to this patient?
7. What are the potential complications from the treatment ordered?
8. What are the additional specific laboratory tests you may consider ordering?
9. What additional patient teaching may be needed?
10. Will you be looking for a consultation?

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CHAPTER 18

Endocrine and Metabolic Disorders

Laurie Kennedy-Malone

ASSESSMENT

With the multiple hormonal and metabolic changes that occur with aging, the incidence of endocrine and metabolic age-related conditions, such as type 2 diabetes, osteoporosis, and hyperlipidemia, increases as adults age (Lewiecki, 2021; Spinelli et al., 2020). Recognizing that normal aging changes of the endocrine system are primarily related to a decrease in pancreatic function (inability to sufficiently secrete insulin) and alterations in thyroid function, the nurse practitioner needs to screen older adults periodically when signs and symptoms of underlying endocrine conditions become apparent (Cai et al., 2012). Endocrine disorders in older adults are commonly detected when screening for other medical conditions. For example, a new onset of atrial fibrillation can result from undiagnosed hyperthyroidism (Jones & Boelaert, 2015; Modawal et al., 2004), and Paget's disease may be evident when a person sustains a fracture (Cundy, 2018).

Overall, the nurse practitioner managing the care of older adults needs to differentiate among four clinical states:

1. Endocrine function that is altered relative to that of younger patients but is an expected consequence of normal aging
2. Altered endocrine function secondary to coincident nonendocrine disease, but is not of known pathological significance
3. Iatrogenic changes in endocrine function that largely reflect the polypharmacy seen in the older adult population
4. Authentic endocrinopathy (Davis et al., 2007)

Recognition of Endocrine and Metabolic Disorders

Accurate history taking of complaints associated with endocrine and metabolic disorders is essential for completing the examination of the older adult. Because changes in the endocrine system may appear subtle to the older person or atypical as compared to younger patients, it may be difficult to pinpoint the onset of the presentation (Silverman, 1990; van den Beld et al., 2018). Reevaluate the patient's family history for endocrine and metabolic disease (Resnick, 2022). Explore with the patient any difficulty with temperature regulation, changes in skin texture, or distribution of body hair. Review with the patient any episodes of unexplained weight loss or gain, new or increased fatigue, weakness, malaise, and recent infections (Ahmed & Haboubi, 2010; Leslie & Hankey, 2015).

Focusing the Endocrine and Metabolic Disorder Review of Systems

Given the vagueness or atypical presentation of endocrine and metabolic disorders in older adults, specific questions directed at these conditions are imperative during the review of systems:

- Is there any alteration in the ability to carry out activities of daily living (ADLs) or instrumental ADLs due to fatigue, lethargy, or weakness?
- Has there been any acute changes in memory or mood?
- Has there been any decrease in appetite or reported change in weight?
- Has the patient noticed any excessive thirst, appetite, or urination?
- Is the patient experiencing incontinence for the first time?
- Has the patient experienced any repeated yeast infections?
- Has the patient had a skin ulcer that has failed to heal?
- Are there any mouth ulcerations?
- Is the patient reporting lethargy or fatigue?
- Are there any new episodes of chest pain, palpitations, tachycardia, dyspnea?
- Is the patient reporting dizziness?
- Is the patient reporting any abdominal area pain?
- Has the patient noticed a new onset of constipation or diarrhea?
- Has the patient noticed any complaints of paresthesias or carpal tunnel syndrome?
- Has the patient reported any hoarseness of the voice?
- Is the patient reporting depression, irritability, or anxiety?
- Has the patient experienced vertigo or gait disturbances?
- Are there any changes in the color or texture of the skin?
- Is there any noticeable dryness to hair, loss of hair?
- Has the patient noticed any intolerance to heat, sweating, or flushing?
- Are there any changes to tolerance of cold or heat?
- Is there any new presentation of abdominal pain and associated symptoms such as nausea or vomiting?
- Any decrease in libido and is the male patient reporting impotence?
- Has the patient reported perceived loss of height?

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- Any reports of back pain?
- Any noted bone pain, especially upon rising and/or deformities in the lower extremities?
- Any recent fractures?
- Has there been any change in hearing?
- Has the patient noticed a need to change hat sizes, or do they experience marks from wearing a hat?

It is important to determine from the patient what therapeutic measures have been initiated or prescribed in the past to alleviate any of the symptoms and what response occurred following treatment (Suneja et al., 2020).

Approach to the Physical Examination

The physical examination should focus on the clinical signs of endocrine and metabolic disorders prevalent in older adults, recognizing, however, that they may present atypically. Evaluation of previously recorded vital signs, weight, and height should be completed when recording current measures; note differences that could indicate unintentional weight loss (malnutrition or frailty), vertebral fractures (reduction in inches), and alteration in temperature, pulse, respiration, and blood pressure (underlying thyroid disease). Any noted change in general appearance since previous visits should be noted. Examine the skin for changes in texture, temperature, evidence of infection and/or rashes, lesions and/or open, nonhealing wounds. Examine for any areas of hyperpigmentation such as acanthosis nigricans found in patients with endocrine disorders (Brady & Rawla, 2021). Look for evidence of eruptive xanthoma—red, yellow papules often found on the elbows or knees in patients with elevated triglycerides.

Inspect the hair distribution and note any dryness, coarseness, or brittleness of hair. Determine whether the hair distribution of the eyebrows has changed (known as madarosis or Queen Anne's sign), which is a presentation found in hypothyroidism (Kumar & Karthikeyan, 2012). Perform a thyroid examination, looking for enlargement, tenderness, and evidence of goiter or nodularity (Williams, 2009). Look for any enlargement of the skull. Examine for any noted bone deformities, such as lateral curvature of femur and anterior curvature of tibia. If positive findings, question the patient about changes in hearing and consider gross hearing screening (Cundy, 2018; Maia et al., 2014).

Note any changes to the nailbeds. Are they brittle, cracked, peeling, or discolored? When examining the hands, look for small muscle wasting of the dorsum of the hand and between the thumb and index finger. Examine for evidence of Dupuytren's contracture, which can be found in patients who have diabetes mellitus (Grazina et al., 2019).

A thorough cardiac and respiratory examination is essential given the new manifestations of conditions such as angina, atrial fibrillation, hypertension, or heart failure in patients with undiagnosed hyperthyroid disease. Has the patient reported a rapid heartbeat or palpitations? Is there any evidence of a new murmur, cardiac arrythmia, or adventitious breath sounds (Knight, 2021)?

A focused examination for suspected pancreatitis may reveal jaundice, palpable mass and, during percussion, an enlarged pancreas with tenderness being elicited when palpating the epigastrium and behind the umbilicus. There may be notable guarding and possible signs of peritoneal irritation with abdominal distension, or rigidity. In severe disease, older adults may present with impaired cognition (Quinlan, 2014).

In patients with suspected osteoporosis, physical examination may reveal skeletal deformities due to a history of fractures. Patients may exhibit a loss of height, kyphosis, or have a diminished rib-pelvis space. Consider testing the patient's balance because of the risk of falls and associated fractures (Lewiecki, 2021).

Examine the lower extremities for edema; nonpitting edema is a clinical sign of pretibial myxedema. Inspect for diabetic dermopathy, which are atrophic, brownish patches usually found on the anterior lower legs of patients with diabetes with peripheral neuropathy. Necrobiosis lipoidica diabeticorum is a rash of raised plaques that may ulcerate and are generally larger than diabetic dermopathy (Lima et al., 2017).

Neurological examination in older patients with undiagnosed diabetes mellitus may reveal alterations in temperature, vibratory sense, and sensation. A fine tremor in the fingers and hands may be noted (Jones & Boelaert, 2015). Reflexes in an older adult may be altered by abnormal thyroid function. Testing the patient's proximal and distal strength is also important because weakness can manifest in thyroid disease. As patients and/or their caregivers may report changes in behavior, or cognition, an objective assessment of mental status is warranted in patients with untreated thyroid disease (Resnick, 2022).

Medication Review

A thorough review of all medications, including over the counter medications and home remedies, is important to discern if drug-drug interactions are responsible for alterations in the absorption of medications. Certain medications may be responsible for a new onset of anorexia, diarrhea, or constipation (Elsawy & Higgins, 2011). Also do a thorough review of how the patient and/or medical facility are administering the medications (timing the doses to not conflict with food). Finally, review patient adherence to and understanding of the medication regimen.

CALCIUM DISORDERS

Signal Symptoms: Many older adults with hypocalcemia or hypercalcemia may be asymptomatic. Calcium (Ca^{2+}) disorders can erroneously be attributed to other disease processes or dangerously dismissed as an expected deviation in the aging process due to the vague presentation.

Hypocalcemia: More severe and emergent presentation of hypocalcemia could include seizures, tetany, paresthesia, laryngospasm, and prolonged QT interval.

Hypercalcemia: Shortened QT interval, headache, and in rare cases coma and stupor may also be seen. Individuals with primary hyperparathyroidism my develop life-threatening severe hypercalcemia. Symptoms can include changes in mental status (cognitive impairment, confusion), bone disease (pain), dehydration, and kidney stones. Some individuals with hypercalcemia or mild hyperparathyroidism later develop parathyroid crisis. In other individuals, a parathyroid crisis can be the

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first sign of the disorder (Fuleihan & Silverberg, 2020). Hypercalcemic crisis is defined by a rapid-onset, albumin-corrected serum calcium level greater than 14 mg/dL and signs or symptoms of multiorgan dysfunction (Wilhelm et al., 2016).

Description: The human body tightly regulates calcium to maintain physiological homeostasis to control bidirectional fluctuations in the 1% of extracellular Ca^{2+} at the level of the intestine, bone, and kidney via the parathyroid (PTH) hormone, vitamin D, and serum Ca^{2+} axis (Tinawi, 2021; Veldurthy et al., 2016). Extracellular Ca^{2+} is tightly regulated by the parathyroid gland to maintain minimal variations in extracellular Ca^{2+} (Goldfarb, 2021). PTH hormone, vitamin D, and serum Ca^{2+} are integral components of a feedback loop to maintain physiological homeostasis with minimal variance (Tinawi, 2021; Veldurthy et al., 2016). Normal serum calcium levels are 8.8 to 10.3 mg/dL (2.2–2.6 mmol/L or 4.4–5.2 mEq/L [Yu et al., 2021]). Serum calcium concentration is determined by the state of hydration and the total of calcium bound to proteins (15%, mostly albumin), calcium bound to organic and inorganic anions (40%, sulfate, citrate, phosphate, and lactate), and calcium circulating as physiologically active ionized (free) calcium (45% [Tinawi, 2021; Yu et al., 2021]). Bone is a calcium reservoir that maintains normal plasma ionized calcium concentration (Goldfarb, 2021).

Etiology: PTH is the main regulator of renal Ca^{2+}; therefore, elevation in PTH with elevated serum calcium is indicative of disease. PTH deficiency affects the gastrointestinal (GI) tract, kidneys, and bones with resulting hypocalcemia. Disruption in Ca^{2+} absorption from small intestines, bone turnover or resorption, and renal excretion adversely affects extracellular Ca^{2+}. In response to low Ca^{2+}, PTH increases, which triggers the bone to release Ca^{2+} and phosphate. The PTH triggers the kidney to increase phosphate excretion, increase calcium reabsorption, calcitriol production, and intestinal dicalcium phosphate. The net effect is an increase in serum calcium with no change in phosphate levels (Veldurthy et al., 2016).

Hypocalcemia: In the absence of PTH, homeostasis is maintained by reclaiming calcium from the kidney and GI tract and depleting skeletal calcium, leading to evidential bone mass remodeling and hyperphosphatemia (Bilezikian et al., 2016). The most common cause of hypocalcemia in an older adult is low serum albumin; therefore, measurement of the serum albumin is essential to distinguish true hypocalcemia and factitious hypocalcemia. Hypocalcemia may be acquired or hereditary. Acquired causes include hypoparathyroidism, liver or kidney disease, COVID-19, dietary deficiency, medication, and surgery (Goltzman et al., 2018).

Primary hypoparathyroidism may be due to an autoimmune response against the parathyroid gland or activating antibodies against calcium sensor receptors (CaSR) that regulate PTH secretion from the parathyroid gland (Tinawi, 2021).

Hypercalcemia: Primary hyperparathyroidism is most commonly due to a benign adenoma in 99% of the cases (Wilhelm et al., 2016). Secondary hyperparathyroidism is an adaptive parathyroid gland hyperplasia with increased production of PTH in response to another disease process.

Occurrence: Hypercalcemia due to primary hyperparathyroidism is common in the general population and affects 2 million Americans each year (Dombroskwy et al., 2018). Prevalence of primary hyperparathyroidism is higher in women (233/100,000) than men (85/100,000). Data are lacking on incidence and prevalence in transgender populations (Sluis et al., 2019). A single parathyroid adenoma is responsible for 80% to 85% of hyperparathyroidism-related hypercalcemia; double adenomas account for 4% to 5%; and parathyroid hyperplasias are seen 10% to 12% of cases (Wolfe & Sharma, 2021). Parathyroid carcinomas are very rare causes of hyperparathyroidism and account for less 1% of disease (Wolfe & Sharma, 2021).

Older adults are more likely to have undiagnosed primary hyperparathyroidism. Rationales found in the literature include lack of acknowledgement of elevated calcium, frequent provider turnover, abnormal calcium noted but not evaluated, PTH was high and symptoms were present but undiagnosed, evaluation of hypercalcemia was planned but not completed, attribution of high calcium to other reasons (chronic kidney disease [CKD], calcium supplementation) without appropriate diagnostic evaluation, patient deference, physician decision, and surgeon deference (Dombrowsky et al., 2018).

Age: Variable based on chronic disease states. Increases for both sexes with advancing age (Dombrowsky et al., 2018; Sluis et al., 2019). Primary hyperparathyroidism prevalence peaks in women 60 to 79 years of age (492/100,000) and in men older than 80 years of age (264/100,000) (Sluis et al., 2019).

Ethnicity: The incidence is highest among Blacks, followed by Whites, then Asians, Latinx, and other ethnicities.

Contributing Factors:

Hypocalcemia: Certain gadolinium-based contrast agents (gadodiamide, gadoversetamide) may cause spurious hypocalcemia by interfering with laboratory measurement of total calcium (Goltzman et al., 2018).

Hypercalcemia: Hyperparathyroidism and malignancies account for 90% of hypercalcemia (Shane, 2020). Vitamin D deficiency triggers a transient increase in PTH to maintain normal extracellular calcium levels that resolves with treatment (Sterns, 2021).

Signs and Symptoms:

Hypocalcemia: Most patients with chronic hypocalcemia are asymptomatic; however, symptoms can range from asymptomatic to life-threatening. Mild hypocalcemia may present with muscle weakness, fatigue, confusion, depression, and memory loss. Hypocalcemia may be present with other electrolyte disorders, specifically phosphorus, magnesium.

Hypercalcemia: Symptoms of chronic hypercalcemia are also nonspecific and may present with other electrolyte disorders (e.g., phosphorus, magnesium). Fatigue, increased sleepiness, vague GI symptoms (nausea, abdominal pain, constipation), and renal manifestations (polyuria, nephrolithiasis), and musculoskeletal symptoms (variable bone pain).

Diagnostic Tests: The hormone regulators for Ca^{2+} homeostasis are PTH and calcitriol (1,25 dihydroxyvitamin D [the most active form of vitamin D]) and serum ionized (free) Ca^{2+} (or albumin-bound serum Ca^{2+} corrected calculation). Abnormal total serum calcium concentration in the presence of normal ionized calcium (free) can occur in hypoalbuminemia or hyperalbuminemia and multiple myeloma.

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Laboratory Studies: Complete metabolic panel. Total serum calcium levels is variable and will change based on the amount of Ca^{2+} bound to albumin; therefore, it is important to evaluate both total and ionized (free) Ca^{2+} (Yu et al., 2021). Commonly used correction formulas have poor accuracy in a variety of populations including those with chronic kidney disease; thus, measurement of ionized calcium is the gold standard for evaluating Ca^{2+} status and confirmation of an elevated result (Yu et al., 2021).

In some instances, the ionized Ca^{2+} will differ from total serum Ca^{2+}. Confirm elevated serum calcium level with ionized calcium (Goltzman et al., 2018). If the ionized calcium level is not available, use the corrected calcium (for albumin) regardless of albumin level to confirm the calcium elevation (Shane, 2020). If used, Yu et al. (2021) suggests this formula:

$$\text{Corrected } [Ca^{2+}] = \text{Measured total } [Ca^{2+}] + (0.08 \times (4.0 - [\text{Albumin}]))$$

Upon confirmation of the elevated Ca^{2+}, measure intact PTH (elevation with elevated ionized or corrected calcium is indicative of primary hyperparathyroidism), 1, 25-dihydroxyvitamin D (if elevated, suspect lymphoma or granulomatous disease); 25-hydroxyvitamin D (elevation indicative of vitamin D toxicity). If vitamin D results are normal, consider serum protein electrophoresis and urine protein electrophoresis to evaluate for multiple myeloma. Other diagnostic tests needed are 24-hour urine calcium to evaluate absorption abnormalities, thyroid panel to evaluate for hyperthyroidism, serum magnesium (low levels may suppress PTH secretion or cause PTH resistance; associated with normal, low, or high PTH levels), and serum phosphorus (Goldfarb, 2021; Shane, 2020). Inappropriate normal PTH results refers to the failure of the homeostatic negative feedback system (and disease state), whereby calcium levels fail to suppress PTH levels as expected (Mizamtsidi et al., 2018).

Physical Examination: Findings are variable depending on the underlying cause and may be nonspecific. Acute mental confusion, hypotension, tachycardia, tachypnea, Grey-Turner's sign, Cullen's sign, Fox's sign, Chvostek's sign, and Trousseau's sign are strongly suggestive of hypocalcemia (Goltzman et al., 2018). Assess for musculoskeletal pain (pattern and intensity), cognitive impairment (possibly transient in hyperparathyroidism and responsive to parathyroidectomy), and depression. Check for ankle reflexes by having the patient place both feet firmly on the floor and then use your reflex hammer to tap behind the Achilles' tendon and feel for muscle contraction in the base of the gastrocnemius and soleus muscles.

Differential Diagnosis:

Hypocalcemia: History of present illness, past medical history, clinical clues, and electrolyte imbalances guide differential diagnosis. Autoimmune diseases; HIV; isolated, infiltrative, or pseudohypoparathyroidism; iatrogenic hypoparathyroidism post-parathyroidectomy; hungry-bone syndrome post-parathyroidectomy; and systemic illness (sepsis, acute pancreatitis, renal failure, burns, rhabdomyolysis, tumor lysis syndrome) should be considered.

Iatrogenic differentials include treatment with inhibitors of bone resorption (especially in vitamin D deficiency), cinacalcet (parathyroid calcium receptor sensitivity enhancer in chronic disease), calcium chelators, foscarnet (due to intravascular complexing with calcium), and phenytoin (due to conversion of vitamin D to inactive metabolites). Laboratory investigation should include PTH, serum phosphorus, magnesium, 25-hydroxyvitamin D, 1,25 dihydroxyvitamin D, and serum creatinine to differentiate pathophysiological etiologies.

Hypercalcemia: Differential diagnoses can be categorized by metabolic, oncological, congenital, or iatrogenic.

- **Metabolic differentials with laboratory findings**
  - Parathyroid-mediated disease (hereditary or acquired): Classic presentation—serum Ca^{2+} ↑, 24-hour Ca^{2+} ↑, PTH ↑ or inappropriately normal in comparison to calcium; bone density T-score <–2.5
  - Hyperthyroidism: Serum Ca^{2+} ↑; PTH normal or ↓; TSH ↓
  - Secondary hyperparathyroidism due to CKD: Serum Ca^{2+} varies; serum creatinine ↑, vitamin D varies
  - Sarcoidosis: Serum Ca^{2+} ↑; PTH normal or ↓; Chest x-ray: hilar adenopathy, Calcitriol ↑
  - Paget's disease: Serum Ca^{2+} ↑; PTH undetectable; alkaline phosphatase ↑; lytic or sclerotic changes on x-ray
- **Oncological**
  - Multiple myeloma: Serum Ca^{2+} ↑; ionized Ca^{2+} normal or ↑; PTH ↓; serum protein electrophoresis: monoclonal gammopathy
  - Osteopenia, osteolytic lesions, or pathological fractures
  - Secondary malignancy: Serum Ca^{2+} ↑; parathyroid hormone related protein (PTHrP) normal or ↑
- **Iatrogenic differentials for hypercalcemia (consider risk versus benefit of continuance; change in treatment or discontinuance)**
  - Lithium (~15% of long-term use)
  - Amiloride
  - Thiazide diuretics
  - Vitamin D or A toxicity
  - Teriparatide
  - Abaloparatide
  - Theophylline toxicity

(Fuleihan & Silverberg, 2020; Shane, 2020; Sterns, 2021)

Other differential diagnoses to consider include prolonged immobilization, milk-alkali syndrome (particular in postmenopausal women), granulomatous disease (tuberculosis), acromegaly, pheochromocytoma, adrenal insufficiency, or lymphoma (Shane, 2020).

Treatment: Treatment depends on the patient's goals of care, longevity, functional capacity, and the disease-related etiology and sequelae (Galassi et al., 2019).

Hyperparathyroidism can create a significant disruption in quality of life. Discuss all options and expected outcomes with all patients.

Primary Hyperparathyroidism: The standard of care to manage primary hyperparathyroidism to achieve cure is surgical removal (Kuo et al., 2019; Perrier et al., 2020; Wilhelm et al., 2016). However, this standard is less clear in older patients over the age of 85 (O'Sullivan et al., 2021; Sluis et al., 2019).

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Benefits of parathyroidectomy include advantages in survival, increased bone density, reduced fatigue, and improve subjective measures (Sluis et al., 2019). Criteria for parathyroidectomy to resolve primary hyperparathyroidism are age <50 years, serum calcium >11.3 mg/dL, T-score ≤–2.5 at any site (normal ≥–1), 24-hour urine calcium >400 mg (reference ≤300 mg/24 hr), or nephrolithiasis (likely calcium based). Additional indications for parathyroidectomy include fracture or other neurocognitive, GI, or cardiovascular sequelae of primary hyperparathyroidism (Kuo et al., 2019; Perrier et al., 2020; Wilhelm et al., 2016). Bone hunger syndrome and transient hypoparathyroidism are expected sequelae post-parathyroidectomy (Milas, 2020). Calcium supplementation is based on the elemental calcium in supplements (Kuo et al., 2019).

Medical management may include isotonic saline hydration therapy to increase calcium excretion, a calcium-sensing receptor agonist to reduce PTH (indicated for parathyroid carcinoma, secondary hyperparathyroidism in CKD), loop diuretics (judiciously), and glucocorticoids (decreases intestinal absorption), bisphosphonates (inhibit bone resorption) depending upon renal function, tolerability, and comorbid conditions (Sluis et al., 2019; Tinawi, 2021).

Secondary Hyperparathyroidism Due to Chronic Kidney Disease: Chronic kidney disease mineral and bone disorder (CKD-MBD) encompasses abnormalities in biochemicals (i.e., calcium, PTH, phosphate, and vitamin D). The approach to management is driven by the estimated glomerular filtration rate. The risk of hypercalcemia is greater than mild and symptomatic hypocalcemia; therefore, correction of vitamin D deficiency and hyperphosphatemia may be of benefit (Quarles & Berkoben, 2020). Those with end-stage renal disease (ESRD) who are symptomatic with markedly elevated PTH levels with symptoms that are recalcitrant to medical management should be referred for surgical consult. Preoperative hypocalcemia is a contraindication to surgery (Milas, 2020). Postoperatively, ESRD patients are more likely to develop transient hypocalcemia after parathyroid surgery due to hungry bone syndrome (Milas, 2020).

The prognosis for a cure of hyperparathyroidism with traditional bilateral neck exploration is more than 95%, with complication rates less than 3% (Wolfe & Sharma, 2021).

Follow-Up: Nurse practitioners are critical to appropriate and prompt diagnosis, evaluation, and management of older adults with calcium disorders. Follow-up is dependent upon therapeutic intervention (surgery versus nonsurgical management), changes made in the treatment plan, response to treatment, specialist involvement (with the primary care provider as the team leader and gatekeeper), and clinical judgment based on medical necessity. Order DEXA scan, PTH with calcium (together), measurement of renal function, intestinal resorption (24-hour urine calcium), and vitamin D every 3 to 6 months or based on medical necessity long term to monitor homeostatic stability and response to treatment.

Sequelae: Sustained elevation in PTH can cause high-turnover bone disease, fracture, hypercalcemia, osteitis fibrosa, nephrolithiasis, and hyperphosphatemia. Postsurgical risk includes hungry bone syndrome, infection, vocal cord dysfunction (rare), constipation, and transient hypocalcemia requiring aggressive calcium supplementation. Stool softeners or fiber laxatives are critical to prevent constipation from calcium supplement (Kuo et al., 2019; Wilhelm et al., 2016).

Prevention/Prophylaxis: Review diet, prescription and nonprescription medications, herbal preparations, calcium intake, and vitamin supplements to assess for milk-alkali syndrome and drug-induced hypercalcemia.

Referral: Refer to an endocrinology surgical specialist trained in parathyroidectomy if surgery is indicated and desired. A team approach including endocrinology and nephrology is indicated for these patients and those who choose conservative management and have concomitant kidney disease.

Education: Patients should be advised of the risk and benefit of all treatment options and included in the decision making process. Instruction about the complications associated with each decision (surgical or nonsurgical) should be provided in lay language verbally and in written format with family members present so the information can be reinforced.

With the exception of patients with contraindications due to ESRD or other comorbid condition, routine postsurgery care will include patient education on pain and its management, incision care, potential complications, and postoperative medications.

Medications: Anticoagulant and antiplatelet therapy resumption is under the surgeon's discretion. Calcium supplements (2,000 mg of Tums Ultra three times a day) will be needed for 1 week post-surgery. Calcium will be continued at 1,000 mg dosage three times a day. Additional calcium may be needed if symptoms of hypocalcemia develop. Daily cholecalciferol 2,000 IU is recommended (Milas et al., 2021). Concomitant vitamin D deficiency should be corrected slowly post parathyroidectomy (Milas et al., 2021; Perrier et al., 2020).

Clinical Recommendation	Evidence Rating	References
Diagnostic work-up for primary hyperparathyroidism should include repeated measurement of ionized Ca^{2+}, with PTH, creatinine, 25-hydroxyvitamin D, and 24-hour urine calcium.	A	Goltzman et al., 2018 Kuo et al., 2019 Wilhelm et al., 2016 Yu et al., 2021
Parathyroidectomy is indicated for patients with osteoporosis, hypercalciuria >400 mg/dL with increased kidney stone risk, or calcium greater than 1 mg/dL above normal, regardless of presence or absence of symptoms.	A	Kuo et al., 2019 Purkiss et al., 2020 Wilhelm et al., 2016

Continued

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Clinical Recommendation	Evidence Rating	References
Use bone imaging with dual-energy x-ray absorptiometry of the hip, lumbar spine, and distal radius to guide therapeutic decisions.	A	Kuo et al., 2019 Purkiss et al., 2020 Wilhelm et al., 2016
Parathyroidectomy is the only definitive treatment of primary hyperparathyroidism. Symptomatic patients are expected to derive clear benefits from curative surgery.	A	Kuo et al., 2019 Shane, 2020 Wilhelm et al., 2016
Criteria for parathyroidectomy to resolve primary hyperparathyroidism are age <50 years, serum calcium >11.3 mg/dL, T-score ≤–2.5 at any site (normal ≥–1), 24-hour urine calcium >400 mg (reference ≤300 mg/24 hr), or nephrolithiasis (likely calcium based).	C	Kuo et al., 2019 Wilhelm et al., 2016
Patients who choose not to undergo surgical intervention should have routine biochemical monitoring. Surgery is recommended for those who cannot follow monitoring protocols.	A	Kuo et al., 2019 Wilhelm et al., 2016
Observational studies have yielded conflicting results as to the benefits of parathyroidectomy to improve cardiovascular risk.	B	Kuo et al., 2019 Wilhelm et al., 2016
Patients with neurocognitive and or neuropsychiatric symptoms have demonstrated neurocognitive benefits of surgery vs. observation.	A	Purkiss et al., 2020 Roman & Sosa, 2007 Wilhelm et al., 2016
Treatment of secondary hyperparathyroidism in the older adult should consider physiopathology, quality of life, symptoms, subjective perception of disease, polypharmacy load, and the potential effect of treatment on disease-related outcomes.	C	Galassi et al., 2019 Sluis et al., 2019
Parathyroidectomy in the older adult is safe; therefore, age-associated morbidity should not preclude parathyroidectomy.	A	O'Sullivan et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

DIABETES MELLITUS, TYPES 1 AND 2

Signal Symptoms: Anorexia, paresthesias, proteinuria, chronic skin infections, blurred vision, nausea, gastroparesis, yeast vaginitis, impotence, fatigue, weight loss or gain, polydipsia, polyuria, polyphagia.

Description: Diabetes mellitus is a chronic state of hyperglycemia that is divided primarily into two types: type 1 and type 2. Formerly, type 1 diabetes was called *juvenile diabetes or insulin-dependent diabetes.* There are two subtypes of type 1 diabetes that have a slower onset: latent autoimmune diabetes of the adult (LADA) and latent autoimmune diabetes of the young (LADY). LADY will not be discussed in this text but is considered as a similar disease entity as LADA but occurring in the younger patient.

Type 2 diabetes was formerly called *adult-onset diabetes or non–insulin-dependent diabetes,* primarily to signify the age of onset of disease and whether insulin therapy was the required treatment. Diabetes in the older adult is increasing in prevalence—mostly due to increased life expectancy (Sesti et al., 2017). With the general population living longer, risk for diabetes goes up for many, including multi-organ functional alterations, impaired function of insulin secreting beta cells, impaired insulin sensitivity, age-related variations in body composition including a reduction in fat-free mass such as muscle, bone, and water, as well as functional impairments (Sesti et al., 2017). This combination of normal changes with aging and lack of typical presentation results in the underdiagnosis of diabetes in the older adult.

Etiology: Type 1 diabetes most often occurs in childhood. It is characterized by low or absent levels of insulin, often resulting from an autoimmune response leading to pancreatic beta cell antibodies. Individuals with type 1 diabetes require insulin therapy for survival. Type 2 diabetes usually occurs in adulthood and is thought to be the result of insulin resistance and deficiency. This early understanding of diabetes has been expanded by the discovery of other hormones involved in the regulation of glucose, including insulin, glucagon, amylin, and incretin hormones. These discoveries have resulted in new classes of medications to treat diabetes. Genetic predisposition for developing diabetes is more evident in type 2 diabetes. Hyperglycemic states that have not reached levels that warrant a type 2 diabetes diagnosis are identified as impaired glucose tolerance. Evidence indicates that individuals with impaired glucose tolerance have an increased risk of developing type 2 diabetes within 5 to 10 years of onset.

LADA accounts for 2% to 12% of all patients with diabetes (Buzzetti et al., 2020). LADA has features of both type 1 and type 2 diabetes and has considerable variability; however, because of its autoimmune nature it is considered a part of the type 1 diabetes spectrum with slow but variable beta cell failure (Buzzetti et al., 2020).

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Occurrence: According to the Centers for Disease Control and Prevention (CDC, 2020), it is estimated that 34.2 million people in the United States, or approximately 10.5% of the population, have diabetes, and of those, 7.3 million people (21.4% are undiagnosed). Type 1 diabetes is only about 5% to 10% of that total. There are 88 million people older than the age of 18 in the United States with prediabetes, which is 34.5% of the total adult population. Of those, 24.2 million are 65 years of age or older. Type 1 diabetes and LADA affect men and women equally. Type 2 diabetes affects men more commonly than women.

Age: The onset of type 1 diabetes usually occurs in childhood, with the major incidence of disease occurring in individuals younger than 30 years old. Onset of LADA occurs after age 30 years (Buzzetti et al., 2020). The onset of type 2 diabetes usually occurs after age 40 years, with a mean age of 51 years. Age, however, cannot be the only factor used to determine the classification of diabetes because type 1, LADA, or type 2 diabetes can occur at any age.

Ethnicity: Type 1 diabetes primarily affects individuals who are White. LADA is reported more frequently in individuals of northern European and Chinese descent, compared with African American and Hispanic individuals (Buzzetti et al., 2020). Native Americans and Alaskan Natives have the highest prevalence of type 2 diabetes for both men and women, with non-Hispanic African Americans and Hispanics next, followed by Whites and Asian Americans.

Contributing Factors: Although the exact causes of type 1 diabetes and LADA are unknown, they have been linked to environmental, autoimmune, and viral toxins. A predisposition for acquiring type 1 diabetes has not been identified. Contributing factors for the development of type 2 diabetes have strongly been associated with obesity, sedentary lifestyle, and familial history. The following risk factors have been identified as significantly increasing an individual's risk of developing type 2 diabetes: age 45 years and older, a positive family history (parents or siblings with diabetes), hyperlipidemia, a history of gestational diabetes, obesity (body mass index [BMI] greater than or equal to 25 kg/m^2), smoking, physical inactivity (exercising less than 150 minutes per week, spread over 3 days [American Diabetes Association (ADA), 2021]), high blood pressure (greater than 140/90 mm Hg,), and a history of impaired fasting glucose or impaired glucose tolerance.

There is a known association between the use of statin drugs and increased insulin resistance and progression to diabetes (Mansi et al., 2021). High-potency statins are particularly diabetogenic, causing insulin insensitivity and decreased insulin secretion. Pravastatin is the least diabetogenic statin. The value of statins' ability to decrease the risk of cardiovascular disease outweighs the risk of developing diabetes, but it does provide another indication for vigilant monitoring for the development of diabetes. The greater number of risk factors present increases the risk of development of the disease.

Signs and Symptoms: Among adults 40 years and older, diabetes often is discovered as an incidental finding during the work-up for cardiovascular, renal, neurological, or infectious diseases. The primary presentation may be due to complications of underlying and undiagnosed hyperglycemia in conditions such as stroke, myocardial infarction (MI) and ischemia, intermittent claudication, impotence, peripheral neuropathy, proteinuria, retinopathy, slow wound healing, or fatigue. Often the classic symptoms of polyuria, polydipsia, and polyphagia with weight loss are attributed to other disease entities and overlooked among older adults. The classic triad may be absent entirely due to an impaired thirst mechanism and an increased renal threshold for glucose. Screening is recommended for adults of any age who are overweight and present with any of the additional risk factors (ADA, 2021). Screening should begin for the general population at 45 years old and be repeated at 3-year intervals. More frequent and earlier screening is recommended for individuals with several risk factors.

The determination of whether the diabetes is type 1, LADA, or type 2 is based on a variety of characteristics to include age of onset, serum markers of autoimmunity and beta cell function, and BMI. The most definitive diagnostic tools available to distinguish between them include the use of antibody testing and testing C-peptide levels. In terms of antibody testing, glutamic acid decarboxylase antibody (GADA) is considered the most sensitive marker of autoimmune type 1 diabetes and LADA, with approximately 90% of patients with type 1 diabetes and LADA being positive (Buzzetti et al., 2020). Antibodies to islet cells and beta cells are present in 70% to 80% of individuals with type 1 diabetes. In terms of beta cell function, C-peptide is a by-product of insulin production, and extremely low levels are consistent with type 1 diabetes. Type 2 diabetes primarily occurs in individuals who are 40 years and older, and have a BMI of more than 27, as well as preservation of beta cell function (albeit with some decline). Beta cell function should be quantified anytime a diagnosis of diabetes is made and needs to be repeated and monitored because it can vary with disease progression. C-peptide should be checked with any significant loss of glycemic control or any development of ketonemia.

Diagnostic Tests: The criterion for the diagnosis of diabetes is either two fasting blood glucose readings with results greater than or equal to 126 mg/dL or a random blood glucose reading greater than or equal to 200 mg/dL if symptoms of diabetes are present. In many people older than the age of 60, diabetes and prediabetes is not diagnosed unless an oral glucose tolerance test (OGTT) is performed (LeRoith & Halter, 2020). This is due in part to the physiological changes in glucose regulation that occur as a result of aging (Lodhi, 2021). Therefore, diabetes will be diagnosed sooner with the OGTT than with fasting glucose alone. Hemoglobin A1c (Hb A1c) measurement greater than or equal to 6.5 is indicative of type 2 diabetes (ADA, 2021). In the absence of unequivocal disease, the same test should be repeated at least once; so, for example, if the Hb A1c is greater than or equal to 6.5, a second Hb A1c result should be compared rather than comparing it to a fasting glucose level (ADA, 2021). An advantage of using the Hb A1c is that fasting is not required and it is less effected by day-to-day issues in the patient, such as illness or stress. An individual with a casual plasma glucose level greater than or equal to 200 mg/dL, but without symptoms, should have fasting plasma glucose, 2-hour OGTT, or Hb A1c measured. Fasting is defined as no caloric intake for at least 8 hours. Parameters for the estimated average glucose levels based on Hb A1c levels can be found in Table 18-1.

When hyperglycemia has been established, C-peptide levels and GAD antibodies will help to differentiate between

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TABLE 18-1 Comparison of Hb A1c to Average Glucose Level

Hb A1c (%)	GLUCOSE (MG/DL)
6.0	126
6.5	140
7.0	154
7.5	169
8.0	183
8.5	197
9.0	212
9.5	226
10.0	240

Source: Adapted from American Diabetes Association. (2010). https://diabetes.org/diabetes/a1c

type 1 and type 2 diabetes. C-peptide levels can vary. At the onset of type 1 diabetes, there may be some lingering beta cell function, thus C-peptide alone is not enough to help make the diagnosis; GAD antibodies should also be measured. After about 1 year those with type 1 diabetes will usually have undetectable C-peptide levels as beta cell function declines. This process often takes much longer in LADA. With type 2 diabetes, varying levels of C-peptide are usually detectable throughout the disease.

Differential Diagnosis:

- Drug toxicity and endocrine disorders that may affect glucose tolerance, interfere with insulin secretion, and induce insulin resistance.
- Drugs associated with hyperglycemia include alcohol, beta-adrenergic agents, calcium channel blockers, corticosteroids, lithium salts, rifampin, asparaginase, diazoxide, diuretics, glycerol, niacin, phenytoin, and sympathomimetics.
- Drugs associated with hypoglycemia include anabolic steroids, beta-adrenergic blockers, chloroquine, disopyramide, pentamidine, salicylates, warfarin, ethanol, and sulfonamides.
- Endocrine disorders that may induce hyperglycemia include Cushing's syndrome, glucagonoma, acromegaly, and pheochromocytoma.

Treatment: The goal of treatment for patients with type 2 diabetes is good glycemic control, good nutritional status with weight management, and exercise. Evidence shows that patients with type 2 diabetes benefit from maintaining near-normal glucose levels. The 2021 ADA Diabetes Standards of Care outline recommendations for glucose control, blood pressure goals, cholesterol goals, and recommendations for screening for both microvascular and macrovascular complications. They recommend patient-centered care plans with individualized goals based on several factors, including duration of diabetes, age/life expectancy, comorbid conditions, known cardiovascular disease (CVD) or advanced microvascular complications, hypoglycemia unawareness, and individual patient considerations. The specific framework that the ADA utilizes is broken up into three categories based on the presence of chronic illnesses and functional status: healthy, complex/intermediate, and very complex/poor health. For example, fasting values vary from 80 to 130 and an Hb A1c target of 7% to 7.5% for the healthy older adult to a fasting value of 100 to 180 and avoiding reliance on the Hb A1c for clinical judgment and instead making decisions based on prevention of hypoglycemia and symptomatic hyperglycemia in those with very complex/poor health (Table 18-2). These new guidelines are based in part on the data from the Action to Control Cardiovascular Risk in Diabetes (ACCORD) study, which concluded that the risk of hypoglycemia and the morbidity resulting from those episodes may outweigh the benefits of tighter control. Aggressive glycemic control that compromises functional independence and quality of life and increases the risk of hypoglycemic episodes would be counterproductive.

The 2021 ADA recommendations focus on patient-centered care plans that include head-to-head trials of antihyperglycemic agents. Treatment goals and the choice of agent to reach those goals should be made after a careful assessment of the patient's health beliefs, comorbidities, life expectancy, cognitive function, functional status, economic situation, and availability of support services.

Nonpharmacological Treatment: Nonpharmacological therapy is recommended as first-line therapy for newly diagnosed type 2 diabetes with mild-to-moderate hyperglycemia. Lifestyle modifications of weight loss and exercise are particularly important in lowering Hb A1c. Although weight loss in frail older adults is not recommended due to the risk of sarcopenia, exercise of even a modest nature can be beneficial in decreasing insulin resistance. If after 3 to 6 months nonpharmacological treatment fails or the hyperglycemia is severe (fasting plasma glucose 200 to 300 mg/dL or casual plasma glucose 250 to 350 mg/dL), oral agents may be added to the treatment regimen. Metformin is also recommended for prevention or delay of type 2 diabetes in patients with a BMI greater than or equal to 35 kg/m^2 or anyone with a history of gestational diabetes or patients with a rising Hb A1c despite lifestyle modifications (ADA, 2021).

Pharmacological Treatment: Pharmacological treatment options for diabetes include oral agents and injectable agents. There are now seven classes of oral glucose-lowering agents: biguanides, sulfonylureas, meglitinides, thiazolidinediones, dipeptidyl peptidase-4 (DPP-4) inhibitors, alpha-glucosidase inhibitors, sodium-glucose cotransporter 2 (SGLT2) inhibitors, and one oral preparation of a glucagon-like peptide–1 (GLP-1) receptor agonist. Other oral agents that may be used in the management of type 2 diabetes include the bile acid sequestrant and the dopamine-2 agonist. Injectable agents include insulin and the GLP-1 receptor agonists.

Oral Agents: Metformin (Glucophage, Glucophage XR) is a biguanide that acts by decreasing hepatic glucose production, decreasing glucose intestinal absorption, and increasing insulin sensitivity. It is considered first-line therapy in treating type 2 diabetes and may be initiated with lifestyle changes in many individuals (ADA, 2021). This agent generally does not increase endogenous insulin production and has few hypoglycemic effects. In addition to glucose control with improved Hb A1c of 1% to 2%, patients may lose weight and improve lipid profiles.

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TABLE 18-2 **Framework for Considering Treatment Goals for Glycemia, Blood Pressure, and Dyslipidemia in Older Adults With Diabetes**

PATIENT CHARACTERISTICS/ HEALTH STATUS	RATIONALE	REASONABLE A1c GOAL‡	FASTING OR PREPRANDIAL GLUCOSE	BEDTIME GLUCOSE	BLOOD PRESSURE	LIPIDS
Healthy (few coexisting chronic illnesses, intact cognitive and functional status)	Longer remaining life expectancy	<7.0–7.5% (53–58 mmol/mol)	80–130 mg/dL (4.4–7.2 mmol/L)	80–180 mg/dL (4.4–10.0 mmol/L	<140/90 mm Hg	Statin unless contraindicated or not tolerated
Complex/intermediate (multiple coexisting chronic illnesses* or 2+ instrumental ADL impairments or mild-to-moderate cognitive impairment)	Intermediate remaining life expectancy, high treatment burden, hypoglycemia vulnerability, fall risk	<8.0% (64 mmol/mol)	90–150 mg/dL (5.0–8.3 mmol/L)	100–180 mg/dL (5.6–10.0 mmol/L)	<140/90 mm Hg	Statin unless contraindicated or not tolerated
Very complex/poor health (LTC or end-stage chronic illnesses** or moderate-to-severe cognitive impairment or 2+ ADL impairments)	Limited remaining life expectancy makes benefit uncertain	Avoid reliance on A1c; glucose control decisions should be based on avoiding hypoglycemia and symptomatic hyperglycemia	100–180 mg/dL (5.6–10.0 mmol/L)	110–200 mg/dL (6.1–11.1 mmol/L)	<150/90 mm Hg	Consider likelihood of benefit with statin

This table represents a consensus framework for considering glycemic treatment and treatment goals for glycemia, blood pressure, and dyslipidemia in older adults with diabetes. The patient characteristic categories are general concepts. Not every patient will clearly fall into a particular category. Consideration of patient and caregiver preferences is an important aspect of treatment individualization. Additionally, a patient's health status and preferences may change over time. ADL, activities of daily living; LTC, long-term care.

‡A lower A1c goal may be set for an individual if achievable without recurrent or severe hypoglycemia or undue treatment burden.

**Coexisting chronic illnesses are conditions serious enough to require medications or lifestyle management and may include arthritis, cancer, heart failure, depression, emphysema, falls, hypertension, incontinence, stage 3 or worse chronic kidney disease, myocardial infarction, and stroke.*

*** The presence of a single end-stage chronic illness, such as stages 3–4 heart failure or oxygen-dependent lung disease, chronic kidney disease requiring dialysis, or uncontrolled metastatic cancer, may cause significant symptoms or impairment of functional status and significantly reduce life expectancy.*

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Side effects include nausea, vomiting, diarrhea, abdominal pain, anorexia, and taste disturbances.

A rare but potentially life-threatening reaction is the development of lactic acidosis. Metformin is contraindicated in patients with renal insufficiency because the risk of lactic acidosis is increased in these patients as metformin depends on adequate renal function for clearance from the body. Although uncommon, lactic acidosis has a very high mortality rate. The estimated glomerular filtration rate (eGFR) at which metformin was contraindicated had been less than 60, but recent recommendations are that it may be used safely in patients with estimated glomerular filtration rate ≥30 mL/min/1.73 m (ADA, 2021). In hospitalized patients at risk for acute or chronic renal insufficiency, consider holding metformin. Other contraindications include hepatic insufficiency, heart failure, and alcohol abuse.

Care should be taken when patients who are taking metformin undergo IV contrast studies. It is important to withhold the medication for 1 to 2 days after the contrast agent has been administered to ensure normal renal function. Usually, metformin is started at 500 mg once a day, given before the evening meal, and increased gradually to a maximum dose of 2,000 mg daily in the older adult. This slow uptitration can minimize gastrointestinal (GI) side effects that can result in patient intolerance. When given with food, the GI side effects tend to be decreased and absorption is increased. An extended-release formulation is available and may be very useful for increasing adherence to therapy and decreasing side effects. When switching from regular release to extended-release metformin, the total daily dose should remain the same. For some patients on 2,000 mg of extended release a day, dividing the dose into two 1,000 mg tablets may be more effective.

Sulfonylureas are insulin secretagogues and act by increasing pancreatic insulin secretion. They tend to lower Hb A1c by 1% to 2% (Cornell, 2014). The second generation sulfonylureas include glipizide (Glucotrol, Glucotrol XL), glimepiride (Amaryl), and glyburide (DiaBeta, Micronase, Glynase). All of these preparations with the exception of glipizide are on the *Beers List: Potentially Inappropriate Drugs for Elderly* and, along with the first generation agents (chlorpropamide, tolazamide, and tolbutamide), should be avoided. They may be continued only in patients who are already adequately controlled on those medications and not experiencing side effects. Because sulfonylureas are renally cleared and renal function declines with aging, an increase of the level of sulfonylurea in the blood may result in an increased risk of hypoglycemia. If sulfonylureas are used, the preferred choice would be glipizide because it has the shortest half-life. Side effects of this class of medications include weight gain, nausea, hypoglycemia, weakness, and photosensitivity. These agents should not be used in patients who have had diabetic ketoacidosis and caution should be exercised in patients who are allergic to sulfonamides. The starting dose depends on the particular drug but should be initiated at the lowest possible dose and increased as tolerated.

Meglitinides are another class of insulin secretagogues and include nateglinide (Starlix) and repaglinide (Prandin). They act quickly to increase the endogenous release of insulin from the pancreas and must be taken 1 to 30 minutes before a meal, typically three times a day. They have less effect on Hb A1c than sulfonylureas, with about a 1% reduction (Cornell, 2014). Though frequent dosing may be seen as a drawback, it can be an advantage in patients with irregular eating habits when the medications are not taken if a meal is skipped. Side effects include hypoglycemia, headache, upper respiratory infection, nausea, vomiting, constipation, diarrhea, muscle aches, and chest pain. Repaglinide is metabolized by the liver, with less than 10% renally excreted, and does not need dose adjustment in renal insufficiency. It is also somewhat better in lowering Hb A1c than nateglinide, so repaglinide can be initial therapy in patients who are not candidates for metformin or sulfonylureas. All insulin secretagogues should be used with caution in those with hepatic insufficiency.

Thiazolidinediones (TZDs), which include pioglitazone (Actos) and rosiglitazone (Avandia), are insulin sensitizers. They act by increasing sensitivity to insulin by acting on adipose, muscle, and liver to increase glucose utilization and decrease hepatic glucose production. TZDs have a favorable effect on lipids and can improve beta cell function. They reduce Hb A1c by 1% to 1.5% (Cornell, 2014). Side effects include headache, weight gain, edema, and anemia. TZDs should not be used in patients with heart failure, bladder cancer, osteoporosis, or liver disease. Serious reactions include liver toxicity and worsening heart failure. Liver function tests should be performed prior to initiation and periodically after that. TZDs have a very slow onset of action. Initial effects are noted in 2 weeks, but as monotherapy the maximum effect is not seen for 10 to 16 weeks.

Dipeptidyl peptidase-4 (DPP-4) inhibitors include sitagliptin (Januvia), linagliptin (Tradjenta), saxagliptin (Onglyza), and alogliptin (Nesina). All are once-daily oral medications that help the body reduce its own blood sugar levels. They have a unique action by inhibiting the enzyme DPP-4, which breaks down GLP-1, thereby increasing the bioavailability of GLP-1. GLP-1 is secreted by the small intestinal L cell, and it is a potent anti-hyperglycemic hormone that works by glucose-dependent insulin stimulation (so the risk of hypoglycemia is low). It also suppresses inappropriate glucagon secretion, slows gastric emptying, and reduces food intake. DPP-4 inhibitors also improve beta cell function. Hb A1c reduction is comparable to that of sulfonylureas and TZDs (Cornell, 2014). When used as monotherapy, DPP-4 inhibitors have a low risk of hypoglycemia but may increase the risk of hypoglycemia when used with sulfonylureas. Side effects of DPP-4 inhibitors include upper respiratory tract infection, nasopharyngitis, and headache. Dose reduction in patients with moderate to severe renal insufficiency is required for all DPP-4 inhibitors except linagliptin, and they should not be used in patients with a history of pancreatitis.

The alpha-glucosidase inhibitors acarbose (Precose) and miglitol (Glyset) act to decrease or delay glucose absorption and lower blood glucose levels. Serum triglycerides tend to be lowered also, and this may be their greatest benefit. Side effects include flatulence, diarrhea, abdominal pain, and rash. Both are dosed three times a day and should be taken with the first bite of each meal. This class of medications is contraindicated in patients who have had ketoacidosis, inflammatory bowel disease, intestinal obstruction, or renal impairment. The primary side effect of these medications is flatulence and patients' lack of tolerance to this side effect results in this class rarely being used. There is only a minor reduction in Hb A1c, 0.8%, which further contributes to their minor clinical usefulness.

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The newest addition to the oral options is the SGLT2 inhibitors, dapagliflozin (Forxiga), canagliflozin (Invokana), empagliflozin (Jardiance), and ertugliflozin (Steglatro). They block glucose reabsorption in the proximal renal tubule by inhibiting the action of SGLT2, which reduces glucose reabsorption and increases urinary glucose excretion. The action of SGLT2 inhibitors is not dependent on insulin and has a modest effect on glucose lowering (ADA, 2021). Specific to the brand Invokana (canagliflozin) is a black box warning regarding a twofold increase of leg and foot amputation in those patients with type 2 diabetes and established cardiovascular disease. Risk factors include prior amputation, history of peripheral vascular disease, neuropathy, and history of diabetic foot ulcers. The recommendation is to monitor patients at risk for infection, new pain or tenderness, and sores or ulcers on lower extremities.

The choice of an appropriate oral agent is a complex clinical decision. The SGLT2 inhibitors empagliflozin, canagliflozin, and dapagliflozin have also demonstrated benefit for cardiorenal outcomes, especially for heart failure hospitalization, risk of kidney disease progression, and mortality (ADA, 2021). When compared with placebo, the GLP-1 receptor agonists liraglutide, semaglutide, and dulaglutide demonstrated favorable atherosclerotic cardiovascular and renal outcomes (ADA, 2021). These benefits were found serendipitously when certain agents were being tested for cardiovascular effects as a standard set forth by the FDA for all diabetic drugs. In 2008, the U.S. Food and Drug Administration added long-term cardiovascular outcomes trials as another safety step in the approval process for diabetes agents because of the possible adverse cardiovascular effects of some diabetes drugs that came to light well after they had been approved (Seaborg, 2020).

Based on these findings, the American Diabetes Association Standards of Medical Care (2021) recommend that patients with type 2 diabetes who have established atherosclerotic cardiovascular disease or indicators of high risk, established kidney disease, or heart failure include a sodium-glucose cotransporter 2 inhibitor or glucagon-like peptide 1 receptor agonist with demonstrated cardiovascular disease benefit as part of the glucose-lowering regimen independent of A1c and in consideration of patient-specific factors (ADA, 2021). Other considerations for selection of agents include the severity of the hyperglycemia and the need for Hb A1c reduction. The newest guidelines specifically indicate that a biguanide (metformin) should be the first-line agent; however, if atherosclerotic heart disease, heart failure, or chronic kidney disease exists—independent of A1c, A1c target, or metformin use—an SGLT2 inhibitor or GLP-1 agonist should be initiated (ADA, 2021).

If there are contraindications to the use of metformin, GLP-1 RA, or SGLT2-inhibitors, a sulfonylurea could be an alternative, keeping in mind that it carries the risk of hypoglycemia and often results in weight gain. DPP-4 inhibitors are another possibility for initial treatment with a similar effect on Hb A1c to that of sulfonylureas without the risk of hypoglycemia, but they are expensive. The newest agents, SGLT2 inhibitors, are also approved for monotherapy, but are also expensive and have less effect on Hb A1c. If monotherapy with any of these agents is unsuccessful after 3 months, combination therapy with metformin, sulfonylurea, thiazolidinedione, DPP-4 inhibitors, SGLT2 inhibitors, GLP-1 receptor agonists, or basal insulin should be considered. If irregular meals are an issue, adding a meglitinide to either metformin or a DPP-4 inhibitor, or an SGLT2 inhibitor may be a reasonable option. The injectable glucagon-like peptide–1 (GLP-1) receptor agonists are non-insulin options for combination therapy and have a side benefit of weight loss as well as the cardiorenal benefits mentioned above. Insulin therapy is a reasonable choice at any point in the patient diagnosed with type 2 diabetes, but it is usually reserved as second-line therapy when combination therapy fails. Insulin therapy may be required either as a single agent or in addition to a sulfonylurea, metformin, DPP-4 inhibitor, SGLT2 inhibitor or GLP-1 agonist.

Injectables: Glucagon-like peptide–1 (GLP-1) receptor agonists are within the drug class called incretins. Those available in the United States include exenatide (Byetta), liraglutide (Victoza), lixisenatide (Lyxumia), albiglutide (Tanzeum), dulaglutide (Trulicity), and semaglutide (Ozempic). Unlike endogenous GLP-1, these medications are resistant to degradation by the DPP-4 enzyme and have a longer half-life than endogenous GLP-1. These medications are effective in reducing glucose levels, as well as inducing weight loss, and also have the added benefit of improving cardiovascular and renal outcomes as outlined above. They can lower Hb A1c by 0.5% to 1.5% and can induce weight loss of 2% to 5%. They may also be prescribed for patients with impaired fasting glucose to delay the onset of type 2 diabetes. Side effects include nausea and a feeling of fullness that may dissipate after a few weeks of treatment. Other common side effects include hypoglycemia when used with sulfonylureas or insulin, vomiting, diarrhea, headache, nervousness, and stomach discomfort. Patients may also experience decreased appetite, acid reflux, and increased sweating. GLP-1 agonists are contraindicated for use in type 1 diabetes and patients with a history of diabetic ketoacidosis. A black box warning exists for patients with medullary thyroid carcinoma or a family history of that disease or with multiple endocrine neoplasia syndrome type 2 (MEN2). GLP-1 agonists should be used with caution in patients with a history of pancreatitis or gastroparesis. All of these drugs are expensive, but the benefits may outweigh the cost.

Insulin Therapy

After many years of having type 2 diabetes, almost all patients will require insulin therapy due to the decline of beta cells in the pancreas and endogenous insulin supply. The body's normal production of insulin is biphasic, with about one-half slowly released around the clock to suppress glucagon release from the liver between meals and while we sleep, and one-half released in response to a rise in blood sugar after food intake. Insulins are the most natural agents and are always effective in lowering blood sugar. They all work alike; the difference is in the onset and duration of action. Insulin therapy may be added when optimal glycemic control is not achieved with an oral regimen or the addition of a GLP-1 agonist.

Every patient with type 2 diabetes needs to understand that the longer they live with diabetes the more likely it is that they will need to use insulin. The ADA Standards of Medical Care in Diabetes 2021 emphasize the importance of introducing the role of insulin from the beginning to avoid the implication that insulin is punishment for poor diabetic

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control. Insulin should always be used as first-line therapy in type 1 diabetes or with patients who have had diabetic ketoacidosis. A variety of regimens are used in the administration of insulin based on the time of onset of action, time of peak effects, and the duration of action. Currently, the most frequently used regimen is the basal/bolus insulin concept. This reflects the body's physiological insulin response. Basal insulins have an intermediate to long duration of action, whereas bolus insulins, which are immediate or rapid in their action, provide postprandial coverage.

Basal Insulins: Basal insulins suppress glucose production between meals and overnight and provide nearly constant levels of insulin. Basal insulin includes the intermediate-acting insulin, neutral protein Hagedorn (NPH); long-acting insulins, glargine (Lantus, Toujeo, Basaglar) and insulin detemir (Levemir); and ultra-long-acting insulin, degludec (Tresiba). Head-to-head studies comparing insulin glargine to NPH found a higher incidence of hypoglycemia and increased weight gain with the NPH (Owens et al., 2017). Administration of insulin glargine and detemir in the morning had even less incidence of nighttime hypoglycemia. Whereas NPH insulin has a distinct peak of action at 4 to 12 hours, insulin glargine and detemir are considered to have no peak. NPH and insulin detemir both may be dosed twice a day.

Bolus Insulins: Mealtime bolus insulins include regular human insulin and the analogues aspart (NovoLog), glulisine (Apidra), or lispro (Humalog). Regular insulin is considered fast acting, with an onset and duration of action that exceeds that of the analogues. It is given 30 minutes before eating and has a peak in 2 to 4 hours. The analogues are considered immediate acting, with an onset within 15 minutes and a peak in 1 to 2 hours. The analogues should not be given until the person is eating and may be given immediately after a meal if the injection was forgotten. Bolus insulins have the advantage of being adaptable to the day. Less can be given if the person is exercising after a meal, and they may not be given at all if a meal will be missed. It is important to understand how to adjust the dose of bolus insulin. It is not sliding scale adjusted in response to the pre-prandial glucose of the meal that is about to be consumed, but rather it should be adjusted based on the preprandial glucose of the next meal (so the dose given at breakfast would be changed based on the lunchtime pre-prandial glucose).

Premixed insulin combinations of long- and short-acting insulins are available and offer less control but more convenience than the basal/bolus concept. A classic mixture has been the combination of NPH and regular insulin 70/30, with the NPH being 70% and Regular being 30% of that mixture. By adding protamine to insulin aspart or insulin lispro, the release of those insulins is delayed. Humalog mix is the delayed-acting insulin lispro protamine and the immediate-acting lispro and is available as 50/50 or 75/25. The protamine lispro is 75% of that mixture and the immediate-acting lispro is 25%. Novolog mix 70/30 is the delayed-acting insulin aspart protamine with the immediate-acting aspart. The insulin protamine aspart is the 70% and the immediate-acting aspart is 30% of that solution. These mixtures are often dosed twice a day before breakfast and again before dinner.

Although the ability to control mealtime spikes in blood glucose is decreased with these split mixed insulins, the fact that fewer injections are required may be more agreeable to the patient. The participation of the patient in decision making is an essential part of individualized care. To further improve convenience of administration, insulin pens are available for all of these mixtures. Insulin pens are not self-explanatory, however, and taking the time to demonstrate their use with the patient returning the demonstration is essential for accurate insulin administration. Insulin pumps are available and most often used for type 1 diabetes. Documentation of very low C-peptide levels is often required for coverage of insulin pumps by insurance companies. The types of insulin, their onset, peak, and the duration of action and how the insulin is normally used are delineated in Table 18-3.

The frequency and timing of self-monitoring of blood glucose levels (SMBGs) need to be individualized based on several factors, including age, ability to adhere, and oral versus insulin therapies. SMBG aids in promoting glycemic control and reinforcing adherence to therapy. Even patients maintaining glucose levels by nonpharmacological means may benefit from intermittent SMBG either postprandial or fasting. Patients requiring oral medications who are capable of SMBG should test glucose levels two to three times per week, preferably alternating before breakfast, the evening meal, and at bedtime, as well as an occasional 2-hour postprandial measurements. Patients receiving insulin therapy should perform SMBG at least two to three times daily. For all patients with diabetes, SMBG monitoring should increase during illness, changes in diet and exercise, or a change in medications.

Follow-Up: Patients with diabetes should be scheduled for appropriate follow-up to evaluate response, tolerability to therapy, goal reassessment, and management of acute and chronic complications. Response to treatment is judged based on home glucose monitoring results and Hb A1c. The Hb A1c reflects the average control over the past 3 months and is not useful for judging the response to recent treatment adjustments. Older patients and patients on insulin therapy may need to be seen every 3 months. When there is a sudden change in health status or treatment regimen, follow-up of 1 month or less may be indicated. For stable patients who are able to maintain treatment goals, follow-up may be every 3 to 6 months.

The following evaluations are recommended at follow-up visits: blood pressure, review records of home glucose monitoring, review of medications, examination of the feet for complications, annual eye examination including dilation of pupils and inspection of retina and eye grounds, routine urinalysis including evaluation for albuminuria and albumin to creatinine ratio, serum creatinine levels and eGFR, annual electrocardiogram and fasting lipid profile, Hb A1c every 3 to 6 months, evaluation for neurovascular complications, self-management education, immunization update including influenza and pneumococcal vaccines, and a biannual oral examination. A special nutritional benefit is available from Medicare for patients with diabetes and should be taken advantage of yearly. Medicare also covers the yearly ophthalmological examination for patients with diabetes.

Sequelae: Acute complications requiring immediate attention include diabetic ketoacidosis, recurring fasting hyperglycemia of greater than 300 mg/dL, Hb A1c of greater than 13%, or severe hypoglycemia with changes in sensorium, altered behavior, seizures, or coma. Complications resulting from

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TABLE 18-3 Insulin Types—Onset, Peak, Duration of Action, and Typical Use

TYPE OF INSULIN (INCLUDES BRAND NAMES)	ONSET OF ACTION	PEAK ACTION	DURATION OF ACTION	ROLE OF INSULIN IN MEAL PLANS
Rapid Acting				
Lispro (Humalog)	15–30 min	30–90 min	3–5 hr	Take at same time as meal along with longer-acting insulin.
Aspart (Novolog)	10–20 min	40–50 min	3–5 hr	
Glulisine (Apidra)	20–30 min	30–90 min	1–2.5 hr	
Short Acting				
Regular-Humulin or Novolin	30 min–1 hr	2–5 hr	5–8 hr	Take within 30–60 min of eating along with longer-acting insulin.
Vesosulin (pump)		2–3 hr	2–3 hr	
Intermediate Acting				
NPH (N)	1–2 hr	4–12 hr	18–24 hr	Covers insulin needs for one-half day or overnight. Often combined with rapid- or short-acting insulin.
Long Acting				
Glargine (Lantus, Toujeo)	1–1.5 hr	No peak	20–24 hr	Covers up to 1 full day. May be combined with short- or rapid-acting insulin.
Detemir (Levemir)	1–2 hr	6–8 hr	Up to 24 hr	
Ultra Long Acting				
Degludec (Tresiba)				Greater than 24-hr coverage but dosed daily and may be combined with short or rapid acting insulin.
Premixed				
Humulin 70/30	30 min	2–4 hr	16–24 hr	Usually taken twice a day before meals. Premixed are combination intermediate- and short-acting insulin. The numbers indicate how much of each type of insulin.
Novolin 70/30	30 min	2–12 hr	Up to 24 hr	
Novolog 70/30	10–20 min	1–4 hr	Up to 24 hr	
Humulin 50/50	30 min	2–5 hr	18–24 hr	
Humalog mix 75/25	15 min	0.5–2.5 hr	16–20 hr	

prolonged hyperglycemia include renal failure, blindness, coronary artery disease, stroke, peripheral vascular disease, slow-healing wounds, autonomic neuropathies, hypertension, sexual problems, and genitourinary system disorders. Macrovascular complications from diabetes substantially increase the risk of morbidity and death from coronary artery disease, stroke, and peripheral vascular disease. End-stage renal disease and lower extremity amputations may also occur. Complications may result from either type 1 or type 2 diabetes. Evidence indicates that the degree of severity with respect to microvascular, neuropathic, and possibly macrovascular complications seems in part to be related to the number of years a patient has had hyperglycemia and the magnitude of the glucose elevation.

Prevention/Prophylaxis: The focus of prevention for developing type 2 diabetes is diet modification and exercise with subsequent weight loss. In adults with obesity and diabetes even a modest weight loss of 7% can improve glycemic control (ADA, 2021). When a patient is diagnosed with type 2 diabetes, the maintenance of glucose levels at as near-normal levels as possible is extremely beneficial in preventing complications from the disease. Monitoring and controlling serum lipid levels and blood pressure can greatly reduce complications from coronary artery disease and stroke. The ADA (2021) recommends considering the use of aspirin (75 to 162 mg daily) as primary prevention in both men and women aged 50 years and older with diabetes and at least one additional major risk factor. Equally important is maintaining routine examinations recommended by the primary care provider.

Referral: Patients with type 2 diabetes should be referred when acute complications requiring hospitalization develop, such as ketoacidosis, severe hyperglycemia, or hypoglycemia. Patients with fasting glucose levels that are consistently greater than 300 mg/dL or Hb A1c of greater than 13% also should be referred to an endocrinologist for further assessment. Annual eye and oral examinations should be referred to appropriate providers. Patients with uncontrolled hypertension, hyperlipidemia, unmanageable skin disorders, or renal insufficiency should be referred to appropriate providers. Consider referring all patients interested in greater control of self-management of the disease to diabetes educators.

Education: The cornerstone of education for patients with diabetes is disease self-management. Assess the patient's knowledge and understanding of the disease, treatment goals, management, and response to complications. Include in the

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assessment barriers to treatment, which include cultural influences, health beliefs and behaviors, socioeconomic status, psychological factors, and education and skills deficits that may preclude the ability to self-manage diabetes adequately. Explicit instructions should be given to patients who participate in daily SMBG. For optimal results, families of patients with diabetes should always be included in the education and management of the disease. Information and helpful tools that may be printed pertaining to diabetes can be obtained from the American Diabetes Association, 2451 Crystal Drive, Suite 900, Arlington, VA 22202, 1-800-DIABETES (1-800-342-2383), www.diabetes.org.

Clinical Recommendation	Evidence Rating	References
Diagnosis of type 2 diabetes mellitus: two fasting blood glucoses ≥126 mg/dL or two random blood glucoses ≥200 mg/dL.	C	American Diabetes Association (ADA), 2021
In a systematic review of the evidence, support is given to the use of Hb A1c as a measure for screening. The ADA endorsed Hb A1c as a diagnostic test for diabetes at a cut-off of ≥6.5% with the provision that this be measured in a laboratory using a NGSP-certified assay aligned to the Diabetes Control and Complications Trial, and that in the absence of unequivocal hyperglycemia the test should be repeated. It is important to understand that values <6.5 does not exclude the diagnosis. Using this criteria, one-third of patients will be missed that would have been diagnosed with the use of a fasting glucose of ≥126 mg/dL.	A	ADA, 2021
The 2-hour plasma glucose during an oral glucose tolerance test rises much more steeply than fasting glucose levels with aging.	A	Lodhi, 2021
For some patients, Hb A1c may not accurately reflect control. Other options include fructosamine and glycated albumin.	C	ADA, 2021
Counsel patients regarding lifestyle modification (weight loss, exercise) (expected decrease in Hb A1c 1%–2%).	C	ADA, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

HYPERLIPIDEMIA

Signal Symptoms: Body mass index (BMI) greater than 25, central obesity, metabolic syndrome, diabetes, familial hypercholesterolemia, thyroid dysfunction, corneal arcus, xanthelasma, xanthoma.

Description: Hyperlipidemia is a major cardiovascular risk factor that increases the rate of atherosclerotic cardiovascular disease (ASCVD) in the general population as well as in older adults. Other terms used to denote this condition are *hypercholesterolemia, hypertriglyceridemia, dyslipidemia,* and *mixed dyslipidemia*. Hyperlipidemia is generally classified as primary or secondary.

Cholesterol is significant for body functions, including nerve conduction, intracellular transport of vitamins (A, D, E, and K), being a precursor of molecules such as steroid and sex hormones, and being part of all cell membranes (Orkaby, 2020). As with frailty and other declining states that are common in older adults, elevated levels of cholesterol have been hypothesized as protective in the very old age. Guidelines from the American College of Cardiology and American Heart Association (ACC/AHA) (Carson, et al., 2020) and the National Lipid Association (NLA) Part 2 (Orringer, et al., 2020), however, both support the pharmacological treatment of hyperlipidemia in the older adult with risk factors.

Etiology: Cholesterol is essential to the structure and function of cell membranes and the synthesis of vitamins and hormones. It is formed in the human body in three different ways: food absorption, bile acids produced by the liver and reabsorbed through the intestinal tract, and cellular synthesis. The latter two have a strong genetic component. Cholesterol is transported in our circulation by lipoproteins. Cholesterol and triglycerides are insoluble in water and are transported in association with proteins (Feingold, 2020). Lipoproteins in the blood are divided into seven classes based on their size, densities, and apolipoproteins. These are chylomicrons, chylomicron remnants, very low-density lipoproteins (VLDLs), intermediate-density lipoproteins (IDLs), low-density lipoproteins (LDLs), high-density lipoproteins (HDL), and Lp(a), which is an LDL particle that has a lipoprotein (a) and is proatherogenic (Feingold, 2021). The degree of lipid in a lipoprotein affects its density—the lower the density of a lipoprotein, the more lipid it contains relative to protein. The total plasma cholesterol measured in a lipid panel is determined by the supply of cholesterol from VLDL, IDL, LDL, and HDL (Healthwise Staff, 2021).

Occurrence: According to data from 2013–2016 Heart Disease and Stroke Statistics (Virani et al., 2020), an estimated 28.5 million adults 20 years of age and older have

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serum total cholesterol levels greater than or equal to 240 mg/dL, with a prevalence of 11.7%. These data indicate a steady decline in the prevalence of high LDL cholesterol over the past four decades. According to the Centers for Disease Control and Prevention (CDC), the number of people in the United States with high cholesterol has decreased by >30%. These data reveal that the national guidelines are making a difference in the management and treatment of patients. Most groups of people met the goal of Healthy People 2020, which aimed to reduce the percentage of adults with elevated cholesterol to 13.5% (Upham, 2020).

Age: Hyperlipidemia can occur at any age due to genetic syndromes that are associated with accelerated atherosclerosis and early cardiovascular disease (CVD). The effects of cholesterol levels on coronary artery disease mortality rates are much higher in the older adult. In men, the level of total cholesterol increases with age from puberty until age 45 to 55 years, followed by a plateau until age 70 years, at which time a mild decrease is observed. In women, the level continues to rise another 10 years before it begins to decrease. However, the levels in women usually remain higher than men of similar age-group. This mild drop in total cholesterol with aging is thought to be a result of a decrease in LDL synthesis related to a decline in liver function because of decreased hepatic blood flow. An age-related decrease in glomerular filtration rate (GFR), changes in cytochrome P450 (CYP450) enzymes, and diminished drug esterase associated with frailty (Streja & Streja, 2020) also occur.

Until recently, women have been underrepresented in randomized controlled trials of lipid-lowering therapies. The most recent data available indicate that more women than men die annually from CVD and women account for 60% of deaths due to stroke (Garcia et al., 2016).

Ethnicity: Patients who are Hispanic have a lower coronary calcium burden than non-Hispanic Whites and Asian Americans (Reiter-Brennan et al., 2020). However, mortality rates remain higher in Hispanics compared to Whites and Asian Americans. Black Americans also have higher rates of coronary artery disease, even though they also have lower coronary calcium store.

Contributing Factors: Both modifiable and nonmodifiable influences contribute to the risk of hyperlipidemia. Age, sex assigned at birth, and family history are risk factors that cannot be changed; however, diets high in saturated and trans fats, inactivity, and excess weight are strong controllable factors that have a significant impact on cholesterol parameters. Obesity is associated with increased total cholesterol, LDL, VLDL, and triglycerides and decreased levels of HDL. Other contributing factors to hyperlipidemia include alcoholism, steroid use, and smoking. Cigarette smoking lowers HDL levels and is an independent risk factor for CVD. The pathological process of atherosclerosis is influenced by many other factors as well. Age (older than 45 years for men and 55 years for women); male gender; genetic abnormalities in lipoprotein metabolism; and comorbidities such as diabetes, chronic kidney disease (CKD), and hypertension all contribute significantly to this disease process. Guidelines from the 2019 ACC/AHA and the NLA both focus on primary prevention strategies to include a plant-based diet instead of animal-based protein. The guidelines also recommended limiting dietary cholesterol to <200 mg/dL to lower LDL cholesterol (Carson et al., 2019). Secondary causes of hypercholesterolemia include hypothyroidism, liver disease. Systemic disease processes can also stimulate the inflammatory process and can cause atherosclerotic problems and dyslipidemia such as psoriasis, Crohn's disease, depression, chronic pain, and irritable bowel syndrome (Hill & Bordoni, 2021).

Certain medications can influence hyperlipidemia. Older adults are often on polypharmacy; therefore, medications should be evaluated thoroughly. Herinkand Ito (2015) did a review looking at medications that induced changes in lipid and lipoproteins. Medications listed in their report include:

- Antihypertensive drugs (diuretics and β-adrenergic blockers)
- Other cardiovascular drugs (amiodarone)
- Steroid hormones (estrogens and progestins)
- Anabolic steroids (Danazol)
- Androgens (testosterone replacement)
- Retinoids (oral isotretinoin)
- Antipsychotics (clozapine)
- Immunosuppressives (corticosteroids, cyclosporine, and tacrolimus)
- HIV therapy (protease inhibitors)
- Interferons

Signs and Symptoms: Hyperlipidemia is typically asymptomatic and is usually detected during a routine lipid screening. Occasionally, in patients with genetic disorders such as familial hypercholesterolemia, xanthelasma and xanthomas may be present. These are fatty deposits under the skin surface, on the hands, elbows, knees, heels, or eyelids, and found in patients with very high cholesterol. Ocular signs of hyperlipidemia may include arcus senilis and xanthelasma palpebrarum. Arcus senilis is a yellowish white ring around the cornea that is caused by lipid deposition in the peripheral cornea. Xanthelasma palpebrarum is a plaque-like yellow lesion near the inner canthus of the eyelids that is caused by lipid deposition in the dermis (Dahl, 2021).

Diagnostic Tests: Screening for lipid disorders should include a total cholesterol (TC), LDL, HDL, and triglyceride level, as well as a measurement of non-HDL cholesterol (non–HDL-C). This number is simply the difference between the TC concentration and the HDL cholesterol concentration. The non-HDL number provides a single index of atherogenic cholesterol particles, and many researchers believe this provides a better assessment of heart disease risk (Jacobson et al., 2017).

Table 18-4 displays the NLA recommendations for lipid management according to risk category. The atherogenic cholesterol (non–HDL-C and LDL-C) levels are considered the appropriate targets of therapy. In patients 65 years of age and older, for whom treatment with medication is questionable, a coronary artery calcium (CAC) score may be considered to obtained additional objective information for treatment decisions. A CAC score of zero in asymptomatic patients may indicate nonpharmacological treatment as an option (Orringer et al., 2020).

Both the ACC/AHA and the NLA utilize risk calculation tools in their primary prevention risk assessment. These tools are used in select older adult individuals with one additional risk factor to further assess risk. However, the two organizations differ in their cut points of high risk and the use of specific treatment goals. Instead of the traditional NLA ATP III risk factor stratification, treat-to-goal approach, the ACC/AHA

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TABLE 18-4 Treatment Goals and Levels to Consider Drug Therapy According to Risk Category

	TREATMENT GOAL	CONSIDER DRUG THERAPY
RISK CATEGORY	**Non-HDL-C mg/dL**	**LDL-C mg/dL**
Low	<130	≥190
	<100	≥160
Moderate	<30	≥160
	<100	≥130
High	<130	≥130
	<70	≥100
Very High	<100	≥100
	<70	≥70

2020 guidelines group patients according to their risk (high risk versus very high risk) and recommend non-statin therapies as add-ons when LDL remains greater than 70. Statins and non-statin therapy will be discussed in more detail in the section on Treatment. The four "at risk" patient groups that were identified by the ACC/AHA task force include:

1. Patients with clinical ASCVD
2. Patients with primary elevations in LDL cholesterol greater than or equal to 190 mg/dL
3. Patients with type 1 or 2 diabetes between the ages of 40 and 75 years
4. Patients with an estimated 10-year ASCVD risk greater than or equal to 7.5%

The 10-year risk estimator tool is called the ASCVD Risk Estimator Plus (previously called the Pooled Cohort Cardiovascular Risk Estimator) and was updated in October 2021 (ACC, 2021). This risk calculator combines the original ASCVD risk calculator with the 2016 Million Hearts Longitudinal ASCVD Risk Assessment tool and allows for 10-year risk calculation for those patients already on statin therapy (ACC, 2021). The ASCVD Risk Estimator Plus is recommended instead of the traditional Framingham Risk Score (FRS). Components assessed in the risk calculation include sex, age, race, TC, HDL, systolic blood pressure, treatment for hypertension, diabetes, and smoking status. The new tool adds diabetes, race, and CAC. The risk calculation includes stroke in the outcome; however, it can only be used to calculate the 10-year risk in patients between 40 and 79 years of age (Lloyd-Jones et al., 2019). The risk calculator can be found at http://tools.acc.org/ASCVD-Risk-Estimator.

The CAC test is an expedient and highly reproducible computed tomography (CT) scan of the heart. This does not require use of contrast or intravenous access to perform the test. It can be performed on any CT scanner that also has the capability to perform electrocardiogram (ECG) gating. This gating technique uses data obtained during a specific part of the cardiac cycle (Orringer et al., 2020). The CAC reports the score for each individual coronary artery and the total score for the patient. The absolute CAC score has been found to be the most efficient predictor of near-term absolute risk over a 5-year time and best for guiding lipid-lowering therapy. The lower the score the lower the risk. For example, someone who is 50 on any CAC score is classified as a high lifetime risk.

Conversely, a patient who is older than 70 years of age with a score of 10 can have a similar risk as a younger person but a lower risk when compared to age, sex, and race/ethnicity-matched peers; therefore, they will have a lower lifetime risk in light of other competing risks in older adults (Orringer et al., 2020). The addition of the CAC score is effective in stratifying risk and improves risk estimation (Reiter-Brennan et al., 2020).

Recommendations are for adults between the ages of 40 and 75 years, with LDL of 70 to 189 mg/dL and a 10-year ASCVD risk of 5% to 19.9%, CAC may be useful to help the practitioner decide whether to use intense preventive therapy with statins. In older patients whose estimated 10-year risk using the Pooled Cohort Equations is driven by age, a CAC = 0 or a low CAC score can influence the decision to hold statin therapy. CAC is not recommended for those with ASCVD (Orringer et al., 2020).

Recommendations for lipid management from the 2017 NLA Expert Panel on older patients differs somewhat from that of the ACC/AHA. A 10-year ASCVD risk greater than or equal to 15% is used instead of greater than or equal to 7.5% in the ASCVD Risk Estimator Plus, and the ATP III Framingham Risk Calculator is recommended. The use of risk calculators should be used with caution in the older adult because advanced age is often the major driver of increased ASCVD risk and could result in potential overtreatment of lower risk older adult individuals.

Differential Diagnosis: When evaluating older patients with hyperlipidemia it is important to think through other potential medical causes. Differential diagnosis is discussed here based on their lipoprotein abnormality. Hypercholesterolemia (elevated TC and LDL) can be attributed to hypothyroidism, nephrotic syndrome, and malnutrition. Hypertriglyceridemia (elevated triglycerides) can be secondary to diabetes mellitus, obesity, metabolic syndrome, alcohol use, oral estrogen, renal failure, hypothyroidism, retinoic acid, and lipodystrophies. Combined hyperlipidemia (high TC, LDL, and triglycerides) can be caused by diabetes mellitus, obesity, metabolic syndrome, nephrotic syndrome, hypothyroidism, and lipodystrophies. Lastly, low HDL cholesterol can be linked to diabetes mellitus, obesity, metabolic syndrome, hypertriglyceridemia, smoking, and the use of anabolic steroids. Specifically, in type 2 diabetes, patients will have increased serum triglycerides, VLDLs and IDLs, but LDL levels are no different than in those patients without diabetes (Feingold, 2020). Medication causes are discussed in the section Etiology. Investigating and treating these secondary causes can often improve abnormal lipid disorders without aggressive statin therapy.

Treatment: Managing modifiable risk factors such as hyperlipidemia remains the primary method to prevent ASCVD. Hypercholesterolemia is common in the older population and decision making regarding treatment can be challenging. Ideally, patients at risk for ASCVD should begin treatment well before they reach older age. Treatment strategies in this population require careful consideration and should be made on an individual patient basis.

Older adults should follow the general principals of a healthy lifestyle recommended by the 2015–2020 Dietary

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Guidelines for Americans (DGA). A balance between energy intake (calories in) and expenditure (calories out) is emphasized to maintain a healthy body weight. The following are key general recommendations that can help older individuals achieve healthy eating patterns within calorie limits:

- Consume less than 10% of calories per day from added sugars.
- Consume less than 10% of calories per day from saturated fats.
- Consume less than 2,300 mg per day of sodium.
- If alcohol is consumed, it should be consumed in moderation (seven drinks or less per week for women and 14 drinks or less per week for men) (U.S. Department of Agriculture and U. S. Department of Health and Human Services, 2020).

A recent recommendation from the NLA expert panel, based on results from randomized controlled trials, indicates that dietary cholesterol has modest effects on levels of TC, LDL, and HDL cholesterol, and that saturated fatty acids and trans fatty acids have a more predictable impact on levels of atherogenic cholesterol (Jacobson et al., 2017). The Mediterranean style diet and the Dietary Approaches to Stop Hypertension (DASH) diets are recommended for the reduction of cholesterol. These diets focus on fruits, vegetables, whole grains, fat-free or low-fat foods, lean protein, nuts, seeds, and liquid vegetable oils. Choosing plant-based protein sources are an effective way to limit cholesterol intake (Carson et al., 2019).

Regular physical activity is essential for healthy aging. Adults aged 65 years and older gain substantial health benefits from regular physical activity. According to the Office of Disease Prevention and Health Promotion (DPHP), older adults should follow these recommendations for exercise:

- All older adults should avoid inactivity. Some physical activity is better than none, and older adults who participate in any amount of physical activity gain some health benefits.
- For substantial health benefits, older adults should do at least 150 minutes (2 hours and 30 minutes) a week of moderate-intensity, or 75 minutes (1 hour and 15 minutes) a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity aerobic activity. Aerobic activity should be performed in episodes of at least 10 minutes, and preferably, it should be spread throughout the week.
- For additional and more extensive health benefits, older adults should increase their aerobic physical activity to 300 minutes (5 hours) a week of moderate-intensity, or 150 minutes a week of vigorous-intensity aerobic physical activity, or an equivalent combination of moderate- and vigorous-intensity activity. Additional health benefits are gained by engaging in physical activity beyond this amount.
- Older adults should also do muscle-strengthening activities that are moderate or high intensity and involve all major muscle groups on 2 or more days a week, as these activities provide additional health benefits.
- When older adults cannot do 150 minutes of moderate-intensity aerobic activity a week because of chronic conditions, they should be as physically active as their abilities and conditions allow.
- Older adults should do exercises that maintain or improve balance if they are at risk of falling.
- Older adults should determine their level of effort for physical activity relative to their level of fitness.
- Older adults with chronic conditions should understand whether and how their conditions affect their ability to do regular physical activity safely.

It has been well established in multiple clinical trials and in more than 27 years of clinical use that 3-hydroxy-3-methyglutaryl-coenzyme A (HMG-CoA) reductase inhibitors (statins) are one effective treatment to reduce ASCVD risk, particularly for secondary prevention. In addition to their cholesterol-lowering properties, statins also have anti-inflammatory effects that are believed to contribute to plaque stabilization. There are currently seven statin medications available: rosuvastatin, atorvastatin, pitavastatin, simvastatin, lovastatin, pravastatin, and fluvastatin. Statins should be prescribed according to potency and intensity as recommended in both the NLA and ACC/AHA guidelines (see Table 18-5).

Safety of these agents, particularly in the older adult, remains a concern. Advancing age, multiple comorbidities, and polypharmacy can cause pharmacokinetic and pharmacodynamic variability, resulting in potential adverse effects (Grundy et al., 2019).

Unfortunately, the subject of deprescription of statin therapy in older adult patients has a paucity of recommendations or guidelines. In a systematic review of guidelines for the instructions and suggestions of discontinuing statin therapy in older adults by van der Ploeg and colleagues (2020), the researchers identified 18 international guidelines on statin therapy. Of these, three groups of instructions were identified for statin discontinuation *only* in the setting of statin intolerance. None were specific to older patients. Three guidelines did include a recommendation for discontinuation of statins in patients with poor health (van der Ploeg et al., 2020). Higher level evidence and new guidelines are suggested to meet the needs of providers. More detailed recommendations regarding the discontinuation of statins in the treatment of dyslipidemia in older adults is warranted.

The National Institute for Health and Care Excellence (NICE) guidelines do recommend that providers should treat older patients up to the age of 84 as they would adults of any age. They further recommend that moderate intensity statins

TABLE 18-5 Intensity of Statin Therapy

HIGH INTENSITY DAILY DOSE ↓ LDL-C ≥50%	MODERATE INTENSITY DAILY DOSE ↓ LDL-C 30 TO <50%
Atorvastatin 40–80 mg	Atorvastatin 10–20 mg
Rosuvastatin 20–40 mg	Fluvastatin 40 mg bid
	Fluvastatin XL 80 mg
	Lovastatin 40 mg
	Pitavastatin 2–4 mg
	Pravastatin 40–80 mg
	Rosuvastatin 5–10 mg
	Simvastatin 20–40 mg

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should be considered for the prevention of non-fatal myocardial infarctions (MIs) in individuals older than 85 years (Horodinischi et. al., 2019). Patients who are frail are susceptible to adverse effects of statin therapy. However, these patients can still benefit from just 1 year of therapy and have been found to have lower mortality rates and slower functional decline (Last et al., 2017). As with any clinical decision in patient care, the medication benefit must outweigh the associated risk.

Elevations in liver enzymes and hepatic damage have been a concern since the first statin was introduced in 1987. However, there is no evidence that routine monitoring of hepatic function is effective in identifying the rare case of liver injury. According to a prospective study by Guo and associates (2019) that evaluated liver enzyme elevation in older adults, the prevalence of elevated liver enzymes (transaminases) was found to be more pronounced in the very old. However, statins were found to be safe for patients older than 80 years. Consequently, liver enzyme tests are recommended prior to beginning statin therapy and as clinically indicated thereafter (U.S. Food and Drug Administration [USDA], 2016).

There are many non-statin therapy regimens available to treat hyperlipidemia. No clinical trial has studied the effect of combination therapy on ASCVD risk reduction in the older population and met the primary endpoint. The ACC/AHA guidelines only recommend non-statin therapies in high-risk patients who either fail therapy on a maximum tolerated statin or are completely intolerant to statins. However, the NLA recommends treating to specific LDL and non-HDL cholesterol goals, making the addition of non-statin medication an option to reach these goals in high-risk patients.

Non-statin therapy includes PCSK9 inhibitors, ezetimibe, niacin, fibrates, bile acid sequestrants, and omega-3 fatty acids (O3FAs). When making clinical decisions regarding the use of non-statin or combination therapy, careful consideration of polypharmacy, drug-drug interactions, and adverse effects must be a priority. Equally, it is important to recognize that older adults are less likely to tolerate high-dose statins and some lower-dose combination therapies may be an excellent choice to achieve treatment goals with minimal side effects.

Proprotein convertase subtilisin/kexin type 9 (PCSK-9) inhibitors are now being considered for a specific cohort of patients. These patients are of higher risk for ASCVD, have a high burden of ASCVD, have poorly controlled hyperlipidemia, or have adverse risk factors. In a consensus statement by the NLA in 2019, PCSK9 inhibitors can provide reasonable value when LDL is ≥70 in patients with very high risk ASCVD without peripheral arterial disease and lower levels of poorly controlled risk factors (Robinson et al., 2019). This treatment regimen can also be considered for patients with less prominent ASCVD but high risk, heterozygous familial hypercholesterolemia, or severe hypercholesterolemia with untreated LDL levels ≥220.

These drugs lower LDL by 50% to 60% by binding PCSK9 labeling of LDL receptors for degradation, and thereby prolonging LDL receptor activity in the cell membrane. This prevents LDL receptors from returning to the surface of the hepatocyte to bind to additional LDL particles resulting in reduced LDL levels (Rosenson et al., 2018). Alirocumab and evolocumab are available for those patients who are not well controlled on statin therapy and/or lifestyle modifications. Alirocumab (Praluent) is provided in 75 mg and 150 mg subcutaneous injections given every 2 weeks and 300 mg subcutaneous injection once a month. Evolocumab (Repatha) is provided in 140 mg subcutaneous injections every 2 weeks and 420 mg subcutaneous injections once monthly. Often patients can perform self-injections after instructions from the pharmacist or provider. Both of these PCSK9 inhibitors have been shown in clinical trials to raise HDL cholesterol by 5% to 10%, lower LDL from 48% to 60%, lower triglycerides by 10% to 15%, and lower lipoprotein (a) by 25% to 30% (Rosenson et al., 2018). Both the FOURIER trial in 2017 and ODYSSEY OUTCOMES trial in 2018 found benefits of PCSK-9 inhibitors in patients older than 65 years of age without cognitive deficits or myalgias (Rosenson et al., 2018).

Ezetimibe is a cholesterol absorption inhibitor and is the only agent in its class. It can be used alone for a modest LDL lowering effect (18%) or in combination with a statin for a more robust lowering effect (54%).

Niacin, or nicotinic acid, is a form of vitamin B_3 and has been available for the treatment of cholesterol disorders since the early 1950s. Niacin's primary use has been in the treatment of low HDL cholesterol disorders, but it has also been used to treat elevated LDL cholesterol. Its main mechanism of action is in the reverse transport of cellular cholesterol and macrophages from the body. Niacin is used with caution in older adults due to safety and tolerability concerns. In addition, recent secondary prevention studies have failed to show any additional benefit of using niacin with maximum dose statins (i.e., AIM-HIGH, HPS2-THRIVE) (Feingold, 2020).

Fibrates are a non-statin therapy that is primarily used to treat high triglycerides and VLDL cholesterol, but they also have a modest effect on raising the HDL cholesterol. These medications work by enhancing the catabolism of triglyceride-rich particles and reducing the secretion of VLDL. Gemfibrozil use is contraindicated with simvastatin due to increased risk of myopathies. Fenofibrate is therefore preferred in combination with statins. The researchers of the FIELD study (2011) found that fenofibrate reduced albuminuria and delayed GFR impairment in type 2 diabetes (Davis et al., 2011). However, gemfibrozil is preferred in patients with CKD because its effect on serum creatinine levels is more favorable when compared with fenofibrates.

Bile acid sequestrants (BASs), sometimes referred to as resins, include cholestyramine, colesevelam, and colestipol. They are recommended in patients with hypercholesterolemia without hypertriglyceridemia. These drugs bind with cholesterol-containing bile acids in the intestines and are then eliminated in the stool. The primary effect of BASs is a 5% to 30% reduction in LDL cholesterol; however, these medications also have a beneficial clinical effect in the treatment of diabetes. These drugs can cause significant GI side effects and are contraindicated in patients with biliary obstruction. Therefore, their use is usually limited to those patients unable to tolerate a statin (Feingold, 2020).

Omega-3 fatty acids (O3FAs) refer to the long-chain polyunsaturated fatty acids docosahexaenoic (DHA) and eicosapentaenoic (EPA). There are currently two prescription strength O3FAs on the market, omega-3-acid ethyl esters (Lovaza) and icosapent ethyl (Vascepa), which are indicated for the treatment of moderate to severe hypertriglyceridemia. These products are generally well tolerated but can inhibit platelet aggregation and should be used with caution in patients taking antiplatelet or anticoagulation therapies. With the antiplatelet effect on O3FA products, the FDA prescribing information recommends that in those patients taking an

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anticoagulant or antiplatelet medication should be monitored periodically, but no specific schedule is suggested. The REDUCE-IT trial (2019) did report a trend in increased bleeding, but no fatal bleeding events (Skulas-Ray et al., 2019).

Follow-Up: The NLA Recommendations for Patient-Centered Management of Dyslipidemia – Part 1 (Reiter-Brennan et al., 2020) advise a follow-up visit 4 to 6 weeks after the primary diagnosis of hyperlipidemia and repeated every 3 to 12 months as needed. Patients on drug therapy should be evaluated every 3 to 6 months to monitor compliance and potential side effects. Weight, dietary adherence, and exercise level should be evaluated. This visit should also include a lipid panel to measure atherogenic cholesterol response to TLC. If the patient is not at goal, these recommendations should be reinforced, and a referral to a dietitian for medical nutritional therapy should be considered. If the patient is not to goal, then TLC should be intensified, and drug therapy should be considered. For patients at high risk for ASCVD, drug therapy and TLC may be initiated concurrently.

Sequelae: Complications related to untreated or undertreated hypercholesterolemia include heart disease (acute coronary syndrome and ischemic heart disease), stroke, organ insufficiency (erectile dysfunction, CKD), peripheral vascular disease (PVD), aneurysms, type 2 diabetes, and pancreatitis. High cholesterol can also create bile imbalance, raising the risk of cholelithiasis (Luo & Grey, 2020). Early screening and management of high cholesterol is the cornerstone of preventing these life-threatening conditions.

Prevention/Prophylaxis: Primary prevention strategies in patients 65 to 79 years old should follow the NLA Recommendations of Patient-Centered Management of Dyslipidemia-Part 1. Prevention focuses on a healthy lifestyle of good nutrition and physical activity. The NLA Expert Panel supports a cardioprotective eating pattern for the management of dyslipidemia. This includes minimal intake of trans fatty acids, viscous fiber intake (5 to 10 g/day), fiber-rich whole grains that have 1.1 g or more of fiber per 10 g of carbohydrate, vegetables, nuts, and restriction of alcohol and refined carbohydrates. The recommended minimal frequency, intensity, and duration of exercise for improving the lipid profile (reduce triglyceride and modestly raise high-density lipoprotein cholesterol [HDL-C]) are 5 or more days/week at 40% to 75% aerobic capacity, and at least 30 to 60 minutes of accumulated daily physical activity (at least 150 minutes per week). This level of physical activity is consistent with the NLA expert panel and public health recommendations.

Other NLA recommendations include:

1. Consideration of moderate- or high-intensity statin medication for patients 65 to 75 years of age with ASCVD or diabetes mellitus.
2. Similar statin doses are recommended for patients 75 to 80 years of age after careful risk-benefit ratio assessment.
3. For patients older than 80 years of age, moderate-intensity statin may be considered after careful evaluation of polypharmacy and drug-to-drug interaction, comorbidities, cost, and patient preference.

Referral: The treatment of lipid disorders in older patients can generally be managed by the practitioner in primary care; however, a team-based collaborative approach, including a dietitian for medical nutritional therapy and a personal trainer who specializes in cardiovascular fitness for seniors, is an excellent approach. Patients with ASCVD should also be monitored by a cardiologist to track progression or stabilization of the disease. Lipid clinics are available if practitioners feel a lipid specialist is necessary.

Education: Education should focus on improving patient outcomes. When patients do not understand their disease or condition and the importance of the treatment regimen, they are less likely to be compliant. Take the time to educate patients on what to expect from their treatment, as well as the risks versus benefits. Considerations in the older adult include cost, dosing frequency of medication, physical difficulties in taking the drug, and risk of adverse drug reactions as perceived by the patient. Identify and discuss any barriers to adherence and formulate strategies for overcoming them.

Clinical Recommendation	Evidence Rating	References
In treating patients more than 65 years to less than 80 years of age with ASCVD or diabetes mellitus, moderate- or high-intensity statin therapy should be considered after a careful consideration of the individual risk-benefit ratio.	A	Jacobson et al., 2017
Older, primary prevention patients who are statin-eligible should undergo a patient-centered discussion with their provider about the risks and benefits of statin therapy so that they can make a more informed decision about taking statins over the long term.	C	Jacobson et al., 2017 Dixon et al., 2015
For patients reporting statin intolerance, consider the use of alternate statin regimens such as low-intensity statin therapy or non-daily moderate-intensity statin therapy; low-dose statin combination therapy with ezetimibe, bile acid sequestrants, or niacin; or non-statin as a second-line option.	B	Jacobson et al., 2017 Dixon et al., 2015
When treating for secondary prevention of hyperlipidemia in patients >80 years of age, consider using one of the moderate-intensity statins based on a provider-patient discussion of the risks and benefits of such therapy, consideration of drug-drug interactions, polypharmacy, concomitant medical conditions including frailty, cost considerations, and patient preference.	B	Jacobson et al., 2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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OSTEOPOROSIS

Signal Symptoms: Kyphosis, decreased height, vertebral or hip fractures, severe back pain.

Description: Osteoporosis is a systemic skeletal disease characterized by low bone mass and deterioration of bone tissue leading to bone fragility and an increased risk of fractures (National Osteoporosis Foundation [NOF], 2021). It is a major public health problem growing into a global epidemic. It has an impact on quality and quantity of life with medical, social, and economic consequences. It is seen in all age-groups, sexes, and races, but is more common in Whites, women, and older adults (Sözen et al., 2017). Patients with osteoporosis are at high risk for fractures and at moderate risk for low bone mass or osteopenia. Of those who have had at least one osteoporotic fracture, 80% are neither identified nor treated for osteoporosis (International Osteoporosis Foundation [IOF], 2021). Patients are either not being prescribed appropriate medications or, if prescribed, not taking them. Widespread media coverage of lawsuits over rare adverse events—atypical femur fractures and osteonecrosis of the jaw—has created fear among patients, leading to a decline in the use of osteoporosis drugs (*The Lancet*, 2018). Bone mineral density (BMD) screening rates within 6 months of a new osteoporotic fracture—when the need for treatment and action is higher—is only 8% for all Medicare beneficiaries (NOF, 2021). Earlier screening, diagnosis, and treatment of this disease before fractures occur can prevent osteoporosis with all its sequalae and cost burden.

Etiology: BMD results from both the peak bone mass achieved by the mid-twenties and the amount of bone loss after maturity. Men experience a gradual decline of bone mass into old age, whereas women experience a plateau followed by an accelerated period of bone loss for several years after menopause. Although osteoporosis is considered a disease of older adults, the origins of the disease begin in adolescence when there is a failure to achieve a high quality of bone. Peak bone mass is determined by genetic factors, with contributions from nutrition, endocrine status, physical activity, and health during growth. Once peak bone mass has been achieved in adulthood, the bone mass and structural integrity are maintained by a process called remodeling. Remodeling is the replacement of old tissue lost by resorption by new bone tissue and continues throughout life so that most of the adult skeleton is replaced every 10 years (IOF, 2021). Bone remodeling is used to repair microfractures and prevent them from becoming macrofractures, thereby assisting in maintaining a healthy skeleton. Osteoporosis results from an imbalance between bone resorption and bone formation, causing a reduction in bone tissue. Fractures occur because of both the qualitative and quantitative character of bone. Falls are the principal cause of fractures, which in older adults are related to a deteriorated sense of balance and low levels of muscular strength.

Occurrence: Per the IOF (2021), more than 200 million people are suffering from osteoporosis. Based on 2010 data, 54 million Americans aged 50 and older are impacted by osteoporosis (10.2 million) and low bone mass (39.8 million) with a risk for fracture (NOF, 2021). According to a Millman analysis commissioned by the NOF (2021), 1.8 million Medicare beneficiaries suffered 2.1 million osteoporotic fractures in 2016. More than 80% of those diagnosed with osteoporosis are women. One in three women and one in five men older than age 50 will suffer an osteoporotic fracture worldwide (IOF, 2021). Men aged 50 and older account for 25% of hip fractures but have a higher mortality rate after (IOF, 2021).

Age: Age is as great a risk factor for osteoporosis because of low BMD. A fracture at any major skeletal site in an adult older than 50 years should be considered a significant risk factor for osteoporosis, even when they occur without significant trauma. The most common fractures are those of the spine, hip, wrist, and distal forearm. Almost 75% of hip, spine, and distal forearm fractures occur among patients aged 65 and older (IOF, 2021).

Ethnicity: Peak bone mass and bone density are influenced by diet and lifestyle; however, genetics are the primary influence. The NOF (2021) report found substantial racial/ethnic disparities in fracture incidence, care, and deaths in Medicare beneficiaries. North American Natives suffered fractures at a rate 20% higher, Whites at 6% higher, Blacks 50% lower, Asians 32% lower, and Hispanics 19% lower than the national average. Rates of subsequent fractures within 12 months ranged from Blacks 11%; Whites 15%; Hispanic, Asian, and North American Natives all 14%. Tibia/fibula fractures were more common for Blacks; vertebral fractures were more common for Asians. Blacks had higher hospitalization rates, higher death rates, and lower BMD screening rates. Mortality rates were Blacks 22%, Whites 19%, Asians 16%, and Hispanic and North American Native 18%.

Contributing Factors: Many risk factors predispose individuals to osteoporosis. Some of these risk factors cannot be changed, including age, family history of the disease, low peak bone mass, female sex, race/ethnicity, small body structure, certain chronic disease states, and history of medication use. Chronic diseases that increase risk include hyperthyroidism, diabetes mellitus, rheumatoid arthritis, chronic kidney disease (CKD), Cushing's syndrome, previous gastric surgery, major organ transplantation, liver disease, epilepsy, alcoholism, malabsorption states, anorexia nervosa, hyperparathyroidism, and women having menopause before age 40 years without hormonal replacement. A history of falling puts a person at increased risk for sustaining an osteoporotic fracture. Patients taking medications such as corticosteroids, thyroid hormones, anticonvulsants, anticoagulants, lithium, chemotherapeutic agents, aluminum antacids, and tetracycline are at increased risk, and these medications need to be reviewed to determine whether alternatives are possible. A decrease in physical activity levels and aerobic capacity can result in changes in balance, increased susceptibility to falls, and impairment in functional capacity in older age. Other modifiable risk factors are tobacco use, excessive alcohol use, sedentary lifestyle, low gonadal hormone levels, low body mass index (BMI), and diet.

Signs and Symptoms: Osteoporosis is a silent disease, commonly displaying no signs or symptoms until a fracture occurs. Evaluate all postmenopausal women aged 50 years and older

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for osteoporosis risk. A detailed history, physical examination, and clinical fracture risk assessment with the Fracture Risk Assessment Tool (FRAX) should be included. Consider measuring bone strength using BMD testing based on FRAX profile. Patients need to be questioned about all the risk factors for osteoporosis. Inquire about a personal history of fractures. Inquire about a family history of hip fractures and obtain a thorough menstrual history in women. Dietary history, exercise patterns, and habits should be reviewed with patients. Physical examination may reveal loss of height with associated kyphosis of the spine. Height should be measured at the initial visit and yearly using a wall mounted stadiometer. Height loss (difference between the current height and peak height at age 20 years) of 1.5 inches (4 cm) or more is significant. If the patient is uncertain of what their peak height was, the arm span measurement is known to be an equivalent to adult height. Gait should be assessed, and the patient's body mechanics should be observed at the same time. It is helpful to do tests of basic functional mobility and balance such as the Timed Up and Go (https://www.cdc.gov/steadi/pdf/TUG_Test-print.pdf), Functional Reach (Duncan et al., 1990), Romberg, or the four-stage balance test (https://www.cdc.gov/steadi/pdf/4-Stage_Balance_Test-print.pdf). The mouth should be examined to assess oral hygiene, dentition, and any evidence of oral bone loss. The thyroid gland should be palpated. Observe for restrictive respiratory problems due to decreased volume of the thoracic cage and poor expansion with breathing. The spine should be examined in detail, including configuration. The most common site for vertebral fractures in patients with osteoporosis is the lower thoracic (T12) or upper lumbar (L1) region. Any tenderness to palpation over the spinous processes and evidence of swelling, tenderness, and ecchymosis present at the sight of an injury should be noted. Range of motion (ROM) should be determined, noting limitations or painful movement. An abdominal examination reveals whether the abdomen is protuberant from spinal changes. The distance between the rib cage and the anterior iliac crest should be recorded.

Diagnostic Tests: When BMD is measured, axial dual-energy x-ray absorptiometry (DXA) measurement (lumbar spine and hip; 1/3 radius) should be used. The World Health Organization (WHO) (1994) defines osteoporosis as a BMD less than 2.5 standard deviations (SDs) or more below the mean of a "young normal" adult (T-score of −2.5 or lower). When bone density is between 1.0 and 2.5 SD below the mean, the patient is said to have low bone mass or osteopenia (T-score between -1.0 and −2.5). The T-score is an important predictor of fracture risk, with the highest risk in those with the lowest BMD. Use of T-scores alone in the diagnosis of osteoporosis is inappropriate because age is as great a risk factor as BMD, and not all patients have access to a DXA (WHO, 1994). Results cannot be compared from different machines or following major software changes without appropriate adjustment or recalibration. Clinicians need to be able to accurately interpret DXA reports according to the criteria set forth by the International Society for Clinical Densitometry (ISCD). Clinicians can become a Certified Clinical Densitometrist (CCD) through the ISCD (https://ISCD.org). The percent change in BMD (from initial or previous) should be used to monitor treatment, not the T-score or FRAX (Camacho et al., 2020).

The FRAX Fracture Risk Assessment Tool developed by the WHO in 2008, accessible at www.shef.ac.uk/FRAX/tool.jsp, is the most widely used computer-based algorithm developed to assist clinicians in the identification of patients at high risk for fractures. The tool is intended to screen patients with low bone density who are not currently receiving treatment to help determine need for treatment. FRAX integrates validated clinical risk factors and BMD of the femoral neck to calculate the 10-year probability of hip fracture and the 10-year probability of a major osteoporotic fracture (clinical spine, forearm, hip, or humerus). Treatment of osteoporosis should be considered for patients with low BMD, as well as a 10-year risk of hip fracture of 3% or more or a 10-year risk of a major osteoporosis-related fracture of 20% or more. The FRAX is recommended for screening in most of the current clinical guidelines and the results are often incorporated into the standard bone density test results. FRAX may underestimate fracture risk among patients with diabetes, and the American Association of Clinical Endocrinologists (AACE) recommended rheumatoid arthritis be entered into the FRAX algorithm as a surrogate for fracture risk associated with diabetes (Camacho et al., 2020).

Using the FRAX algorithm, the AACE (Camacho et al., 2020) and the Endocrine Society's (Shoback et al., 2020) definitions of risk categories for fracture risk are listed in Table 18-6.

Lateral x-rays of the thoracic and lumbar spine or vertebral fracture assessment can assess the development or progression of asymptomatic vertebral fractures. Biomechanical computed tomography (BCT) analysis measures both bone strength and BMD at the hip or spine and is now available as a Medicare screening benefit (Keaveny et al., 2020). It is not ordered as a stand-alone test but for *opportunistic use* when the patient already has a hip or spine CT ordered for any medical condition and the software is available for this add-on test (VirtuOst BCT test). The BMD measurements from BCT can be used to identify osteoporosis, assess fracture risk, and monitor treatment. Laboratory testing should be considered for all women with postmenopausal osteoporosis and those at high fracture risk to identify coexisting medical conditions that cause or contribute to bone loss. Include a complete blood count (CBC), comprehensive metabolic profile, 25(OH)D, parathyroid hormone (PTH), phosphate, and a 24-hour urine collection for calcium, sodium, and creatinine. If medical history, physical findings, or laboratory test results suggest causes of secondary osteoporosis, additional laboratory evaluation may be warranted.

Differential Diagnosis: Osteoporosis is usually diagnosed based on low BMD in the absence of fracture but can also be diagnosed in patients with low bone mass at increased fracture risk using FRAX (Camacho et al., 2020). Clinically, osteoporosis can be diagnosed if there is a low-trauma/fragility fracture in the absence of other metabolic bone disease, independent of the BMD T-score (Camacho, et al., 2020). An osteoporotic or fragility fracture is defined as a fracture sustained from force similar to a fall from a standing height or less that would not have occurred in healthy bone, excepting fractures of the skull, face, fingers, and toes, which tend to occur due to trauma (Camacho et al., 2020). Vertebral fractures can occur during routine daily activities without a specific fall or injury. Other considerations are multiple myeloma, hyperparathyroidism,

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TABLE 18-6 Stratification of Fracture Risk Categories

RISK CATEGORY	CRITERIA
Low Risk Normal	• No prior hip or spine fractures • Bone mineral density (BMD) T-score at the hip and spine above –1.0 • 10-year hip fracture risk <3% • 10-year risk of major osteoporotic fracture (OF) <20%
Moderate Risk Low bone mass	• No prior hip or spine fractures • BMD T-score at the hip & spine both between –1 to –2.5 • 10-year fracture risk <3% • 10-year risk of major OF <20%
High Risk Osteoporosis	• Prior spine or hip fragility fracture • BMD T-score at the hip or spine –2.5 or below • 10-year hip fracture risk ≥3% • Risk of major osteoporotic fracture risk ≥20%
Very High Risk Severe Osteoporosis	• Multiple spine fractures • BMD T-score at the hip or spine of –2.5 or below • Recent hip, spine fracture within the past 12 months* • High risk of falls or history of injurious falls* • Those who experience fractures while receiving approved osteoporosis therapy* • Those who experience multiple fractures* • Those who experience fractures while receiving drugs that cause skeletal harm, e.g., long-term corticosteroids* • BMD T-score <–3, 10-year risk of major osteoporosis fracture >30%, hip fracture >4.5%*

**Criteria by American Association of Clinical Endocrinologists only*

osteomalacia, hyperthyroidism, Cushing's syndrome, Paget's disease, and hypogonadism, based on abnormal laboratory results.

Treatment: Management of osteoporosis requires a comprehensive approach. The goal of treatment is to prevent fractures. Adequate intake of calcium is a fundamental aspect of any osteoporosis prevention or treatment program and part of a healthy lifestyle for all ages. Vitamin D is important for calcium absorption and bone health, and is important for muscle performance, balance, and falling risk. Women and men 50 years and older need 1,200 mg of calcium a day to maintain bone health (Camacho et al., 2020). There is limited benefit in increasing calcium intake above 1,500 mg, and the risk of renal stones is increased. Safety questions have been raised about the use of calcium supplements with or without vitamin D because of a potential increased cardiovascular risk. Reports have been conflicting and currently, there is no conclusive evidence that calcium supplements increase cardiovascular risk (Vandenbroucke et al., 2017). Food sources of calcium are preferable because they provide other nutrients as well. Vitamin D deficiency due to insufficient skin exposure to sunlight or reduced efficacy of vitamin D synthesis is common in patients with osteoporosis and may hinder the effectiveness of treatment if not corrected. Patient factors such as obesity, race or ethnicity, malabsorption, those on medications affecting vitamin D metabolism, and history of transplant may increase the necessary vitamin D dose to achieve adequate levels (Camacho et al., 2020). Vitamin D replacement is available as ergocalciferol (vitamin D_2) or cholecalciferol (vitamin D_3). Both are effective in raising the level of serum vitamin D, but Binkley and Wiebe (2018) only recommend vitamin D_3 for replacement. Ergocalciferol is a prescription preparation and carries the potential advantage of insurance coverage. Determining the proper vitamin D requirement for a given patient is based on expert recommendations in conjunction with clinical judgment. The AACE and the Endocrine Society recommend basing a dose required to maintain a 25 (OH) level at 30 to 50 ng/ml for an optimal and safe range (Camacho et al., 2020; Shoback et al., 2020). This often requires at least 1,000 to 2,000 IU of vitamin D daily. The combined supplementation of calcium and vitamin D is preferred because it has shown to have more benefit in reducing fractures than either component alone (Chen et al., 2019; Vandebroucke et al., 2017). Calcium and vitamin D supplementation are an essential but not sufficient component of osteoporosis treatment. Indications for pharmacological therapy are low T-score, increased fracture risk based on FRAX, or fragility fracture. Recommendations for pharmacological therapy are based on the risk of fracture, individual drug considerations, and patient medical history. Patient acceptance of treatment, insurance coverage, and out-of-pocket costs all play a role. Full prescribing information should be reviewed before recommending any specific agent. Currently available osteoporosis therapies are relatively safe with no significant differences in the incidence of most adverse events in even very old adults compared to the general population (Vandenbroucke et al., 2017). The AACE's (Camacho et al., 2020) and the Endocrine Society's (Shoback et al., 2020) recommendations for pharmacological treatment for prevention and treatment of osteoporosis based on fracture risk are found in Table 18-7. Table 18-8 lists available pharmacological treatments for osteoporosis with dosing based on prevention or treatment. Many random controlled trials have given evidence supporting the superiority of anabolic agents over antiresorptive agents in reducing vertebral fracture risk in patients at very high risk for fractures, causing some experts to

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TABLE 18-7 Initial Pharmacological Treatment Based on Risk of Fracture

Low Risk	Reassess fracture risk in 2–4 years
Moderate Risk*	Bisphosphonates
High Risk*	Alendronate, denosumab, risedronate, zoledronic acid
Very High Risk*	Abaloparatide, denosumab, romosozumab, teriparatide, zoledronic acid

* *calcium + vitamin D as adjunct therapy*

advocate for this treatment approach (Camacho et al., 2020). Although at one time a treatment of choice for postmenopausal treatment, estrogen has only ever been approved by the U.S. Food and Drug Administration (FDA) for prevention and is to only be considered for women at significant risk of osteoporosis and for whom non-estrogen medications are not considered to be appropriate. Given the concerns regarding the increased risk of cardiovascular disease and breast cancer with estrogen use, AACE only recommends estrogen for the relief of menopausal symptoms in the lowest dose necessary and for the shortest time possible (Camacho et al., 2020).

Concomitant use of two or more osteoporosis drugs has not been shown to have a greater impact on fracture reduction, increases the cost of care and possibly side effects and is not routinely recommended by AACE (Camacho et al., 2020). However, drug combinations have been used when fracture risk is especially high or there is demonstrated suboptimal effects of certain drugs. For example, patients at high risk of hip fracture who are taking raloxifene to reduce their risk of breast cancer can add a bisphosphonate or denosumab (Camacho et al., 2020). Administration of denosumab with 20 mcg teriparatide resulted in a larger increase in BMD than either drug alone; results were even better using 40 mcg (Tsai et al., 2019). Two rare events have been associated mostly with long-term bisphosphonate therapy (more than 5 years duration), but causality has not been determined. Osteonecrosis of the jaw (ONJ) was first reported in patients with advanced cancer receiving high-dose zoledronic acid and denosumab, but the incidence is rare/much lower with drug doses for osteoporosis (Camacho et al., 2020). Risk factors are dental pathological conditions, invasive dental procedures, and poor dental hygiene. Delay initiation of treatment until dental issues are corrected. If a patient already receiving bisphosphonates or denosaumab needs invasive dental procedures, there is no evidence that discontinuing or interrupting treatment will change the outcome or reduce the risk of ONJ, but you can consider stopping treatment (Camacho et al., 2020). Atypical femur fracture (AFF) of the subtrochanteric area occurs with little or no trauma. Patients may present with a history of prodromal groin or thigh pain, bilateral fractures and bilateral radiographic abnormalities, and delayed healing (Camacho et al., 2020). These fractures are also seen in patients with low BMD who are not on any osteoporotic treatment. The number of fractures prevented with osteoporotic treatment far outweighs the risk of ONJ and AFF. Because bisphosphonates accumulate, they may have a prolonged residence time in bone and a residual therapeutic effect after stopping. A drug holiday may be considered to decrease risk of AFF and ONJ. A drug holiday is commonly believed to be 5 years; decision for initiation and duration must be individualized (not yet evidenced-based). Table 18-9 gives the AACE and Endocrine Society's guidelines on duration of pharmacological treatment, drug holidays, and (only for bisphosphonates) and drugs for transition.

Lifestyle: Nutritional recommendations include adequate intake of protein in the diet (0.8 to 1 g/kg) and reduction of excessive alcohol (3 or more drinks/day), caffeine (more than 2 servings/day), and high-phosphorus foods and carbonated beverages. Tobacco should be stopped. Patients should engage in regular weight-bearing exercises (e.g., walking, jogging, tai chi, stair climbing, dancing), which help to reduce the rate of bone loss and increase strength. Muscle-strengthening exercises (weight training and other resistive movements) improve strength, balance, and flexibility, which are important in preventing falls. The most effective exercise interventions associated with BMD changes and fracture reduction are those that include multiple exercise types and resistance exercise undertaken for 60+ minutes, 2 to 3 times/week for 7+ months (Pinheiro et al., 2020). All patients should be counseled on fall prevention. Measures to enhance safety in the home and environment should be emphasized. Personal risk factors should be minimized, such as compromised vision, orthostatic blood pressure drop, wearing high-heeled shoes, and drug or alcohol use. Individuals with severe osteoporosis should use caution when engaging in activities that involve forward spine flexion and rotation, lifting heavy weights, or even side bending of the trunk because these maneuvers exert compressive forces on the spine and may lead to fracture (Camacho et al., 2020). The NOF offers advice on exercise at www.nof.org.

Follow-Up: Serial BMD testing can be done to monitor the response to treatment, or the need for treatment. Frequency is clinically individualized, but in treated patients, BMD testing every 1 to 2 years may be appropriate (Camacho et al., 2020). In treated patients, if BMD decreases significantly, evaluate patients for nonadherence, secondary causes of osteoporosis, or use of drugs that might cause bone loss. Treatment failure can be a significant decrease in BMD or recurrent fractures in a patient who is adherent to therapy. Bone turnover markers (BTM) are useful for assessing patient adherence and efficacy of therapy (Camacho et al., 2020). Significant reductions in BTMs are seen with antiresorptive therapy and have been associated with fracture reduction, and significant increases indicate good response to anabolic therapy.

Sequelae: Any previous fracture is associated with an 86% increased risk of a future fracture (*The Lancet*, 2018). In the Millman Analysis of Medicare beneficiaries (NOF, 2021), more than 40% were hospitalized across all types of fractures, but 90% of those with hip fractures were hospitalized. Of those with a new osteoporotic fracture, 19% (154,000 women, 91,000 men) died within 12 months, 421,900 of them became institutionalized in nursing homes and 56,000 became eligible for Medicaid within

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TABLE 18-8 Pharmaceutical Prevention and Treatment of Osteoporosis

MEDICATION	DIRECTIONS	PREVENTION	TREATMENT
Antiresorptives			
Bisphosphonates			
Alendronate	Take first thing in the morning with a full glass of plain water at least 30 minutes before eating, drinking anything else, or taking any other medication	5 mg PO daily 35 mg PO weekly	10 mg PO daily 70 mg PO weekly 70 mg + D (2,800 IU or 5,600 IU) weekly
Ibandronate	*PO:* Take first thing in the morning with a full glass of plain water at least 30 minutes (2.5 mg) or 60 minutes (150 mg) before eating, drinking anything else, or taking any other medication *IV:* Administered by a health-care provider	2.5 mg PO daily 150 mg PO monthly	2.5 mg PO daily 150 mg PO monthly 3 mg IV every 3 months
Risedronate	Take first thing in the morning with a full glass of plain water at least 30 minutes (5, 35 mg) or 60 minutes (150 mg) before eating, drinking anything else, or taking any other medication	5 mg PO daily 35 mg PO weekly 150 mg PO monthly	5 mg PO daily 35 mg PO weekly 150 mg PO monthly
Zoledronic acid	Over no less than 15 minutes	5 mg IV every second year	5 mg/100 mL IV once yearly
Selective Estrogen Receptor Modulator			
Raloxifene		60 mg PO daily	60 mg PO daily
RANKL (Osteoclast) Inhibitor			
Denosumab	Administered by the health-care provider in the upper arm, upper thigh, or abdomen	—	60 mg/mL subcutaneous injection every 6 months
Sclerostin Inhibitor			
Romosozumab	Administered by a health-care provider in the abdomen, thigh, or upper arm; give as 2 separate injections consecutively	—	Two prefilled syringes 210 mg subcutaneously once monthly
Calcium Metabolism Modifier			
Calcitonin		—	100 IU daily subcutaneously or IM or 200 IU (1 spray, one nostril) daily
Anabolic (also includes romosozumab, which has dual action)			
Teriparatide	Into thigh or abdominal wall, requires refrigeration	—	20 mcg subcutaneously once daily
Abaloparatide	Into thigh or abdominal wall; no refrigeration required	—	80 mcg subcutaneously daily
Over the Counter			
Calcium Dietary calcium preferred; total calcium intake should not exceed 1,500 mg/day. Calcium citrate is more expensive but better tolerated than calcium carbonate; if tablets are difficult to swallow, soft chews and gummies are available	If calcium carbonate, take with food; do not take >500–600 mg/dose for optimal absorption	Part of a healthy lifestyle for any age; recommended daily allowance for calcium is age dependent	Ages ≥50: 1,200 mg/day
Vitamin D	Take with a meal with some fat in it to aid absorption	1,000 IU–2,000 IU daily or an appropriate dose to maintain adequate 25(OH)D level	Dose needed to correct deficiency varies based on 25(OH)D level; if <30, try 50,000 IU once weekly or 5,000 IU daily of vitamin D_2 or D_3 daily for 8–12 weeks

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TABLE 18-9 Duration of Pharmacological Treatment for Osteoporosis and Transition

DRUG	DURATION OF TREATMENT	DRUG HOLIDAY	TRANSITION TO
Bisphosphonates	Risk-benefit ratio for treatment >10 years unknown (Camacho et al., 2020)	Low risk: Consider after 3–5 years of stability on oral or 3 years on IV zoledronic acid	Low risk: No other treatment but reassess fracture risk at 2- to 4-year intervals and consider resuming treatment if fracture or significant bone mineral density loss occurs
		High risk: 10 years for oral, 6 years for IV zoledronic acid	High risk: Parathyroid hormone or raloxifene
Calcitonin	Safety data available through 5 years	No	When stopped, skeletal benefits are quickly lost over next 1–2 years
Denosumab	Reassess fracture risk after 5–10 years; if patient remains at high risk continue or change as long as clinically appropriate	No	Start an antiresorptive to prevent accelerated bone loss that occurs with stopping anabolic treatments
Parathyroid hormones	18–24 months	No	Bisphosphonate or denosumab to prevent accelerated bone loss that occurs with stopping anabolic treatments; can use romosozumab if patient remains high risk
Raloxifene	As long as clinically appropriate	No	When stopped, skeletal benefits are quickly lost over next 1–2 years
Romosozumab	1 year	No	Bisphosphonate or denosumab to prevent accelerated bone loss that occurs with stopping anabolic treatments
Zoledronic acid	Up to 6 years in very-high-risk patients	Consider after 3 years in high-risk patients or until fracture risk is no longer high	Not applicable

Source: Camacho et al., 2020; Arceo-Mendoza & Camacho, 2021

3 years. Those with a hip fracture had the highest mortality rate at 30%. Within a 3-year follow-up period, 14% had a subsequent fracture. For those who suffered subsequent fractures, the total estimated allowed medical cost in the 6-month period following was $5.7 billion in 2018. This estimate did not cover costs related to the loss of productivity, absenteeism, nonskilled home and nursing home costs, or pharmaceutical drugs. After a vertebral fracture, there may be acute pain that may resolve or may become chronic.

Prevention/Prophylaxis: The basic level of prevention and treatment includes diet, exercise, and fall prevention strategies.

Referral: Primary care providers may be knowledgeable about prevention and screening of fractures but may refer to an orthopedic surgeon for management of a fracture or to an osteoporosis specialist or clinical endocrinologist for management of osteoporosis. Fracture liaison services programs, a model of coordinated care where patients with recent fractures may be referred for secondary fracture prevention, have successfully reduced repeat fractures and lowered costs (NOF, 2021). Referral to such osteoporosis specialists is important in patients with fragility fractures, those with normal BMD and fracture without major trauma, those with recurrent fractures or continued bone loss while receiving therapy without obvious treatable causes of bone loss, those with less common secondary conditions (e.g., hyperthyroidism, hyperparathyroidism, hypercalciuria or elevated prolactin). those with osteoporosis with unexpectantly severe or unusual features, those with a condition that complicates management like CKD (glomerular filtration rate [GFR] <35) or malabsorption (Camacho, 2020). Consider a referral to physical or occupational therapy for significant kyphosis, back discomfort, and gait instability to improve gait and strength, reduce the risk of falling, and instruct the patient on proper body mechanics to prevent fractures and the use of adaptive treatment.

Education: Providers need time with a patient for a balanced discussion about their risks of probable osteoporosis, the risks and benefits of treatment options, reducing behavioral risks, diet, exercise and a fall reduction program, the risks of fracture and their consequences, and risks and benefits of discontinuing therapy. It is important to learn from the patient about their cultural beliefs, previous treatment experiences, fears, and concerns. The provider needs to present data in simple language that is understandable to the patient, sometimes with the use of decision aids such as brochures, cartoons, graphs, videos, and skeleton models. These are all important in patient-centered, shared decision making and should result in a management plan that is acceptable to the patient as well as better clinical outcomes.

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Clinical Recommendation	Evidence Rating	References
A 12-month-long, 3-times-weekly 30-minute balance-training program significantly improved postural balance and increased aerobic capacity and reduced falls in women with osteoporosis.	A	Miko et al., 2018
To prevent osteoporosis, post-menopausal women who have identified low bone mass should participate in bone-loading exercise and have adequate calcium and vitamin D supplementation.	A	Waltman et al., 2022
Optimal intake and utility of calcium supplements are controversial; dietary calcium is preferred over supplemental calcium; AACE. NOF, the Institute of Medicine (IOM) (now National Academy of Medicine [NAM]), and the Endocrine Society recommend calcium intake for adults ≥50 years of age 1,200 mg/day, including diet, plus calcium supplements if necessary; total calcium intake should not exceed 1,500 mg/day.	B	Camacho et al., 2020
Optimal serum 25(OH)D level controversial; AACE and the Endocrine Society recommend 30–50 ng/mL.	B	Camacho et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PANCREATIC DISORDERS

PANCREATIC CANCER

Signal Symptoms: Pancreatic cancer is called the "silent disease" because often the disease is advanced before any symptoms begin. Symptoms include weight loss, pain in the upper abdomen spreading to the back that may come and go and be worse after eating and at night, jaundice of the skin or eyes, dark urine and light-colored stools, bowel movements that look greasy and float in the toilet, weakness, loss of appetite, and nausea and vomiting (Fernandez del-Castillo, 2021).

Description: Pancreatic cancer is difficult to detect, hard to diagnose, early to metastasize, and resistant to treatment. Pancreatic tumors can be characterized as either endocrine or exocrine, depending on the cells of origin. Exocrine pancreatic tumors are the most common, with adenocarcinoma being the most common subtype (American Cancer Society [ACS], 2021a). Cancers can arise from both exocrine and endocrine portions of the pancreas, though 95% develop in the exocrine portion. Approximately 75% of pancreatic cancers occur within the head or neck, 20% in the body, and 5% to 10% in the tail of the pancreas. The most common type of pancreatic cancer is pancreatic duct adenocarcinoma. Generally, it metastasizes to regional lymph nodes, then to the liver or, less commonly, the lungs (National Comprehensive Cancer Network [NCCN], 2021).

Etiology: Pancreatic cancer is fundamentally a disease caused by damage to the DNA. These mutations can be inherited, or they can be acquired as one ages. DNA can also be damaged by certain behaviors, such as smoking, or simply by chance (ACS, 2021b).

Occurrence: More than 60,000 cases of pancreatic cancer are diagnosed annually in the United States. Pancreatic cancer accounts for over 48,000 deaths annually (NCCN, 2021; National Cancer Institute [NCI], 2021). The overall 5-year survival rate for pancreatic cancer is 10.8%. Incidence is slightly higher in men than in women (NCI, 2021).

Age: The disease is rare in patients younger than 45 years. The median age of diagnosis is 70 years. Approximately two-thirds of patients are at least 65 years old (NCI, 2021).

Ethnicity: Blacks are only slightly more likely to have pancreatic cancer compared with Whites. Asian/Pacific Islanders have the lowest incidence rate (NCI, 2021).

Contributing Factors: Pancreatic cancer has been linked to smoking, obesity, diabetes, and chronic pancreatitis. Exposure to chemicals and heavy metals including beta-naphthylamine, benzidine, pesticides, asbestos, benzene, and chlorinated hydrocarbons is associated with pancreatic cancer (ACS, 2021b). Certain hereditary conditions are associated with pancreatic cancer, including hereditary breast and ovarian cancer syndrome (*BRCA1* and *BRCA2* genes), hereditary breast cancer (*PALB* gene), familial atypical multiple mole melanoma (FAMM) syndrome (*p16/CDKN2A* gene), familial pancreatitis (*PRSS1* gene), Lynch's syndrome or hereditary nonpolyposis colon cancer (*MLH1* or *MSH2* genes), and Peutz-Jeghers' syndrome (*STK11* gene) (ACS, 2021b; NCCN, 2021).

Signs and Symptoms: Patients should be questioned about abdominal and midback pain, anorexia, depression, nausea, vomiting, and changes in bowel movements. Along with significant weight loss and moderate epigastric tenderness, the patient may have a palpable gallbladder (Courvoisier sign) and skin excoriation from pruritus. One of the most characteristic signs of pancreatic cancer of the head of the pancreas is painless obstructive jaundice (Fernandez del-Castillo, 2021). However, patients may notice a darkening of the urine and lightening of stools before the jaundice is visually evident. When questioned, they may indicate that their stools float. They may also have ascites, and an abdominal mass may be noted in those with advanced pancreatic cancer. Left supraclavicular lymphadenopathy (Virchow's node) may be palpated in some patients with widespread disease. Many

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patients with advanced disease have Trousseau's syndrome (a hypercoagulable state) and there is a high incidence of thromboembolic events as well (Fernandez del-Castillo, 2021).

Diagnostic Tests: Liver function testing may show an elevated bilirubin and alkaline phosphatase. Bilirubin may be noted in urine and stool samples as well. The most useful tumor marker for pancreatic cancer is the ca19.9 antigen. A pancreatic protocol computed tomography (CT) scan of the abdomen is recommended when pancreatic cancer is suspected. Cases should be reviewed by an experienced multidisciplinary team to determine whether the disease is resectable, borderline resectable, locally advanced, or metastatic. Additional testing may include a CT scan of the chest, endoscopic ultrasound (EUS), magnetic resonance imaging (MRI) of the abdomen, endoscopic retrograde cholangiopancreatography (ERCP) with stent placement, and positron emission tomography (PET) scan. A biopsy will be done using fine-needle aspiration after a CT scan or EUS is done (NCCN, 2021).

Differential Diagnosis:

- Aortic aneurysm
- Duodenal or gastric ulcers
- Ampullary carcinoma
- Bile duct strictures or tumors
- Cholangitis
- Cholecystitis
- Choledocholithiasis
- Cholelithiasis (Fernandez del-Castillo, 2021; NCCN, 2021)

Treatment: The extent of surgery depends on the location and size of the tumor, the stage of the disease, and the patient's general health. The Whipple's procedure is the most common surgery for pancreatic cancer, especially if the tumor is in the head of the pancreas. A distal pancreatectomy removes the body and the tail of the pancreas, and a total pancreatectomy removes the entire pancreas, part of the small intestine, a portion of the stomach, the common bile duct, the gallbladder, the spleen, and nearby lymph nodes. After surgery the patient may have radiation therapy, chemotherapy, or a combination of both. FOLFIRINOX (chemotherapy regimen made up of the following: folinic acid [FOL], fluorouracil [F], irinotecan [IRIN], and oxaliplatin [OX]) or a regimen that contains gemcitabine are the recommended systemic treatment options (NCCN, 2021). Pain relief is crucial in palliative care. This can be done with narcotic analgesics alone or by combining them with tricyclic antidepressants or antiemetics. Radiation therapy can also palliate pain but does not affect patient survival. Obstructive jaundice warrants relief if the patient has pruritus or right upper quadrant pain. Anorexia may also improve after relief of biliary obstruction. Pancreatic insufficiency and subsequent malabsorption are treated with pancreatic enzyme replacement.

Follow-Up: Follow-up after surgery and/or treatment modalities is important to ensure that any changes are seen and dealt with as early as possible. This will include visits to the primary care provider, the surgeon (if surgery was done), and oncologist if that treatment modality was selected (NCCN, 2021).

Sequelae: Patients with pancreatic carcinoma are often anorexic. Patients with malabsorption diarrhea and weight loss may benefit from pancreatic enzyme supplementation. Visits to a dietitian may also be useful for nutritional assistance (NCCN, 2021).

Prevention/Prophylaxis: Although pancreatic cancer is not completely preventable, patients need to be aware of probable modifiable risks associated with the development of pancreatic cancer, such as smoking and excessive alcohol intake (a contributor to chronic pancreatitis). It remains controversial whether people with given risk factors should be screened for pancreatic cancer.

Referral: Current guidelines recommend that decisions about treatment and resectability involve input from a multidisciplinary group of specialists. Patients selected for surgery should be based on the probability of cure (NCCN, 2021). Other factors include comorbidities, overall performance, and age. In advanced pancreatic cancer, patients and family should be informed of availability of palliative care measures and hospice as indicated by the patient's progression of disease.

Education: The best decisions are made with a solid knowledge base, so one needs to learn as much about pancreatic cancer as possible. The patient and family will need end-of-life education. Although some patients may live up to 2 years or more, most with advanced pancreatic cancer die within months of diagnosis. There are support groups that can give information on possible clinical trials pertinent to the patient's condition (NCCN, 2021).

Clinical Recommendation	Evidence Rating	References
FOLFIRINOX or a gemcitabine-containing regimen is recommended as first-line chemotherapy for patients with metastatic pancreatic cancer.	A	National Comprehensive Cancer Network (NCCN), 2021
Asymptomatic, high-risk patients should be considered for pancreatic cancer screening using EUS.	C	NCCN, 2021
Pancreatic protocol abdominal CT scan is the best initial imaging test for diagnosis and staging of suspected pancreatic cancer.	B	NCCN, 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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PANCREATITIS, ACUTE

Signal Symptoms: Mild-to-severe sharp epigastric pain with possible radiation to the back, chest, or flanks; pain can be exacerbated by eating, drinking, or lying flat. Nausea and vomiting often accompany the abdominal pain, as does mild to moderate fever.

Description: Acute pancreatitis is the result of acute inflammation of the pancreas, an organ that produces enzymes such as amylase, lipase, trypsin, and chymotrypsin to aid in digestion, as well as the hormone insulin, which controls the level of glucose in the blood. It is located in the upper abdomen, behind the stomach. The enzymes are secreted into the duodenum through the pancreatic duct and join with bile produced by the liver to digest food. Generally, these enzymes do not become active until they reach the small intestine. However, with a precipitating event the acinar cells within the pancreas can become damaged triggering a cascade activation of digestive enzymes within the pancreas causing pancreatic autodigestion which leads to pancreatic damage and inflammation (Mederos et al., 2021). Acute pancreatitis typically has a sudden onset and in a majority of patients resolves in 3 to 5 days with treatment and without complications. However, some patients progress to developing complications, which can include chronic pancreatitis, pancreatic pseudocyst, necrosis, organ failure, and death with a mortality rate of up to 30% in patients with severe acute pancreatitis (Quinlan, 2014).

Etiology: The two most common causes of acute pancreatitis are obstruction by gallstones, accounting for 21% to 33% of cases, and alcohol, accounting for 16% to 27% of cases (Zilio et al., 2019). If not due to gallstones or alcohol use, two less common but useful causes to investigate in the older adult are drug-induced pancreatitis and hypertriglyceridemia-induced pancreatitis, typically with serum triglycerides over 1,000 mg/dL (Gapp et al., 2019; Goyal et al., 2016; Papachristou et al., 2017; Simons-Linares et al., 2019). Other possible causes of acute pancreatitis are many and include viral infections (mumps, coxsackie B, mycoplasma pneumonia, and campylobacter), abnormalities of the pancreas itself, obstruction by pancreatic neoplasm, hereditary diseases such as cystic fibrosis, autoimmune disorders such as systemic lupus erythematosus, complication of endoscopic retrograde cholangiopancreatography (ERCP) (occurs in approximately 3% of post-ERCP patients), and trauma to the abdomen (Forsmark, Baillie, AGA Institute Clinical Practice and Economics Committee, & AGA Institute Governing Board, 2007). More than 500 drugs have been implicated in acute pancreatitis including acetaminophen, enalapril, furosemide, losartan, nadolol, statins, antibiotics such as tetracycline, and many others (Nitsche et al., 2010; Simons-Linares et al., 2019).

Cigarette smoking has been identified as a risk factor for both recurrent acute pancreatitis and progression to chronic pancreatitis (Ahmed Ali et al., 2016; Magnusdottir et al., 2019). In addition to smoking, older age, obesity, and HIV-positive status have been identified as risk factors for acute pancreatitis (Forsmark et al., 2016). Despite numerous etiologies, it should be noted that many cases of acute pancreatitis are idiopathic with no identifiable cause (Mederos et al., 2021).

Occurrence: Acute pancreatitis is the leading gastroenterological cause of hospitalization with nearly 275,000 hospitalizations annually (Forsmark et al., 2016). Eighty percent of pancreatitis is considered mild, and those persons generally recover without complication. The other 20% have severe disease with local and systemic complications. The mortality rate for acute pancreatitis varies based on severity but can range from approximately 1%, to over 30% in the most severe cases (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013). Disease severity scoring systems have been developed to attempt to predict patient mortality rate based on variables that influence disease severity such as age, presenting signs/symptoms, and laboratory values (Mederos et al., 2021). Acute pancreatitis affects males and females nearly equally (Yadav & Lowenfels, 2013); however, alcohol-related etiology is more common in men than in women, although the rates equalize when level of alcohol consumption is equal. Gallstone etiology is more common in women compared to men.

Age: Acute pancreatitis is more common in older adults, with the incidence rate (per 100,000 population) for those age 75 years and older double that of those age 35 to 44 years in males and nearly triple that in females for the same age comparison groups (Yadav & Lowenfels, 2013). Mortality, likewise, increases with age. A study by Fan and associates (1988) found mortality for acute pancreatitis at 5.9% for those age 50 years and younger and 21.3% for those age 75 years and older. The reasons are attributed to diminished organ function, comorbid illnesses, increased susceptibility to infection and ischemia, and age-associated changes in the pancreas and biliary system (Skolnick et al., 2008).

Ethnicity: In the United States, Blacks have a two to three times higher risk of acute pancreatitis than do Whites (Yadav & Lowenfels, 2013). The hospitalization rates of Blacks are three times higher than for Whites and are more pronounced for males than females.

Contributing Factors: Biliary tract disease, binge alcohol use, recent surgery, family history of high triglycerides (typically over 1,000 mg/dL), and increasing age are some of the contributing factors. There is some disagreement on other potentially contributing factors. Some studies cite medications as causing up to 2% of acute pancreatitis cases (Quinlan, 2014); others assert that factors such as medications, hypercalcemia, hyperparathyroidism, and infection are falsely attributed as causative factors to acute pancreatitis because the evidence supporting these is lacking and therefore causative links are only theoretical (Tenner et al., 2013).

Signs and Symptoms: Examination findings will vary depending on severity of the attack. With a mild attack, the epigastric area may be minimally tender; however, with severe episodes, there may be abdominal distention, tenderness, guarding, and decreased bowel sounds (Mederos et al., 2021). Respirations may be shallow due to diaphragmatic irritation. There may be ecchymotic discoloration of the flank (Grey-Turner's sign) or in the periumbilical area (Cullen's sign), which occurs in less than 1% of cases, reflects intra-abdominal hemorrhage

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typically associated with severe necrotizing acute pancreatitis, and is associated with a high mortality (Pannu et al., 2017).

Diagnostic Tests: Amylase and lipase amounts are elevated during acute pancreatitis and are the most common laboratory markers used to establish a diagnosis of acute pancreatitis. While these tests tend to be ordered together in about 90% of cases, there is research demonstrating lipase as a superior test (Barbieri et al., 2016). Continued use of amylase is often attributed to more familiarity with the test, belief that both tests are necessary to establish a diagnosis, and order sets that bundle the tests together. However, lipase has been shown to have higher sensitivity and specificity, increased ability to detect both early- and late-stage cases of pancreatitis, and more specificity to the pancreas compared to amylase. Because of this, it has been suggested that amylase offers no increased diagnostic value and lipase should be ordered alone (Barbieri et al., 2016; Ismail & Bhayana, 2017). Another potential marker of acute pancreatitis is trypsinogen activation peptide (TAP) that becomes markedly increased and may be useful in detection of early acute pancreatitis. Additional useful laboratory tests include the metabolic panel to look at blood urea nitrogen (BUN), creatinine, glucose, and calcium levels, as well as liver function tests, triglycerides, a complete blood count (CBC), arterial blood gases (ABGs), and a urinalysis, all of which can help establish disease severity, help predict outcomes, and identify complications (Mederos et al., 2021).

Radiological evidence is used to confirm or exclude the clinical diagnosis, establish a cause, assess severity, and provide guidance for therapy. An abdominal x-ray is generally done first and helps to exclude other causes of abdominal pain, such as an obstruction or bowel perforation. A finding in more severe disease is an ileus or "colon cut-off sign," reflecting paucity of air in the colon due to spasm of the descending colon. This may be followed by an abdominal ultrasound, which is 87% to 98% sensitive for detection of gallstones, as well as for showing a diffusely enlarged hypoechoic pancreas. Abdominal computed tomography (CT) scan or magnetic resonance imaging (MRI) can be performed to confirm the diagnosis of acute pancreatitis, especially with normal lipase and/or amylase levels, or to evaluate patients who fail to show improvement after 72 hours (Vivian et al., 2019). However, it is not necessary at initial presentation and management unless diagnosis is unclear (Mederos et al., 2021).

Endoscopic ultrasonography (EUS) and magnetic resonance cholangiopancreatography (MRCP) can be especially helpful in documenting stones, tumors, changes in pancreatic ducts and anatomic structural abnormalities. It can also be useful in determining which patients with acute pancreatitis would benefit from a therapeutic ERCP (100% sensitive and 91% specific for gallstones). MRCP is a newer, noninvasive technique and is comparable to ERCP for cholelithiasis detection but does not have the interventional capacity for stone extraction, stent insertion, or biopsy, as the ERCP does. Additionally, advantages of MRCP include no radiation exposure compared to CT scan; gadolinium contrast in MRI has a lower risk of renal complications than iodine contrast in CT scan; and for patients with contraindication to contrast, nonenhanced MRI can still detect pancreatic necrosis. ERCP may be used for the less common causes of pancreatitis such as sphincter of Oddi dysfunction or pancreatic duct strictures. It is indicated for those persons who have not passed a stone during the acute attack and those with evidence of sepsis, biliary obstruction, cholangitis, elevated bilirubin worsening, or persistent jaundice or worsening pain in the presence of an abnormal ultrasound (Carroll et al., 2007; Cherian et al., 2007). For patients with acute cholangitis and persistent obstruction, ERCP should be performed in less than 24 hours to lessen disease severity (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Most patients will have mild disease; however, it is important to know as early as possible whether the attack is mild or severe for purposes of management and use of resources. There are several scoring systems used to identify early prognostic signs to predict the severity of pancreatitis, including the Revised Atlanta Classification (REC), Ranson criteria, the Acute Physiology and Chronic Health Evaluation (APACHE II) model, the Systemic Inflammatory Response Syndrome (SIRS) Score, and the Computed Tomography Severity Index (CTSI). Each has its pros and cons. With all scoring systems, the higher the prognostic score, the poorer the clinical outcome will be.

The REC is both used to diagnose acute pancreatitis and rate the severity of pancreatitis. Diagnosis is made based on the REC when two of three criteria are met: abdominal pain consistent with acute pancreatitis, serum amylase and/or lipase three times the normal limit, and cross-sectional (CT or MRI) imaging findings consistent with acute pancreatitis. To rate severity, the RAC uses the Modified Marshall Score to grade existence and duration of organ failure, as well as the presence of localized (pancreatic) complications. Patients with mild disease typically have a short, self-limiting course and hospital discharge within 7 days; moderate pancreatitis has a more prolonged course for weeks or even months due to organ dysfunction and localized complications (such as pseudocyst or necrosis) (Mederos et al., 2021).

Several scores can be used to predict outcome, such as mortality; they can also be used to guide management such as level of care and required resources. The Ranson criteria was the first system and remains the best known and most widely used. However, drawbacks include the need for information both at diagnosis and within the first 48 hours of admission and that it can be difficult to use (Mederos et al., 2021). The sensitivity and specificity for disease severity is 0.79 and 0.78, respectively; for mortality sensitivity and specificity are 0.91, 0.72 (Mikó et al., 2019). The criteria include:

On Admission:

- Age of more than 55 years
- White blood cell (WBC) count greater than 16,000/mm^3 (16.0×10^9/L)
- Blood glucose greater than 200 mg/dL (11.1 mmol/L)
- Serum lactate dehydrogenase (LDH) greater than 350 U/L
- Aspartate aminotransferase (AST) greater than 250 U/L

During the Initial 48 Hours:

- Hematocrit decrease greater than 10%
- BUN increases greater than 5 mg/dL (1.8 mmol/L)
- Serum calcium less than 8 mg/dL (2 mmol/L)
- Base deficit greater than 4 mmol/L (4 mEq/L)
- Fluid sequestration greater than 6,000/mL
- PaO_2 less than 60 mm Hg

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Scoring: One point for each criterion met. The prognostic implication is as follows: 0 to 2 means 2% mortality; 3 to 4 means 15% mortality; 5 to 6 means 40% mortality; and 7 to 8 means 100% mortality.

The APACHE II score can be used to assess the patient at any point during the illness, but it is cumbersome to use. Sensitivity is 71% and specificity is 80% for disease severity and 92% and 79% for mortality (Mikó et al., 2019). The equation includes multiple factors, including history of severe organ insufficiency or immunocompromised state, age, rectal temperature, measures of respiratory status, heart rate, serum electrolytes, serum creatinine, hematocrit, WBC count, Glasgow Coma Scale score, FIO_2, and others. Scoring can be calculated at https://www.mdcalc.com/apache-ii-score.

The CT Severity Index (CTSI) developed by Balthazar (2002) is the only scoring system to use evidence of necrotic pancreas as criteria. A key criterion for identification of patients at higher risk for fatal pancreatitis is pancreatic necrosis. Although the CTSI requires a CT scan to be performed, it is both easy to calculate and provides reliable information on both disease severity and mortality (Mikó et al., 2019).

CT Grade:
- A is normal pancreas (0 points)
- B is edematous pancreas (1 point)
- C is B plus mild extrapancreatic changes (2 points)
- D is severe extrapancreatic changes plus one fluid collection (3 points)
- E is multiple or extensive fluid collections (4 points)

Necrosis Score:
- None (0 points)
- Less than 30% (2 points)
- Greater than 30% but less than 50% (4 points)
- Greater than 50% (6 points)

Scoring: CT grade plus necrosis score. Scores range from 0 to 10 with 0 to 2 equated to mild disease, 4 to 6 moderate disease, and 8 to 10 severe disease (Mortele et al., 2004).

The presence of systemic inflammatory response syndrome (SIRS) has been associated with an increase in mortality from acute pancreatitis. A score based on the presence of SIRS can be used daily to reliably predict acute pancreatitis severity. When SIRS is persistent for 48 hours despite the patient being adequately hydrated, a poor prognosis may be indicated (Forsmark et al., 2016). One study found that patients with persistent SIRS from admission, presence of SIRS on admission that was not persistent, and no SIRS had mortality rates of 25%, 8%, and 0%, respectively (Mofidi et al., 2006). SIRS is present if the patient meets two or more of the following criteria:

- Temperature greater than 38.3°C (100.4°F) or less than 36.0°C (96.8°F)
- Heart rate greater than 90 beats/minute
- Respiratory rate greater than 20 breaths/minute or $PaCO_2$ less than 32 mm Hg
- WBC count greater than 12,000 cells/mL, less than 4,000 cells/mL, or greater than 10% immature (band) cells

At initial presentation, pancreatitis severity should be estimated using an established classification method, such as the Atlanta classification system, rather than clinical judgment alone. Additionally, hemodynamic status should be assessed immediately on presentation, and fluid resuscitation should be started at the time of diagnosis even in the emergency department (Crockett et al., 2018; Ketwaroo et al., 2019; Vivian et al., 2019).

Differential Diagnosis:
- Cholangitis
- Cholecystitis
- Choledocholithiasis
- Cholelithiasis
- Colon cancer
- Colonic obstruction
- Diabetic ketoacidosis
- Dissecting aneurysm
- Diverticulitis with/without perforation
- Duodenal or gastric ulcers
- Gastric or pancreatic cancer
- Gastric outlet obstruction
- Gastric volvulus
- Hepatitis
- Intestinal infarction
- Mesenteric ischemia
- MI
- Perforated peptic ulcer
- Pneumonia
- Tubo-ovarian abscess (Quinlan, 2014)

Treatment: The acronym PANCREAS can be used to remember management particulars: **P**erfusion, **A**nalgesia, **N**utrition, **C**linical management, **R**adiology, **E**RCP, **A**ntibiotics, and **S**urgery (Khaliq et al., 2010). For acute pancreatitis, a short stay in the hospital is generally required for IV fluid replacement and pain management. Persons admitted with severe acute pancreatitis or certain high-risk patients (older adults, gross obesity, diabetes) may require intensive care because multiple complications can develop within hours or days. In rare cases, acute pancreatitis can cause hypoxia, and this is more common in the older adult. If there is vomiting, a nasogastric tube may be inserted to remove fluid and air (Neoptolemos, 2009).

Fluid resuscitation is key to treatment of acute pancreatitis. Previous recommendations included aggressive fluid resuscitation of 5 to 10 mL kg/hr, unless contraindicated due to cardiac, renal, or other conditions (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013). However, more recent research has dialed this back to less than 3 mL/kg/hr or has recommended against specific, blanket recommendations in favor of goal-directed therapy based on laboratory values and physiological data (Ketwaroo et al., 2019; Vivian et al., 2019). Fluid status should be frequently reassessed based on BUN and hematocrit. Clinical signs and adequate fluid resuscitation have been linked to reduced mortality (Working Group IAP/APA Acute Pancreatitis Guidelines, 2013).

Antibiotics are generally not indicated for most cases of pancreatitis, even with findings of necrosis unless fever and/or leukocytosis are present (Ketwaroo et al., 2019). For patients with gallstone pancreatitis, a cholecystectomy should be performed during the hospital stay, generally after at least 24 hours of treatment but within 2 weeks (Ketwaroo et al., 2019). Acute cholangitis resulting from biliary pancreatitis is potentially life threatening and should be treated with antibiotics; an ERCP may be required as well in these cases (Vivian et al., 2019).

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Patients with mild disease can begin on a low-fat, low-residue, soft diet within 24 hours of symptom control; with severe disease precluding an oral diet, parenteral nutrition should begin within 3 days of diagnosis (Vivian et al., 2019). Enteral nutrition (via oral, nasogastric, or nasojejunal route) is the preferred route of nutrition due to lower cost, decreased length of stay, and prevention of complications, organ failure, and mortality in acute pancreatitis (Ketwaroo et al., 2019; Vivian et al., 2019).

Follow-Up: Treatment of the patient must address underlying causes of pancreatitis and should follow a health-care team approach. If the culprit is alcohol consumption, treatment should go beyond just telling the patient to quit drinking and rather focus on a multidisciplinary team approach to alcohol cessation including medical care, behavioral health, and counseling. An endocrinology consultation may be assistive for those with hypertriglyceridemia or hypercalcemia-induced pancreatitis. Multidisciplinary care should also address triglycerides with lifestyle modification, weight control, and diet in addition to pharmacological therapy. Those with medication-induced pancreatitis may benefit from a pharmacology consultation to identify possible offenders and reasonable alternatives.

Sequelae: Gallstones may be the cause of acute pancreatitis and will need to be removed, which may be done by cholecystectomy if the pancreatitis is mild. However, surgery should occur within 2 weeks to prevent recurrent gallstone pancreatitis (Ketwaroo et al., 2019). If the pancreatitis is more severe, the gallstones may be removed using ERCP and a cholecystectomy performed after a full recovery from acute pancreatitis. Other possible complications can be an abscess or pseudocysts. Newly diagnosed patients with acute pancreatitis have a twofold increased risk of developing prediabetes or diabetes in the 5 years following acute pancreatitis (Das et al., 2014). Primary care providers should be vigilant with aggressive monitoring and prevention strategies in these patients. Acute pancreatitis can also cause kidney failure through acute tubular necrosis, although this risk can be lessened with adequate hydration during hospitalization. However, impaired kidney function after acute pancreatitis is possible, and a nephrology consultation may be beneficial. Finally, repeated episodes of acute pancreatitis can lead to chronic pancreatitis and the sequelae of this including pancreatic insufficiency, pseudocysts, and chronic pain.

Prevention/Prophylaxis: Depending on the cause of the acute pancreatitis episode, the person needs to be counseled on the cause, such as hypertriglyceridemia, alcoholism, hypercalcemia, or gallstone pancreatitis. The patient should be educated on steps related to prevention strategies such as alcohol cessation, evaluation for causes of hypercalcemia like hyperparathyroidism, and lifestyle modification for hypertriglyceridemia (Mederos et al., 2021). Additionally, triglyceride management with fibrates, statins, or omega-3 fatty acids (O3FAs) would be beneficial.

Referral: A dietary consultation and endocrinology referral may be helpful for the patient with acute pancreatitis that is due to high triglycerides or calcium. Endocrinology may also assist in management of diabetes that can result from pancreatitis. A referral for behavior modification, behavioral health, or a treatment program can be useful for the person who continues to drink alcohol. Nephrology can assist in any renal complications that result from acute pancreatitis.

Education: It is necessary for persons who have had an episode of acute pancreatitis to understand the mechanism behind the episode of pancreatitis to promote necessary changes including lifestyle management, diet, exercise, alcohol cessation, and others. Alcohol, specifically, increases the likelihood of recurrent attacks and development of chronic pancreatitis; education should be initiated in the hospital and occur as an outpatient at 6-month intervals for a minimum of 2 years (Mederos et al., 2021).

Clinical Recommendation	Evidence Rating	References
For patients with acute biliary pancreatitis, surgery should be consulted to consider cholecystectomy before discharge.	A	Vivian et al., 2019
Patients should NOT receive antibiotics to prevent infected necrosis, even in the presence of sterile necrosis.	B	Ketwaroo et al., 2019
If a patient has acute pancreatitis and cholangitis, they should undergo ERCP and appropriate endoscopic therapy within 24–48 hours, depending on hemodynamic stability.	B	Ketwaroo et al., 2019 Vivian et al., 2019
Enteral nutrition is preferred over parenteral nutrition in patients with acute pancreatitis.	A	Vivian et al., 2019
Enteral nutrition should be initiated within 24 hours, unless contraindicated.	B	Crockett et al., 2018 Vivian et al., 2019
In patients who cannot tolerate oral feeding, enteral nutrition via nasogastric or nasojejunal tube feedings should be initiated within 3–5 days.	B	Ketwaroo et al., 2019 Vivian et al., 2019
Lactated Ringer's solution is preferred over normal saline for fluid resuscitation, unless contraindicated.	B	Crockett et al., 2018 Ketwaroo et al., 2019 Working Group IAP/APA Acute Pancreatitis Guidelines, 2013 Vivian et al., 2019

Continued

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Clinical Recommendation	Evidence Rating	References
Enteral nutrition should be initiated for patients with mild acute pancreatitis within 24 hours of symptom control.	B	Crockett et al., 2018 Ketwaroo et al., 2019
Patients with acute pancreatitis should receive aggressive fluid intravenous hydration (minimum 3 mL/kg/hr) unless contraindicating comorbidities exist.	B	Ketwaroo et al., 2019
Aggressive hydration in patients with acute pancreatitis is most crucial, and should be initiated in the first 24–48 hours.	A	Tenner et al., 2013
For patients undergoing aggressive hydration, serum blood urea nitrogen (BUN), hematocrit, and creatinine should be monitored every 8–12 hours in the first 24–48 hours to guide hydration.	B	Ketwaroo et al., 2019 Vivian et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PANCREATITIS, CHRONIC

Signal Symptoms: As many as 80% of people experience upper abdominal pain, described as dull, and often in the epigastric area with radiation to the back (Barry, 2018; Singh et al., 2019; Wilcox et al., 2015). The pain may feel worse after eating or drinking and is sometimes relieved by leaning forward. The pain can be intermittent or constant. Overall, the severity, duration, character, and timing are variable between patients. Pain may also be accompanied by nausea and/or vomiting. The majority of patients experience intermittent attacks of pain at unpredictable intervals over years. Other associated symptoms can include fatigue, weight loss, steatorrhea, diarrhea, and decreased appetite (Kemalasari et al., 2018; Singh et al., 2019).

Description: Chronic pancreatitis is a chronic inflammatory condition as a result of pancreatic insult(s) resulting in irreversible structural and functional damage (Hart & Conwell, 2020; Kemalasari et al., 2018; Singh et al., 2019). It occurs due to the same underlying causes of acute pancreatitis and can be a consequence of recurrent acute pancreatitis episodes. In the presence of a trigger, such as alcohol, acinar cells are damaged and release digestive enzymes and inflammatory cytokines causing parenchymal damage that progresses to inflammation, fibrosis, and calcification; over time pancreatic ducts can become stenosed and obstructed, resulting in tissue loss and pancreatic atrophy (Kemalasari et al., 2018; Singh et al., 2019).This, in turn, results in exocrine and endocrine insufficiency, which can lead to diabetes mellitus, steatorrhea, chronic pain, malabsorption, vitamin deficiency, weight loss, osteoporosis, and pancreatic adenocarcinoma (Barry, 2018). The TIGAR-O (Toxic-metabolic, Idiopathic, Genetic, Autoimmune, Recurrent/severe acute pancreatitis, and Obstructive) classification system is based on risk factors for chronic pancreatitis (Barry, 2018).

Etiology: The three most common causes of chronic pancreatitis are alcohol and idiopathic and genetic causes (Singh et al., 2019). The majority of chronic pancreatitis cases have been attributed to excessive alcohol use and can account for approximately 50% of cases, or as many as 77% of cases (Singh et al., 2019). One study found the relative risk of chronic pancreatitis in patients who consume either 35 drinks a week or 48 drinks a week to be 2.7 and 3.3, respectively (Kristiansen et al., 2008). Idiopathic etiology simply means that after testing and work-up, no specific cause could be found; anywhere from 28% to 80% of cases have been found to be idiopathic, and this is generally considered the second most common etiology (Kemalasari et al., 2018; Singh et al., 2019). Genetic causes are the third most common etiology. Recently, several pathological genetic variants have been identified linked to pancreatitis and may be responsible for more cases than initially thought. A study in the United States found pathological variants of four specific genes in 47.8% of the study's patients previously diagnosed with idiopathic pancreatitis (Jalaly et al., 2017). In a study of Chinese patients with idiopathic pancreatitis, similar variants of the same genes were found in 50% of patients compared to 5.9% in the control group (odds ratio [OR] 16.1, $p < 0.001$) (Zou et al., 2018). Alcohol plays a larger role in chronic pancreatitis in men; women tend to have chronic pancreatitis of idiopathic, autoimmune, or gallstone origin.

Other, less common, etiologies of chronic pancreatitis include ductal obstruction (such as from stones, stricture, or tumor), hypercalcemia, severe hypertriglyceridemia, autoimmune diseases (such as inflammatory bowel disease, celiac disease, systemic lupus erythematosus, Sjögren syndrome), other chronic diseases (such as cystic fibrosis), and pancreatic anatomical abnormalities (such as annular pancreas) (Kemalasari et al., 2018; Singh et al., 2019).

Occurrence: Overall, chronic pancreatitis is a relatively rare disease, with prevalence having been estimated by several studies of between 35 to 73/100,000 in the United States and incidence ranging from 4 to 12/100,000/year, which translates to <200,000 U.S. patients living with chronic pancreatitis (Hart & Conwell, 2020; Singh et al., 2019). Chronic pancreatitis is more common in men then in women, although the degree of difference varies. Some newer studies find minimal difference in genders of about a 5% increased frequency in men than women (Machicado et al., 2019; Yadav et al., 2011). Others have found men 1.5 to 3 times more likely to have chronic pancreatitis, although these are typically older studies (Etemad & Whitcomb, 2001).

Age: Patients with chronic pancreatitis have an average age of 35 to 55 years old at diagnosis. However, there are age variations dependent on etiology. Average diagnostic age in alcohol-associated pancreatitis is 40 to 60 years old; genetic etiology is

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10 to 40 years old. Idiopathic pancreatitis can be classified as early-onset (average 19 years old at diagnosis) and late-onset (56 years old) (Layer et al., 1994; Singh et al., 2019). However, because of the lifelong nature of chronic pancreatitis, older patients are simply less likely to be newly diagnosed.

Ethnicity: As with age, ethnicity tends to affect variations in etiology. Blacks are more likely to have alcohol-related chronic pancreatitis than Whites; more broadly, non-Whites have higher rates of alcohol-related chronic pancreatitis than Whites (68% versus 42% in one study) (Beyer et al., 2020; Conwell et al., 2017; Singh et al., 2019). Additionally, Blacks with chronic pancreatitis have been shown to be more likely to be male, current or former smokers, and have etiology related to alcohol consumption (Wilcox et al., 2016). Finally, Blacks were more likely to have more advanced pancreatic morphological changes on imaging than Whites (Hart & Conwell, 2020).

Contributing Factors: Alcohol use remains the most common contributing factor (Barry, 2018; Kemalasari et al., 2018; O'Brien & Omer, 2019; Singh et al., 2019); it has been attributed to as much as 70% of cases (Barry, 2018). Idiopathic "late-onset" pancreatitis is more common in older adults. Obstructive chronic pancreatitis can be caused by an ampullary tumor or adenocarcinoma of the pancreas as well as pancreatic duct stricture (Barry, 2018; Kemalasari et al., 2018). Pancreatic stones also have been known to develop in older adults (Shah et al., 2008). Polypharmacy, common in older adults, raises the risk of pancreatitis-inducing medication use. Cigarette smoking has also been identified as a risk factor for chronic pancreatitis and accelerates disease progression (Barry, 2018; Hart & Conwell, 2020; Kemalasari et al., 2018; Singh et al., 2019). Other contributing factors include concomitant autoimmune diseases (such as inflammatory bowel disease, celiac disease, primary biliary cholangitis, and Sjögren syndrome) and genetic links with four recently identified gene variants linked to chronic pancreatitis development (Barry, 2018; Hart & Conwell, 2020; Kemalasari et al., 2018; Singh et al., 2019).

Signs and Symptoms: The most important clue to a proper diagnosis of chronic pancreatitis is an accurate medical history and subjective interview. The most common symptoms for chronic pancreatitis include abdominal pain, typically dull, epigastric, and with radiation to the back, neck, or flank, that can be worsened by food intake (Barry, 2018; Drewes et al., 2017; Hart & Conwell, 2020; Kemalasari et al., 2018; Singh et al., 2019). The pain is typically variable between patients but can be debilitating, result in social impairment, and significantly impact quality of life. Other symptoms can accompany pain including nausea, vomiting, weight loss/malnutrition, and steatorrhea (Kemalasari et al., 2018; O'Brien & Omer, 2019; Singh et al., 2019). Although pain is the most common symptom of chronic pancreatitis, as many as 20% of patient may have "silent" pancreatitis; additionally, pain can subside in patients as the pancreas fails (Barry, 2018).

The pancreatic enzymes (lipase and amylase) that are grossly elevated in acute pancreatitis may be normal or only mildly elevated and are considered nonspecific for chronic pancreatitis. Liver function tests may be elevated in obstructive pancreatitis such as with chronic strictures or mass. Serum triglycerides may be significantly elevated if related to the etiology, although this is rare. There may also be abnormal pancreatic function tests, such as fecal elastase, fecal fat, and serum trypsinogen (Barry, 2018).

As discussed, pain may subside as the pancreas fails; when 90% of pancreatic function is lost, exocrine dysfunction may result and impede the body's ability to break down complex foods and properly absorb products of digestions (Barry, 2018). Symptoms in these cases may include weight loss, diarrhea, steatorrhea, fat-soluble vitamin deficiencies, and osteopenia/osteoporosis. Even if the patient's appetite is unaffected by abdominal pain, patients with chronic pancreatitis may suffer weight loss due to these malabsorption deficiencies (Barry, 2018; O'Brien & Omer, 2019; Singh et al., 2019).

Occasionally on physical examination a tender fullness or mass may be palpated in the epigastric area, suggesting a pseudocyst or an inflammatory mass in the abdomen. Patients who have protein and fat deficiencies associated with advanced disease may exhibit decreased subcutaneous fat, temporal wasting, sunken supraclavicular fossa, and other signs of malnutrition. Severe or rapid weight loss should be a red flag for the health-care provider because it is generally worrisome for pancreatic cancer, which has a 15% to 40% incidence in patients with chronic pancreatitis (Barry, 2018).

Diagnostic Tests: Symptoms between acute and chronic pancreatitis can be similar. Serum amylase and lipase levels may be slightly elevated in chronic pancreatitis but are often normal or even decreased with the atrophy of the gland itself. If there is obstruction of the biliary tract, one may see elevated bilirubin, serum alkaline phosphatase, and hepatic transaminase levels (liver function tests). In the more advanced stages of pancreatitis, when malabsorption is present, the health-care provider may order blood, urine, and stool tests (testing fecal fat content) to help diagnose and monitor progression. However, maldigestion and malabsorption do not occur until more than 90% of the pancreas is destroyed (Barry, 2018).

Pancreatic function tests at present are direct tests, such as determining duodenal aspirates, but although they are sensitive, they are invasive and expensive. Generally, x-rays of the abdomen may show pancreatic duct calcifications in 30% of patients with chronic pancreatitis, although this is not diagnostic. In patients with suspected chronic pancreatitis, the first imaging modality for diagnosis is computed tomography (CT scan). If diagnosis is not established, the next imaging choice is magnetic resonance imaging (MRI). If diagnostic criteria are still not met, then endoscopic ultrasound (EUS) may be further used and may show calcifications, pancreatic enlargement, pancreatic pseudocysts, or pancreatic ductal dilation. Finally, endoscopic retrograde cholangiopancreatography (ERCP) can be performed. It must be considered that both EUS and ERCP are invasive tests and carry risks, such as acute pancreatitis (Mederos et al., 2021). The sensitivity/specificity for chronic pancreatitis are 75%/91% for CT, 78%/96% for MRI, and 81%/90% for EUS (Barry, 2018).

Although EUS has the highest possible sensitivity and specificity, it is invasive, has associated risks, and its accuracy is limited by the skill of the ultrasonographer/endoscopist with high interrater variability. Magnetic resonance imaging/magnetic resonance cholangiopancreatography (MRI/magnetic resonance cholangiopancreatography [MRCP]) is becoming the choice test for diagnosing chronic pancreatitis because of its ability to identify calcifications and duct obstructions in the disease without the radiation exposure associated with CT scan imaging and invasive procedural risks of EUS and ERCP.

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However, there is still low sensitivity for small calcifications and small duct calculi. Although CT has similar sensitivity and specificity to MRI/MRCP, there is low sensitivity for early disease, nonoptimal pancreatic duct visualization, and high levels of radiation exposure (Barry, 2018).

Differential Diagnosis:

- Pancreatic cancer
- Intestinal ischemia/infarct
- Cholecystitis
- Chronic gastritis
- Peptic ulcer disease (PUD)
- Biliary obstruction
- Crohn's disease
- Intestinal obstruction
- Ovarian cyst
- Myocardial infarction (MI)
- Irritable bowel syndrome (IBS)
- Ectopic pregnancy
- Acute appendicitis (Barry, 2018)

Treatment: Optimal management of chronic pancreatitis includes lifestyle changes, pain management, improvement of exocrine pancreatic insufficiency leading to malabsorption, and management of any complications. Lifestyle modifications that should be cornerstone to chronic pancreatitis treatment include smoking cessation and alcohol abstinence (Barry, 2018; Drewes et al., 2017; Gardner et al., 2020; Singh et al., 2019). Continued smoking and alcohol have been associated with continued disease progression; cessation can lead to decreased complications such as pancreatic cancer (Barry, 2018). Smoking may also be associated with decreased efficacy of endoscopic and surgical treatments (Singh et al., 2019). However, there is limited evidence associating smoking cessation and reduction in pain (Drewes et al., 2017). Alcohol abstinence in patients with chronic pancreatitis can improve pain, reduce frequency of recurrent acute pancreatitis, and limit hospitalizations (Drewes et al., 2017; Gardner et al., 2020). Both smoking and alcohol cessation should be addressed using a multidisciplinary approach, including pharmacological and nonpharmacological interventions such as support groups and behavior health/counseling.

Treatment of pain generally follows a stepwise approach, starting with nonopioid medications, such as nonsteroidal anti-inflammatory drugs and acetaminophen, with escalation based on clinical response (Barry, 2018; Beyer et al., 2020; Gardner et al., 2020; Hart & Conwell, 2020; Singh et al., 2019). If nonopioids are not effective in managing the patient's pain, then the next option would include weak opioids such as tramadol, followed by strong opioids such as oxycodone or morphine (Barry, 2018; Singh et al., 2019). If there is a need for opioid therapy, long-acting formulations should be strongly considered and appropriate attention should be paid to the risks of opioid use; follow tenants of safe prescribing (Beyer et al., 2020; Gardner et al., 2020). Another potential treatment option for pain includes antioxidants, especially in early disease, although research is limited and results are mixed (Barry, 2018; Gardner et al., 2020). Additionally, coanalgesics, such as antidepressants (e.g., gabapentin) and anticonvulsants (e.g., pregabalin), may reduce the need for opioids, although caution should be used with anticonvulsants (Beyer et al., 2020). Pancreatic enzymes, often used for malnutrition and pancreatic exocrine insufficiency, have limited data on effectiveness in pain management, although for patients who report pain improvement these can be continued given their low risks (Gardner et al., 2020). Finally, endoscopic, and surgical options (such as celiac plexus block) can be used to aid in pain management, although studies are conflicting in regard to timing and effectiveness (Beyer et al., 2020; Gardner et al., 2020). As noted by the complexity of pain management in these patients, it should be approached by a team including primary care, gastroenterology, and pain management specialists.

Patients with chronic pancreatitis are at risk for subsequent exocrine pancreatic insufficiency, malabsorption, and malnutrition and need to be appropriately managed. All patients with chronic pancreatitis should undergo regular nutrition assessment (Beyer et al., 2020; Gardner et al., 2020; O'Brien & Omer, 2019). Most patients' nutrition can be managed orally with supplementation, although some may require tube feeding (O'Brien & Omer, 2019). All patients with documented exocrine pancreatic insufficiency and/or malnutrition should receive pancreatic enzyme supplementation with weight-based dosing per treatment guidelines (Beyer et al., 2020; Gardner et al., 2020; Hart & Conwell, 2020). Enzyme supplementation may even improve or reduce complications from chronic pancreatitis (Gardner et al., 2020). Many organizations recommend a healthy diet that is low fat and consists of small, frequent meals to reduce risk of pain and complications (Barry, 2018; Beyer et al., 2020). Finally, assessment of fat-soluble vitamin deficiencies should be periodically done, with supplementation added as needed (Gardner et al., 2020; O'Brien & Omer, 2019).

Finally, as previously discussed, patients with chronic pancreatitis are at increased risk for several complications including diabetes, bone density loss and osteopenia/osteoporosis, and risks for pancreatic cancer, and should be subsequently monitored and treated (Gardner et al., 2020; Hart & Conwell, 2020). For patients who develop diabetes as a complication of chronic pancreatitis, management recommendations include metformin as the first-line treatment followed by insulin (Hart & Conwell, 2020). Use of insulin has also been thought to potentially reduce catabolic side effects of chronic pancreatitis (Hart & Conwell, 2020). It is reasonable that patients with chronic pancreatitis should undergo baseline dual x-ray absorptiometry (DEXA) scanning for bone mineral density (BMD) to evaluate for bone density losses because of the risk of osteopenia/osteoporosis. Subsequent screening and treatments, including weight-bearing exercises, supplementation with calcium and vitamin D, smoking cessation, and cautious use of bisphosphonates (if needed) should follow established general guidelines (Hart & Conwell, 2020). Finally, patients with chronic pancreatitis have an increased risk of pancreatic cancer (Barry, 2018). However, routine pancreatic cancer screening with imaging is not recommended for multiple reasons, although care providers should be vigilant in evaluating for warning signs that may raise suspicion for pancreatic cancer (Gardner et al., 2020; Hart & Conwell, 2020).

Follow-Up: If alcohol use and/or smoking are among the habits of the patient, these are best treated by a team approach using a chemical dependency counselor, psychologist, or mental health nurse practitioner. An alcohol treatment program may be appropriate. The patient will be seen back for follow-up on symptoms and clinical progression of

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the disease, with any treatment modifications needed, based on symptoms and presentation. Involvement of the multidisciplinary team, possibly including gastroenterology, pancreatic disease specialist, pain management, and endocrine, can be initiated for more complex patients.

Sequelae: There are several possible complications of chronic pancreatitis (Beyer et al., 2020; Gardner et al., 2020; Hart & Conwell, 2020; O'Brien & Omer, 2019; Singh et al., 2019). Chronic pancreatitis can also lead to calcification of the pancreas, where the tissue hardens, and surgery may be necessary to remove part of the pancreas. Long-standing inflammation in the pancreas caused by chronic pancreatitis is a risk factor for developing pancreatic cancer. Benign cysts, called pseudocysts, are formed of pancreatic fluid and surrounded by a fibrous wall. However, these cysts can also fill with fluid and debris, become infected, and rupture (Barry, 2018). Biliary obstruction and gastric outlet obstruction may occur because of compression of the bile duct necessitating endoscopic or surgical intervention (Barry, 2018). If the beta cells of the pancreas are destroyed, diabetes may develop, and insulin and diet will be recommended along with frequent blood glucose monitoring. Other risks include osteoporosis and risk of bone fracture, fat-soluble vitamin deficiency.

Other complications of chronic pancreatitis include development of duodenal obstruction, pancreatic ascites, and pleural effusion from fluid accumulation, pseudoaneurysms, and splenic vein thrombosis (Barry, 2018). When medical management no longer relieves pain, when patients are significantly malnourished, or when quality of life is decreased greatly, surgical intervention should be considered (Kemalasari et al., 2018; O'Brien & Omer, 2019). To date, the most recent Cochrane review of surgical intervention in obstructive chronic pancreatitis found that early surgical intervention seemed beneficial but could not be definitively demonstrated (Ahmed Ali et al., 2012). Caution is advised when regulating glycemic control in older adults to prevent episodes of hypoglycemia regardless of diabetic etiology.

Prevention/Prophylaxis: A cornerstone of prevention of chronic pancreatitis is smoking cessation and alcohol abstinence (Gardner et al., 2020). For patients already diagnosed with the disease, a diet low in fat with frequent small meals is generally recommended (Barry, 2018; Beyer et al., 2020). Additionally, patients with exocrine pancreatic insufficiency (EPI) should be placed on pancreatic enzymes for treatment/prevention of malabsorption and worsening malnutrition (Beyer et al., 2020; Gardner et al., 2020). The dosing is generally 500 units lipase/kg/meal and half that for snacks, and attempts should be made to ensure patient takes the supplements correctly to promote intended effect (O'Brien & Omer, 2019). The enzymes should be taken with every meal and snack (not before or long after) and should be taken whole with adequate fluids. A diet low in fiber may help, as dietary fiber can reduce the effectiveness of pancreatic enzymes (O'Brien & Omer, 2019). Various other supplements may be considered to help prevent nutritional issues due to malabsorption and malnutrition. A daily proton pump inhibitor may be added for those with refractory therapy because gastric acid may denature exogenous enzymes. Those persons with a known reason for chronic pancreatitis, other than smoking or alcohol, should have those reasons treated or corrected, if possible.

Referral: Surgical intervention is indicated when there is an anatomical complication correctable by mechanical intervention and includes an abscess, fistula, and fixed obstruction such as a stone, pseudocyst, stenosis, or a varietal hemorrhage due to splenic vein thrombosis. Additionally, surgery may be needed as a pain management intervention for some patients. Pancreatic resection with islet auto transplantation (TPIAT) is reserved for those with small duct disease or pain unresponsive to medical management, although this is only offered at a limited number of facilities and will likely require tertiary care referral (Barry, 2018; Beyer et al., 2020).

Education: All persons with chronic pancreatitis should have a consultation with a dietitian concerning a diet low in fat. They should also have instruction on how to cook low-fat meals and how to portion out small, frequent meals. Additionally, there should be education on smoking cessation, alcohol abstinence, risks of complications, and warning signs to be aware of.

Clinical Recommendation	Evidence Rating	References
Pancreatic enzyme supplementation is indicated for steatorrhea and malabsorption and may help relieve pain in patients with chronic pancreatitis.	B	Barry, 2018
Contrast-enhanced computed tomography scan is the recommended initial imaging study in patients with suspected chronic pancreatitis.	C	Barry, 2018 Gardner et al., 2020
Genetic testing is recommended in chronic pancreatitis patients with unclear etiology, especially younger patients.	C	Gardner et al., 2020
Endoscopic retrograde cholangiopancreatography drainage of pseudocysts results in a similar rate of pain relief as surgery, with equivalent or lower mortality.	B	Barry, 2018
Pancreatic enzyme supplementation should be given to chronic pancreatitis patients with weight loss or abdominal signs/symptoms attributable to malabsorption or maldigestion.	A	Mayerle et al., 2013

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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THYROID DISORDERS

HYPERTHYROIDISM

Signal Symptoms: Apathy, fatigue, confusion, weakness, course tremors, anorexia, palpitations, orbitopathy, weight loss.

Description: Hyperthyroidism occurs when there is an excessive synthesis and secretion of thyroid hormone. Whereas the clinical signs and symptoms of hyperthyroidism are generally well recognized in younger patients, older adults may present atypically with symptoms such as mood, cognitive changes, or heart arrhythmias (Ross et al., 2016). Overt hyperthyroidism is defined as a suppressed thyroid-stimulating hormone (TSH) level and elevated free T4/T3 levels. Subclinical hyperthyroidism is defined as suppressed TSH levels and normal free T4/T3 levels. Subclinical thyroid disease is clinically relevant in older adults, potentially leading to progression to overt hyperthyroidism, along with multiple complications such as cardiac issues, bone loss, fractures, and dementia (Biondi & Cooper, 2018).

Etiology: The most common cause of hyperthyroidism in adults is Graves' disease; however, the proportion of patients with toxic multinodular goiter (Plummer's disease) and toxic adenoma increases with age and iodine deficiency. Graves' disease is a familial autoimmune disorder in which thyrotropin receptor antibodies stimulate the TSH receptor, resulting in increased thyroid hormone production (Ross et al., 2016). In toxic multinodular goiter or toxic adenoma, the nodules are thought to independently produce excess thyroid hormone. Thyroiditis may occur, which is caused by the release of thyroid hormone due to the autoimmune or viral destruction of the tissue (Hughes & Eastman, 2021).

Occurrence: Hyperthyroidism occurs in about 1.2% of the U.S. population (0.5% overt and 0.7% subclinical) (Ross et al., 2016). Women are 5 to 10 times more likely to develop Graves' disease than men (Antonelli, et al., 2020).

Age: Of all cases of hyperthyroidism, 15% to 25% occur in people 60 years and older (Papaleontiou & Haymart, 2012).

Contributing Factors: Patients with other autoimmune conditions, such as type 1 diabetes, rheumatoid arthritis, and myasthenia gravis, are at risk for developing hyperthyroidism. A familial tendency for developing hyperthyroidism exists (Antonelli et al., 2020). Patients prescribed amiodarone or radiographic contrast media can develop iodine-induced hyperthyroidism (Ross et al., 2016). Hyperthyroidism may occur rarely in patients with metastatic follicular thyroid cancer, certain ovarian tumors, and TSH-secreting pituitary tumors. Laboratory findings that suggest hyperthyroidism in a patient with known hypothyroidism is due to over-replacement with exogenous thyroid hormone. The dose of levothyroxine should be adjusted to ensure a euthyroid status. Environmental factors may include viruses, a high-iodine diet, smoking, and selenium and/or vitamin D deficiency (Antonelli et al., 2020).

Biotin is a common supplement that can lead to an error in the laboratory reporting of thyroid labs. High doses of biotin make TSH appear falsely suppressed and T4/T3 levels falsely elevated, which can lead clinicians down the incorrect path of a hyperthyroidism diagnosis. Biotin has also been shown to cause falsely positive thyroid antibodies (TRab) that suggest autoimmune hyperthyroidism. It is imperative that patients who take biotin supplements stop them at least 2 days before their laboratory draw to provide the most accurate report (Ardabilygazir et al., 2018).

Signs and Symptoms: For patients of all ages, weight loss, fatigue, heat intolerance, tremor, and palpitations are the most common symptoms (Smith & Hegedüs, 2016). Older patients commonly report weight loss, decreased appetite, and cardiac manifestations. Atrial fibrillation occurs in more than 10% of patients older than 60 years with hyperthyroidism (Smith & Hegedüs, 2016). Thyroid hormones play an essential role in mood and cognition, along with emotional regulation. A wide range of symptoms may occur, such as depression, anxiety, or apathy, particularly in untreated patients (Riguetto et al., 2019). Older adults may experience diarrhea; a prior history of constipation may resolve with the onset of undiagnosed hyperthyroidism. A reduction or increase in appetite may be revealed; patients with severe hyperthyroidism may become cachectic. Photophobia and blurred and/or double vision may be reported.

Known as apathetic thyrotoxicosis, patients and/or caregivers may report that the patient is withdrawn, anorexic, and experiencing new onset of proximal muscle weakness, all contributing to inactivity (Samuels & Franklyn, 2018).

On physical examination, ophthalmological changes in the older adult such as exophthalmos are not as common; however, the risk of opthalmopathy is higher in older men (Smith & Hegedüs, 2016). Physical examination findings related to the eye may include proptosis, eyelid swelling, eyelid retraction, exophthalmos, extraocular muscle dysfunction, or increased lacrimation (Smith & Hegedüs, 2016). Patients may report ocular pain.

The examiner needs to remember that the thyroid is found lower in the neck and substernal area in older adults than in a younger person. Palpate the thyroid to determine presence or absence of nodules and/or tenderness. Thyroiditis may or may not be painful (Hughes & Eastman, 2021).

Because cardiac findings are prevalent in older adults with hyperthyroidism, a thorough cardiac examination is essential. Accurate measurement of pulse and blood pressure is important for the initial work-up and ongoing surveillance of patients with hyperthyroidism. Tachycardia, angina, atrial fibrillation, heart failure, and cardiovascular death may occur in patients with hyperthyroidism, particularly if untreated (Lillevang-Johansen et al., 2019). New onset of atrial fibrillation is much more common in the older adult with thyrotoxicosis. Look for evidence of peripheral nonpitting edema with asymmetrical plaques or nodules (pretibial myxedema).

A reduction in muscle mass may be detected (proximal weakness is common in hyperthyroidism), so muscle strength should be tested. Ask patients to demonstrate their ability to stand up from a seated position. If patients report recent falls, observe gait and assess the patient's ability to maintain balance. A coarse tremor may be evident; note for presence in

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outstretched fingers. Brisk tendon reflexes may occur; however, this manifestation is less common in older adults.

Although the signs, symptoms, and physical examination of patients with hyperthyroidism may be dramatic, it is important to recognize that many older adults with subclinical hyperthyroidism may be asymptomatic (Biondi & Cooper, 2018).

Diagnostic Tests: The TSH level is decreased in patients with hyperthyroidism. If the serum-free T4 result is normal following a decreased TSH, a serum-total T3 should be ordered. This value is sometimes increased, indicating T3 toxicosis (Ross et al., 2016). If the T3 result is also normal, the patient is said to have subclinical hyperthyroid disease. Serum antibody tests are useful in determining the cause of hyperthyroidism. Testing should include TRabs, which have a 96% sensitivity for detecting Graves' disease (Ross et al., 2016). Antibody testing is the preferred initial approach to reduce overall cost of diagnostic testing (Ross et al., 2016). Radioactive iodide uptake (RAIU) may be ordered to differentiate the cause of the thyrotoxicosis. For patients with Graves' disease, toxic adenoma, or toxic multinodular goiter, the RAIU will indicate increased iodine uptake, whereas other causes will show a low uptake, including thyroiditis (Ross et al., 2016). There is a diffuse uptake of RAIU in Graves' disease, whereas there is focal uptake in toxic nodular disease. In older adults, an electrocardiography is warranted to rule out associated cardiac arrhythmias, particularly if there is clinical concern. The use of thyroid ultrasound is indicated if the patient requires evaluation for thyroid nodules as thyroid cancer may coexist in up to 10.6% of with hyperthyroidism and nodules (Ross et al., 2016). Additional baseline laboratory tests should include a complete blood count and liver enzymes. Routine laboratory tests of patients with hyperthyroidism may reveal impaired glucose tolerance, increase in serum calcium levels, and elevated liver enzymes.

Differential Diagnosis:

- Anxiety
- Depression
- Diabetes mellitus, type 1 or type 2
- Severe anemia
- Leukemia
- Atrial fibrillation
- Pheochromocytoma
- Medication side effects

Treatment: Hyperthyroidism needs immediate attention in older adults because it is commonly associated with involvement of other organ systems, especially cardiac. Long-acting beta blockers are indicated in the early treatment of hyperthyroidism to control palpitations and tachycardia, unless limited by other concomitant conditions such as asthma or heart failure (Ross et al., 2016).

The three main treatments for hyperthyroidism are antithyroidal agents (thioamides), radioactive iodine ablation, and thyroidectomy. Methimazole is the preferred antithyroidal agent for older adults with hyperthyroidism. Methimazole works by blocking thyroid hormone synthesis. Current guidelines recommend that adults can remain safely on methimazole for up to 18 months or longer with careful monitoring. Potential rare but serious side effects include agranulocytosis (<0.5% of patients) and hepatic injury (<0.1% of patients) (Biondi & Cooper, 2018). For patients who are high risk for surgery or who have a limited life expectancy, methimazole treatment is the preferred long-term treatment (Ross et al., 2016). Radioactive iodine ablation is a definitive treatment option for patients with Graves' disease or toxic nodules, with a cure rate of approximately 75% in the 6 months following treatment (Hughes & Eastman, 2021). Ablation therapy may be preferred for patients who are healthier with a longer life expectancy and patients should be euthyroid before proceeding for treatment. Thyroid ablation is not recommended for patients who have moderate or severe orbitopathy due to the potential for worsening of the eye disease (Ross et al., 2016). Thyroidectomy is a final option but is generally not recommended in older patients unless they have a large goiter causing compressive symptoms, have concomitant thyroid cancer, or other options have failed to control the hyperthyroidism (Hughes & Eastman, 2021).

The treatment of subclinical hyperthyroidism has long been an area of debate in endocrinology. Current recommendations support treating older adults with subclinical disease due to the potential for harm from cardiac involvement, bone loss, or cognitive decline (Biondi & Cooper, 2018).

Follow-Up: Patients with hyperthyroidism require monitoring during the course of treatment, including symptoms, thyroid levels, and cardiac status. The patient must be aware of the potential of converting to hypothyroidism due to overtreatment or reversal of the underlying condition. Diagnostic studies, including TSH, free T4 (with or without T3) should be monitored every 6 to 8 weeks following treatment for Graves' disease until a euthyroid state is achieved and the patient is stable (Ross et al., 2016). Following radioactive iodine ablation, most patients eventually develop hypothyroidism within 2 to 6 months and will require thyroid hormone replacement such as levothyroxine. For patients with autoimmune hyperthyroidism, it is possible that they will enter remission after taking thioamides. Patient counseling of signs and symptoms of both hypothyroidism and hyperthyroidism is important. Careful monitoring of thyroid function is required on a regular basis. In patients with subclinical hyperthyroidism who do not have obvious sequalae or symptoms such as arrhythmias, it is reasonable to wait and repeat thyroid labs in 2 to 3 months to assess trends before deciding on treatment (Biondi & Cooper, 2018). Subnormal TSH levels are transient in up to 50% of patients (Biondi & Cooper, 2018). Autoimmune hypothyroidism occurs in 10% to 20% of patients during long-term follow-up (Smith & Hegedüs, 2016).

Sequelae: Complications that can develop in hyperthyroidism include ischemic heart disease, angina, cardiac arrhythmia, atrial fibrillation, myocardial infarction (MI), and heart failure. Bone density may decrease, rendering the patient susceptible to the development of osteoporosis. For patients who remain on antithyroidal treatments, potential side effects of methimazole should be evaluated continually, including agranulocytosis and hepatic injury. It is generally not recommended to follow laboratory studies (complete blood count [CBC], hepatic panel) unless the patient presents with signs and symptoms (e.g., severe infection).

Prevention/Prophylaxis: Hyperthyroidism is not known to be preventable; however, because thyroid disease is prevalent in older adults, regular screening for signs and symptoms of

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hyperthyroidism in patients with a history of other autoimmune conditions and/or family history of thyroid disease should be considered.

Referral: Patients with complicated hyperthyroidism should be treated by an endocrinologist, especially in the presence of complications or multiple comorbid conditions. Patients who wish to discuss treatment options or long-term management may also benefit from referral to a provider experienced in the care of thyroid disease.

Education: Patients should have a discussion with their health-care provider outlining the signs and symptoms of both hyperthyroidism and hypothyroidism. All three treatment options should be discussed, along with pros and cons of each. Patients should understand that the treatment of hyperthyroidism will require ongoing monitoring and screening for potential complications such as cardiac issues. Prescribed medications should be taken daily. Weight gain is common in patients after being treated for hyperthyroidism as the euthyroid state is recovered (Hughes & Eastman, 2021). Patients should be counseled to take measures to ensure a well-rounded diet with an appropriate calorie amount for their activity level to avoid unnecessary weight regain.

Clinical Recommendation	Evidence Rating	References
Older patients with subclinical hyperthyroidism who are high risk (heart arrythmias, bone loss) should be treated.	C	Biondi & Cooper, 2018
The use of beta-adrenergic blockade agents should be prescribed for older adults with symptomatic thyrotoxicosis.	A	Ross et al., 2016
Methimazole is typically the first-line treatment for hyperthyroidism. A baseline complete blood count and hepatic function panel should be drawn.	A	Hughes & Eastman, 2021
Definitive treatment (radioactive iodine) or thyroidectomy should be explored; however, remaining on methimazole may be a good option for many older adults.	B	Ross et al., 2016
Thyroid function studies (thyroid-stimulating hormone, free T4) should be followed every 6–8 weeks until stable and then every 3–6 months thereafter.	A	Ross et al., 2016
Older adults should be followed closely to ensure that thyroid function tests remain normal, and no sequelae develop (osteoporosis, weight loss, atrial fibrillation, cognitive changes).	A	Samuels, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

HYPOTHYROIDISM

Signal Symptoms: Weakness, cold intolerance, myalgias, depression, apathy, impaired memory, fatigue, hair thinning and/or loss, weight gain.

Description: Hypothyroidism is classified as either primary hypothyroidism, which is the failure of the thyroid gland to produce hormones; or secondary hypothyroidism, which occurs when the pituitary gland fails to secrete adequate amounts of thyroid-stimulating hormone (TSH). Hypothyroidism can further be divided into either overt (elevated TSH and low free T4) or subclinical (elevated TSH and normal free T4).

Etiology: Autoimmune thyroiditis, known as Hashimoto's thyroiditis, is the most common cause of hypothyroidism in people of all ages, causing 90% of hypothyroidism (Calsolaro et al., 2019). Other causes of primary hypothyroidism include thyroidectomy, radioiodine treatment, infection, or infiltration of the thyroid gland. Hypothyroidism can be iatrogenic from medications such as amiodarone, lithium, or tyrosine-kinase inhibitors (Calsolaro et al., 2019). Severe iodine deficiency or mild to severe iodine excess can cause hypothyroidism (Taylor et al., 2018). Causes of secondary (central) hypothyroidism include hypothalamic failure, pituitary adenoma or apoplexy, or, rarely, thyroid hormone resistance (Taylor et al., 2018).

Occurrence: Hypothyroidism occurs in up to 3.7% of the population of the United States (Taylor et al., 2018)

Age: Hypothyroidism is more common in adults older than 65 years, affecting 5% to 10% of women and 3% to 8% of men (Duntas & Yen, 2019). Women are up to 10 times as likely to be diagnosed with the condition (Taylor et al., 2018). Subclinical hypothyroidism may be present in up to 15% of the older population (Jasim & Gharib, 2018).

Ethnicity: Hypothyroidism is most common in White populations compared to Black, Asian, or mixed-race populations (Taylor et al., 2018).

Contributing Factors: Patients with previous thyroid dysfunction or goiter may develop hypothyroidism. Patients who have had extensive neck surgery, radiation, or prior thyroid surgery may develop hypothyroidism. Hypothyroidism can result from pituitary disease and certain infiltrative diseases such as sarcoidosis and scleroderma. Patients with first-degree relatives with thyroid disease are at risk.

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Signs and Symptoms: The symptoms of hypothyroidism may be commonly mistaken for the normal aging process. Older adults with hypothyroidism are more likely to present with mild, absent, or even atypical symptoms (Leng & Razvi, 2019). The most common symptoms in older adults are constipation, psychiatric problems, balance problems, and joint/muscle pain (Duntas & Yen, 2019). Other signs and symptoms may include dry skin, cold intolerance, weight gain, puffiness, slow heart rate and slow thinking (Jonklaas et al., 2014). Older patients may experience cognitive changes that could include confusion, disorientation, impairment in word fluency, or even dementia (Leng & Razvi, 2019). Additionally, patients with undiagnosed hypothyroidism may experience dyspnea and sleep apnea (Jonklaas et al., 2014). Given that the signs and symptoms of hypothyroidism are neither sensitive nor specific, it is recommended that they be correlated with laboratory findings (Jonklaas et al., 2014).

On physical examination, the overall appearance of the patient may reveal brittle nails, puffiness of the face and eyelids, thinning of the outer halves of the eyebrows, and xerosis (Watson & Guilbeau, 2021). During the thyroid examination, the examiner should first observe the thyroid while the patient swallows and then proceed to hands-on examination. A goiter may be present that feels rubbery, is not tender, and is possibly nodular. Thyroiditis may cause a tender thyroid gland. Thyroid nodules, common in older adults, are more likely to be benign if they feel smooth and easy to manipulate, whereas malignant nodules are more likely to be hard, irregular, fixed, and tender on palpation.

Other physical examination findings may include macroglossia, bradycardia, elevated diastolic blood pressure, diminished bowel sounds, delayed relaxation of deep tendon reflexes, nonpitting edema in the lower extremities (pretibial myxedema), carpal tunnel disease, and ataxia (Watson & Guilbeau, 2021). A mental status screening examination should be performed.

Diagnostic Tests: Overt hypothyroidism is defined as an elevated TSH and a suppressed free T4. It is important to note that TSH levels increase with the normal aging process. Some studies suggest that TSH can rise to around 8 mU/L in adults older than 80 years who do not have underlying thyroid disease (Duntas & Yen, 2019). Using age-specific intervals for thyroid levels may be the most appropriate evaluation method in older adults. An elevated TSH and a normal free T4 occurs in subclinical hypothyroidism. Thyroid antibodies should be drawn to assess for autoimmune disease. Antithyroid peroxidase antibodies and anti-thyroglobulin (TgAbs) are the most sensitive and specific (Calsolaro et al., 2019). An electrocardiogram may indicate sinus bradycardia, prolonged QT intervals, and possibly atrioventricular block and conduction disturbances (Jonklaas et al., 2014). A thyroid ultrasound is warranted in patients with thyroid nodule(s) or goiter (Jonklaas et al., 2014).

Differential Diagnosis: A number of conditions can mimic hypothyroidism. It is imperative for clinicians to conduct a full history and physical to determine the potential for comorbid conditions. The following diagnoses should be considered in addition to hypothyroidism:

- Dementia
- Anemia
- Depression
- Heart failure
- Ascites
- Chronic fatigue syndrome
- Fibromyalgia
- Sleep disorder (insomnia or obstructive sleep apnea)

Treatment: The goals of treatment for hypothyroidism are to resolve symptoms, achieve normalization of thyroid hormones, and avoid overtreatment (Jonklaas et al., 2014). Older adults with an underactive thyroid should be prescribed levothyroxine. Although most younger patients are started on weight-based levothyroxine dosing (1.6 mcg/kg/day), older adults should typically start with more conservative dosing. Generally, levothyroxine can be initiated at 50 mcg/day. For those who are underweight, frail or who have underlying cardiovascular disease, the starting dose should be 12.5 to 25 mcg/day. Patients should be reevaluated in 4 to 6 weeks for assessment of clinical presentation and TSH level. The dose can then be adjusted upward by 12.5- to 25-mcg intervals every 4 to 6 weeks (Jonklaas et al., 2014).

A thorough medication history is necessary when prescribing levothyroxine. Cholestyramine, ferrous sulfate, sucralfate, and antacids containing aluminum hydroxide can reduce medication absorption and effectiveness. Phenytoin, carbamazepine, rifampin, and anticoagulants may increase the drug metabolism. Patients taking levothyroxine should allow a 4- to 6-hour interval between these medications (Jonklaas et al., 2014). Dietary fiber and soy can also interfere with absorption, so levothyroxine needs to be taken on an empty stomach in the morning, at least 30 minutes before any other food, medication, supplement, or even coffee.

There is ongoing debate about whether older adults with subclinical hypothyroidism should be treated. Some studies suggest that symptoms do not improve in patients treated with thyroid replacement (Saifi et al., 2017). Other studies suggest that subclinical hypothyroidism is a risk factor for the development or exacerbation of type 2 diabetes, hyperlipidemia, hyperuricemia, and hypertension (Jasim & Gharib, 2018). The American Association of Clinical Endocrinologists recommends treating patients with subclinical hypothyroidism who have a TSH >10, have a TSH between 5 to 10 with a goiter, cardiac symptoms, or positive antibodies, or if there is significant concern about the progression to overt hypothyroidism (Jasim & Gharib, 2018; Peeters, 2017).

Treatment with thyroid formulations other than levothyroxine is not recommended in older patients as alternate treatments can be difficult to titrate, are often associated with higher rates of side effects, and have a lack of long-term safety data (Jonklaas, et al., 2014).

Follow-Up: Patients who are still needing dose adjustments should have thyroid levels checked every 4 to 6 weeks until the TSH is normal. Once stable, patients should have a routine TSH evaluation every 6 to 12 months. Patients with secondary hypothyroidism need a free T4 test because the TSH will not be accurate given lack of pituitary function. Monitor clinical signs and symptoms in all patients. Patients with subclinical hypothyroidism should be reevaluated every 3 to 6 months to determine whether hypothyroidism treatment is clinically indicated (Jonklaas et al., 2014).

Sequelae: Patients with untreated (or undertreated) hypothyroidism may develop hyperlipidemia and/or coronary artery disease or heart failure (Jonklaas et al., 2014). Patients who are overtreated with too high of a levothyroxine dose may experience bone loss leading to fracture, weight loss, or atrial

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fibrillation (Jonklaas et al., 2014). Patients with subclinical hypothyroidism and positive antibodies (TRAb and/or TgAb) convert to overt hypothyroidism at a rate of 4.3% per year (Calsolaro et al., 2019).

Prevention/Prophylaxis: Although the value of regular screening for thyroid disease has been debated for the general population, it is advocated for older adults who have higher rates of thyroid disease (Duntas & Yen, 2019).

Referral: If the patient has numerous complications or is not responding to treatment despite compliance, referral to an endocrinologist is appropriate.

Education: Remind patients about the potential for drug interactions that have been shown to interfere with L-thyroxine absorption, including over-the-counter products that contain iron, aluminum-containing antacids, and calcium carbonate. Patients should not increase their dosage if they are experiencing symptoms of hypothyroidism; instead, they should contact their health-care provider. Alert patients to contact their health-care provider if they experience signs and symptoms of hypothyroidism or hyperthyroidism. In most cases, the diagnosis of hypothyroidism will require lifelong management and follow-up.

Clinical Recommendation	Evidence Rating	References
Levothyroxine is recommended as the preparation of choice for the treatment of hypothyroidism.	B	Jonklaas et al., 2014
Levothyroxine needs to be consistently taken either 60 minutes before breakfast or at bedtime (3 or more hours after the evening meal) for optimal, consistent absorption.	A	Jonklaas et al., 2014
Levothyroxine should be separated from other potentially interacting medications and nutritional supplements (e.g., calcium carbonate and ferrous sulfate).	A	Jonklaas et al., 2014
Most older adults can be started on low-dose levothyroxine (50 mcg/day) and titrated up every 4–6 weeks as needed.	B	Jonklaas et al., 2014
Older adults with subclinical hypothyroidism should be treated if they have TSH >10, TSH between 5 and 10 with a goiter or positive antibodies, or cardiac involvement, or if there is significant concern about the progression to overt hypothyroidism.	C	Jasim & Gharib, 2018
The goals of treatment for hypothyroidism are to resolve symptoms, achieve normalization of thyroid hormones, and avoid overtreatment.	A	Jonklaas et al., 2014

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THYROID NODULES

Signal Symptoms: Neck mass, hyperthyroidism, thyroid cancer.

Description: A thyroid nodule is a lesion within the thyroid gland that is radiologically distinct from the surrounding thyroid parenchyma. There can be one or multiple thyroid nodules within the thyroid gland. The majority of thyroid nodules are benign, but each nodule holds independent risk for malignancy and should be evaluated individually (Durante et al., 2018).

Etiology: The majority of thyroid nodules are caused by overgrowth of normal thyroid tissue without a known cause. Iodine deficiency has been associated with increased risk of thyroid nodules (Kant et al., 2020). Ionizing radiation is a known risk factor for both benign and malignant nodules of the thyroid, with rates of nodule development up to 2% annually (Zamora et al., 2021). There can be a familial association in some disorders including multiple endocrine neoplasia type 2 leading to medullary thyroid cancer and familial adenomatous polyposis (Kant et al., 2020).

Occurrence: Thyroid nodules are very common; between 20% to 50% of asymptomatic patients examined with ultrasound or at autopsy have one or more thyroid nodules. Durante et al. (2018) state that about 16 million individuals in the United States have palpable thyroid nodules, whereas up to 219 million individuals have ultrasound detectible nodules. Most thyroid nodules, however, are small and not of clinical significance. Approximately 5% of women and 1% of men will come to clinical attention because of a thyroid nodule. Women are about four times more likely to have thyroid nodules than men (Castellnou et al., 2020).

The number of incidentally found thyroid nodules is growing with increased imaging modalities for other reasons not related to the thyroid. Although most thyroid nodules are benign, between 7% and 15% of thyroid nodules are found to be thyroid cancer of which the majority are differentiated thyroid cancer (Haugen et al., 2016). (This number may be higher with additional risk factors discussed below.)

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Age: The prevalence of thyroid nodules increases with age.

Ethnicity: Thyroid nodules are found in all ethnic groups, but most commonly in Whites. The rate of differentiated thyroid cancer is also highest in Whites. A study by Iwata et al. (2018) reported that 12.9% of incidentally discovered thyroid nodules were found to be differentiated thyroid cancer in Whites versus 4.9% in non-White patients.

Contributing Factors: There are multiple potential contributing factors to development of thyroid nodules. Iodine deficiency has been found to increase the risk of thyroid nodules, but this is now very rare in the United States after the introduction of iodized salt in 1924 (Kant et al., 2020). Increased age, obesity, and smoking are also potential contributing factors (Zamora et al., 2021). Head and neck radiation, occupational radiation exposure, or nuclear fallout increases the risk of thyroid nodule and thyroid cancer development. This is especially true if exposure occurred as a child (Durante et al., 2018). As stated above, family history of thyroid nodules and thyroid cancer can also contribute to increased risk (Haugen et al., 2016).

Signs and Symptoms: Most thyroid nodules are asymptomatic. If symptoms are present, they are typically related to size and location of the thyroid nodule. Globus sensation, dysphagia, dysphonia, and voice hoarseness can occur (Durante et al., 2018). Large goiters may lead to supine compression and fullness of the neck. Pemberton's sign is defined as facial plethora when the patient is instructed to lift both arms above their head. This is used to evaluate for venous obstruction of the thoracic outlet in large goiters (Pishdad, 2020). Reports of a rapidly growing nodule raises concern for more aggressive thyroid cancer and should be promptly evaluated (Haugen et al., 2016).

Diagnostic Tests: All patients with thyroid nodules should be evaluated with ultrasonography of the neck and a baseline thyroid-stimulating hormone (TSH) level. If the TSH is low, a radionuclide uptake scan should be performed to evaluate for a hyperfunctioning thyroid nodule. Thyroid nodules that are hyperfunctioning have a very low risk of malignancy and should not routinely be biopsied (Haugen, et al., 2016).

Thyroid ultrasound provides valuable information to stratify risk of malignancy based on nodule characteristics and size. There are multiple classification systems to stratify risk and determine when fine needle aspiration (FNA) should be performed. Many providers follow the American Thyroid Association (ATA) guidelines which vary slightly from the American College of Radiology (ACR) Thyroid Imaging Reporting & Data System (TI-RADS) that is frequently used by radiologists when reporting ultrasound results. Both systems label cystic nodules as benign and do not require an FNA. Very low risk nodules are partially cystic or spongiform nodules without other concerning features. A biopsy should be considered when then nodule is around 2 cm in size or larger. Low risk nodules are isoechoic (same color as the surrounding thyroid tissue) or hyperechoic (lighter than surrounding tissue) and solid. The size used to recommend an FNA varies among sources, but it is typically 1.5 cm in the largest dimension for nodules with low-risk characteristics. The estimated risk of malignancy for these nodules is about 5%. Hypoechoic nodules (darker than surrounding thyroid tissue) are considered intermediate risk for cancer, with about a 5% to 20% risk of malignancy. Thus, biopsy is usually recommended for hypoechoic nodules at 1 cm. The characteristics of nodules considered high risk include hypoechoic pattern and solid form with any of these additional features: microcalcifications, irregular borders, taller than wide, rim calcifications, or evidence of extension beyond the thyroid. These nodules should also be biopsied when they are 1 cm in the largest dimension and carry up to a 90% risk of malignancy according to the ATA (Durante et al., 2018). It is important to remember that each nodule carries independent risk for malignancy; therefore, multiple thyroid nodules may need to be biopsied in a particular patient with a multinodular goiter (Haugen et al., 2016).

The Bethesda Classification System is used to classify FNA results. Bethesda category 1 is nondiagnostic. This indicates there were insufficient cells to classify the sample and the patient will require a repeat FNA. Bethesda category 2 indicates a benign nodule. This holds a 0% to 3% predicted risk of malignancy. Bethesda category 3 is atypia of undetermined significance or follicular lesion of undetermined significance and holds a 5% to 15% risk of malignancy. Bethesda category 4 includes cytology results labeled follicular neoplasms or suspicious for follicular neoplasm and holds a 15% to 30% risk of malignancy. Both Bethesda category 3 and category 4 are considered indeterminate results and require repeat biopsy, usually 6 to 12 weeks after the initial biopsy. This is typically performed with the addition of molecular testing to help stratify risk by identifying genetic mutations or changes in gene expression associated with thyroid cancers. Bethesda category 5 indicates suspicious for malignancy with 60% to 75% risk and Bethesda category 6 show malignancy at 97% to 99% risk. Both Bethesda categories 5 and 6 should be referred to a surgeon with specialized training in thyroid surgery to discuss thyroidectomy or thyroid lobectomy (Haugen et al., 2016).

Differential Diagnosis: Other diagnoses to consider when evaluating a thyroid nodule include infectious or inflammatory diseases (including lymphadenopathy, sialadenitis, or neck abscess), congenital conditions (including brachial anomalies or thyroglossal duct cysts), goiter, or other head and neck malignancies (Durante et al., 2018).

Treatment: Treatment is determined based on thyroid nodule size and FNA biopsy results. Nodules that are benign or nodules that are too small to meet criteria for biopsy do not require any treatment. Nodules that have FNA results suspicious for malignancy or that are malignant should be referred to endocrine surgery for discussion of thyroid lobectomy or total thyroidectomy. Nodules that were indeterminate but with higher risk molecular testing results should also be referred for consideration of thyroidectomy. Other considerations for surgery include thyroid nodules that are causing aerodigestive compromise or nodules that are over 4 cm in size (Haugen et al., 2016).

Patients with hyperfunctioning thyroid nodules should be referred to endocrinology for treatment of hyperthyroidism through either radioactive iodine ablation, thioamide medication therapy, or surgery (Durante et al., 2018).

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Follow-Up: Follow-up is dependent on the risk of malignancy and if a biopsy has been performed. Nodules that have not been biopsied that are low risk should have a repeat ultrasound around 24 months. Intermediate to high-risk nodules that did not meet FNA size criteria should have a repeat ultrasound in 12 months (Haugen et al., 2016).

Thyroid nodules with benign pathology on FNA should still have repeat ultrasound monitoring in 12 months if they had high-risk features. Low- to intermediate-risk nodules should have repeat ultrasound monitoring in 12 to 24 months. Nodules that grow more than 20% (and at least 2 mm) in two dimensions or have an increase in total volume of 50% or more should have a repeat FNA given the potential for missed malignancy. If a nodule has had two benign biopsies, the nodule no longer needs ultrasound surveillance. Evidence is lacking for specific guideline recommendations for long term monitoring of thyroid nodules (Haugen et al., 2016).

Patients who have undergone a thyroid lobectomy should have TSH monitoring following surgery. About 22% of patients who had a thyroid lobectomy will have biochemical hypothyroidism and require thyroid hormone replacement therapy. The risk of postoperative hypothyroidism increases if the patient has positive thyroid antibodies or high normal TSH prior to surgery. All patients who have had a total thyroidectomy will require lifelong thyroid hormone replacement therapy (Haugen et al., 2016). Follow-up after surgery for thyroid cancer should initially be managed by an endocrinologist.

Sequelae: There are typically no long-term effects from thyroid nodules because most thyroid nodules are asymptomatic. Hyperfunctioning thyroid nodules that are untreated can lead to symptoms of hyperthyroidism, including tachycardia, palpitations, and diaphoresis. Long-term complications of untreated hyperthyroidism include atrial fibrillation, osteoporosis, and weight loss (Ross et al., 2016).

Prevention/Prophylaxis: The U.S. Preventive Services Task Force (USPSTF) does not recommend a screening ultrasound to evaluate for the presence of thyroid cancer in asymptomatic people because earlier detection did not lead to reduced mortality (2017). It is not recommended to routinely measure thyroglobulin or calcitonin in patients with thyroid nodules (Haugen et al., 2016).

Referral: Primary care providers should consider referral to endocrinology for management of thyroid nodules when there are high risk features for thyroid cancer including history of head/neck radiation, proximity to a nuclear fallout zone, or family history of thyroid cancer. All patients with a low TSH on initial screening should be referred to endocrinology for management of hyperthyroidism (Walker et al., 2019). Patient reports of a rapidly growing neck mass should prompt urgent referral for ultrasound and surgical evaluation. Surgical referrals can be determined based on pathology results (Bethesda 5 and 6 and high-risk molecular markers), large nodules (more than 4 cm), or thyroid nodules causing aerodigestive compromise (Haugen et al., 2016).

Education: It is important to reassure patients that most thyroid nodules are benign. The cornerstone of management includes ultrasound monitoring to assess size and characteristics of the thyroid nodule and will guide the decision for biopsy. A small percentage of thyroid nodules are toxic nodules, leading to hyperthyroidism. This is managed by either anti-thyroid medication, radioactive iodine ablation, or thyroidectomy (Kant et al., 2020).

Clinical Recommendation	Evidence Rating	References
Imaging with ultrasound remains an accurate method to guide recommendation for management of thyroid nodules.	A	Haugen et al., 2016
Initial evaluation of a thyroid nodule should include family history, evaluation of risk factors (including occupational exposures to radiation, radiation to the head or neck, and proximity to nuclear fallout zone), and symptoms of aerodigestive compromise or rapid nodule growth.	A	Haugen et al., 2016
A baseline thyroid-stimulating hormone (TSH) should be performed in all patients with a thyroid nodule to evaluate thyroid hormone function. If the TSH is low, a radionuclide uptake scan should be completed.	A	Kant et al., 2020
In the absence of concerning features or rapid growth, most nodules (including those that have been biopsied and are benign) can be followed with ultrasound annually. Low-risk nodules that have not been biopsied should have a follow up ultrasound in 24 months.	C	Haugen et al., 2016
The decision to biopsy a thyroid nodule should be based on the nodule's size and characteristics. The ATA classification or ACR TI-RADS system are commonly used to stratify nodule risk.	C	Durante et al., 2018
Surgical referral for thyroid lobectomy or total thyroidectomy should be considered for nodules >4 cm, symptoms of aerodigestive compromise, or thyroid nodules with cytopathology suspicious for malignancy (Bethesda 5), diagnostic malignancy (Bethesda 6), or high-risk molecular testing results.	C	Haugen et al., 2016

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CASE STUDY

A 65-year-old man presents with pain in the left-upper quadrant and epigastric area of his abdomen. He states that he had an episode of acute pancreatitis 10 years ago without any real sequelae. He does say that he has had episodes of abdominal pain in the epigastric and upper abdominal area over the years, but generally over time it goes away within hours or days, and he does not seek medical care.

On further questioning, he admits to drinking anywhere from two to six beers at least 3 days a week. He does not feel this is a problem; he does remember being told to watch his alcohol intake when he had acute pancreatitis, but after several years without pain he decided that alcohol must not be a factor in his abdominal pain. Further questioning about his symptoms has him telling you that his pain radiates to the left scapular area of his back. He admits to being thirstier recently and has been urinating more frequently as well. He has had to notch his belt two holes within the last year. He has not been trying to lose weight. He denies diarrhea but has had nausea without vomiting. Eating aggravates the pain but bending over at the waist helps the pain lessen.

Objective: Blood pressure (BP) 135/80 mm Hg, heart rate (HR) 80 beats/min, BMI 21.

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What are the differential diagnoses that you are considering?
4. What laboratory tests will help you rule out some of the differential diagnoses?
5. What imaging studies are generally ordered for a patient with these symptoms?
6. What is your treatment plan for this patient?
7. Will you be looking for a consultation?

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CHAPTER 19

Hematological Disorders

Evelyn Duffy

ASSESSMENT

Assessment of the hematological system needs to include a detailed history, physical examination, and diagnostic testing. The presenting symptoms of hematological deficiency can include excessive bruising, petechiae, unexplained bleeding, epistaxis, or inflamed lymph nodes. Older adult patients with severe anemia may complain of fatigue, dizziness, heart palpitations, headache, shortness of breath with exertion, and exercise intolerance (Ianni et al., 2021). Confusion, depression, and cold intolerance are also common. Some patients present with unusual food cravings, referred to as pica. In many cases, symptoms are absent, subtle, or erroneously attributed to the aging process, and anemia is identified on routine complete blood count (CBC). Identification is important because anemia in older adults has been associated with an increase in all-cause mortality (Lanier et al., 2018).

The medical history obtained from the patient should include history of anemia, hemoglobin abnormalities (sickle cell or thalassemia), recent surgery or blood transfusion, lymphadenopathy, clotting disorders, and occupational or other known exposure to toxic agents or radiation. Inquire about comorbid conditions and any family history of anemia. Review current medications both prescribed and over-the-counter. Particularly important are anticoagulants, including aspirin, chronic use of NSAIDs, metformin, levodopa, or the use of proton pump inhibitors (PPIs) or histamine-2 blockers.

Some of the most common causes of hematological disease in the older adult include iron-deficiency anemia, anemia of chronic disease, and nutritional deficiencies, which have an increased incidence in patients older than 60 years. Myelodysplastic syndromes and leukemias are also becoming more common. Systemic disease and severe clotting disorders need to be included in the differential diagnosis.

Physical Examination and Diagnostics

The physical examination should be complete and thorough. Assess the eyes for pale conjunctiva or icteric sclera, which occur with some anemias. Inspect the skin for pallor or jaundice and note the temperature of the skin (Ianni et al., 2021). Check for petechiae, bruising, and pale mucous membranes. Assess the nails for the presence of koilonychia (concave spoon nails), which is seen with chronic iron deficiency (Rathod & Sonthalia, 2021). Check for lymphadenopathy. On oral examination there may be several signs of possible anemia. A red, painful, beefy tongue can be present with pernicious anemia. In iron deficiency, angular cheilitis, atrophic glossitis, and erosion of the buccal mucosa may be evident (Halim et al., 2018). Tachypnea and tachycardia can be seen with severe anemia. Auscultate the heart for any systolic murmurs; severe anemia can cause a loud apical and mid-precordial murmur. An early diastolic murmur may also occur, heard best at the left sternal border. Palpate the abdomen for tenderness or hepatosplenomegaly. A rectal examination and stool guaiac should be completed if the history indicates possible gastrointestinal (GI) blood loss. Hematuria can be indicative of hemolytic anemia. Complete an assessment of mental status and, if indicated by the history, do a complete neurological examination. The absence or presence of physical findings on examination helps to narrow the clinical diagnosis. Ultimately hematological diagnoses cannot be made without laboratory work-up; they cannot be based on signs and symptoms alone.

Based on the history and physical examination, choose appropriate diagnostic tests to complete the hematological assessment:

- CBC with differential will guide additional choice of diagnostics
- Comprehensive metabolic panel (CMP)
- Hemoglobin A1c
- Urinalysis
- Erythrocyte sedimentation rate (ESR)
- Iron, total iron-binding capacity (TIBC), and ferritin if iron-deficiency or microcytic anemia is considered
- Vitamin B_{12} and folate levels to rule out pernicious anemia or other megablastic anemia
- Reticulocyte count to assess for blood loss or blood cell destruction
- Hemoglobin (Hgb) identification (electrophoresis) to assess for Hgb abnormalities or thalassemia

When the assessment is complete, plans will address the specific diagnosis. If etiology is unclear or the probable diagnosis is complex, consultation or referral to hematology is necessary to evaluate the older adult patient further.

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APPROACH TO INTERPRETING THE COMPLETE BLOOD COUNT

The CBC is essential to the diagnostic decision-making process when assessing the hematological system. Therefore, every advanced practice registered nurse (APRN) should be fluent in the language of the CBC. Although inexpensive and readily available, it should not be ordered routinely. Know the rationale for the choice of the test and how it will inform the care of the older adult.

The CBC provides information on three cell lines: white blood cells (WBCs), red blood cells (RBCs), and platelets. All three are the result of the differentiation of the hematopoietic stem cells in the bone marrow. Only mature blood cells are detected in a normal CBC. The CBC also includes a determination of hemoglobin (Hgb), hematocrit (Hct), and RBC indices. The differential, if added, includes identification of the different WBC types. Common abnormalities on the CBC include anemia, leukemia, polycythemia, thrombocytosis, and thrombocytopenia. Other abnormalities can occur because of infection, inflammation, coagulopathies, malignancies, and exposure to toxins. Abnormal results on the CBC may be the first sign of disease in an asymptomatic patient.

Red Blood Cells

The RBCs, or erythrocytes, supply oxygen to the tissues and remove carbon dioxide waste. Their biconcave shape provides for a large surface area to accomplish the gas exchange. RBCs survive in the circulation for about 120 days. They have no nucleus and cannot divide. To create a healthy RBC the older adult needs to have functioning bone marrow, adequate erythropoietin production by the kidneys, and adequate substrates (iron, cobalamin [vitamin B_{12}], and folate [vitamin B_9]).

In response to low oxygen states, rather than a decrease in RBCs, the kidneys produce erythropoietin, which in turn stimulates RBC production in the bone marrow. RBC production has the potential to increase to 10 times the normal rate. Renal disease decreases erythropoietin production and can be a cause of anemia. Inadequate substrates, iron, B_{12}, or folate also result in anemia. B_{12} and folate are needed for cell growth, DNA synthesis, and reproduction. Iron is needed for Hgb synthesis. Hgb is the iron-containing protein in red blood cells that carries oxygen. Hgb is about 90% of the weight of the RBC.

Reticulocytes are the immediate precursors to RBCs. In healthy patients they only remain in circulation for 1 day before becoming fully mature. An increase in reticulocytes occurs when there is an acute blood loss or if there is hemolysis. The reticulocyte is a percentage of RBCs, so in anemia it may be erroneously elevated. Calculating a reticulocyte production index (RPI), or corrected reticulocyte count, is indicated. The RPI is the reticulocyte percentage times the patient's Hct/normal Hct (normal value is usually 45%). A normal RPI is between 0.5% and 2.5%. An RPI less than 0.5% is a hypoproliferative state, whereas a value greater than 3% indicates a hyperproliferative state due to hemolysis or acute blood loss. If hemolysis is suspected, additional tests, including lactate dehydrogenase (LDH), total bilirubin, and haptoglobin, can confirm the diagnosis (Phillips & Henderson, 2018). After identifying the cause of anemia and treating it effectively, there will be an increase in reticulocytes as much as 20%. In the setting of bone marrow failure, reticulocytes are not adequately produced.

The CBC includes a report of the RBC count. The result is the number of RBCs per liter of blood in International Units, for example 5.43 × m/uL (a normal count). The Hgb and Hct add information to further define the result. Hgb is produced in the immature RBC and is complete when the RBC matures. Hgb is measured in grams per deciliter; for example, 14 g/dL (a normal result for both men and women). There are different types of Hgb: A (healthy adult), F (fetal and newborns), S (sickle cell), C, and E (those of Southeast Asian descent). The heme portion of Hgb provides the red color to the RBC, and binds the oxygen. The globin portion is made up of four amino acid chains, each of which is associated with a heme. The amino acid chains (also called globin chains) of a healthy adult (HgbA) include two alpha and two beta chains, whereas fetal Hgb (HgbF) has two alpha and two gamma chains. HgbA2, a normal variant of HgbA, has two alpha and two delta chains. HgbA2 is present in low levels in adults and is increased in beta thalassemia. In the disease alpha thalassemia, there is a lack or absence of alpha chains and excess beta chains. In beta thalassemia there is a lack or absence of beta chains and an excess of alpha chains. Both are the result of a genetic defect and can occur with either a major or minor presentation, which may severely affect health or have no symptoms at all. To determine the type of Hgb, a Hct identification or hemoglobin electrophoresis can be ordered.

The Hct represents the ratio of RBCs to total whole blood volume and is reported as a percent. Total whole blood volume includes RBCs, WBCs, platelets, and plasma. The Hct is normally about three times the Hgb level, which is about three times the number of RBCs; this is referred to as the rule of 3s. Hyperglycemia and hypernatremia can result in enlarged RBCs and will increase Hct. In dehydration, which is not uncommon in older adults, the RBCs, Hgb and Hct will all appear higher. Comparison with blood urea nitrogen level (BUN) can help to assess the accuracy of the result. In the situation of fluid overload, the opposite occurs.

Other RBC measures of significance include the reticulocyte count, the mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH), mean corpuscular hemoglobin concentration (MCHC), and the often-overlooked red cell distribution width (RDW). The MCV should be assessed after the RBC, Hgb, and Hct. The normal MCV value is between 80 and 100 fL and is referred to as normocytic. Values below 80 fL are considered microcytic (smaller than normal), while values above 100 fL are considered macrocytic (larger than normal). The size of the RBC can be helpful in identifying the cause of any anemia as well as other hematological disorders.

MCH measures the average weight of the Hgb in the RBC—a ratio of Hgb/RBC. It may not be reported on current CBC results. Because the MCH is a calculated value, its value can decrease by the same conditions that elevate the RBCs. The MCHC can be helpful to judge contributing factors to the CBC results. It is a ratio of the Hgb to the Hct and should be about 1/3 (remember the rule of 3s). If the result is lower than the reference range, the cells are hypochromic or have less hemoglobin. Values greater than the norm are not referred to as hyperchromic because the RBCs cannot accumulate more than the normal concentration of Hgb. If cells have an elevated MCHC, it may be due to a change in the shape of the cell.

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The RDW describes the discrepancy in the size of the cells, anisocytosis, reported as the standard deviation. The greater the deviation in the RDW the greater the variation in cell size. The RDW-CV is the width of the frequency distribution of the cell volumes at one standard deviation from the mean divided by the MCV. Normal range is 13% + 1%. Variations can be another indication of the type of abnormality responsible for any irregular values.

White Blood Cells

The WBCs, or leukocytes, can be divided into two main categories: phagocytes and immunocytes. All WBCs have nuclei, and they may be categorized as myeloid or lymphoid depending on their origin. Myeloid cells, or myelocytes, include neutrophils, eosinophils, basophils, and monocytes. Monocytes and neutrophils are phagocytes that kill unwanted microorganisms.

Myelocytes that contain granules in their cytoplasm and are classified as granulocytes include neutrophils, eosinophils, and basophils. Granulocytes take about a week to develop in the bone marrow, remain in circulation for 6 to 12 hours, then are sequestered for 2 to 3 days in the spleen tissue before ultimately being eliminated. Neutrophils are mature granulocytes and make up 60% to 70% of WBC types. They are also called segmented neutrophils (segs) or polymorphonuclear neutrophils (PMNs) or polys. They are the most common cell type in the early stage of inflammation. With increased demand, additional neutrophils can be released from the bone marrow. In inflammation they migrate out of the capillaries and into the tissue where they digest organisms and debris and form pus. Eosinophils are about 2% to 4% of the WBC total. Eosinophils increase in response to allergies, collagen disease, and disease of the spleen and central nervous system. Eosinophils are also seen in mucous membranes. Basophils respond in allergies and in antigen responses by releasing histamine and dilating blood vessels. Basophils circulate in the bloodstream. They are less than 0.5% of WBC count.

Monocytes and lymphocytes do not contain granules. Monocytes are myelocytes and are the largest of the WBCs in size. They are young cells in the bloodstream then move to tissue where they become mature macrophages. Monocytes are the major cell population in the body tissues. Their levels increase in response to wounds, malignancy, and inflammation and form the mononuclear phagocytic system.

Lymphocytes are also nongranulocytes and are responsible for the immune response. They are the second most numerous WBC circulating in the bloodstream but are more common in the lymphatic system. Lymphocytes include two cell types: B cells, which make antibodies and enhance pathogen destruction, and T cells. T cells mature in the thymus and are responsible for cell-mediated immunity, which does not involve antibodies. T cells can stimulate B cells, which trigger humoral or antibody-mediated immunity.

An elevation of WBCs is called leukocytosis. It commonly occurs in infection, inflammation, or tissue necrosis that occurs in myocardial infarction, burns, leukemia, or lymphoma. Elevations in WBCs have also been noted after ischemic stroke. In leukemia, elevations in WBCs may be greater than 100,000. Stress can also cause an elevation in WBCs, but they should rapidly return to normal. After identification of an increase in WBCs, further review of the cell constituents can help clarify the diagnosis. Unsegmented neutrophils, or bands, are immature neutrophils that are released when there is an increased demand. This may be referred to as a *shift to the left* or bandemia. This result may be noted before there are other overt signs of infection.

Platelets

The smallest of the three population of cell types are the platelets or thrombocytes. They are nonnucleated disk-shaped cells with a life span of 9 to 12 days. Platelets are fragments of megakaryocytes that are located in the bone marrow. They are important in the clotting cascade. They are the initial reactants when there is damaged epithelium. Their response is rapid, occurring in 3 to 5 minutes. Excessive platelets, known as thrombocytosis, can result in clotting disorders. Very elevated platelet counts are present in myeloproliferative disorders. Thrombocytopenia is a low platelet count and can result in bleeding disorders.

Clarifying Complete Blood Count Results

After the CBC has been evaluated, several additional laboratory studies can further clarify the finding. If there is an unexpected result on the CBC that seems inconsistent with the patient's presentation, a reasonable response might be to order a repeat CBC. It is also possible to ask the laboratory to do a peripheral blood smear. A peripheral blood smear provides the opportunity for direct visualization of the cells. It is a sample of blood that is smeared on a microscope slide by a laboratory professional and examined under magnification to add more clarity regarding the size, shape, and number of cell types. The visualization allows for identification of other types of cells such as spherocytes or sideroblasts. An indication for a smear might be a wide RDW noted on the CBC.

ANEMIA

Anemia is a decrease in the whole-body red cell mass (RCM). It is not a disease; it is the sign of an underlying disease. Anemia is ultimately a laboratory diagnosis, with Hgb and Hct being representative of the RCM. However, these may not accurately represent RCM when there is a volume increase, such as in pregnancy or when patients have received IV fluids, referred to as relative anemia or dilutional anemia. Determining the cause of the anemia is the challenge for the provider. Treatment should not be introduced based on an abnormal laboratory value alone.

Anemia in older adults has a prevalence of 10% to 24% overall, including 7% to 11% in those living in the community, 47% of those in long-term care, and 40% of hospitalized older adults (Stauder et al., 2018). Even slightly low hemoglobin levels have been independently associated with increased morbidity and mortality, affecting functional ability and both cognitive status and mood (Lanier et al., 2018; Stauder et al., 2018). Anemias have been associated with cardiovascular disease, decrease in cognitive function, mood disorders, falls, and fractures. Patients with anemia have more frequent hospitalizations with longer stays.

The thresholds for definition of anemia were established by the World Health Organization study group on nutritional anemia in 1968 and remain the overall reference values. These values are a Hgb of less than 13 g/dL in an adult male and less than 12 g/dL in an adult female. Recent attempts to

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modify this definition based on race or age have not been universally adopted (Stauder et al., 2018).

Many patients with anemia are asymptomatic. The anemia is noted when the provider receives the abnormal result from a complete blood count (CBC). Lack of symptoms in an older adult is not uncommon, particularly if the anemia developed over time and the body has adjusted to the reduced number of red blood cells (RBCs) (Ianni et al., 2021). An older adult may attribute symptoms to their older age, and the provider may assume symptoms, such as fatigue or dyspnea, are due to an existing chronic illness. Even without concerns from the patient, a thorough review of systems should not be omitted.

Laboratory assessment of anemia begins with the CBC. A systematic approach to analysis of the CBC is critical to the accuracy of the final diagnosis. After determining that the Hgb is low, comparison to previous results adds additional data. A Hgb of 9.0 g/dL may not require an urgent response if it has been in that range historically. However, if recent Hgb results were all in the normal range, a Hgb of 9.0 g/dL would indicate a definite change in condition and an urgent response would be necessary. If the choice is to send the patient for a more urgent work-up, it is necessary to communicate the details of your concern to the acute care providers. In acute care settings a Hgb below 7.0 g/dL is the criteria most often used to order a blood transfusion, so anything higher may be dismissed as non-urgent unless there is evidence of an acute bleed. This is an example of the communication necessary for a successful handoff between primary and acute care providers.

After determining that the Hgb and Hct values are low, the next step is to review the mean corpuscular volume (MCV) and the red cell distribution width (RDW). The MCV is most informative, and its interpretation informs the follow-up analysis. Recall that the normal range for the MCV is 80 to 100 fL (normocytic). Results below 80 fL indicate that the RBCs are smaller than normal (microcytic). Results greater than 100 fL indicate that the RBC is larger than normal (macrocytic). The RDW is helpful, particularly in interpretation of values that are normocytic or macrocytic. A large RDW indicates a mixed cell population, and a normocytic result could occur if the patient has a combination of an iron and a B_{12} deficiency. In that circumstance, a large RDW identifies the variation in cell size and requires an expanded differential diagnosis (Ianni et al., 2021). After the anemia has been defined as normocytic, microcytic, or macrocytic, further diagnostic tests are required to clarify the cause and develop a treatment plan.

The following sections will address each of the abnormal presentations in detail, normocytic anemia, microcytic anemia, and macrocytic anemia. The sections include the common causes of each type, their treatment, as well as those less common hematological concerns that should not be missed.

NORMOCYTIC ANEMIA

Description: A low Hgb and Hct and a normal MCV between 80 and 100 fL on a CBC is classified as normocytic anemia. This means that the cells are the normal shape and size but have a low Hgb. To verify that the cells are all a normal size, check the RDW. If it is elevated, it indicates that the cells are a mixture of sizes, and a peripheral blood smear can be requested to further identify the cell types. In anemia of inflammation (AI) there may be a normal or even an increased amount of iron stores, but a low level of iron in the cells. The inflammation prevents the cells from using the stored iron.

Etiology: In the past normocytic anemia was often identified as the anemia of chronic disease (ACD). This label was not inaccurate, but it failed to identify the chronic diseases responsible and the potential treatments appropriate to the cause. Normocytic anemia often occurs due to chronic inflammation characteristic of chronic kidney disease, cancer, or autoimmune diseases (Stauder et al., 2018). A more appropriate label may be AI rather than ACD (National Institute of Diabetes and Digestive and Kidney Diseases [NIDDKD], 2018). Chronic kidney disease (CKD) is a primary contributor to AI. In CKD there is a decline in the synthesis of erythropoietin (EPO). EPO promotes the survival, proliferation, and differentiation of erythrocyte precursors. As the glomerular filtration rate decreases and CKD progresses, EPO is reduced and results in deficiency. If kidney function continues to decline, the progression of anemia may ultimately result in true microcytic iron-deficiency anemia. Even a mild decline in GFR can compromise a robust synthesis of EPO. Inflammation inhibits EPO function and may decrease hepcidin level, which influences iron metabolism (Begum & Latunde-Dada, 2019). Hepcidin is produced in the liver and regulates the metabolism and transport of iron. It has a major role in AI. AI can shorten the RBC survival, normally about 120 days.

Hemolytic anemia should also be included in the differential diagnosis of normocytic or macrocytic anemia (Phillips & Henderson, 2018). Hemolytic anemias can be intrinsic or extrinsic. Intrinsic destruction of the RBCs is due to a defect in the cells themselves such as in hereditary spherocytosis, or a problem with a red cell enzyme, as in G6PD deficiency. Extrinsic hemolytic anemia occurs when RBCs that are normal undergo destruction from direct trauma, infection, malignancies, autoimmune disorders, or medications. Another consideration is the cause of the hemolysis, which can be extravascular (most common) or intravascular. Extravascular hemolysis occurs when the RBCs are removed prematurely from circulation by the liver and spleen due to hemoglobinopathies such as sickle cell or thalassemia. Extravascular hemolysis can also be due to enzymopathies such as G6PD deficiency, membrane defects such as spherocytosis, or be a result of medications. Intravascular hemolysis occurs when the cells are broken up within the circulatory system which can result from a transfusion reaction or infection. Causes of hemolytic anemia are numerous. If identified referral to hematology for a complete work-up is the appropriate next step.

Occurrence: With their high burden of chronic conditions, AI is a common cause of anemia in older adults, accounting

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for more than one-third of the cases. The prevalence of anemia increases twofold over the general population in patients with CKD. In those with CKD, the prevalence of anemia increases with declining function, approaching 53.4% at Stage 5 (Portolés et al., 2021). About 1 million people older than 65 years have anemia due to inflammation (NIDDKD, 2018).

Age: Normocytic anemias due to inflammation or CKD can occur at any age, but older adults are more likely to have AI because they are more likely to have chronic diseases that cause inflammation (NIDDKD, 2018). Before age 75 women are more likely to have anemia than men, but after age 75 men are more likely to have anemia than women. Sex distribution varies based on the underlying cause of anemias. Some of the difference may be due to the World Health Organization's sex-specific value of less than 13 g/dL being used for males across all ages (as opposed to less than 12 g/dL for females). Because Hgb declines slightly and anemia prevalence rises with aging, the prevalence rate for men is higher with advancing age (Cappellini & Motta, 2015).

Contributing Factors: The presence of one or more chronic conditions, such as cancer, chronic infection, chronic inflammation, or autoimmune conditions, is a contributing factor to the development of AI and is also a factor in hemolytic anemia.

Signs and Symptoms: Onset of signs and symptoms in AI can be confounding and is usually masked by the underlying conditions. The typical symptoms of anemia, such as fatigue, weakness, dyspnea, and palpitations, may be present but are nonspecific. In older adult patients these symptoms tend to be attributed to the aging process. Additionally, many older patients adjust their activities as their bodies make physiological adaptations for the underlying disease. Signs specific to hemolytic anemia include jaundice or hematuria. With chronic hemolysis, lymphadenopathy or hepatosplenomegaly may be detected on physical examination (Phillips & Henderson, 2018). Although it may be difficult to assess in the older adult population, conjunctival pallor is a reliable sign. Its absence, however, cannot exclude anemia. Other signs may be discovered through incidental laboratory testing. Cognitive decline, depression, and decreased quality of life may also accompany AI. The clinician should have a high index of suspicion of AI in older adult patients with chronic conditions, and any presentation of the previous symptoms should prompt further evaluation.

Diagnostic Tests: A first step in confirming AI is to review the RDW to evaluate the possibility that the MCV includes a consistent cell size. A smear may be requested to determine more specifics regarding the cell population. Checking the reticulocyte count and calculating RPI can identify if the anemia is hypoproliferative or hyperproliferative. If hyperproliferative, additional laboratory work should be ordered to assess for hemolysis, including LDH, haptoglobin, total bilirubin and urinalysis. In hemolytic anemia, in addition to reticulocytosis, there will be an increased LDH, increased total bilirubin, and decreased haptoglobin levels. Ordering a direct antiglobulin test (Coombs') will evaluate for an autoimmune hemolytic anemia (Phillips & Henderson, 2018). To evaluate kidney function as a cause of normocytic anemia, check the blood urea nitrogen (BUN), creatinine and estimated glomerular filtration rate. To differentiate AI from iron-deficiency anemia (IDA), a serum ferritin is key. Serum ferritin is a measure of iron stores, and the main abnormality in AI is the impaired ability to use iron stores in the reticuloendothelial system (liver/spleen). Values in AI are reflected in a normal to high ferritin level (i.e., iron is present but inaccessible for use). In contrast, ferritin levels in IDA are low (below 30 ng/mL). Ferritin is an acute phase reactant and is increased in the presence of inflammation. That explains the higher levels in AI, but it is also less reliable as a measure to define IDA. Other measures such as serum transferrin can be helpful. If measurement of serum hepcidin becomes more readily available, it would be an excellent choice in the differential diagnostic process, as it is very low in IDA and elevated in AI.

Inflammatory markers of concern in AI include tumor necrosis factor alpha (TNF-alpha), interleukin-1 (IL-1), interferon gamma (IFN-gamma), and IL-6. Decision regarding these less-common tests could be deferred until initial assessment is complete. Referral to hematology for additional work-up is always an option.

Table 19-1 compares the laboratory data in AI and IDA. Research is being directed to look at new serological markers, such as hepcidin, that may be used in the future to better distinguish AI from IDA.

Differential Diagnosis: Differential diagnosis may include almost any cause of anemia. Early or partially treated IDA is the main differential diagnosis for AI because microcytosis may be present or absent in either disorder. Normocytic indices may be the result of a mixed anemia due to vitamin B_{12} and/or folate deficiency in addition to IDA. Due to potential neurological complications, it is important not to miss a vitamin B_{12} deficiency. Hypoproliferative anemias (e.g., renal disease, endocrine disorders) and thalassemia are also considerations. Blood loss and hemolysis are other optional causes.

Treatment: Treatment of AI focuses on management of the underlying disorder. Although there is no specific treatment for AI, if anemia is severe or underlying disease is resistant to treatment, erythropoiesis-stimulating agents (ESAs) (e.g., Epogen, Procrit) may be used (Begum & Latuda-Dada, 2019). Large trials highlighted the harm of using high-dose ESA with a goal of complete correction of anemia and raising the Hgb above 11 g/dL, which was associated with poor outcomes. The poor outcomes included increased risk of stroke, rapid progression of malignancies, and increased mortality. Current guidelines recommend the use of lower doses of ESA and only if Hgb is below 10 g/dL (Begum & Latuda-Dada, 2019). Coverage for ESAs by Medicare and other third-party reimbursement requires documentation of laboratory test findings indicative of AI. Current recommendations include the addition of iron, either oral or parenteral. Dosage for a patient with renal disease should be individualized and be as low as possible to reduce risk of poor outcomes while also reducing the need for transfusion.

Vitamin D reduces hepcidin gene transcription, lowers serum levels by 50%, enhances erythropoiesis, and reduces inflammation. It was not as effective in mild to moderate anemia. Cholecalciferol (vitamin D_3) is the formulation of choice and is also useful in the prevention of mineral and bone disorders common in CKD.

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TABLE 19-1 Laboratory Data in AI and IDA[1]

LABORATORY TEST	AI	IDA
CBC		
• Hemoglobin	<12 g/dL (120 g/L) women <13 g/dL (130 g/L) men Rarely <10 g/dL (100 g/L)	<12 g/dL (120 g/L) women <13 g/dL (130 g/L) men
• Mean corpuscular volume: (MCV)[2]	80–96 mcm^3 (normocytic)	70–80 mcm^3 (microcytic)
• RBC distribution width: (RDW)	Normal	Increased
Serum ferritin	Normal or increased	Decreased
Serum iron	Decreased	Decreased
Total iron-binding capacity	Decreased	Increased
Transferrin	Normal to low	Increased
Transferrin saturation	Reduced	Reduced
Reticulocyte production index	Decreased	Decreased
Reticulocyte count	Decreased	Decreased
Peripheral smear	Normochromic	Microcytosis, hypochromic

[1] *Changes in relation to respective normal values*
[2] *Overlap, may be normal with AI + IDA*

Abbreviations: *AI = anemia of inflammation; CBC = complete blood count; IDA = iron deficiency anemia; RBC = red blood cell; g/dL = grams per deciliter, L = liter*

Follow-Up: Follow-up is individualized depending on underlying cause and extent of the anemia. A robust rise in a reticulocyte count completed 5 to 10 days after initiating treatment may confirm the correct course.

Sequelae: Variable depending on the underlying condition.

Prevention/Prophylaxis: Early education regarding healthy lifestyle may prevent or delay onset of some chronic conditions. Avoidance of renal toxic substances such as NSAIDs can protect the kidneys. Use of tobacco and frequent alcohol intake may also contribute to the development of AI or hemolytic anemia.

Referral: Referral is indicated for progression of anemia and/or resistance to treatment of underlying condition; significant anemia of unknown causation; and severe, symptomatic anemias.

Education: Teaching the patient and family about the importance of lifestyle modifications and adherence to a treatment plan for management of underlying conditions may be a factor in preventing or slowing the progression of chronic diseases. A healthy balanced diet is indicated to prevent or correct dietary deficiencies that can contribute to other forms of coexisting anemias.

Clinical Recommendation	Evidence Rating	References
Anemia is an independent risk factor for increased morbidity and mortality and decreased quality of life in community-dwelling older persons.	B	Joosten, 2018 Lanier et al., 2018
Anemia is associated with increased length of stay, hospital readmissions, and mortality in older adults.	B	Joosten, 2018 Lanier et al., 2018
IV iron therapy may have a beneficial effect in treating AI.	A	Begum & Latunde-Dada, 2019
ESAs should be initiated at lower doses and only if the hemoglobin is below 10g/dL.	B	Begum & Latunde-Dada, 2019
When possible, treatment of the underlying disease is the therapeutic approach of choice for anemia of chronic disease.	C	Begum & Latunde-Dada, 2019 Stauder et al., 2018
After hemolytic anemia is identified a peripheral blood smear should be ordered.	C	Phillips & Henderson, 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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MICROCYTIC ANEMIA

Signal Symptoms: Fatigue, weakness, pica, koilonychias (spoon nails), pale conjunctiva, cheilitis, glossitis. The patient may be completely asymptomatic.

Description: Microcytic anemias are identified by red cells that are smaller than normal. A mean corpuscular volume (MCV) less than 80 is indicative of microcytosis. However, microcytic anemias can occur concurrent with other anemias. When the MCV is 80 to 100 (normocytic) or above 100 (macrocytic) but the red cell distribution width (RDW) is wide, it can be an indication of a mixed anemia. In that presentation ordering a follow-up peripheral blood smear can help to identify the presence of microcytic cells.

Etiology: The small cell size is due to a decreased production of Hgb. In microcytic anemia the cells are also hypochromic. Causes of microcytic anemia include a lack of iron (iron-deficiency anemia), a problem of iron delivery (chronic kidney disease [CKD], inflammation) or a lack of globin production, the protein that binds iron (thalassemia).

Iron-deficiency anemia (IDA), the most common cause, can be a result of inadequate intake, decreased absorption, increased demand, or increased loss of iron. In the United States, IDA is less often a result of dietary deficiency because iron is added to many foods for enrichment and fortification. Because of this addition of iron in foods, iron deficiency is most often caused by blood loss (Lanier et al., 2018). Most older adults with IDA have an underlying gastrointestinal (GI) tract abnormality. A GI source of blood loss should be assumed until proven otherwise, it cannot afford to be missed. Anemia of inflammation (AI) may initially be normocytic, but as the disease process advances it can develop into a microcytic anemia.

Thalassemias are a group of inherited disorders resulting in a defect of the Hgb chains. The globin part of Hgb has four amino acid chains and in healthy adults there are two alpha and two beta chains. In alpha thalassemia there is a lack of alpha chains and an excess of beta chains. In beta thalassemia there is lack of beta chains and an excess of alpha chains. There is a reduced amount of HgbA on Hgb analysis. The extent of the reduction or absence determines whether the disease is major or represents thalassemia trait. The imbalance of globin chains can cause hemolysis or impair erythropoiesis and result in microcytosis and possibly anemia. Thalassemia major would be diagnosed in childhood; however, because of the subtle nature of thalassemia minor the patient may have been labeled as having iron-deficiency anemia and treated presumptively with iron replacement. This is a reason to include this diagnosis in your differential of microcytic anemia.

Occurrence: Anemia affects 27% of the population worldwide, with iron deficiency as the dominant cause (greater than 60%) (Kassebaum et al., 2016). Between 1% and 10% of these patients have undiagnosed GI cancer. Thalassemia occurs in about 5% of the world's population (Muncie & Campbell, 2009).

Age: IDA is most common in children and younger women of childbearing age; in older adults, incidence increases with age. AI/anemia of chronic disease (ACD) can occur at any age but increases with aging. Thalassemia is an inherited disorder and is present from birth. With aging, complications of thalassemia increase, such as vascular and hepatic disease. In addition, hepatic, hematological, and solid cancers have occurred related to the chronic stress on the bone marrow from thalassemia (Taher et al., 2021).

Ethnicity: Alpha thalassemia occurs most often in those with African or Southeast Asian heritage, and beta thalassemia is most common in those of Mediterranean, African, and Southeast Asian descent. Thalassemia trait is present in 5% to 30% of those in these ethnic groups (Muncie & Campbell, 2009).

Contributing Factors: In the older adult patient, decreased oral intake or inadequate diet, GI-related surgery, benign prostatic hypertrophy, malabsorption syndromes, low socioeconomic status, medications (i.e., salicylates, NSAIDs, proton pump inhibitors [PPIs], H_2 blockers, and antacids), combination of medication and alcohol, and chronic blood loss—most frequently from the GI tract—are contributing factors for IDA. Some GI causes include malignancy, esophagitis, peptic ulcer disease, gastritis, diverticular disease, or bleeding caused by inflammatory bowel disease. *Helicobacter pylori* infection can decrease iron absorption and can also lead to microerosions that cause bleeding. Surgeries such as gastrectomy, duodenal bypass, or bariatric surgery (Roux-en-Y gastric bypass) can result in decreased iron absorption (Camaschella, 2015).

Recent evidence suggests that obesity may also play a role in IDA due to inflammation that can cause impaired duodenal absorption and an increase in hepcidin, a peptide that regulates iron homeostasis. Higher hepcidin levels may reduce iron absorption and blunt the effects of iron fortification (Stoffel et al., 2020). In patients with prosthetic heart valves, intravascular hemolysis may lead to IDA related to increased hemosiderin loss in the urine. Epistaxis, hematuria, dysfunctional uterine bleeding, and bleeding diathesis are other possible contributing factors in older adults.

In thalassemia there is ineffective erythropoiesis and peripheral hemolysis that can cause a chronic microcytic anemia. A key diagnostic feature is the presence of a very low MCV in the presence of a mild decrease in Hgb. Many of these patients have been treated presumptively with iron for many years and face the very real possibility of iron overload. Proper identification of the patient who may have thalassemia can prevent overuse of iron replacement and risk of iron overload.

Signs and Symptoms: Diagnosis of IDA may be the result of an incidental finding on CBC, requiring further investigation. Clinical presentation of IDA can be vague, unreliable, and, in many cases, asymptomatic. In the older adult, symptoms may be incorrectly attributed to the aging process or chronic comorbid conditions. Anemia that develops slowly tends to present with fewer signs and symptoms then anemia that is of a rapid onset (e.g., acute bleeding). Fatigue, weakness, lethargy, tachycardia, palpitations, dyspnea on exertion,

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headache, irritability, inability to concentrate, neuralgia, sore tongue, paresthesia, restless legs syndrome, alopecia, and susceptibility to infection are possible symptoms. Dizziness, faintness, claudication, exercise intolerance, or angina also may be present.

Thalassemia, unless diagnosed in childhood, is generally asymptomatic. Patients may report a history of iron therapy for anemia without evidence of a specific cause of blood loss.

A thorough history should include questions about diet, symptoms (especially GI-related), signs or sources of blood loss, surgeries, and family history of GI malignancies such as stomach or colon cancer. Pica or pagophagia (i.e., compulsive consumption of ice or iced drinks) may be reported. Medication history, including over-the-counter (OTC) drugs, is especially important to rule out NSAID-induced bleeding.

Physical examination may be unremarkable. Pallor, common in patients with significant anemia, is also common in aging and may be discounted as a normal age-related finding. Conjunctival pallor is the only sign attributable specifically to anemia. Angular cheilitis, glossitis, brittle ridged nails, or "spoon" nails (koilonychia) may also be present. Cardiovascular and respiratory examination may reveal tachycardia, systolic murmur, or signs of heart failure (HF). In some patients, splenomegaly may be present, owing to hemolysis of iron-deficient RBCs. Lymphadenopathy, weight loss, bruising, and jaundice are physical signs that require further evaluation.

Diagnostic Tests:

- CBC will reveal Hgb of less than 12 g/dL in women and 13 g/dL in men. Note that patients who are smokers and those with chronic hypoxemia have a higher premorbid Hgb and therefore can be anemic at higher Hgb levels (Sharma et al., 2019).
- RBC indices reveal an MCV/RBC size that will be decreased to less than 80 fL in adults; MCH will be low, consistent with hypochromia. In thalassemia the MCV is usually less than 75 fL and MCH will be low.
- RDW-CV% may be increased in IDA indicating a mixture of mature and immature RBCs. In thalassemia the RDW is normal or may occasionally be increased.
- Serum ferritin level is the most accurate initial test for IDA; patients with IDA are expected to have low levels. It is important to consider that ferritin is an acute phase reactant and increases in the face of inflammation. Given the many chronic inflammatory diseases that are more common in older adults, a normal serum ferritin may be misleading. A ferritin level of less than 25 ng/mL is highly predicative of IDA, whereas a level of greater than 100 ng/mL indicates adequate iron stores with a decreased likelihood of IDA. In thalassemia serum ferritin is normal.
- TIBC: increased in IDA and is especially helpful in coordination with consideration of the possible falsely normal ferritin. TIBC is normal in thalassemia.
- Serum iron: decreased in IDA, also helpful if serum ferritin is normal. Serum iron is normal to increased in thalassemia.
- Transferrin saturation: decreased in IDA. This finding indicates that there is a decreased amount of iron available to bind to transferrin, which is an iron-carrying protein. Transferrin saturation is normal to increased in thalassemia.
- Peripheral smear in IDA reveals microcytosis, hypochromia, and poikilocytosis (abnormally shaped RBCs). In thalassemia nucleated red blood cells appear on the peripheral smear.
- Hgb identification for suspected thalassemia
- With referral to hematology, bone marrow iron stain: may be helpful in an unclear presentation

If IDA is confirmed, further diagnostic studies to determine the cause must be undertaken. The presence of IDA in adults, especially men and postmenopausal women, is presumed to be the result of blood loss in the GI tract, and the possibility of malignancy must be ruled out. Endoscopic evaluation usually begins with colonoscopy, if indicated, and when the patient is 50 years or older to identify any lower GI bleeding. Esophagogastroduodenoscopy (EGD) investigates for upper GI bleeding. Evaluation of mid and distal small bowel can be done through several methods, including capsule endoscopy, and should be done if the colonoscopy and EGD findings are negative (Joosten, 2018; Lanier et al., 2018). The choice and sequence of procedures is dependent on clinical suspicion and presenting signs and/or symptoms.

Differential Diagnosis: Differential diagnosis for microcytic, hypochromic anemias by etiology includes:

- Defective iron utilization: thalassemia trait, sideroblastosis, G6PD deficiency
- Defective iron reutilization: infection, inflammation, cancer, and other chronic diseases
- Hypoproliferation: decreased erythropoietin from renal failure, hypothyroidism, and other hypoproliferative states (Prath & Miller-Chism, 2019)

In adult men and postmenopausal women, differential diagnosis for microcytic anemia includes the following in decreasing order of frequency: IDA, AI, unexplained anemias, and thalassemia trait.

Treatment: Oral iron therapy is usually first-line treatment for patients with IDA. An initial medication of choice is ferrous sulfate 325 mg (65 mg of elemental iron) bid–tid. Depending on the severity of the IDA, adults will usually require a daily dose in the range of 100 to 200 mg of elemental iron (Lanier et al., 2018). This treatment is not well tolerated and associated with dark or black stools, constipation, diarrhea, abdominal discomfort, nausea, and vomiting. Interventions to reduce GI symptoms include dose reduction of iron or starting with one-half the dose and gradually increasing it. Switching from ferrous sulfate to better tolerated formulations, ferrous gluconate 325 mg (35 mg of elemental iron) or ferrous fumarate 325 mg (99 to 108 mg of elemental iron), may also help. Other options include taking iron with food, which may increase patient compliance with therapy but may also reduce absorption by 50%. Measures to alleviate constipating effects of iron therapy include gentle laxatives, stool softeners, fiber, and adequate liquid intake. There is some new evidence that iron given at lower doses and less frequently may reduce the adverse effects. Further research, especially with older adults, is needed to determine optimal dosing efficacy.

Ideally, a dose is administered on an empty stomach, 1 hour before meals. Absorption of iron is enhanced with ascorbic acid (vitamin C). Other measures to improve iron absorption include avoidance of foods high in tannate (tea,

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bran, cereal) and medications that increase gastric pH (milk, antacids, PPIs, H_2-histamine blockers, quinolones, and tetracycline). Liquid iron preparations are recommended for those who are unable to dissolve the coating of iron pills, which leads to decreased iron absorption. Sustained-release formulations (enteric coated) of iron for initial therapy should be avoided because they reduce the amount of iron presented for absorption by the GI tract (Pasricha et al., 2021).

Treatment effectiveness should be demonstrated after 3 to 4 weeks of therapy, and Hgb and Hct should be normalized in 6 to 8 weeks. The duration of therapy is not specifically identified, but it is generally continued for 3 to 6 months after Hgb and Hct are normalized (Lanier et al., 2018).

Parenteral iron therapy is indicated in the following situations: chronic uncorrectable bleeding, intestinal malabsorption, intolerance to oral therapy, nonadherence, or Hgb level less than 6 g/dL with signs of poor perfusion in those who would otherwise receive transfusions (e.g., those with religious objections), and coexisting inflammatory conditions that can interfere with iron homeostasis. Several different IV iron products are available in the United States.

Blood transfusions may be necessary initially (e.g., acute bleeding) and should be considered for patients who are symptomatic (i.e., fatigue, dyspnea on exertion), as well as for asymptomatic cardiac patients with an Hgb level less than 7 g/dL (Lanier et al., 2018). The decision to transfuse should consider the clinical status and comorbidities.

In addition to medical therapy, a healthy diet with foods rich in iron should be encouraged. Dietary sources of iron include meat, fish, poultry, fruits, green leafy vegetables, beans, nuts, and grain products.

Follow-Up: The restoration of iron stores is the primary goal of treatment. The Hgb level should increase by 1 g/dL every 2 to 3 weeks, but restoration of iron stores may take 3 months after Hgb is corrected, during which time iron therapy should be continued (Lanier et al., 2018). The patient should be seen at regular intervals to reassess symptoms or side effects from the treatment plan. Patients should be evaluated in 2 to 4 weeks for examination and repeat CBC after the initiation of therapy. Referral should be considered if failure to respond to a 4- to 6-week trial of oral iron occurs (Pasricha et al., 2021). Frequency of subsequent evaluations with repeat CBC should be based on the identified cause and whether it was reversed.

Sequelae: Possible complications in the evaluation of a microcytic anemia include failure to identify an occult bleeding source, particularly one related to malignancy. Failure to identify thalassemia can result in unnecessary treatment with iron and possible iron overload.

Prevention/Prophylaxis: IDA can be prevented by promoting proper nutrition with adequate iron intake, identifying those at high risk, and prompt evaluation and treatment of any symptoms or bleeding.

Referral: Referral to a specialist (e.g., gastroenterology for diagnostic studies, hematology, oncology if malignancy is suspected) is indicated to aid in the diagnosis and treatment of the causation. Collaborative management is appropriate for complex cases. Referral to a nutritionist can assist with the evaluation of dietary inadequacies and with meal planning or with congregate or home-delivered meals.

Education: The patient should be educated about the mechanism of anemia, the expected course of therapy with respect to frequency of office appointments and blood tests, any referrals, the importance of adhering to the treatment regimen, and the need to notify the patient's health-care provider about problems with the regimen. A guide to the dietary sources of iron to supplement oral iron medication is helpful to both the patient and any person responsible for meal planning and preparation. If iron is prescribed, inform the patient of possible side effects, including the black stools, and offer treatment options for GI side effects.

Clinical Recommendation	Evidence Rating	References
Serum ferritin is the best test for iron-deficiency anemia (IDA).	C	Ianni et al., 2021 Lanier et al., 2018
Adult men and postmenopausal women with IDA should be screened for GI malignancy.	C	Lanier et al., 2018
Thalassemia trait should be considered in the differential of microcytic anemia to avoid over treatment with iron and iron overload.	B	Taher et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

MACROCYTIC ANEMIA

Signal Symptoms: Weakness, shortness of breath, glossitis, dizziness, neuropathy. Often asymptomatic and only noted after receiving results of a routine CBC.

Description: Macrocytic anemia presents with macrocytosis (MCV greater than 100) on the CBC. Macrocytic anemia can be megaloblastic, a result of deficiency or impaired utilization of B_{12} (cobalamin) or folate (vitamin B_9), or non-megaloblastic due to disease such as myelodysplastic syndrome, liver disease, hypothyroidism, medications, or inherited disorders of DNA synthesis (Nagao & Hirokawa, 2017). The RBCs are the result of impaired DNA synthesis that inhibits nuclear division in the reticulocytes. The maturity of cytoplasm in RBCs is dependent

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on RNA and protein synthesis and continues normally. Adequate vitamin B_{12} and folate levels are necessary for DNA synthesis. When levels are inadequate, a nuclear-cytoplasmic asynchrony allows the cells to grow bigger before the nucleus signals division, resulting in large, nucleated RBCs, known as megaloblasts (Hariz & Bhattacharya, 2021).

Etiology: Megaloblastic anemia is primarily the result of a nutritional deficiency, particularly insufficient B_{12} and folate. Such deficiencies are often related to social determinants of health, such as lack of access to fresh food or alcohol abuse. Malabsorption of B_{12} and folate can be the result of the absence of intrinsic factor (IF) due to pernicious anemia or can occur after gastric surgery. Some medications interfere with the DNA synthesis, and some research has shown copper deficiency plays a role in megaloblastic anemia (Hariz & Bhattacharya, 2021).

Vitamin B_{12} is bound to IF produced by gastric parietal cells and then absorbed in the terminal ileum. Vitamin B_{12} is stored in the liver (about 2 to 3 mg total, which is an adequate supply for 2 to 4 years) (Hariz & Bhattacharya, 2021). The hepatic supply is one explanation for the length of time it can take for serious symptoms to develop. Pernicious anemia is an autoimmune condition resulting in a lack of IF causing poor vitamin B_{12} absorption from the ileum. Initially pernicious anemia was considered a primary cause of vitamin B_{12} deficiency, but more recent research has determined that it is relatively rare (Stauder et al., 2018). Other factors, such as *Helicobacter pylori* infections, acid-reducing agents, or atrophic gastritis that can cause hypochlorhydria, more frequently lead to cobalamin malabsorption syndrome (Stauder et al., 2018). Dietary sources of vitamin B_{12} include meats, fish, eggs, and dairy products. Strict vegetarian and vegan diets are low in vitamin B_{12}, and those patients should be screened for deficiency (Hariz & Bhattacharya, 2021).

Folate is from the Latin word *folium*, meaning "leaf." It is present in dark green leafy vegetables, legumes, fruits, grains, seafood, and liver. Folic acid is the synthetic form of folate and is a frequent additive in foods because of its role in prevention of neural tube defects in pregnancy. Folic acid is better absorbed than folate (85% vs. 50%). In addition to its role in RBC development, folate helps to break down homocysteine, which has harmful effects if elevated. About 5 mg of folate is stored in the liver—enough supply to meet the dietary requirement for 3-4 months (Hariz & Bhattacharya, 2021).

Macrocytic anemias that are non-megaloblastic can be due to liver disease, alcohol abuse, hypothyroidism, medications, myelodysplastic syndrome, and certain inherited disorders (Nagao & Hirokawa, 2017). One explanation of how liver disease without nutritional deficiency can cause macrocytosis is that increased deposition of cholesterol on the membranes of RBCs increases their surface area. Liver disease can also result in increased hemolysis. resulting in a hemolytic anemia (Yang et al., 2018).

Many medications can cause a megaloblastic anemia by impairing the availability or utilization of folate or vitamin B_{12}. Medications are also responsible for macrocytic non-megaloblastic anemias: Antineoplastics, folate antagonists, antimetabolite, antibacterial, antimalarial, anticonvulsant, anti-inflammatory, and antivirals.

Alcohol intake of greater than 85 ml a day can have a direct effect on the development of RBCs. Macrocytosis may be present in alcoholics before anemia develops (Nagao & Hirokawa, 2017). Abstinence may return the MCV to normal. Thyroid hormone helps to stimulate erythropoietin and hematopoiesis, so a low level of thyroid hormone may cause either normocytic or macrocytic anemia.

Myelodysplastic syndrome (MDS) is a hematopoietic stem and progenitor cell disorder identified by cytopenia, myelodysplasia, ineffective hematopoiesis, and risk of progression to acute myeloid leukemia (AML) (Hellström-Lindberg et al., 2020; Nagao & Hirokawa, 2017). In addition to cytopenia, MDS is defined by the presence of morphological dysplasia of precursor and mature bone marrow RBCs (Hellström-Lindberg et al., 2020). MDS is a variety of disorders that present with different degrees of anemia, dysplasia, and risk of AML. Subtypes include MDS with a single blood component (WBC, RBC, or platelet) that is low in number or abnormal. Another subtype may have two or three abnormal cell types. Ring sideroblasts, RBCs with rings of excess iron, are present in another subtype of MDS. MDS may include a subtype with a specific DNA mutation known as del(5q) chromosome abnormality. MDS with excess blasts includes any of the three types of blood cells and very immature blasts in the blood and bone marrow. Finally, there may not be a clear classification of the MDS.

Occurrence: Most sources acknowledge that megaloblastic anemia is common, but concrete data on prevalence are rare. One study published in 2017 found that megaloblastic anemia was present in 3.6% of all cases of anemia (Kaur et al., 2018). In the same study, no association between vegetarian diet and megaloblastic anemia was noted. Nagao and Hirokawa (2017) report that in family practice 2% to 4% of patients were found to have macrocytosis, and in older adults living at home macrocytosis was noted in 6.3% of men and 3.3% of women.

Age: The incidence of megaloblastic anemia increases with age. Older adults are at highest risk for pernicious anemia. Older adults are more likely to have a lack of stomach acid and intrinsic factor preventing the small intestine from absorbing vitamin B_{12}. Most patients presenting with MDS are older than 60 years.

Ethnicity: Vitamin B_{12} deficiency is more common in older White women than in Black women. Folate deficiency is more prevalent in Black than in White older women. Pernicious anemia is more common in people of Northern European and African descent (Ankar & Kumar, 2021).

Contributing Factors: Because megaloblastic anemia is often due to nutritional insufficiency, careful assessment of lifestyle and social habits are important. Alcoholism has been a chief component in both megaloblastic and non-megaloblastic macrocytic anemia. Any patient noted to have a macrocytosis with or without anemia should be assessed for alcohol misuse.

As noted above several classes of medications can contribute to the development of macrocytic anemia. These include some common medications such as allopurinol, disease-modifying antirheumatic drugs, hydroxyurea, 5 fluorouracil, trimethoprim, penicillin antibiotics, erythromycin, metformin, and triamterene. These medications can cause changes in the bone marrow or reduce the intestinal absorption of folic acid or vitamin B_{12} or metabolism of these vitamins (Hariz & Bhattacharya, 2021). A recent focus on a link between metformin and vitamin B_{12} deficiency has

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resulted in patients questioning the use of this first-line treatment for diabetes.

Patients with previous chemotherapy or radiation are at an increased risk of MDS. Exposure to benzene has been linked to MDS.

Signs and Symptoms: Most often there are no concerns expressed by the patient, but the abnormality is noted on routine laboratory findings. Because most macrocytic anemia is megaloblastic and caused by nutritional deficiency, and the liver has stores of vitamin B_{12} and folate, the anemia may take years to develop, and any insidious symptoms go unrecognized. The neurological manifestations of vitamin B_{12} deficiency are most concerning. Paresthesia and balance disorders are common, but the deficiency can also result in peripheral neuropathy, visual disturbances caused by optic atrophy, or dementia. Vitamin B_{12} is included in any laboratory evaluation of possible contributing factors to dementia.

Patients with MDS may have no symptoms until the disease advances. Complaints that can occur with any anemia include fatigue, shortness of breath, and pallor. Patients with MDS may develop a pancytopenia and, due to thrombocytopenia (low platelets), present with bruising, bleeding, or petechiae. With leukopenia (low WBCs) they may experience frequent infections.

On physical examination the provider may note a decrease in vibratory sensation, proprioception, or (in extreme cases) a positive Romberg test in patients with a B_{12} deficiency. Although less common, a Babinski reflex, hyporeflexia, and clonus may be noted in advanced neurological decline (Hariz & Bhattacharya, 2021). Depending on how long the deficiency has been present and the severity of the symptoms, the disorders may not be completely reversible.

The astute provider will recognize that comorbidities are common in older adults and expand the assessment to include concurrent factors such as hypothyroidism or hepatic dysfunction.

Diagnostic Tests:

- CBC will reveal Hgb of less than 12 g/dL in women and 13g/dL in men. Note that patients who are smokers and those with chronic hypoxemia have a higher premorbid Hgb and therefore can be anemic at higher Hgb levels (Sharma et al., 2019).
- RBC indices reveal an MCV/RBC size that will be increased to more than 100 fL in adults; MCH will be high, consistent with hyperchromia.
- Reticulocyte count, if elevated, may indicate hemolysis, which can occur in advanced liver disease. If low, serum vitamin B_{12} and folate levels will be the only additional tests needed.
- Vitamin B_{12} above 300 pg/mL is considered normal. If the level is between 200 and 300 pg/mL, additional testing with methylmalonic acid and homocysteine levels should be obtained.
- Folate levels of 2 to 4 ng/mL are considered borderline; levels below 2 ng/mL are diagnostic of folate deficiency.
- Methylmalonic acid can help to differentiate between vitamin B_{12} and folate deficiency. It is only elevated in vitamin B_{12} deficiency. In severe renal disease, methylmalonic acid levels are unreliable.
- Homocysteine is elevated in both vitamin B_{12} and folate deficiencies.
- In patients diagnosed with vitamin B_{12} deficiency, consider antibody assays against intrinsic factors.
- To evaluate for hypothyroidism, thyroid-stimulating hormone (TSH) level with reflex to T4 if abnormal.
- Hypersegmented neutrophils may be present on a stained peripheral smear in megaloblastic anemia.
- Poikilocytosis (RBCs of varying shapes) and anisocytosis (RBCs of varying sizes) are common due to ineffective erythropoiesis.
- Referral to hematology for bone marrow biopsy is essential in a patient suspected of having MDS.
- Ring sideroblasts, excess blasts, and chromosomal abnormalities on bone marrow biopsy are consistent with the diagnosis of MDS.

Differential Diagnosis: Differential diagnosis for macrocytic, hyperchromic anemia includes:

- Alcoholic hepatitis
- Atrophic gastritis
- Hypothyroidism
- Gastric cancer
- Celiac sprue
- Liver disease
- Tropical sprue
- MDS
- Aplastic anemia
- Acquired sideroblastic anemia
- Homocystinuria

Treatment: Vitamin B_{12} and folic acid can be given orally or parenterally. Vitamin B_{12} is absorbed in the terminal ileum and is dependent on intrinsic factor; however, oral vitamin B_{12} can be absorbed passively independent of intrinsic factor (Chan et al., 2016). The preferred route is oral unless there are malabsorption issues. Oral treatment takes time, so when severe neurological symptoms are present, a more rapid treatment response with parenteral vitamin B_{12} is required. If anemia is symptomatic, a blood transfusion may be necessary because vitamin B_{12} and folate, even given parenterally, will not correct anemia rapidly (Hariz & Bhattacharya, 2021).

The recommended dose of vitamin B_{12} is 1,000 mcg parenterally once a week until the deficiency is corrected, or an oral dose of 1,000 mcg daily. Duration of treatment depends on the cause. If the cause is corrected, diet improved, alcohol intake addressed, the supplement can be stopped when vitamin B_{12} levels are normal. When comorbidities such as history of gastric bypass or pernicious anemia exist, supplementation needs to be ongoing.

Folic acid supplement to correct a folate deficiency is 1 mg orally once a day until the deficiency is corrected or in the case of an ongoing condition, indefinite supplementation is needed. For non-megaloblastic causes of anemia, treatment needs to address the underlying cause. Treatment for alcohol misuse syndrome involves initiating thyroid replacement hormone and deprescribing medications that cause macrocytosis if possible. For MDS, refer to hematology and follow-up with the patient for support and management of other comorbidities.

Follow-Up: With treatment for vitamin B_{12} or folic acid deficiency, bone marrow should respond within 1 week and Hgb and Hct will normalize in 1 to 2 months

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(Hariz & Bhattacharya, 2021). The neurological effects of vitamin B_{12} deficiency will take longer to correct and may be permanent depending on how long the deficiency occurred undetected.

Follow-up for patients with non-megaloblastic macrocytic anemia is dictated by the identified cause. Care is often comanaged with specialists.

Prevention/Prophylaxis: A diet with leafy greens, meats, fish, and fresh fruits helps prevent folate deficiency. Diets that include meat, fish, eggs, and dairy products are important to provide adequate vitamin B_{12}. To reduce alcohol-related complications, patients should consume two or less drinks a day for men or one or less drinks a day for women. A drink is considered 12 ounces of a beer with 5% alcohol content, 5 ounces of wine (which is typically 12% alcohol content), or 1.5 ounces of distilled spirits (which are typically 40% alcohol content) (National Institute on Alcohol Abuse and Alcoholism [NIAAA], 2021). Remember that in alcohol misuse syndrome and hypothyroidism, patients may have macrocytosis without anemia. Perform a careful medication review to evaluate for medications that can contribute to the development of macrocytic anemia and deprescribe if possible.

Sequelae: Support patients who have severe neurological effects from chronic vitamin B_{12} deficiency to understand that while symptoms may not completely resolve, treatment success is measured is resolution of anemia and preventing further decline. Patients with MDS need to follow with hematology and consider referral to palliative care. Many of these patients will go on to develop AML.

Referral: If cause is not clear or the patient does not respond to treatment, referral to hematology is indicated to aid in the diagnosis and treatment. Collaborative management is appropriate for complex cases. Referral to a nutritionist can assist with the evaluation of dietary inadequacies and with meal planning or with congregate or home-delivered meals. Patients with alcohol misuse syndrome should be referred for counseling.

Education: The patient should be educated about the mechanism of anemia, the expected course of therapy with respect to frequency of office appointments and blood tests, any referrals, the importance of adhering to the treatment regimen, and the need to notify the patient's health-care provider about problems with the regimen. A guide to the dietary sources of vitamin B_{12} and folate are helpful to both the patient and any person responsible for meal planning and preparation. If vitamin B_{12} or folic acid are prescribed, inform the patient of expected length of treatment. Patients who are strict vegetarians or vegans need to understand the rationale for including vitamin B_{12} as a supplement.

Clinical Recommendation	Evidence Rating	References
Adequate Vitamin B_{12} and folate are necessary for DNA synthesis.	A	Nagao & Hirokawa, 2017 Hariz & Bhattacharya, 2021
Alcohol intake of greater than 85 ml a day can have a direct effect on the development of RBCs. Macrocytosis may be present in alcoholics before anemia develops.	A	Nagao & Hirokawa, 2017
Myelodysplastic syndrome is a hematopoietic stem and progenitor cell disorder identified by cytopenia, myelodysplasia, ineffective hematopoiesis, and risk of progression to acute myeloid leukemia.	A	Hellström-Lindberg et al., 2020 Nagao & Hirokawa, 2017
Methylmalonic acid can help to differentiate between vitamin B_{12} and folate deficiency. It is only elevated in vitamin B_{12} deficiency. In severe renal disease. methylmalonic acid levels are unreliable.	A	Hariz & Bhattacharya, 2021
Vitamin B_{12} is absorbed in the terminal ileum and is dependent on intrinsic factor; however, oral vitamin B_{12} can be absorbed passively independent of intrinsic factor.	A	Chan et al., 2016

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

PLATELET DISORDERS

As noted earlier in this chapter, platelets are the smallest population of blood cells. They are nonnucleated and disk-shaped fragments of megakaryocytes located in the bone marrow, with a life span of 9 to 12 days. Platelets are important in the clotting cascade. When damage occurs to a vessel wall, they form a hemostatic plug to close the leak. Their response is rapid, occurring in 3 to 5 minutes. Thrombopoietin regulates the production of platelets just as erythropoietin regulates production of RBCs. Thrombocytopenia is defined as a platelet count below 150×10^9/L. Thrombocytopenia can result in bleeding disorders due to the lack of platelets available to respond to injury. Thrombocytosis is defined as a platelet count above 450×10^9/L. Thrombocytosis may result in clotting disorders but in some cases can paradoxically cause bleeding.

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THROMBOCYTOPENIA

Signal Symptoms: There may be no symptoms and the low platelet count may be an incidental finding on the CBC. Before they become symptomatic, a patient's platelet count is typically less than 30×10^9/L, at which point minimal trauma may cause bleeding. A patient with a very low platelet count, less than 10×10^9/L, may present with petechiae, bruising, or oral mucocutaneous bleeding.

Description: Thrombocytopenia is classified as mild when the platelet count is between 100 and 150×10^9/L, moderate between 50 and 99×10^9 /L, and severe if less than 50×10^9/L. Sources may define these classifications differently, with some labeling a platelet count between 70 and 150×10^9/L as mild and severe as less than 20×10^9/L. With counts greater than 50×10^9/L, patients are rarely symptomatic unless they suffer a major trauma. Platelet counts can vary with age, sex, and race. Younger adults have higher counts than older adults, women have higher counts than men, and platelet counts in non-Hispanic Blacks are higher than in Whites. The baseline platelet count is important because if a patient has a high normal platelet count, 450×10^9/L for example, and it declines by greater than 50%, 247.5×10^9/L, it would still be well within the normal range but could indicate a clinically significant problem that should be evaluated.

Etiology: Thrombocytopenia can result from decreased platelet production, sequestration, or increased platelet destruction.

Decreased Platelet Production: Decreased platelet production can result from bone marrow disorders due to deficient nutrients, myeloid disorders (MDS, myeloproliferative syndromes), lymphoid malignancies, and metastasis from other cancers. Infection can cause thrombocytopenia.

Medications that can cause platelet destruction include antibiotics, antiepileptics, and (of classic concern), heparin. Treatment with radiotherapy or high-dose chemotherapy can affect the production of platelets in the bone marrow.

Thrombocytopenia can occur in chronic liver diseases including drug-induced, infectious hepatitis, and nonalcoholic liver disease. Liver disease or chronic alcohol abuse can affect both production of platelets as well as sequestration of platelets in the spleen. Production of platelets can be affected because thrombopoietin, which regulates platelet production, is produced in the liver.

Sequestration: Monocytes in the spleen are called reticular cells and act to remove old cells from circulation and act as phagocytes for inflammatory and immune responses. When platelets circulate through the spleen they may be identified by the reticular cells as abnormal and remove them. This may be due to portal hypertension, sarcoidosis, lymphomas, or chronic lymphocytic leukemia.

Platelets can also shift into the spleen, resulting in a low platelet count, even though the total number of platelets is actually normal or increased. Dilution occurs when there is a massive fluid resuscitation or transfusion. Redistribution/hypersplenism occurs when the normal one-third of platelet mass is altered either due to an increase in spleen size or congestion due to portal hypertension due to alcoholic liver disease. As noted above platelet sequestration can occur because of alcohol abuse even without liver disease.

Increased Platelet Destruction: Platelet destruction or consumption can be the result of idiopathic thrombocytopenic purpura (ITP), medications, disseminated intravascular coagulation (DIC) or hemolytic uremic syndrome which can be autoimmune or due to a bacterial infection.

Occurrence: Immune thrombocytopenia occurs in 2 to 4 cases per 100,000 person years (Cooper & Ghanima, 2019).

Age: Immune thrombocytopenia has two age peaks. The first is between 20 and 30 years and disproportionately affects females, due to causes resulting from pregnancy. The second much larger peak occurs after the age of 60 when autoimmune diseases of all types are more likely to occur (Cooper & Ghanima, 2019).

Ethnicity: Not significant.

Contributing Factors: Viral infections, such as HIV, Epstein-Barr, rubella, mumps, varicella, hepatitis-C, and COVID-19, result in thrombocytopenia due to bone marrow suppression. Bacterial infections, including malaria and tuberculosis (TB) cause low platelet counts through immune-mediated destruction, sequestration, and a shortened platelet survival time. TB can infiltrate the bone marrow and decrease platelet production or cause immune thrombocytopenia. *Heliobacter pylori* infection has also been associated with both ITP or as a secondary cause of immune thrombocytopenia.

Thrombocytopenia can occur due to alcohol abuse, even in the absence of liver disease. It may be associated with megaloblastic anemia due to vitamin B_{12} and folic acid deficiency, but those deficiencies may not be present. Discontinuing alcohol use can restore the platelet count. Other autoimmune diseases, such as systemic lupus erythematosus, Grave's disease, and sarcoidosis, can cause secondary immune thrombocytopenia.

Signs and Symptoms: Bleeding, petechiae, purpura, ecchymosis, enlarged liver or spleen. There may be no symptoms, but a routine blood test may show thrombocytopenia with no other abnormalities. Severe bleeding is usually only a concern if platelet count falls under 10×10^9/L (Cooper & Ghanima, 2019). The concurrent presence of an autoimmune disorder favors secondary ITP (Cooper & Ghanima, 2019).

Diagnostic Tests: CBC with peripheral blood smear (PBS) will reflect thrombocytopenia but otherwise be normal. PBS may show larger than normal platelets but normal RBC and WBC morphology. If there are other abnormalities in the PBS, a bone marrow biopsy is required to rule out other problems. In patients older than 60 years, bone marrow biopsy is realistic due to an increase in MDS.

Differential Diagnosis:

- Pseudothrombocytopenia
- Renal or liver disease
- Acute leukemia
- Chronic lymphocytic leukemia
- MDS

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- Aplastic anemia
- Thrombotic thrombocytopenic purpura
- Other autoimmune diseases
- Infection (HIV, Epstein-Barr, hepatitis, cytomegalovirus)
- Vasculitis
- Vitamin K deficiency
- DIC
- Hemolytic uremic syndrome (HUS)
- Hypersplenism

Treatment: The goal of treatment is to sustain a safe (not normal) platelet count to avoid bleeding. This may include withholding certain drug therapy, where risks outweigh benefits. If counts are above 80×10^9/L and the patient is asymptomatic, repeating the CBC and evaluating factors that may contribute to the thrombocytopenia is a reasonable first step. One study of the long-term outcomes of patients with incidental thrombocytopenia with platelet counts from 100 to 150×10^9/L followed for 10 years found that 64% normalized or remained stable (Gauer & Braun, 2012). Only 7% developed ITP, and 12% developed an autoimmune disorder. Four cases of MDS were diagnosed—all in older adults. A hematology referral should be initiated for assessment and management of patients with platelet counts less than 80×10^9/L, for those who have bleeding on examination, or for any patient for whom the advanced practice registered nurse (APRN) is not confident regarding the diagnosis and treatment. Treatments are indicated for those with 20 to 30×10^9/L who present with bleeding or plan surgical procedures (Al-Samkari & Kuter, 2020). Emergent conditions include those with new-onset acute thrombocytopenia. ITP only occurs in 100 cases per 1 million each year and half of these are in children, but immediate referral for management is critical (Gauer & Braun, 2012). For patients with platelet counts less than 10,000/mm^3, platelet transfusions may be indicated. For ITP, prednisone 1 mg/kg/day orally or IV immunoglobulin (IVIG) is used initially; a 4-day burst of dexamethasone (40 mg/day) may also be initiated or used in lieu of steroid treatment. In cases where platelet counts are less than 20,000/mm^3 with severe mucocutaneous bleeding or any significant bleeding, hospitalization is indicated to stabilize the patient. For RhD-positive patients who have not had a splenectomy, anti-D products, such as WinRho and Rhophylac, are as effective as IVIG in refractory cases (Cooper & Ghanima, 2019).

Splenectomy is a second-line option; the risks and benefits of surgery must be weighed (Cooper & Ghanima, 2019). Newer therapies include the monoclonal antibody rituximab and thrombopoietic growth factors for recalcitrant cases (Lambert & Gernsheimer, 2017). Other drugs that have been used successfully include cyclosporine, antifibrinolytics, and certain chemotherapy agents.

For many adult patients with ITP and a platelet count 30,000 to 40,000, watchful monitoring is all that is required if they are asymptomatic. The course of ITP in older adults tends to be chronic with initial responses to treatment, with a reversal back to baseline after a few months.

Follow-Up: Follow-up is variable depending on symptoms, platelet levels, causative agent, and response to treatment (if initiated). Patients with moderate or severe ITP will be followed by hematology and comanagement will be helpful in support of the patient.

Sequelae: Mortality rate is less than 1%, usually related to infections, bleeding, or refractory disease. There are some spontaneous remissions.

Prevention/Prophylaxis: Causes of thrombocytopenia are numerous and many of them can be addressed and treated. Adequate treatment of viral or bacterial causes can result in resolution of the low platelet count. Alcohol abuse needs to be addressed and support for recovery provided. Medications or the use of nutraceuticals or street drugs should be carefully assessed and properly managed with deprescribing, encouraging elimination, or referral for treatment.

Referral: Consultation with or referral to hematology is indicated in cases of severe bleeding or cases refractory to treatment. If malignancies are identified, refer to oncology. Autoimmune diseases may be best managed by rheumatology. The goal is accurate diagnosis and treatment.

Education: Patients should be instructed to avoid invasive dental procedures and other activities that could precipitate bleeding episodes. Low-impact exercise is recommended. Aspirin and NSAIDs should be avoided; alcohol intake should be limited to an occasional drink. Patients with hypertension should be encouraged to take their medications as ordered and to have frequent monitoring of their blood pressure to avoid a stroke. Periodic monitoring of platelets will be necessary.

THROMBOCYTOSIS

Signal Symptoms: Thrombocytosis is often asymptomatic and is initially noted on the CBC. If symptoms are present, they are generally related to the secondary cause of the elevated platelets. In patients with primary thrombocytosis, symptoms may be due to blood clots or bleeding.

Description: Thrombocytosis is defined as a platelet count exceeding 450×10^9/L in adults. The problem can be primary (essential thrombocythemia), caused by alterations in the genes of the main regulators of thrombopoietin, which affects the development of hematopoietic cells. Essential thrombocytosis is a subform of myeloproliferative neoplasms. Most often thrombocytosis is the result of a secondary cause (reactive thrombocytosis).

Etiology: Essential thrombocytosis can be familial or sporadic. There may be similarities in the cellular mutations in both forms of the disease, but it is not clear cut. Even those with sporadic disease may have a hereditary component. Myeloproliferative disorder is often a diagnosis of exclusion, meaning that other differentials must first be ruled out as a cause of the elevated platelet count. Reactive thrombocytosis occurs because of elevated levels of thrombopoietin, interleukin-6, other cytokines or catecholamines because of an external cause such as cancer, chronic inflammation, iron deficiency, in situations of stress. or a rebound after splenectomy. When thrombocytosis is noted without clear causation, it is important to consider an occult malignancy.

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Occurrence: The most common cause of thrombocytosis is a reactive process, greater than 90% (Galvez & Stein, 2020). Essential thrombocytosis occurs in the remaining cases. Women are one and a half times more likely than men to develop essential thrombocytosis.

Age: People older than age 60 years are more likely to develop essential thrombocytosis and are also more susceptible to the diseases likely to cause reactive thrombocytosis.

Contributing Factors: May be genetic or due to the disease resulting in reactive thrombocytosis.

Signs and Symptoms: Some symptoms may be due to clotting, such as headaches, dizziness, chest pain, weakness, or numbness and tingling of the hands and feet. Ischemia of the hands or feet may be present with essential thrombocytopenia. There may be paradoxical bleeding complications in essential thrombocytopenia. Forty percent of patients with essential thrombocytopenia have splenomegaly. On peripheral blood smear there may be giant platelets in essential thrombocytopenia which would not be present in reactive thrombocytopenia.

Diagnostic Tests: Screening tests appropriate to rule out the common causes of secondary or reactive thrombocytopenia. Laboratory tests do not offer clear differential diagnosis. Referral to hematology is appropriate for bone marrow biopsy and possible genetic testing.

Differential Diagnosis:
- Other myeloproliferative disorders
- Acute blood loss
- Recovery from thrombocytopenia
- Acute infection or inflammation
- Response to exercise
- Iron deficiency
- Hemolytic anemia
- Cancer
- Chronic inflammatory disease
- Drug reactions
  - Vincristine
  - Cytokines
  - Growth factors

Treatment: In patients with reactive thrombocytosis, platelet-lowering medications are not required because the abnormal platelet count does not increase the risk of vascular events (Galvez & Stein, 2020). The critical concern is identifying the cause of the reactive thrombocytosis and treating the underlying disease.

In essential thrombocytosis treatment to lower the platelet count may be needed. Referral to hematology to guide decision making regarding treatment is the best strategy. Adults over the age of 60 and those with cardiovascular risk factors are at the highest risk for thrombotic and vascular events. Those at high risk may benefit from platelet lowering medication and aspirin. When cerebrovascular events or digital ischemia has already occurred platelet-cytoreductive agents and aspirin may be indicated. All the available treatment options include the potential for serious side effects and ongoing studies are being conducted to determine the best alternatives.

Follow-Up: Regardless of etiology, essential or reactive thrombocytosis, the patient will most likely be comanaged with a specialist. Coordination of care will be of utmost importance and maintaining high degree of vigilance for complications.

Sequelae: Depends on the underlying cause of the elevated platelet count. Gene therapy for essential thrombocytosis may be an option in the future. Adherence to treatment and ongoing monitoring.

Clinical Recommendation	Evidence Rating	References
Treatment decisions are influenced by platelet count and degree of bleeding; therapy is seldom required for platelet counts >30,000/mm^3.	C	Lambert & Gernsheimer, 2017
The goal of treatment is to prevent bleeding, not necessarily to return platelet count to normal.	C	Lambert & Gernsheimer, 2017 Cooper & Ghanima, 2019
Initial management includes treatment with oral prednisone. Other choices for treatment include high-dose dexamethasone, IVIG, and WinRho.	C	Lambert & Gernsheimer, 2017 Cooper & Ghanima, 2019
Chronic refractory ITP is defined as persistence for >3 months, lack of response to splenectomy, and platelet count <50,000/mm^3. Treatment options include glucocorticoids, rituximab, vincristine, cyclophosphamide, and methylprednisolone.	C	Cooper & Ghanima, 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

LEUKEMIA

Leukemia is a hematological malignancy of the blood and bone marrow and arises from the hematopoietic stem cell line. Blood cell development undergoes several steps to mature to erythrocytes (red blood cells), megakaryocytes (platelets), or granulocytes and lymphocytes (white blood cells).

Leukemia develops because of genetic changes in the hematopoietic precursor cell. Abnormal and immature blood cells replicate and invade bone marrow and peripheral blood and impede the normal function of all hematopoietic cell lines (erythrocytes, granulocytes, lymphocytes, and megakaryocytes).

The four main types of leukemia are acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphocytic leukemia (CLL), and chronic myeloid leukemia (CML). Adult leukemias represent 3% of all adult cancers (NCI, 2021). In the adult population, AML and CLL are the most prevalent types of leukemia.

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ACUTE MYELOID LEUKEMIA

Description: In acute myeloid leukemia (AML), myeloid cells grow into leukemia blasts, crowding out the healthy myeloid cell precursors in the marrow, which may result in pancytopenia (low blood counts) (Srinivas, 2021). AML is categorized into subtypes M0 to M7 based on the type of cell it develops from and the maturity of the cell (American Cancer Society [ACS], 2021b). Acute promyelocytic leukemia (APL) is a particularly aggressive subtype of AML with distinct morphology and clinical presentation. APL accounts for 10% of AML cases. There is high risk for early mortality due to coagulopathy (National Comprehensive Cancer Network [NCCN], 2021a).

Occurrence: In 2021, there will be an estimated 20,240 new cases and 11,400 deaths in the United States. Based on SEER program data from 2011 to 2017, 29.5% of patients with AML were alive 5 years after diagnosis (NCI, 2021a).

Age: The median age at diagnosis is 68 years. The median age at diagnosis of APL is 47 years (NCCN, 2021a).

Ethnicity: Not significant.

Signs and Symptoms: Patients present with fever, pallor, fatigue, shortness of breath, bleeding, or bruising due to pancytopenia (Srinivas, 2021).

Diagnostic Tests:

- History and physical examination
- CBC with differential, CMP, lactate dehydrogenase (LDH), uric acid, prothrombin time (PT), partial thromboplastin time (PTT), International Normalized Ratio (INR), fibrinogen
- Additional work-up to be initiated by a hematologist
- Bone marrow aspirate and biopsy (NCCN, 2021a)

The presence of 20% blasts in peripheral blood or bone marrow is diagnostic of AML. Patients are divided into three risk categories based on cytogenetics—favorable, intermediate, and poor risk. Molecular profiling is now a standard diagnostic tool for AML because it further refines prognostic risk groups (NCCN, 2021a).

Differential Diagnosis:

- Acute lymphocytic leukemia
- Anemia
- Aplastic anemia
- B-cell lymphoma
- Bone marrow failure

Treatment: AML treatment is rapidly evolving, with eight new targeted therapy drugs approved since 2017. The options used to be intense chemotherapy with curative intent versus low-intensity palliation (Table 19-2). For the past several decades, the treatment discussion focused on the fitness for intensive therapy. Now, there are new factors: ensuring prompt identification of molecular mutations at diagnosis and relapse, choosing an appropriate therapy, and safe management of adverse effects. Ongoing clinical trials will better define drug response and toxicities (Dinardo & Wei, 2020).

The treatment of AML is divided into induction and post-remission (consolidation) therapy. The goal of induction is to reduce tumor burden and restore hematopoiesis. Induction chemotherapy must be started before cytogenetic and molecular information is known. Therapy is based on age, history of myelodysplasia or cytotoxic therapy, and performance status.

Cytogenetic and molecular analysis provide the best prognostic information for induction and post-remission chemotherapy (NCI, 2021a). There is no standard or ideal salvage chemotherapy regimen for relapsed/refractory AML. For older adults who are frail and with significant comorbidities, a less intense regimen is preferred to control disease and minimize treatment-related mortality (Megías-Vericat et al., 2018). Supportive care with blood product transfusions and hydroxyurea is an appropriate option for patients who are not fit for induction therapy or who choose supportive care and forego chemotherapy (NCCN, 2021a). Supportive care with blood product transfusions and hydroxyurea is an appropriate option for patients who are not fit for treatment or choose not to receive chemotherapy (NCCN, 2021a).

Response to Treatment: Sixty to seventy percent of adults obtain complete remission after induction. Older patients have increased morbidity and mortality during induction. The 3-year survival rate for adults with AML is 25%. Negative prognostic factors include age, central nervous system (CNS) involvement, infection at diagnosis, WBC >100,000/mm^3 at diagnosis, therapy-related malignancy, history of myelodysplastic syndrome (NCCN, 2021a).

TABLE 19-2 Treatment Phases for Acute Myeloid Leukemia

TREATMENT PHASE	GOALS OF TREATMENT PHASE	CONSIDERATIONS
Induction	Reduce leukemic blast burden	Prognostic/genomic features determine treatment plan
	Restore hematopoiesis	
	Achieve clinical remission	If remission is not achieved, a re-induction is initiated.
Post-Remission (Consolidation)	Eradicate remaining leukemia	Move to hematopoietic stem cell transplantation evaluation based on prognostic/genomic features
	Prevent relapse	
Supportive Therapy	Support through myelosuppression caused by treatment	Blood products, anti-infectives, growth factors

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Supportive Care: Patients require CBC every 1 to 3 months for the first 2 years after consolidation and every 3 to 6 months for up to 5 years. Bone marrow biopsies are only performed if the CBC is abnormal.

Patients require antimicrobial prophylaxis, tumor lysis prophylaxis, growth factor support, blood product transfusions, correction of coagulopathies, and electrolyte replacement (NCCN, 2021a). Patients are at increased risk of secondary malignancy and HF due to treatment with anthracycline chemotherapeutic agents. Patients who undergo hematopoietic stem cell transplant (HSCT) may experience acute and chronic graft versus host disease, chronic infections due to immunosuppression, infertility, osteopenia, cataracts, iron overload, chronic fatigue, and secondary malignancies (NCI, 2021a).

Considerations for the Primary Care Physician (PCP): Obtain a CBC in patients who appear anemic and/or have extreme fatigue, unexplained high fevers, infections that are difficult to control or recur, lymphadenopathy, bruising/bleeding, petechiae, or an enlarged spleen. If symptoms persist or blood counts are abnormal, refer to a hematologist for further work-up. In any individual with an abnormal CBC, rapid referral to a hematologist should be considered. Treatment of an individual with AML is considered critically urgent and patients will be admitted to the hospital as soon as the potential diagnosis is made.

CHRONIC LYMPHOCYTIC LEUKEMIA

Description: Chronic lymphocytic leukemia (CLL) is one of the chronic lymphoproliferative neoplastic disorders and is characterized by the progressive accumulation of abnormal and incompetent lymphocytes (Fig. 19-1). Small lymphocytic lymphoma (SLL) is an indolent non-Hodgkin's lymphoma (primarily seen in nodal disease), yet is identical to CLL. However, CLL abnormal lymphocytes are in the blood and bone marrow and SLL is found in lymph nodes and bone marrow.

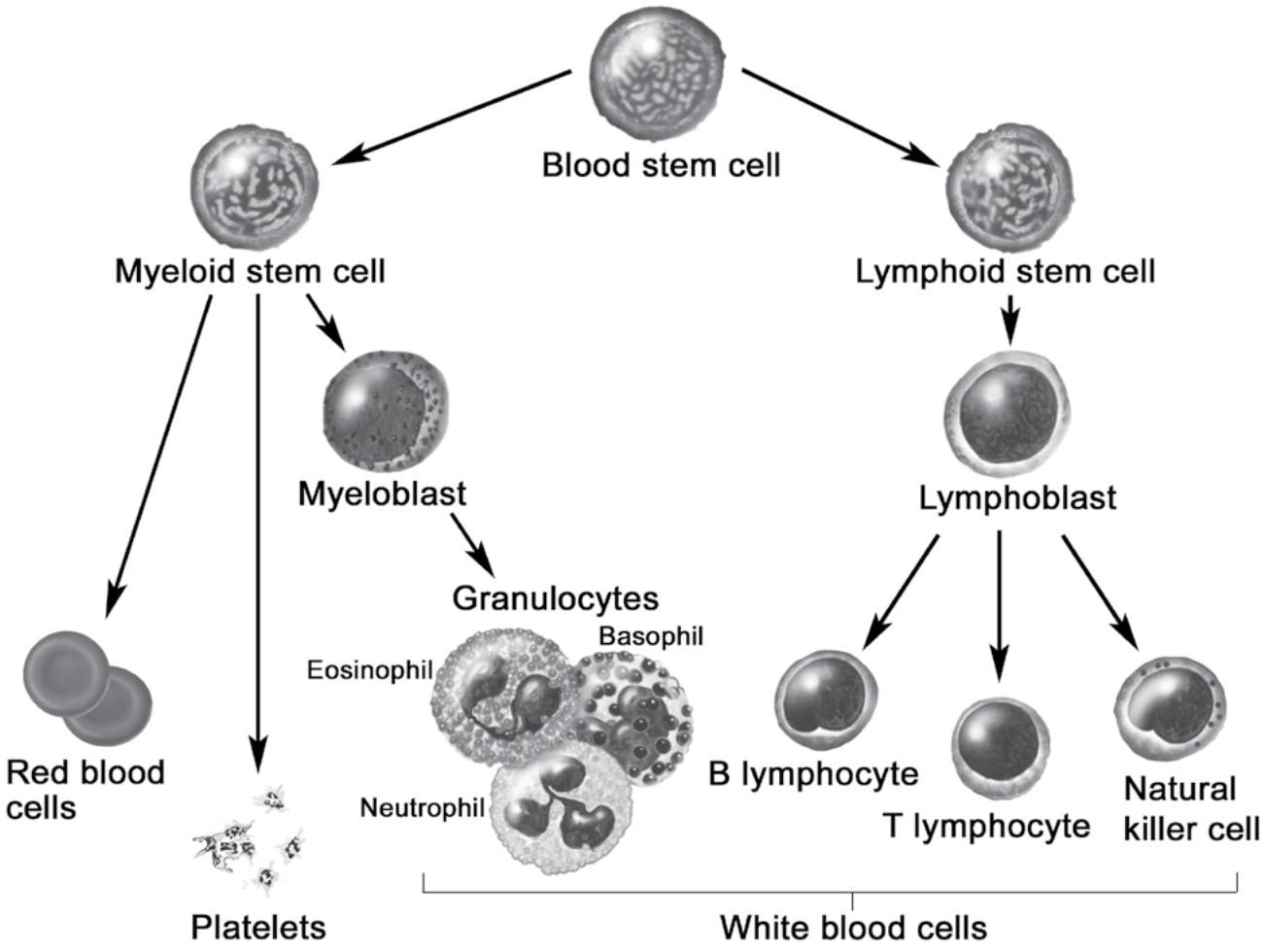

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FIGURE 19-1 Blood cell development.

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Occurrence: CLL is a disease of older adults. It makes up 25% of new leukemia cases. In 2021, there will be an estimated 21,250 new cases and 4,320 deaths in the United States.

Age: Average age at diagnosis is 70 years. It is rarely seen in people younger than 40 (American Cancer Society [ACS], 2021b).

Ethnicity: More common in North America and Europe than in Asia. Asian people who live in the United States do not have a higher risk than those living in Asia (ACS, 2021b).

Signs and Symptoms: Patients are usually asymptomatic in early CLL. Based on the heterogenous nature of CLL, certain subsets of patients have survival rates like the normal population. Symptoms that occur later in CLL progressive disease include painless swelling of lymph nodes, fatigue, weakness, pain, or fullness below ribs (splenomegaly), fever, infection, bruising/bleeding, petechiae, weight loss, night sweats (NCI, 2021b).

Diagnostic Tests:
- History and physical examination
- Measurement of lymph nodes, spleen, and liver
- CBC with differential, chemistry panel, LDH, beta-2 microglobulin
- Reticulocyte count, indirect bilirubin, serum haptoglobin, direct Coombs', and cold agglutinin (if concern for autoimmune hemolytic anemia)
- Additional tests/genetic analysis completed by a hematology/oncology specialist (NCI, 2021b)

CLL diagnosis requires monoclonal B lymphocytes present at 5×10^9/L and clonality of B cells confirmed by peripheral blood flow cytometry. SLL diagnosis requires lymphadenopathy and/or splenomegaly with B lymphocytes of less than 5×10^9/L in the peripheral blood and confirmation with lymph node biopsy.

Differential Diagnosis:
- Infection resulting in lymphocytosis
- Monoclonal B cell lymphocytosis
- Prolymphocytic leukemia
- Mangle cell lymphoma
- Lymphoplasmacytic leukemia
- Hairy cell leukemia
- Follicular lymphoma
- Splenic marginal zone lymphoma

Treatment: Treatment of CLL ranges from observation (providing treatment of infectious, hemorrhagic, or immunological complications) to a variety of therapeutic options administered as targeted single agents or combination therapy. In asymptomatic patients, treatment may be deferred until the disease progresses and symptoms occur. Frequent and careful observation is required to monitor the clinical course, and the patient may experience a long period of stability. Treatment is indicated for patients with disease-related complications, including worsening anemia and/or thrombocytopenia, symptomatic splenomegaly, or constitutional symptoms (significant fatigue/inability to perform usual activities, fevers and/or night sweats greater than 2 to 4 weeks without evidence of infection, and/or unintentional weight loss >10% within the previous 6 months).

Response to Treatment: Targeted therapy treatment regimens have altered the treatment landscape for CLL, providing treatment response/remission without need of traditional chemotherapeutic agents. Apart from allogeneic hematopoietic stem cell transplant (HSCT), however, CLL remains incurable with current treatment options.

Supportive Care: Patients with relapsed CLL are severely immunocompromised. They must receive the influenza vaccine annually and pneumococcal vaccine every 5 years. Herpes virus prophylaxis with acyclovir and PJP prophylaxis with sulfamethoxazole/trimethoprim is indicated. IV immunoglobulin (IVIG) can be effective to prevent recurrent infections. Hepatitis B, cytomegalovirus, and Epstein-Barr virus can be reactivated. Autoimmune hemolytic anemia (AIHA) and idiopathic thrombocytopenic purpura (ITP) are commonly seen in CLL (NCCN, 2021b).

CHRONIC MYELOCYTIC LEUKEMIA

Description: Chronic myelocytic leukemia (CML) is a myeloproliferative neoplasm defined by the Philadelphia chromosome, translocation (9;22), which creates the BCR-ABL1 fusion gene. It is classified into three phases: chronic phase (CP-CML), accelerated phase (AP), and blast phase (BP). Ninety to ninety-five percent of patients present in CP-CML. CP-CML may transform to a more aggressive form of disease (AP or BP) within 3 to 5 years. Increased peripheral blood blast count and cytogenetic changes, as well as fever, bone pain, and change in spleen size can be seen during transformation (NCCN, 2021c).

Occurrence: Fifteen percent of adult leukemias are CML. In 2021, there will be an estimated new 9,110 cases and 1,220 deaths in the United States (ACS, 2021c). Targeted therapy has changed the treatment landscape for Ph-positive CML. Today CML is classified as a chronic disease (Vener et al., 2020). Unfortunately, patients with Ph-negative CML do not respond well to treatment and have a shorter overall survival (NCI, 2021c).

Age: The median age at diagnosis is 67 years.

Ethnicity: Most common in non-Hispanic Whites and least common in non-Hispanic Asian/Pacific Islanders (NCI, 2021c).

Signs and Symptoms: Symptoms of CML are often dependent on the stage of the disease. Chronic phase CML symptoms result from anemia and splenomegaly, including fatigue, weight loss, malaise, early satiety, and left upper quadrant fullness. Bleeding, thrombosis, gouty arthritis, priapism, retinal hemorrhages, and upper gastrointestinal (GI) ulceration are rare symptoms. Headaches, fevers, bone and joint pain, bleeding, infections, and lymphadenopathy are signs that CP-CML is transforming into an AP or BP, which very much resembles AML (Eden & Coviello, 2022).

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Diagnostic Tests:

- History and physical
- Spleen size by palpation
- CBC with differential and chemistry (NCCN, 2021c)

CP-CML is diagnosed when there are less than 10% blasts and promyelocytes in the peripheral blood and bone marrow; AP-CML 10% to 19% blasts; BP-CML 20% or more blasts. When patients with 20% or more blasts also present with fever, malaise, and splenomegaly they are in blast crisis (NCI, 2021c). Transformation between phases is characterized by leukocytosis, thrombocytosis, thrombocytopenia, anemia, splenomegaly, hepatomegaly, fever, bone pain, bone lesions, and thrombotic or bleeding complications (NCI, 2021c).

Differential Diagnosis:

- Leukemoid reactions
- Effect from corticosteroids
- MDS
- Polycythemia vera with iron deficiency
- Philadelphia-negative CML
- Myeloid hyperplasia
- Thrombocythemia

Treatment: There are several first-line targeted therapies (tyrosine kinase inhibitors [TKIs]) for CP-CML. Therapies are chosen based on the patient's comorbidities. (Vener et al., 2020). TKIs are generally well tolerated, but each has a unique side-effect profile ranging from fatigue to renal, pulmonology, hepatic, and cardiology toxicities. All TKIs can cause cytopenias (NCCN, 2021c). Patients with advanced phase CML (AP and BP) should enroll in a clinical trial, if available, as well as be worked up for hematopoietic stem cell transplant (HSCT).

Response to Treatment: Hematological, cytogenetic, and molecular responses to treatment with TKIs are evaluated to assess response (Table 19-3). If patients do not achieve a molecular response at 3, 6, or 12 months after subsequent TKI therapy, they need to be evaluated for appropriateness of HSCT (NCCN, 2021c).

Supportive Care: Compliance with oral TKIs can be a barrier to treatment. Patient education and side effect management is key to adherence. TKIs can interact with many medications and dosing needs to be reviewed with a pharmacist. A multidisciplinary team is best suited to coordinate care for patients with CML (Eden & Coviello, 2022).

TABLE 19-3 Measurement of Treatment Response With TKI for CML

LEVEL OF RESPONSE	DEFINITION	TEST
Hematological	Complete hematological response is noted when the peripheral blood counts are normal with no immature blood cells, leukocyte count is less than 10×10^9/L, and platelet count is less than $450{,}000 \times 10^9$/L.	CBC
Cytogenetic	Cytogenetic response is noted when there is a decrease in the number of Philadelphia-positive metaphases, as determined by bone marrow aspirate and cytogenetics.	Bone marrow cytogenetics
Molecular	Decrease in the amount of BCR-ABL1 chimeric mRNA as measured by the RT-PCR.	Quantitative real time-polymerase chain reaction (RT-PCR)

Adapted from NCCN. (2021). Chronic myelogenous leukemia. Version 1.2021. Retrieved from www.nccn.org

Clinical Recommendation	Evidence Rating	References
CD19CAR T cells are indicated for patients with relapsed/refractory B cell ALL.	I	Grigor et al., 2019
Complete molecular response (CMR) within 3 months of therapy with TKIs predicts for best overall survival for patients with Ph-positive B cell ALL.	2A	Sasaki et al., 2019
A less-intense regimen is preferred to control disease and minimize treatment-related mortality in relapsed/refractory AML patients who are older, frail, or with significant comorbidities.	I	Megías-Vericat et al., 2018
If APL is suspected, ATRA and aggressive supportive care to manage bleeding risk must be initiated urgently while waiting for confirmation of diagnosis.	I	Sanz et al., 2019
Acalabrutinib +/– obinutuzumab is a preferred regimen for CLL for patients without Del(17p) or TP53 mutation.	I	NCCN, 2021b
Ibrutinib monotherapy is a preferred regimen for CLL for all patients.	I	NCCN, 2021b

Continued

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Clinical Recommendation	Evidence Rating	References
Venetoclax +/– obinutuzumab is a preferred regimen for CLL for relapsed/refractory older patients with comorbidities.	2A	NCCN 2021b
Second and third generation TKIs are preferred for patients without significant comorbidities; Imatinib is recommended for less fit patients with comorbidities.	I	Vener, et al., 2020

For an explanation of NCCN's recommendation categories, go to https://www.nccn.org/guidelines/guidelines-process/development-and-update-of-guidelines.

CASE STUDY

Mrs. L., a 68-year-old woman, presents to your office today with a complaint of feeling tired all the time and now, more recently, feeling weak and like "I can't catch my breath sometimes." She has been healthy except for high cholesterol, managed by Lipitor. Her husband died 9 months ago, and she has attributed her fatigue to dealing with his death, but realizes that she is feeling worse and not better as time passes.

No known drug allergies, takes only Lipitor. Past surgical history: Appendectomy in childhood; hysterectomy for uterine myoma 10 years ago. No significant medical history. Has two daughters living nearby. Blood pressure (BP) 106/70 mm Hg, heart rate (HR) 98 beats/min and regular, respiratory rate 18 breaths/min and afebrile, body mass index (BMI) 22 (10-lb weight loss since death of husband).

Slender, quiet-spoken older woman appearing tired. Conjunctiva pale, mucous membranes moist. No lymphadenopathy of neck or femoral area. Chest CT angiogram (CTA), good air movement. Heart tachyarrhythmic with regular rate, soft midsystolic murmur. Abdomen soft, bowel sounds × 4. Urine dipstick negative.

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What national guidelines are appropriate to consider?
4. What tests will you order?
5. Are there any screening tools that you want to use?
6. What are the differential diagnoses that you are considering?
7. What is your plan of care?
8. Are there any *Healthy People 2020* objectives that you should consider?
9. What additional patient teaching may be needed?
10. Will you be looking for a consultation?

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CHAPTER 20

Psychosocial Disorders

Laurie Kennedy-Malone

ASSESSMENT

Psychosocial assessment of the older adult requires a holistic, systematic review and evaluation of the patient, their family, and their environment. The psychosocial assessment provides the foundation for developing and implementing a comprehensive plan of care and a means for evaluating its effectiveness. The psychosocial assessment needs to consider not only the patient's mental health but also their social well-being. The practitioner must understand what happens during the aging process because this knowledge allows differentiation between normal and abnormal symptoms. For the older adult, physical health, mental health, spirituality, and environmental and social problems all interact to complicate the life and function of the older patient, their caregivers, and their family. Differentiating between medical and psychological disorders can be difficult for any clinician due to the possibility of multimorbidity (Varghese & Dahale, 2018).

The assessment of older adults is quite challenging considering the many age-related physiological and metabolic changes, increased number of chronic diseases with potential psychiatric manifestations, medications and their side effects, and often atypical presentation of illness (Meeks et al., 2009).

The psychosocial assessment of the older adult includes evaluation of the following basic needs:

- Autonomy and independence
- Dignity, credibility, and respect
- Identity and individuality
- Communication and belonging
- Touch

A positive correlation exists between social supports and the use of health-care services by older adults. Older adults who are alone and lonely, depressed, or having difficulty adapting to change appear in their practitioner's office more frequently than those with adequate support systems. Social networks are an important aspect of a patient's social functions, as are work, hobbies, and interests. Older adults may be reluctant to reveal social or emotional concerns and, in some cultures, may feel that it is unacceptable to share personal problems with outsiders. However, they may feel comfortable discussing a physical manifestation, such as pain or sleeplessness, with a health-care provider (Kendall, 2019; Varghese & Dahale, 2018).

The older adult population is not a homogeneous group; rather, the population demonstrates a diversity in health, social and environmental supports, financial security, and cultural and personal philosophies. Some distinctive occurrences in the lives of older adults may include:

- Developmental milestones that have an impact on most older adults (e.g., retirement, loss of a spouse)
- Changes in financial and social resources that allow the older adult to cope effectively with age-related phenomena

Relocation, financial concerns, and lack of social supports may be the impetus for physical and mental health problems. The most common life events that place the older adult at risk for psychosocial dysfunction include:

- Retirement/role loss
- Loss of spouse
- Deaths of close friends
- Family problems
- Relocation
- Financial problems (Meeks et al., 2009)

Psychological Health

Because older adult patients may hesitate to discuss social or emotional problems with a health-care provider, physical symptoms may be the chief expression of underlying psychosocial dysfunction. Therefore, measurement of psychological health adds an important component to the older adult assessment. Psychological health is measured based on the two subdomains of cognition (mental status) and affect (anxiety and depression). A variety of tools, mentioned throughout this text, can be used for cognitive and emotional health assessment. Although helpful, screening tools should not replace the interactive relationship between practitioner and patient (Kendall, 2019). The heterogeneity of socioenvironmental factors precludes the use of a single tool for evaluating the older adult; however, to evaluate this domain, an environmental and safety checklist may be helpful, and it may also be used for patient and family

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education. The information derived from this evaluation will direct the practitioner in areas of education for the patient and family.

Chronic disease, physical disability, pain and suffering, cognitive impairment, accumulated losses, and social isolation may occur when an individual is least able to cope with change. Therefore, a psychosocial assessment provides a foundation for developing and implementing a comprehensive plan of care. The expected outcome for the older adult is an enhanced quality of life.

Components of the Psychosocial Assessment

An accurate psychosocial assessment is an interactive process between the practitioner and the older adult that creates an awareness of risks, limitations, and functional changes (Varghese & Dahale, 2018). This enables the older adult to make appropriate lifestyle changes and accommodations to maintain their autonomy, independence, and dignity. The psychosocial assessment should be performed at the initial encounter and annually thereafter for all older adults. Reassessment is appropriate whenever a patient's health status changes. You may want to consider at some time assessing the older adult with and without a family member or caregiver present.

Components of the psychosocial assessment are included in the Welcome to Medicare Examination and the Annual Wellness Visit (Camacho et al., 2017; Pfoh et al., 2015; Simpson et al., 2021), providing the clinician time to review their psychosocial status even if the patient is not forthcoming with their concerns (Lucas et al., 2022).

When considering the approach to the psychosocial assessment in an older adult, use terminology that can be understood by the older adult. It may be a struggle for an older adult to commit to a visit that pertains to mental health issues, so focus on their overall well-being. Address the patient's overall medical information, including presenting problems, history of past conditions, medications (prescription and over-the-counter), known psychiatric history, present level of cognition, screening for changes in behavior or mood, and any psychotic or anxiety symptoms. Ascertain from the patient, family member, or caregiver information about any past treatments (medications, psychological therapy, and electroconvulsive therapy [ECT]) and for a history of psychiatric disorders. Conduct a brief suicide assessment. Evaluate for signs and symptoms of abuse or neglect, current and past use of alcohol and other illicit drugs, changes to functional status. Also ask about the patient's current living environment, family status/history (especially of psychiatric or neurological disorders), friends, and social support network (Varghese & Dahale, 2018).

Review current and past occupational, military, and education history. Determine the patient's engagement in spirituality, leisure activities and hobbies, and what gives them pleasure and meaning in life. Assess the patient's coping skills. If an older adult has experienced significant loss, consider assessing for bereavement overload.

The overall assessment should begin with a test of cognition; however, it is crucial to first establish a rapport and a secure trust with the patient before using a specific screening instrument. The complete mental status assessment includes the appearance, motor movement, speech, affect/mood, thought content, process, perception, cognition, insight, and judgment (Libby et al., 2021; Snyderman & Rovner, 2009). When positive findings of any of the components of the mental status examination are reported or observed, further probing is needed and information should be verified by the patient, family members, or caregivers (Kendall, 2019; Varghese & Dahale, 2018).

Evaluation for Neuropsychiatric Conditions

When considering assessing psychosocial conditions in older adults, the clinician knows that older adults are often not forthcoming about a change in their overall condition or even why they might be experiencing symptoms (medication-related or disease-process–related). Questions about prevalent psychosocial symptoms commonly experienced by older adults, such as apathy, sadness, depressive symptoms (lack of energy, loss of interest, deceased ability to concentrate), agitation, and sleep disturbance, may need to be probed by the clinician if these symptoms are suspected or anticipated because of changes in function, medications, or experienced loss (Kendall, 2019; Meeks et al., 2009). If patients respond to having experienced any of these symptoms, it is important to quantify the duration of the symptom, any known precepting factors and any self-care measures or treatments that the patient has initiated. A more in-depth neuropsychological evaluation can be considered for an objective assessment of multiple cognitive and complicated emotional functions that may require complex treatment plans (Schroeder et al., 2019).

Determining Capacity in Older Adults

Whether or not impaired cognition or progressive psychiatric illness is determined, older adults may be found to have impaired decisional capacity and competency (Meeks et al., 2009; Varghese & Dahale, 2018). *Capacity* is defined as a functional determination that an individual is or is not capable of making a medical decision within a given situation, whereas *competency* is defined as the ability of an individual to participate in legal proceedings (Darby & Dickenson, 2017). Nurse practitioners can determine decision-making capacity in patients (Libby et al., 2020). Establishing capacity is viewed as a complex computation involving a complete mental status assessment and an appraisal of the patient's culture, education level, health literacy skills, and ability to articulate the issues of concern (Goldfrank & Wittman, 2017). A patient has capacity if they:

- Understand information relevant to the decision in question
- Have the ability to weigh risks and benefits and to assess alternative options
- Communicate clearly with medical providers about the decision in question, and verbalize the ultimate decision
- Demonstrate consistency of logic and decision making throughout the encounter (Libby et al., 2021, para 26)

It is highly recommended that older adults be proactive in establishing advance directives before the need to determine capacity and competency (Meeks et al., 2009).

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AGITATION

Signal Symptoms: Change in behavior, also known as *neuropsychiatric symptoms of dementia.*

Description: Various terms are used to describe agitation. These include *aggression, hyperactivity*, and *irritability*. The International Psychogeriatric Association defines *agitation* as manifesting excessive motor activity or verbal or physical aggression that is associated with emotional stress for the person concerned (Schmudderich et al., 2021).

Etiology: Symptoms are related to the changes in the brain structure and function, particularly in the brain circuits and networks that are involved in motivated behavior, emotions, and cognitive processing (Nowrangi et al., 2015).

Occurrence: Agitation occurs most frequently in those with cognitive impairment or dementia, with a higher incidence in females. Ninety percent of people with dementia develop at least one clinically significant neuropsychiatric symptom. The prevalence of agitation can reach 85% based on the assessment tool utilized (Schmudderich et al., 2021).

Age: Predominantly in older adults

Ethnicity: Patients with moderate to severe dementia who are Black or Latino have a higher prevalence of dementia-related behaviors than Whites (Freedman et al., 2018).

Contributing Factors: Cognitive impairment, sensory impairment, social isolation, chronic bedrest, pain, and hunger can precipitate episodes of agitation. Environmental triggers, such as noise, light, and visual cues from television and physical surroundings, can also lead to agitation. Psychosocial triggers, such as the approach taken by staff, interaction with other residents, and anxiety during personal care, may cause a person to become agitated (Schmudderich et al., 2021).

Signs and Symptoms: Behaviors may be displayed in multiple ways. Common behaviors include repeating questions, arguing, pacing, screaming, crying out, making disruptive sounds, physical or verbal aggression, and shadowing a caregiver. When assessing the older adult with agitation, primary psychiatric causes should not be overlooked. Anxiety disorders are the most prevalent psychiatric disorder among older adults. Acute anxiety can present with signs of agitation including restlessness, pacing, irritability and agitation. Individuals with psychotic symptoms such as delusions, paranoia, hallucinations, or disorganized behavior may also be agitated (Kennedy et al., 2020).

Diagnostic Tests: Assessment should include ruling out conditions that can cause agitation. These include hypoxia, hyperglycemia, ST-elevation myocardial infarction (STEMI), electrolyte imbalance, infection, and medication side effects. Obtain complete blood count (CBC), comprehensive metabolic panel (CMP), urinalysis, and electrocardiogram (EKG) (Shenvi et al., 2021).

Differential Diagnosis:

- Delirium
- Psychosis
- Mania
- Infection
- Medication side effects
- Late-life delusional disorder
- Depression
- Pain
- Seizures

Treatment: Depending on the manifestations of agitation, evidence supports the use of antidepressants, antipsychotics, or antiepileptics in conjunction with cholinesterase inhibitors (Table 20-1). Cholinesterase inhibitors have a favorable safety

TABLE 20-1 Psychotropic Drug Management for Agitation

DRUG	DOSE	FORM	CAUTIONS
Antipsychotics (Always Start at Lowest Dose)			
aripiprazole (Abilify)	2.5 mg	Tab, dissolvable	Decreased white blood cells
	Max 30 mg	Liquid, IM	Potentiates antihypertensives
risperidone (Risperdal)	0.25–1.0 mg	Tab, liquid, IM	Dose-related EPS
			Potentiated by proton inhibitors
			May be affected by fluoxetine (Prozac), paroxetine (Paxil)
asenapine (Saphris)	5–10 mg	SL	Weight gain, anxiety, depression
Antiseizure Agents (Off-Label Use)			
carbamazepine (Tegretol)	200–1,000 mg	Tab	Poor tolerability in older adults
			Monitor complete blood count, electrolytes, liver profile
lamotrigine (Lamictal)	25–200 mg	Tab	Slow dose titration
			Stevens-Johnson syndrome
divalproex sodium (Depakote)	250–2,000 mg	Tab, liquid, sprinkles	Monitor complete blood count, platelets, liver function
			Better tolerated by the older adults

Abbreviations: CBC = complete blood count; EPS = extrapyramidal symptoms; IM = intramuscular; SL = sublingual; WBCs = white blood cells.

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TABLE 20-2 Behavioral Interventions for Agitation

Individual approach	Cognitive training
	Redirection and reassurance
	Validation
	Cognitive stimulation
	Increased activity and exercise
	Pain management
	Multisensory stimulation
	Reminiscence
	Reality orientation
Environmental	Cuing with signage and room layout
	Decreased noise levels
	Ambient lighting
	Person-centered care model
	Availability of activities and supplies
Alternative modalities	Music therapy
	Pet therapy
	Massage
	Therapeutic touch
	Multisensory room or environment
	Acupuncture
	Aromatherapy
	Art therapy
Staff/caregiver education	Approach to patient
	Behavioral intervention skills

TABLE 20-3 Acronym for Management of Agitation

T- Take charge
U- Understand possible triggers
R- Reassure and redirect
T- Take away distractions
L- Leave the area with patient
E- Empathize and evaluate

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profile and are generally well tolerated. They may be used long term. An antidepressant may help decrease agitation among those exhibiting depressed mood, anxiety, or paranoia. Start antidepressants at a lower dose and titrate slowly because they are associated with increased fall risk.

Antipsychotics, especially risperidone, aripiprazole, and olanzapine, have been evaluated in multiple studies and demonstrated improvement in severe agitation and aggression. Effects and durations of antiepileptics vary widely. It is recommended they be used for short duration. Valproate has a higher incidence of toxicity. Carbamazepine can cause side effects, requiring liver enzymes and CBC to be monitored. Gabapentin is better tolerated and shows a modest decrease in aggression (McDermott & Grvenewald, 2019).

Follow-Up: Review laboratory reports, treat any infections or acute medical conditions, and review medications. If antipsychotics were prescribed, monitor for extrapyramidal symptoms, falls, and lethargy. If indicated, attempt a gradual dose reduction of any psychotropic medications after the acute episode and further reduction at least once every 3 months.

Sequelae: Falls, sedation, hypotension, gait disturbances, weight gain, gastrointestinal problems (McDermott & Gruenewald, 2019).

Prevention/Prophylaxis: Identify antecedents, avoid triggers, educate staff and caregivers, and introduce behavior modification. Data also support the use of the person-centered care model in long-term care facilities and assisted living communities, along with the use of the nonpharmacological interventions listed in Table 20-2 and Table 20-3. The main focus should include tailored activities based on ability and interest, addressing individual needs, reducing environmental stimuli and improving staff interaction. An overarching activity noted in multiple studies is the use of individualized music (Isaac et al., 2021).

Referral: In refractory cases, a specialist, such as a geriatric psychiatrist, a geriatrician, or a neurologist with specific expertise in pharmacological management, should be consulted.

Education: Education should include patient safety and fall prevention, identification of triggers, reassurance and redirection techniques, simplification of activities, establishment of routine and structure, promotion of rest and sleep, and consistent caregiver assignments.

Clinical Recommendation	Evidence Rating	References
Prevalent symptoms of agitation include repeating questions, arguing, pacing, screaming, crying out, making disruptive sounds, physical or verbal aggression, and shadowing a caregiver.	A	Schmudderich et al., 2021
Occurs most frequently in those with cognitive impairment or dementia; prevalence of agitation can reach 85% based on the assessment tool utilized.	A	Schmudderich et al., 2021
Identified triggers for agitation can include noise, light, and visual cues from television and physical surroundings, and the approach taken by staff, interactions with other residents.	A	Schmudderich et al., 2021 Shenvi et al., 2021

Continued

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Clinical Recommendation	Evidence Rating	References
Nonpharmacological interventions: Tailored activities, addressing individual needs, music therapy, reducing environmental stimuli, and improving staff interaction shown to be beneficial when working with patients who are agitated.	A	Isaac et al., 2021,

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

ANXIETY

Signal Symptoms: Anxiety in older adults involves excessive worrying that is difficult to control and interferes with daily functioning (American Psychiatric Association [APA], 2013). Anxiety is characterized by restlessness, fatigue, difficulty concentrating, irritability, muscle tension, and sleep disturbance (APA, 2013). Older adults with anxiety may present with physical or somatic symptoms, such as headaches, chest pain, palpitations, shortness of breath, dizziness, sweating, or gastrointestinal upset.

Description: Anxiety disorders are common among older adults and continue to require increased efforts in screening, diagnosis, and treatment as the older adult population rises in the United States. The U.S. Census Bureau (2020) reported that the population of older adults aged 65 years and older rose by more than a third since 2010. Most older adults with anxiety initially present to their primary care providers instead of psychiatric providers in mental health-care settings (Brahmbhatt et al., 2021). However, anxiety disorders are often undertreated, underrecognized, underdiagnosed, or misdiagnosed in primary care settings (Bandelow et al., 2017; Brahmbhatt et al., 2021). This lack of diagnosis and treatment of anxiety could be related to comorbid conditions, such as depression, neurocognitive disorder, and other medical conditions, as well as lack of recognition of anxiety by some older adults (Aggarwal et al., 2017).

Anxiety in older adults can present as an exacerbation of anxiety diagnosed earlier in life. However, some older adults experience new-onset late-life anxiety related to pain, loss, physical limitations, and other challenges in later life. According to the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM*-5; APA, 2013), anxiety disorders commonly diagnosed in older adults include generalized anxiety disorder (GAD), social anxiety, specific phobia, agoraphobia, panic disorder, and anxiety disorder related to substance use, medication, or another medical condition. One of the most common anxiety disorders diagnosed in older adult populations overall is GAD (Subramanyan et al., 2018). Among older adults in residential care facilities, GAD and specific phobias were found to be the most common anxiety disorders diagnosed (Creighton et al., 2016). Medical conditions should be considered and ruled out before making a diagnosis of an anxiety disorder.

Etiology: Although anxiety is common among older adults, anxiety is not a normal result of the aging process. The pathogenesis of late-life anxiety likely involves interactions between biological, psychological, and environmental risk factors (Hellwig & Domschke, 2019). Risk factors include genetic factors, structural brain changes, hypothalamic-pituitary-adrenal axis changes, cognitive impairment, loss, social isolation, and other age-related changes (Hellwig & Domschke, 2019). Worry was found to be associated with activation of the frontal brain, amygdala, and insula in older adults with GAD (Mohlman et al., 2017).

Occurrence: Estimates of anxiety disorder prevalence among older adults are unclear due to underdiagnosis, undertreatment, and lack of utilization of reliable diagnostic tools. Anxiety disorders are estimated to be diagnosed in 14% to 17% of older adults (Canuto et al., 2018; Welzel et al., 2019). Older adults in aged care facilities were estimated to experience higher prevalence of anxiety disorders compared to older adults in community settings (Creighton et al., 2016). Researchers discovered that some anxiety disorders have been found to occur more often among older women compared to older men (Canuto et al., 2018; Grenier et al., 2019). Grenier and associates (2019) found that prevalence rates for GAD and social anxiety disorder (SAD) were increased for older women compared to older men. Canuto and associates (2018) concluded that older women were twice as likely to receive a diagnosis of agoraphobia or GAD compared to older men.

Age: Anxiety disorders are common among older adults, but prevalence generally decreases as age increases (Reynolds et al., 2015). Among adults aged 82 years and older, anxiety prevalence is estimated to be 14.5% (Welzel et al., 2019).

Ethnicity: There are limited data available regarding differences in anxiety disorder prevalence between various ethnic groups. Vilsaint and associates (2019) found that non-Latino White Americans experienced higher unadjusted prevalence of anxiety disorders compared to African Americans, Hispanic Americans, and Asian Americans. Nativity and lower education were found to be relevant risk factors for anxiety disorders, especially among racial/ethnic minorities compared to non-Latino White Americans (Vilsaint et al., 2019).

Contributing Factors: Anxiety among older adults is frequently related to functional decline, recent loss, depression, and experience of major stressors during the aging process (World Health Organization, 2017). Occurrence of a past anxiety episode increases risk of anxiety in older adults (Grenier et al., 2019). Anxiety among older adults living in residential aged care was associated with pain, depression, and lower perceived quality of life (Creighton et al., 2017). Among individuals aged 82 years and older, depression, impaired cognitive ability, and recent loss are associated with anxiety and related distress (Welzel et al., 2019).

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Signs and Symptoms: Anxiety among older adults may be manifested by excessive worry, restlessness, and somatic problems, such as gastrointestinal upset, chest pain, or headaches. Older adults with anxiety commonly experience comorbid depression and somatic symptoms (Bakkane et al., 2018; Grover et al., 2019). Older adults commonly experience fear or worry related to falling, pain, death, burdensomeness, physical limitations, health problems, and financial challenges. Worry symptoms may negatively impact neurocognitive performance (De Vito et al., 2019). Clinically significant anxiety in late life has been associated with increased risk of Alzheimer's disease (Santabárbara et al., 2019). Anxiety was also found to be a common symptom among older adults with dementia (Kwak et al., 2017). In older adults with depression, the severity of anxiety symptoms was found to be associated with the severity of depression symptoms and suicidality (Bakkane et al., 2018).

Diagnostic Tests: To diagnose anxiety in older adults, it is important to complete a history and physical examination. Laboratory tests can rule out medical conditions that may be related to anxiety, including a complete blood count (CBC), comprehensive metabolic panel (CMP), and thyroid-stimulating hormone (TSH) test. Additional laboratory tests may be needed based on findings from the history and physical examination. Valid and reliable self-report scales to help diagnosis and assess older adults for anxiety include the Geriatric Anxiety Inventory (GAI) and the Geriatric Anxiety Scale (GAS) (Segal & Mueller, 2019; Szalek et al., 2021). Assess the extent of distress, suicide risk, and functional impairment in addition to considering scores from self-report scales (Szalek et al., 2021). A diagnosis of GAD according to the *DSM-5* requires excessive anxiety, difficulty controlling worry, and associated symptoms (at least three), including restlessness, easy fatigability, difficulty concentrating, irritability, muscle tension, or difficulty falling or staying asleep (APA, 2013).

Differential Diagnosis: When diagnosing an anxiety disorder in an older adult, it is important to rule out medical conditions with similar symptoms, other psychiatric disorders, medication effects, or substance use disorders. Examples of medical conditions that could be ruled out when diagnosing anxiety include thyroid conditions (hyperthyroidism or hyperparathyroidism), cardiac diseases (angina, myocardial infarction, or arrythmias), pulmonary diseases (asthma or obstructive pulmonary diseases), neurological conditions (seizure disorders or transient ischemic attacks), adrenal diseases (pheochromocytoma), and other medical conditions (Craske & Stein, 2016). Anxiety could be induced by substance intoxication or withdrawal. Examples of related substances and medications include alcohol, caffeine, cannabis, opioids, amphetamines, cocaine, phencyclidine, decongestants, albuterol, and levothyroxine, among other substances (APA, 2013). Anxiety symptoms in older adults may overlap with symptoms of depression and dementia (Kwak et al., 2017).

Treatment: Goals for treatment for anxiety in older adults include improved functioning, decreased distress, and relief of anxiety symptoms. Therapeutic communication, active listening, compassion, and respect can help to improve the therapeutic relationship during the treatment of anxiety. Comorbid depression, dementia, and other medical or psychiatric conditions should be treated. Research studies have demonstrated that pharmacological and psychological interventions are effective for treating adults with GAD, but younger adults are more likely to experience anxiety symptom relief compared to older adults (Carl et al., 2020).

First-line treatment for generalized anxiety disorder in older adults includes use of selective serotonin reuptake inhibitors (SSRIs) or serotonin and norepinephrine reuptake inhibitors (SNRIs) due to overall effectiveness, improved tolerance, and a more favorable safety profile compared to other anxiety medications (Crocco et al., 2017). Sertraline, escitalopram, and citalopram are SSRIs that are frequently used in older adults with anxiety (Szalek et al., 2021). Higher doses of SSRIs within therapeutic dosage ranges increased benefit in relieving anxiety (Jakubovski et al., 2019). Gastrointestinal disturbances, sexual dysfunction, insomnia, somnolence, and hyponatremia may occur with SSRI use in older adults, and QTc interval prolongation may occur with doses of citalopram above 40 mg (Crocco et al., 2017; U.S. Food and Drug Administration [FDA], 2017). SNRIs, including venlafaxine and duloxetine, have been shown to be effective in older adults with anxiety, but blood pressure may be increased when taking SNRIs, especially venlafaxine (Crocco et al., 2017; Jakubovski et al., 2019). Tricyclic/tetracyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) are not considered first-line or primary treatments for anxiety disorders in older adults due to risks of adverse effects, including orthostatic hypotension, falls, and confusion (Crocco et al., 2017). Benzodiazepines, such as lorazepam, could be used for the short term, as older adults' initiate treatment with an SSRI or SNRI; long-term use in older adults is not advised (Crocco et al., 2017). There is limited evidence regarding the use of buspirone for anxiety disorders in older adults, but buspirone is a safer adjunct treatment alternative to benzodiazepines (Crocco et al., 2017).

Psychological interventions, especially cognitive behavioral therapy (CBT), can be effective for treating GAD as well as coexisting anxiety and depression in older adults (Hall et al., 2016; Wuthrich et al., 2021). CBT in older adults has been found to be as effective as CBT in working-age adults (Kishita & Laidlaw, 2017). For older adults with GAD, CBT augmentation to treatment with SSRIs could decrease cortisol levels (Rosnick et al., 2016). There is modest evidence that exposure therapy can be effective in decreasing anxiety symptoms in older adults (Jayasinghe et al., 2017). There is limited evidence that mindfulness-based cognitive therapy can be effective for treating anxiety symptoms (Helmes & Ward, 2017). Life review could also be valuable for older adults to improve quality of life, well-being, and other psychosocial outcomes (Lan et al., 2017).

Follow-Up: Evaluation of the effectiveness and tolerability of anxiety treatment depends on the severity of symptoms, impairment in functioning, and use of pharmacotherapy or psychotherapy. Trials of SSRIs may last 6 weeks, and maintenance treatment can last at least 6 months to prevent relapse of anxiety symptoms in older adults (Szalek et al., 2021). Antidepressant use among older adults is associated with hyponatremia, so if antidepressants (especially mirtazapine, escitalopram, or venlafaxine) are prescribed, then the patient should be monitored for possible hyponatremia 2 to 3 weeks after the medication is initiated (Grover et al., 2018; Szalek et al., 2021). Provide education about anxiety for the patient and caregiver, use simple terminology, allow adequate time

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for addressing questions, and allow for description of symptoms in their own words (Subramanyam et al., 2018).

Sequelae: Anxiety disorders have been linked to cognitive impairment, disability, and decreased quality of life (Bower et al., 2015). Anxiety in older adults was also found to be associated with incident impairment in self-care functioning (Simning & Seplaki, 2020).

Prevention/Prophylaxis: Although it may be difficult or not possible to prevent anxiety disorders in older adults, distress and relapse of anxiety symptoms could be mitigated by managing stress, maintaining a support network, sleeping and eating adequately, and exercising regularly.

Referral: Patients expressing suicidal ideation or those at high risk for harming themselves or others should be referred immediately to a psychiatric provider or inpatient psychiatric facility. Psychiatric evaluation by a mental health provider may be beneficial if impaired functioning or anxiety symptoms persist after multiple trials of treatment or if comorbid psychiatric conditions are suspected (Szalek et al., 2021). Refer to a neurological specialist if dementia is suspected (Szalek et al., 2021).

Education: Compared to younger adults, older adults may have decreased knowledge about anxiety disorders (Beaunoyer et al., 2019), so psychoeducation is critical. Educate patients and caregivers to recognize and manage anxiety symptoms and triggers and to understand the connection between anxiety and physical symptoms (Szalek et al., 2021). Discuss physical activity, social networks, nutritional status, and sleep hygiene with the patient.

Clinical Recommendation	Evidence Rating	References
Effective screening tools for anxiety include evidence-based instruments, such as the Geriatric Anxiety Inventory and Geriatric Anxiety Scale.	B	Balsamo et al., 2018 Segal & Mueller, 2019 Szalek et al., 2021
Cognitive behavioral therapy (CBT) can be effective in treating anxiety disorders in older adults.	A	Carpenter et al., 2018
Selective serotonin reuptake inhibitors (SSRIs) are effective treatment options for generalized anxiety disorder.	A	Crocco et al., 2017 Jakubovski et al., 2019
Augmenting SSRIs with CBT results can reduce anxiety and decrease the need for long-term pharmacotherapy in older adults with anxiety.	B	Crocco et al., 2017
Physical activity, mindfulness, exposure therapy, music therapy, and life review have been shown to reduce anxiety symptoms in older adults.	B	Belland et al., 2017 Jayasinghe et al., 2017 Kandola et al., 2018

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

BIPOLAR DISORDER

Signal Symptoms: Patients may present with clusters of symptoms and in various phases of mood changes. Phases include depressive, hypomanic, manic, or rapid cycling (called the *cyclothymic phase*). In the manic phase, individuals may feel energized or have pressured speech or grandiosity or thoughts of grandeur, delusions, distractibility, or fluctuations in mood with persistent insomnia of 4 to 7 nights in a row that impact the domains of social, environmental, occupational, and/or other areas of daily functioning. Bipolar depressive symptoms include trouble with appetite and sleep (*Diagnostic and Statistical Manual of Mental Disorders*, 5th ed.; *DSM*-5; American Psychiatric Association [APA], 2013; Dols & Beekman, 2020).

Description: Bipolar disorder, also called bipolar affective disorder, is a mood spectrum disorder that presents similar to unipolar major depressive disorder until a first manic episode. According to the APA (2013), bipolar disorders are classified as bipolar I, bipolar II, cyclothymic disorder, and other specified bipolar related disorders. Each presentation has a hallmark of intensity and time frame of symptoms. A diagnosis of bipolar I disorder requires an individual to have experienced at least one full manic episode. A manic episode involves changes in mood that are expansive, euphoric, grandiose, or irritable, accompanied by an increase in energy levels despite poor sleep of only 3 hours or less per night for 7 nights in a row. Most patients also have depressive episodes, and although this may be precluded or followed by a manic episode, it is not a required for the diagnosis of bipolar I disorder; only one manic episode is required. A diagnosis of bipolar II disorder requires at least one prior episode of major depression and at least one hypomanic episode, although hypomania lasts at least 4 days/nights and fewer than 7 days/nights (APA, 2013). Cyclothymic disorder is characterized by milder mood fluctuations that occur over a longer period, more specifically 2 years of cycling phases with symptoms that cause clinical impairment, and it does not meet criteria for a full hypomanic episode (APA, 2013). It is important to distinguish bipolar disorder from major depressive disorder, also known as *unipolar depression*, because treatment differs (National Institute of Mental Health [NIMH], 2020).

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Etiology: Scientists have not discovered one precise etiology of bipolar disorder, but factors include brain structure and function, genetics, and stress (National Alliance on Mental Illness [NAMI], 2017). Neurocognitive changes and cerebral vascular comorbidities are more common causes in older-age bipolar disorder (OABD) (Dols & Beekman, 2020). Additional research indicates that progressive central nervous system degenerative changes caused by inflammation, mitochondrial dysfunction, and oxidative stress may influence late onset of bipolar disorder (Madireddy & Madireddy, 2022). Patients with OABD presenting with a new onset of mania should be assessed for a cerebral vascular accident or brain tumor (Dols & Beekman, 2020). Misdiagnosis in older adults is common, although 10% of individuals aged 50 or older will have a first manic episode (Marzani & Neff, 2021).

Occurrence: According to the APA, 6 million Americans have bipolar affective disorder and 1 million of those are 60 years old or older (2013). Epidemiological studies have found the prevalence of new-onset cases of bipolar disorder I, in which individuals experience their first manic episode as an older adult and receive a diagnosis, to be 1% of older adults (Carlino et al., 2013). Overall cases of OABD in older adults who are 60 years old or older is expected to increase by 50% in 2030 (Marzani & Neff, 2021). Over 60% of patients with late-life onset of bipolar disorder are female (Ljubic et al., 2021). More females experience rapid cycling, more depressive episodes, and more comorbidities than males.

Age: Bipolar disorder can occur at any age, with the average age of onset being 20 years (APA, 2013). About 90% of older adults with bipolar disorder experience bipolar disorder symptoms as an adolescent and have a continuation of the disorder lifelong. Less commonly, the condition is diagnosed after the age of 50 years old, although the patient may be diagnosed and treated for unipolar depression for decades and tend to do fair ((Ljubic et al., 2021).

Ethnicity: Bipolar disorder manifests across all ethnic and cultural groups although is lower in Afro-Caribbean than Black or White populations (APA, 2013).

Contributing Factors: According to the Depression and Bipolar Support Alliance statistics (2021), two-thirds of people with bipolar disorder have at least one close relative with bipolar disorder or unipolar depression; however, OABD has less of a genetic link to a family history of bipolar disorder (Tampi et al., 2021). For older adults with new-onset bipolar disorder, stressors from life are postulated to be a contributing factor, including adverse childhood events and traumatic brain injuries (Dols & Beekman, 2020; Tampi et al., 2021).

Signs and Symptoms: Classic symptoms that bring individuals in for treatment are the depressive episodes, and an antidepressant may be prescribed. The danger of antidepressant medication is that it may activate a first manic episode. Elevated mood, presenting as euphoria or irritability, is common in OABD. Dysphoric depression alone may be a common presentation. Rapid cycling includes back-and-forth shifts from subhypomania to depression over longer periods of time or phases. All phases have insomnia (hypomania, mania) or hypersomnia (depressive) implications. Inquiring about suicide ideation or intent should be assessed at every visit. Psychotic symptoms may present in either manic or depressive phases, and cognitive impairment is common in dual diagnoses of substance use disorders (APA, 2013; Dols & Beekman, 2020).

The acronym DIGFAST has been used to describe signs and symptoms during a manic or hypomanic phase (Kadiyala, 2020):

- **D**istractibility
- **I**ndiscretions
- **G**randiosity
- **F**light of ideas
- **A**ctivities are increased (hyperactive, does not feel they need rest)
- **S**leep deficits (and do not miss the sleep)
- **T**alkative (pressured or rapid speech)

According to the *DSM*-5, the individual must also experience increased energy and poor sleep while having DIGFAST symptoms (APA, 2013).

Symptoms during the depressive phase are similar to those of major depressive disorder. Use the acronym SIGECAPS, which requires only 5 symptoms over 2 weeks:

- **S**leep disturbance (although they miss the sleep with unipolar major depressive disorder)
- **I**nterest is lost/anhedonia
- **G**uilt feelings, thoughts of worthlessness or helplessness
- **E**nergy changes/fatigue
- **C**oncentration/attention impairment
- **A**ppetite/weight changes (gain or loss)
- **P**sychomotor disturbances (agitation or retardation)
- **S**uicidal thoughts

Diagnostic Tests: The Mood Disorder Questionnaire (MDQ) is a validated (Hirschfeld et al., 2005) screening tool to assess for bipolar disorder; however, it is not specific to older adults. For patients with depressive features, the Geriatric Depression Scale (GDS), is recommended as a screening tool for unipolar major depressive disorder. Risk factors for the depressive phase include potential risk for suicide, which should be assessed at each visit because OABD have a much higher risk than younger adults.

Diagnostic studies to rule out a medical etiology of mood changes include a complete blood count (CBC), comprehensive metabolic panel (CMP), toxicology drug screen, urinalysis, thyroid function tests, rapid plasma reagin (RPR), venereal disease research laboratory (VDRL) testing, B_{12} and folate levels, electrocardiogram, and other individualized testing as indicated by the individual patient presentation and anticipation of treatment modalities (Shah et al., 2017). In patients with new onset of psychosis, an electroencephalogram (EEG), magnetic resonance imaging (MRI), or computed tomography (CT) scan of the brain may be appropriate to rule out medical pathologies. Other screening tests for cognitive disorders, such as the Mini-Mental State Examination (MMSE) (Folstein et al., 1975) or the Saint Louis University Mental Status (SLUMS), are more sensitive to detecting cognitive impairment, and may be useful in assessing comorbid neurocognitive deficits (Yoelin, & Saunders, 2017).

Differential Diagnosis: Bipolar disorder in older individuals is often undetected or misdiagnosed for decades. The etiology of new-onset mania may be secondary to an underlying

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medical illness. Medical conditions include stroke, brain tumor, multiple sclerosis, hyperthyroidism, traumatic brain injury, medication reaction, vascular dementia, or most commonly delirium (Tampi et al., 2021). Substance use disorder, schizophrenia, schizoaffective disorder, major depressive disorder (MDD) (unipolar), and anxiety disorders are included in comorbid psychiatric diagnoses (APA, 2013; Ott, 2018). A complete medication list review should be assessed to rule out medication-induced mania and to assess polypharmacy.

Treatment: The goal is remission of symptoms and improvement in functionality. There are no guidelines specific to older adults; however, clinical practice guidelines generally suggest similar pharmacological treatment for older adults as used in younger adults (National Institute for Health and Care Excellence [NICE], 2020; Shah et al., 2017). These medications include divalproex sodium (or valproic acid), lithium, carbamazepine, lamotrigine, some atypical antipsychotics, and antidepressants. Patients with bipolar disorder are often challenging to manage because of the fluctuating and chronic nature of bipolar disorder. Depending on the presentation and severity, inpatient treatment may be required to stabilize the patient.

First-line treatment for late-life onset of mania includes the mood stabilizers lithium and valproic acid, or the antipsychotics risperidone, quetiapine, or olanzapine (Dols & Beekman, 2020; Ljubic et al., 2021)). Because older adults are frequently on multiple medications for comorbid conditions, monotherapy has been recommended as a starting point with a backup plan for adding other medications if clinically indicated (Sajatovic & Chen, 2021; Tampi et al., 2021). Patients with coexisting dementia require individualized treatment and comanagement by a geriatric psychiatrist or psychiatric mental health nurse practitioner. There is early evidence of a neuro-protective affects for comorbid dementia in those prescribed lithium (Stahl, 2021). Drug therapy is specific to different bipolar disorder phases, symptoms, and comorbidities (Marzani & Neff, 2021).

Dosing should begin at the lowest dose and be slowly increased, while monitoring comorbidities and potential adverse side effects. Benzodiazepines are sometimes used for adjunct, or acute agitation in mania.

Selective serotonin reuptake inhibitors (SSRIs) are generally not recommended for monotherapy in bipolar depression, because they are often ineffective or may induce mania unless added concurrently with an anticonvulsant and/or an antipsychotic medication (Sajatovic & Chen, 2021); however, they are prescribed in select, resistant depressive cases. Treatment may require a combination of the previously mentioned medications (Stahl, 2021). Electroconvulsive therapy (ECT) is highly effective in resistant cases of bipolar depression, psychosis, or catatonia and should be considered if drug therapy is ineffective (Ljubic et al., 2021).

An integrated care model has been successful for patients with combined chronic medical and mental health disorders. Establishing a therapeutic alliance, including psychotherapy and psychoeducation, is key to management (APA, 2021).

Follow-Up: Regular follow-up, particularly during active periods of mania or depression, is essential and should include monitoring for suicide. Family members or life partners are usually included because bipolar disorder affects the entire family. Patients on lithium require initial evaluation of renal, cardiac, and thyroid function before initiating therapy, and then periodically during treatment. Lithium levels need close monitoring during the initial period and periodic monitoring once stabilized. Concurrent use of NSAIDs, thiazide or loop diuretics, and angiotensin-converting enzyme (ACE) inhibitors may adversely affect lithium levels or impair renal function (Stahl, 2021). Adverse effects of lithium include tremor, hypothyroidism, rash, weight gain, and renal impairment. Patients being treated with valproic acid require close monitoring of serum levels, liver function tests (LFTs), and CBC. Adverse effects include weight gain, hepatotoxicity, pancreatitis, sedation, and thrombocytopenia.

Those on atypical antipsychotics should have weight, glucose, and lipid monitoring. QTc interval prolongation can also occur, especially in comorbid cardiovascular disease. Atypical antipsychotics prescribed for older adults with dementia have been found to increase mortality and should be avoided, if possible, in those with bipolar I disorder (Stahl, 2021).

Sequelae: Bipolar disorder is a chronic mental health disorder with both physical and mental health sequelae. Medications used to treat bipolar disorder often cause adverse effects. Concurrent substance use or sexual hyperactivity or foolish financial sprees may result in legal consequences and can complicate the treatment of bipolar disorder. Individuals with bipolar disorder have a 45% lifetime prevalence of comorbid anxiety disorders such as generalized anxiety disorder (GAD), post-traumatic stress disorder, and obsessive-compulsive disorder (APA, 2013; Ott, 2018). Comorbidities often confound and determine the course of treatment for bipolar disorder in older adults (Marzani, & Neff, 2021).

Prevention/Prophylaxis: Teach patients, caregivers, and families to avoid unnecessary stress that could precipitate an acute manic episode. Promote sleep hygiene and routine activity. Educate caregivers and families to recognize early signs of mania to avoid a full-blown episode. Work with the patient and the family to develop a safety plan strategy if the patient demonstrates injurious behavior directed toward self or others. Educate the patient and family on the importance of regular sleep patterns, medication adherence, and routine follow-up with a designated health-care practitioner (Marzani & Neff, 2021).

Referral: Initial referral to a psychiatrist or an advanced practice psychiatric mental health nurse practitioner experienced in the assessment and management of bipolar disorder is important, particularly in older adults with cognitive deficits or medical comorbidities. Any patient with suicide intent should be referred immediately to psychiatry at an inpatient facility if safety is a concern. Referral of the patient and the family to support services is important.

Education: Those with new-onset bipolar disorder require extensive education on the disorder. Poor insight may be part of the clinical picture, thus frequent re-education is indicated. For patients who are in a group living setting, education of

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caregiving staff is essential so that manic and hypomanic episodes in particular are not misinterpreted as deliberate aggression. Spouse and family, if present, also require education in the disorder phases, triggers, the chronic nature of symptoms, and the importance of medication adherence. Avoidance of alcohol and other addictive substances is an important part of the education.

Resources:

- National Institute of Mental Health: www.nimh.nih.gov
- Depression and Bipolar Support Alliance: www.dbsalliance.org
- National Alliance on Mental Illness: www.nami.org
- Mental Health America: www.mhanational.org/
- American Psychiatric Association: www.psychiatry.org

Clinical Recommendation	Evidence Rating	References
Patients 50 or older who present with a first manic episode: 1. Assess history of presenting illness 2. Obtain medical/surgical history 3. Obtain psychiatric history 4. Review current and past medication list 5. Assess standard mental status examination and formal cognitive testing 6. Complete a focused physical assessment to rule out neurological disorder 7. Order diagnostic testing: B_{12}, folate levels, rapid plasma reagin, VDRL/HIV testing, complete metabolic panel, complete blood count, urine drug toxicology screening, electrocardiography, and neuroimaging studies 8. Determine cause and effect 9. Assess safety and for suicide	B	Tampi et al., 2021. Shah et al., 2017
Assess safety of patient and others and determine the need for psychiatric hospitalization, intensive outpatient treatment with close family monitoring.	B	Shah, et al., 2017
Lithium has been shown to decrease manic symptoms and the risk of suicide in patients with mania or depressive phases.	A	Marzani & Neff, 2021
Anticonvulsant mood stabilizers have been shown effective in the treatment for mixed episodes, rapid cyclers, and individuals with medical or other psychiatric comorbidities.	A	Marzani & Neff, 2021 Tampi et al., 2021
For geropsychiatric patients with acute mania or hypomania, monotherapy lithium, or valproate (Depakote), or antipsychotic medications are first-line psychopharmacologic therapy. If antipsychotic medications are utilized as first-line monotherapy treatment, such as olanzapine, cariprazine, haloperidol, risperidone, paliperidone, ziprasidone or quetiapine caution must be used as the risk of extrapyramidal reactions have a higher incidence. Note there is a risk of cerebrovascular accident with individuals with comorbid dementia.	C	Tampi et al., 2021 Marzani & Neff, 2021
For geropsychiatric patients with bipolar disorder, depressive episode or prominent depressive symptoms, lithium is first-line therapy for initial treatment if renally intact; others are quetiapine, cariprazine, or lurasidone; olanzapine-fluoxetine combination is FDA approved.	C	Rajagopalan et al., 2016 Tampi et al., 2021 Marzani & Neff, 2021
For geropsychiatric patients, in refractory cases with psychotic or catatonic symptoms electroconvulsive therapy is an option.	C	Dols & Beekman, 2021
For geropsychiatric patient's adjunctive treatment of refractory mania or hypomania benzodiazepine medications may be beneficial in 25%–50% of cases. Psychotherapy is an adjunctive treatment that is tolerated and improves mood and acceptance of the diagnosis.	C	Marzani & Neff, 2021 Tampi et al., 2021

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DELIRIUM

Signal Symptoms: Change in mental status, confusion, disorientation (time, place, person), agitation.

Description: According to the American Psychiatric Association's (APA, 2013) *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM*-5), delirium is a neurocognitive disorder that presents as a disturbance "in attention (i.e., reduced ability to direct, focus, sustain, and shift attention) and awareness (reduced orientation to the environment)" (DSM-5 Criterion A). The onset of the disturbance is rapid (hours to days) and typically fluctuates over the course of the day (DSM-5 Criterion B). Cognitive changes (poor memory, disorientation, speech disturbance) and/or perceptual disturbances are distinct

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from a preexisting, established, or evolving neurocognitive disorder (DSM-5 Criterion C and Criterion D). Delirium frequently represents a sudden and significant decline from a previous level of functioning, and there is usually evidence from the history, physical examination, or laboratory tests of a direct physiological etiology of a general medical condition, substance intoxication or withdrawal, use of a medication, toxin exposure, or a combination of these factors (DSM-5 Criterion D and Criterion E; APA, 2013).

The *DSM-5* differentiates delirium into the following categories:

1. Substance intoxication delirium
2. Substance withdrawal delirium
3. Medication-induced delirium
4. Delirium due to another medical condition
5. Delirium due to multiple etiologies (APA, 2013).

Delirium should also be specified as acute or persistent, as well as hyperactive, hypoactive, or mixed level activity. The duration of delirium can range from less than 1 week to more than 2 months and typically resolves within 10 to 12 days. However, for some older persons persistent delirium can last for years. Although delirium was once thought to be reversible, evidence supports that delirium may result in permanent neuronal damage to the brain and increased mortality (APA, 2013; Hshieh et al., 2018a).

Etiology: Causes of delirium are numerous, and in older adult hospitalized patients there are often multiple etiologies (Hshieh et al., 2018a; Percisco et al., 2018):

- Metabolic: renal failure, hepatic failure, anemia, hypoxia, hypoglycemia, thiamine deficiency, electrolyte abnormalities
- Infection: meningitis, encephalitis, sepsis, urinary tract infection (UTI), respiratory infection
- Cardiac: myocardial infarction, heart failure, arrhythmia
- Neurological: stroke, intracranial hemorrhage, head trauma, seizures, undiagnosed pain
- Pulmonary: respiratory failure, chronic obstructive pulmonary disease (COPD) causing hypoxia
- Sensory impairment: visual and/or hearing deficits
- Medications: benzodiazepines, sedative-hypnotics, opioids, anticholinergics, antihypertensives, corticosteroids, lithium
- Toxins: alcohol, amphetamines, cocaine, substance intoxication or withdrawal

Because the cause of delirium is multifactorial, no single neuropathology of delirium has been identified (Oh et al., 2017; Hshieh et al., 2018a). Possible neurological pathways may involve oxidative stress, inflammatory responses, and neurotransmitter deficiencies in acetylcholine and melatonin; excesses of norepinephrine, dopamine, and glutamate; and abnormalities in serotonin, histamine, and gamma-aminobutyric acid (GABA) (Maldonado, 2017; Mulkey et al., 2018). The role of inflammatory biomarkers is thought to be implicated in the pathophysiology of delirium (Hshieh et al., 2018a; Oh et al., 2017).

Changes in brain function, multiple general medical problems, polypharmacy, reduced hepatic metabolism of medications, multisensory declines, and brain disorders such as dementia make older adults particularly vulnerable to delirium (Hsheith et al., 2018a). Reviewing all medications is part of a complete evaluation. Although many medications can be a causative factor, those with anticholinergic effects are frequently responsible (American Geriatrics Society 2015 Beers Criteria Update Expert Panel, 2015; Mulkey et al., 2018).

Occurrence: Prevalence in the community is 1% to 2% but increases to 14% in those aged 85 years and older. The prevalence of delirium ranges from 10% to 30% of older persons in the emergency department, 15% to 53% postoperatively, and 70% to 87% in the intensive care unit. In long-term care residents aged 75 years and older, the prevalence of delirium may be as high as 60% at any given time. Approximately 14% to 24% of persons exhibit delirium on admission to the hospital, and 6% to 56% may develop delirium during their stay. Prevalence varies depending on the underlying condition(s), procedures and surgeries performed, and other medical interventions provided (APA, 2013).

Age: Any medically ill patient can develop delirium; however, older adults are more prone to delirium due to preexisting conditions, aging processes, and greater vulnerability to multiple precipitating factors (Hshieh et al., 2018a; Petrie & Kirschner, 2021).

Ethnicity: Culture and ethnicity should be taken into consideration when evaluating an individual's mental status and capacity. Some patients may not be familiar with information used in cognitive rating scales (general knowledge, geographical information, memory, and orientation/location), and many scales adjust for these factors, as well as educational level, in the interpretation of scores (APA, 2013).

Contributing Factors: See Etiology, Occurrence, and Age. Frailty and delirium are related entities (Hshieh et al., 2018a; Percisco et al., 2018). Approximately half of postoperative patients develop delirium, and the majority of those with terminal illness (up to 83%) develop delirium as they approach death (APA, 2013).

Signs and Symptoms: Symptoms of subclinical delirium, such as restlessness, anxiety, irritability, distractibility, or sleep disturbance, may be manifested in the days before the onset of overt delirium and may progress to full-blown delirium over the course of a few days. The clinical presentation may include confusion; difficulty sustaining and shifting attention; extreme distractibility; reduced or inability to focus, disorientation to time and place; impairment of recent memory; misperceptions about the environment, including illusions and hallucinations; emotional instability; and psychomotor activity that fluctuates between agitation and vegetative state (APA, 2013; Maldonado, 2017; Sherer et al., 2020). Disorientation to other persons occurs commonly. Dysarthria is a frequent speech and language disturbance, and dysnomia (impaired ability to name objects), dysgraphia (impaired ability to write), or aphasia may be observed.

Commonly associated features of delirium include disturbances in the sleep–wake cycle, such as daytime sleepiness, nighttime agitation, and disturbances in sleep continuity. Complete reversal of the sleep–wake cycle or fragmentation of the circadian sleep–wake pattern can occur. Emotional disturbances may include anxiety, fear, depression, irritability, anger, euphoria, and apathy. Affective lability (rapid and unpredictable shifts from one emotional state to another) may occur. Possible autonomic signs associated with delirium include nausea, vomiting, diarrhea, tachycardia, sweating, chest pain, hypoventilation, and elevated blood pressure (Suneja et al., 2020).

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The diagnosis of delirium superimposed on dementia presents challenges for clinicians (Morandi et al., 2017) and results in poor outcomes for older persons, including increased cognitive decline, institutionalization, and mortality (Fick et al., 2013; Inouye et al., 2014b). Delirium is an independent risk factor for dementia and dementia is the leading risk factor for delirium (Fong et al., 2015).

Diagnostic Tests: Laboratory work will assist in identifying potential causative factors, as will rating scales that measure cognition and establish diagnostic data such as the Confusion Assessment Method (CAM), the Delirium Rating Scale – Revised (DRS-R-98), or the Delirium Observation Screening Scale. These scales assist in tracking progress and in the patient's return to baseline functioning (Hshieh et al., 2018a). However, because of fluctuating levels of consciousness and cognition, it may be difficult to assess mental status and cognitive function. When possible, obtain information from the medical record, medical staff, and others, especially family members.

Differential Diagnosis: See Etiology. The most common differential diagnostic challenge is whether the patient has dementia or delirium, has delirium alone, or has a delirium superimposed on a preexisting dementia. Although there are common cognitive disturbances in delirium and dementia, a primary difference is that the patient with dementia usually is alert, whereas the patient with delirium manifests overt disturbances of consciousness or arousal. The rapid onset and course of cognitive impairments and the reversibility of symptoms are helpful in distinguishing between delirium and dementia. The severity of delirium symptoms typically fluctuates over the course of a day, whereas dementia symptoms generally do not fluctuate (Inouye et al., 2014a). Information from medical records, caregivers, and family members may help determine whether dementia was present before the onset of delirium. Depression is another differential diagnosis, because patients often manifest cognitive and psychomotor symptoms common to dementia and delirium (Oh et al., 2017).

Treatment: Nonpharmacological interventions are used as well as treatment for the underlying cause (Hshieh et al., 2018a; Wan & Chase, 2017). Appropriate treatment for delirium involves discovering the causes, many of which are reversible, and preventing complications through prompt treatment of specific, identified disorders. A thorough, comprehensive assessment; evaluation of medications, interactions, and contraindications; and ordering of laboratory work will assist in ruling out/in the many etiologies of delirium. While assessing for probable etiology and definitive treatment, management should focus on ensuring safety from behavioral disturbances by combining environmental, behavioral, and pharmacological therapies.

Nonpharmacological Interventions: Nurses are instrumental in directing the course of treatment for older adults with nonpharmacological interventions (Wan & Chase, 2017). A therapeutic environment would include reassurance and reality orientation by family members; clear communication; caregiver consistency; decreased stimuli (noise reduction, adequate lighting, sufficient time to perform tasks); decreased stress and anxiety through frequent reassurance and provision of a daily routine; comfort maintenance (eyeglasses, hearing aids, personal belongings); reestablishment of a sleep–wake cycle by controlling nighttime noise and unnecessary disruptions; guarantee of adequate daily fluid intake; assurance that elimination needs are met; provision of space and programs for physical activity, ambulation, and range of motion; and avoidance of chemical or physical restraint (Marcantonio, 2017; Marra et al., 2017; Oh et al., 2017). Medication should be used as a last resort (Bellelli et al., 2021). In one observational prospective study (Blandfort et al., 2019), hospitalized adults aged 75 years and older in single-bed rooms experienced a reduced risk for delirium when compared with double room occupancy.

Pharmacotherapy: Data support the use of first generation (e.g., haloperidol) and second generation (e.g., olanzapine, risperidone, ziprasidone, and quetiapine) antipsychotic medications to control behavioral symptoms of delirium and prevent injury to self or others. Antipsychotic medications have significant side effects, especially for older persons with dementia, and should be prescribed at the lowest effective dose and only 1 to 2 days or the shortest interval possible depending upon the setting, such as surgery or intensive care (American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015; Marcantonio, 2017; Reus et al., 2016;). The avoidance of benzodiazepines except for specific indications (e.g., alcohol or *gamma*-hydroxybutyric acid [GHB] withdrawal delirium, delirium related to seizures) continues to be a recommendation (American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015; Marcantonio, 2017).

It is important to reassess the patient's mental status and any other prevailing psychiatric symptoms. Regular monitoring and periodic assessments of mental status and symptoms will allow for the adjustment of treatment strategies and may indicate the effectiveness of interventions and new or worsening medical conditions (American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015; Morandi et al., 2017).

Follow-Up: Close follow-up for treatment efficacy, appropriate laboratory and diagnostic studies to monitor resolution of the underlying cause, and monitoring of mental status and cognitive functioning are essential to ensure full recovery.

Sequelae: During overt periods of delirium, there is risk of injury to self or others due to confusion, altered perception, and impaired insight and judgment. Fear is often a precipitant to injury in patients with delirium and may result in attacking others; falling out of bed; or pulling on IV lines, oxygen tubing, tracheotomy or gastrointestinal (GI) tubes, urinary catheters, or other medical equipment. Although the majority of patients recover fully, delirium may progress to stupor, coma, seizures, or death. Full recovery is less likely in older adults, and persistent cognitive deficits are common (Fong et al., 2015). Such deficits may be due to preexisting dementia that was not clearly established.

Older adults have a significantly increased risk of developing complications, such as pneumonia and decubitus ulcers, which may result in longer hospital stays. In postoperative patients, delirium may limit recovery and contribute to poorer long-term outcomes. Increased risk for postoperative complications, longer postoperative recuperation periods, longer hospital stays, and long-term disability are associated with delirium. Delirious patients with alcohol or sedative-hypnotic withdrawal, cocaine intoxication, head trauma, hypoglycemia, strokes, or extensive burns are at increased risk for seizures.

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Delirium in the medically ill is associated with an increased mortality rate, and patients who develop delirium during a hospitalization also have a very high rate of death during the months following discharge (Hshieh et al., 2018a).

Prevention/Prophylaxis: Preventive measures to lessen the likelihood of delirium include elimination or minimization of risk factors. These measures include judicious use of high-risk medications (Beers criteria; STOPP/START), timely management and good control of acute and chronic medical disease processes, correction of sensory deficits (eyeglasses, magnifying glasses, adequate lighting, hearing aids, cerumen removal), promotion of normal sleep patterns through good sleep hygiene measures, provision of adequate nutrition and hydration with oral/parenteral supplementation as necessary, prompt attention to elimination needs, participation in activities that maintain and stimulate cognitive and physical functioning, and provision of general supportive measures (environmental modifications, reality orientation, control of external stimuli) (Marcantonio, 2017). For hospitalized older adults and long-term care residents, encourage frequent visits by family members to provide familiarity, reality orientation, reassurance, and comfort. Quality improvement models of care and protocols specific to older adults that address hospitalized older adults can also improve outcomes, but further research on their efficacy is needed (Hsieh et al., 2018b; Scheunemann et al., 2018).

Referral: Patients with delirium should be hospitalized so that diagnostic testing, identification of underlying causes, and management can occur in a rapid, coordinated manner during concurrent treatment of acute symptoms to ensure patient safety and comfort. Care of the patient with delirium should be coordinated by the primary care provider and managed jointly with internal medicine, psychiatry, neurology, and other specialty physicians to ensure appropriate comprehensive evaluation and care.

Education: Patients and families should be educated about the etiology of delirium and the expected course of illness, while being provided reassurance that delirium is usually temporary and that the symptoms are part of a medical condition. The American Delirium Society (www.americandeliriumsociety.org) is a multidisciplinary professional group dedicated to delirium research and the education of professionals and families of patients with delirium.

Clinical Recommendation	Evidence Rating	References
Assessment of predisposing/vulnerability factors includes findings from the patient's history and physical assessment. Pre-existing cognitive impairment, severity of presenting illness, and age are the most consistent risk factors identified for the development of delirium.	B	Hshieh et al., 2018a
Research is needed on Framework for Improving the Diagnosis of Delirium Superimposed on Dementia: • Improving attention testing • Impact of arousal/awareness/motor fluctuations • Clinical evaluation of delirium superimposed on dementia • Clinical examination • Laboratory testing • Neuroimaging	B	Morandi et al., 2017
Nonemergency antipsychotic medications should only be used for agitation or psychosis in persons with dementia if the symptoms are severe, dangerous, or are distressing to the patient.	A	Reus et al., 2016
Nurses' recognition and assessment of delirium can be enhanced with education on assessing cognition, cognitive impairment, features of delirium, and factors associated with poor recognition of delirium.	B	Wan & Chase, 2017
In older persons not taking cholinesterase inhibitors, cholinesterase inhibitors should not be prescribed to prevent or treat delirium.	C	American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015
Nursing admission and daily assessment processes should incorporate the use of standardized instruments for assessing cognition and the presence of delirium.	B	American Geriatrics Society Expert Panel on Postoperative Delirium in Older Adults, 2015
Primary prevention multicomponent evidence-based strategies, nonpharmacological interventions and addressing the underlying cause for delirium is essential to improve patient outcomes.	A	Wan & Chase, 2017 Hseish et al., 2018b
Early mobilization is an intervention strategy aimed at prevention of delirium for hospitalized older persons.	B	Marra et al., 2017

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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DEMENTIA

Alzheimer's disease (AD) is the most common cause of dementia and is the primary focus of this section. According to the American Psychiatric Association's (APA, 2013) *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM*-5), dementia is a neurocognitive disorder and is defined as a clinical syndrome with global cognitive decline from a previous level of baseline function that interferes with activities of daily living (ADLs). In the differential diagnosis, it is important to ascertain whether an individual has cognitive impairment or an illness with similar or overlapping signs and symptoms such as delirium, depression, schizophrenia, bipolar disorder, or other neurological disorder (APA, 2013). If there is cognitive impairment, then developmental delay, borderline intellectual functioning, mild cognitive impairment, and other related diagnoses must be ruled out (APA, 2013). To meet the criteria for minor or major neurocognitive disorders according to the *DSM*-5 (APA, 2013), cognitive decline must be in at least one of the following cognitive domains including "complex attention, executive function, learning and memory, language, perceptual motor or social cognition" (APA, 2013). Once dementia is ruled in, the type of dementia can then be determined (APA, 2013).

Signal Symptoms: Cognitive changes including confusion, disorientation (as to time, place, person), and impaired short-term memory. Personality changes, psychiatric symptoms, problem behaviors, and changes in daily functioning (APA, 2013).

Description: Clinicians must consider normal aging processes and factors that may contribute to the overall clinical picture when assessing a patient who presents with signs or symptoms of dementia (Arvanitakis et al., 2019). AD has a gradual onset, and the course of illness and progression is typically slow (Arvanitakis et al., 2019). The duration of AD ranges from 3 to 20 years and averages 10 years as comorbidities complicate the course of illness (APA, 2013). Symptoms vary from person to person, and cognitive deficits cause significant impairment in social and occupational functioning, impaired ability to care for oneself, and altered behavioral patterns. Signs and symptoms progress from memory loss to impaired executive functioning, language deficits, coordination, and perception with total or partial loss of the ability to recognize familiar people or objects. Impairment in memory and learning (amnestic) is the typical presentation for AD (APA, 2013) and neuropsychiatric symptoms almost always occur (Phan et al., 2019).

The National Institute on Aging (NIA) and the Alzheimer's Association workgroup introduced diagnostic staging for AD, including preclinical, mild cognitive impairment due to AD, and dementia due to AD (Albert et al., 2011; Jack et al., 2011; McKhann et al., 2011; Sperling et al., 2011). An update (Jack et al., 2018) from the 2011 NIA and Alzheimer's Association workgroup includes the framework for the three clinical stages and a numeric staging along the Alzheimer's disease continuum.

Etiology: The etiology of dementia includes numerous systemic disorders; however, most cases of dementia are irreversible because dementia is a progressive disease process unto itself.

- Central nervous system (CNS) disorders: mild cognitive impairment (MCI), AD (most common type of dementia [Alzheimer's Association, 2021a, b], 60% to 80%; one-half of cases are mixed dementia related to other pathology), Lewy body dementia (10% to 25%), vascular dementia (10%), primary degenerative dementia, frontotemporal dementia or Pick's disease (10% of persons 45 to 60 years old), Huntington's disease, normal pressure hydrocephalus (5%)
- Cardiovascular disease: cerebral hypoxia/anoxia, vascular insults to brain, cardiac arrhythmias, inflammatory blood vessel disease
- Infectious processes: AIDS, Creutzfeldt-Jakob's syndrome, neurosyphilis
- Liver disease: chronic progressive hepatic encephalopathy
- Neoplastic conditions: intracranial lesions, primary or metastasis
- Pulmonary disease: respiratory encephalopathy, chronic obstructive pulmonary disease (COPD)/CO_2 toxicity
- Urinary tract disease: urinary tract infection (UTI), chronic or progressive uremic encephalopathy

Occurrence: Currently, 6.2 million Americans are living with AD, and 11% people age 65 years and older have AD (Alzheimer's Association, 2021b). By 2060, the number of older persons 65 years and older with AD is expected reach 13.8 million (Alzheimer's Association, 2021b). More women than men have dementia, primarily because women live longer.

Age: Most people have a diagnosis of late-onset AD. In late-onset AD, symptoms are experienced after age 65 years and older (Alzheimer's Association, 2021b).

Ethnicity: African Americans and Hispanics are at highest risk of developing AD. African Americans are approximately twice as likely to develop AD than Whites, and Hispanics have approximately one and one-half times the risk of their White counterparts.

Contributing Factors: Risk factors for AD are designated as actual and probable.

Actual Risk Factors:

- Age
- Genetics/family history (NIA, 2019)
- Gene mutations chromosomes 1, 14, 21
- A 50/50 chance of developing early-onset AD if one parent had AD
- Apolipoprotein E (ApoE) gene on chromosome 19
- ApoE alleles e2, e3, e4
- Possibly chromosomes 9, 10, 12
- Microglial *TREM2* gene increases the risk of AD (Zheng et al., 2018)
- Down's syndrome
- Less than 5% of AD cases are caused by rare genetic variations found in a small number of families worldwide. In these inherited forms of AD, the disease tends to develop before age 65 years, sometimes in people as young as 30 years old. The genetic mutations involve the following chromosomes:
  - Chromosome 21 on the gene for the amyloid precursor protein

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- Chromosome 14 on the gene for the presenilin 1 protein
- Chromosome 1 on the gene for presenilin 2 (APA, 2013; NIA, 2019)

Probable Risk Factors:

- Low educational level, low lifetime achievements
- More years of education (versus fewer years) provides a "cognitive reserve" that enables compensation for symptoms of AD/other dementia
- Differences in education and dementia risk may reflect increased risk for disease in general and less access to medical care in lower socioeconomic groups
- Female gender, low estrogen levels
- Framingham Study: Lifetime risk for any dementia in females who reached age 55 years = 21% and for males = 14%
- Depression, brain injury
- Cardiovascular disease, hypertension, type 2 diabetes mellitus, smoking, obesity

Signs and Symptoms: Signs and symptoms vary according to the stage of dementia and disease progression. AD is a multiyear brain disease; it is thought to begin well before clinical manifestations appear. Preclinical changes in the brain can begin 10 to 20 years before symptoms present. These changes include diffuse cerebral plaques, neuritic plaques and tangles, neuron and synapse loss, and some cognitive impairment (Edwards, 2019; Sperling et al., 2011). The onset of clinical symptoms typically begins with memory loss. The duration of each stage of the disease varies, and functional changes usually occur late in the disease process (see Table 20-4).

Many patients manifest neuropsychiatric symptoms, such as apathy, agitation and aggression, combativeness, delusions, hallucination, depression and anxiety, sleep disturbances, and wandering, years before being diagnosed with dementia. Once dementia is diagnosed, neuropsychiatric symptoms may continue to manifest similarly or progress to symptoms more difficult to manage.

Diagnostic Tests: A thorough diagnostic evaluation aimed at identifying the specific etiology of dementia is necessary and will guide treatment decisions. The evaluation should determine whether any treatable psychiatric or general medical conditions might be causing or exacerbating the symptoms manifested by the patient. The clinician must obtain a comprehensive history, and because of questionable reliability secondary to cognitive deficits, a family member or caregiver should be present to validate and obtain collateral information. Take care to note the patient's attitude toward the family member (e.g., friendly, positive, suspicious, paranoid, angry, hostile) who is answering the examiner's questions. If the family member is frequently "correcting" the patient's answer to a question, consider patient and/or family denial, compensation, inconsistency, and fabrication of information (Arvanitakis et al., 2019). The history should include:

- Family history, past medical history, occupation, current health status
- Onset and frequency of memory and cognitive lapses
- Word-finding difficulties
- Ability to perform ADLs, instrumental ADLs
- Sleep patterns
- Ability to drive without getting lost
- Recognition of known others and recall of names
- Wandering

TABLE 20-4 Stages of Alzheimer's Disease and Associated Symptoms

STAGE	ASSOCIATED SYMPTOMS	DURATION
Preclinical	Impaired memory, excused or covered	2–4 years or longer
	Insidious instrumental activities of daily living (ADLs) losses (money handling, bills)	
	Preserved basic ADLs	
	Poor judgment and decisions	
	Subtle personality changes	
	Decreased spontaneity, sense of initiative	
	Increased anxiety, socially normal	
Mild–moderate	Obvious memory impairment	2–10 years
	Overt instrumental ADL impairment	
	Basic ADLs failing	
	Prominent behavioral difficulties	
	Shortened attention span	
	Language difficulty	
	Variable social skills	
	Supervision required	
Severe	Memory fragments only	1–2 years or longer
	No recognition of familiar people	
	Assistance with basic ADLs required	
	Fewer troublesome behaviors	
	Reduced mobility	
	Weight loss, infections	
	Seizures, dysphagia	
	Incontinence	
	Groaning, moaning, grunting	

Diagnostic and Screening Tests: Evidence-based studies support the following routine laboratory studies: complete blood count (CBC), electrolytes, glucose, blood urea nitrogen (BUN), creatinine, liver function tests (LFTs), thyroid-stimulating hormone (TSH), serum B_{12}, folate, syphilis serology, and urinalysis (American Geriatrics Society, 2021). A noncontrast computed tomography (CT) scan will detect vascular insults (infarcts, stroke), and based on history and physical findings and clinical suspicion, magnetic resonance imaging (MRI) may assist in ruling out medical/neurological processes and assist in differential diagnosis. Tests for early diagnosis of AD or for low diagnostic uncertainty are in investigative stages and include a positron emission tomography (PET) scan and biological markers (American Geriatrics Society, 2021; Arvanitakis et al., 2019).

Mental Status Examination and Cognitive Testing: A full mental status examination may uncover mood and neurovegetative symptoms that indicate treatable comorbid psychiatric conditions (e.g., depression, anxiety) that may contribute to cognitive difficulties. Instruments that assess orientation, attention,

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calculation, and memory should be initiated early to assist in diagnosis and establish baseline and should be routinely repeated to objectively document and measure changes over time.

Although commonly used, the Mini-Mental State Examination (MMSE) has poor specificity for dementia and may exhibit poor sensitivity in highly intelligent or well-educated patients; copyright limitations also apply. Additionally, sensory loss and physical frailty may lower scores. Other cognitive instruments may unmask deficits in executive function, abstraction, praxis, visuospatial performance, and test clock-drawing ability, word fluency, proverb interpretation, and praxis (e.g., ability to brush teeth or comb hair). The Montreal Cognitive Assessment (MoCA) and the St. Louis University Mental Status Exam (SLUMS) are well-validated instruments that may be used in the assessment of dementia. The MoCA is a screening test to detect MCI and has greater sensitivity and specificity in distinguishing normal controls from MCI when compared to the MMSE. The MoCA assesses attention and concentration, executive functions, memory, language, visuoconstructional skills, conceptual thinking, calculations, and orientation (Carlson et al., 2017). The SLUMS is useful for detecting MCI and dementia, is more sensitive than the MMSE, and tests orientation, short-term memory, word fluency, attention, concentration and recall, clock drawing, and identification (Yoelin & Saunders, 2017).

The Clock Drawing Test (CDT) can be administered alone or within other cognitive screening instruments (e.g., SLUMS) and screens for AD and other types of dementia. The CDT offers clues regarding areas of cognitive change or damage and provides information about general cognitive and adaptive functioning (memory, information processing, vision, visual-spatial skills). Of note, the CDT lacks sensitivity for MCI. The patient is asked to draw a clock with all of the numbers and to set the hands to read a certain time (Palsetia et al., 2018).

Physical Examination: A general medical assessment should be completed with emphasis on the cardiovascular, respiratory, neurological, and musculoskeletal systems. Assess for endocrine, inflammatory, and infectious processes that may contribute to cognitive symptoms, and note focal motor or sensory signs and altered reflexes, gait, or coordination. The presence of tremor, rigidity, or cogwheeling may indicate a parkinsonian process and vertical gaze paralysis may suggest supranuclear palsy. Look for funduscopic changes that may indicate vascular damage or intracranial pressure, and vision and hearing loss that can mimic or worsen cognitive decline. Unless there are comorbid medical disease processes, the physical examination does not typically reveal many findings.

Diagnosis: Definitive diagnosis of AD is only possible on autopsy and upon finding disease-specific pathology in the brain. As such, the diagnosis of AD is presumptive and based upon the following diagnostic criteria:

Major or Mild Neurocognitive Disorder Due to AD*

DIAGNOSTIC CRITERIA

A. The criteria are met for major or mild neurocognitive disorder.

B. There is insidious onset and gradual progression of impairment in one or more cognitive domains (for major neurocognitive disorder, at least two domains must be impaired).

C. Criteria are met for either probable or possible AD disease as follows:

For Major Neurocognitive Disorder:

Probable Alzheimer's disease is diagnosed if either of the following is present; otherwise, **possible Alzheimer's disease** should be diagnosed.

1. Evidence of a causative AD genetic mutation from family history or genetic testing.
2. All three of the following are present:
   - **a.** Clear evidence of decline in memory and learning and at least one other cognitive domain (based on detailed history or serial neuropsychological testing)
   - **b.** Steadily progressive, gradual decline in cognition, without extended plateaus
   - **c.** No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological, mental, or systemic disease or condition likely contributing to cognitive decline)

For Mild Neurocognitive Disorder:

Probable Alzheimer's disease is diagnosed if there is evidence of a causative AD genetic mutation from either genetic testing or family history.

Possible Alzheimer's disease is diagnosed if there is no evidence of a causative AD genetic mutation from either genetic testing or family history, and all three of the following are present:

1. Clear evidence of decline in memory and learning
2. Steadily progressive, gradual decline in cognition, without extended plateaus
3. No evidence of mixed etiology (i.e., absence of other neurodegenerative or cerebrovascular disease, or another neurological or systemic disease or condition likely contributing to cognitive decline)

D. The disturbance is not better explained by cerebrovascular disease, another neurodegenerative disease, the effects of a substance, or another mental, neurological, or systemic disorder.

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Differential Diagnosis: Numerous disorders and disease processes have similar or overlapping symptoms to dementia, and a comprehensive assessment is necessary for accurate diagnosis. The primary focus of differential diagnoses for dementia is depression and delirium because symptoms may be very difficult to differentiate in an acutely ill patient (see Table 20-5). Additional differential diagnoses include:

- Psychiatric: depression, delirium, mild cognitive impairment, vascular cognitive impairment, amnesic disorder
- Neurological: multiple sclerosis, normal-pressure hydrocephalus, intracranial tumors, subdural hematoma, dementia pugilistica
- Infection: HIV, neurosyphilis
- Inflammatory: rheumatoid cerebrovasculitis, lupus cerebrovasculitis, neurosarcoidosis
- Endocrine: hypothyroidism, hypoparathyroidism, Cushing's disease, Addison's disease, hyperthyroidism, hyperparathyroidism

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TABLE 20-5 Differential Diagnosis of Dementia, Delirium, and Depression

CLINICAL FEATURES	DEMENTIA	DELIRIUM	DEPRESSION
Onset	Insidious	Rapid	May be abrupt, with life changes
Course	Long, progressive	Short, diurnal variation	Situational
Duration	Months to years	Hours to 1 month	2 weeks, months, years
Awareness	Clear	Reduced	Clear
Alertness	Normal	Impaired	Normal
Orientation	Impaired	Impaired	Selective
Thought process	Poor abstract thinking; diminished thoughts; poor judgment; difficulty with word finding/verbalizing	Disorganized, distorted, fragmented, diminished, or expansive thoughts, incoherence	Intact, linear; themes of hopelessness, helplessness, poor self-esteem
Perception	Frequent misperceptions	Distorted with illusions, delusions, hallucinations	Intact
Psychomotor behavior	Normal, apraxia	Varies/mixed; hypokinetic, hyperkinetic	Varies with restlessness, agitation, retardation
Sleep–wake cycle	Fragmented, disturbed, reversed	Disturbed, reversed	Disturbed sleep patterns (increased/decreased); early, mid-, late insomnia; napping
Associated features	Affect superficial, labile, inappropriate; may be in attempt to conceal deficits	Variable affective changes, increased arousal, personality exaggeration	Affect and mood depressed, increased somatic complaints, preoccupation, rumination
Mental status testing	Increased effort to find appropriate replies, frequent near-miss answers, word searching	Distracted from task, inability to focus	Inability to focus/concentrate; makes little effort; gives up; shows indifference, apathy

- Metabolic: vitamin B deficiency
- Toxins: alcohol/substance abuse/dependence

Once depression, delirium, and systemic causes of dementia are eliminated from the differential, it is important to differentiate the type of dementia manifested by the patient. Dementia that is primarily caused by degenerative CNS processes or sequelae includes vascular dementia, Lewy body dementia (associated with Parkinson's disease), frontotemporal lobe dementia (Pick's disease), AD, and mixed dementia. There are similar/overlapping symptoms and distinct symptoms of each type, which help with the differential diagnosis.

Differentiation of Dementia: Dementia can be classified as vascular, Lewy body/Parkinson's, frontotemporal lobe/Pick's disease, or mixed (Alzheimer's Association, 2021b; APA, 2013).

Vascular Dementia:
- Sequelae from transient ischemic attacks, mini-strokes, cerebrovascular accidents
- No or little cortical shrinkage
- Cognitive, behavioral, and functional losses defined by area of infarct
- Stepwise deterioration over time

Clinical Presentation:
- Abnormal executive functioning
- Impaired psychomotor performance
- Changes in personality and mood
- Disturbances in gait (slow and unsteady)
- Hyper-reflexia, extensor plantar response
- Urinary incontinence
- Hemiparesis, including lower facial weakness
- Hemisensory deficits
- Visual problems (field defect, diplopia)
- Pseudobulbar syndrome (e.g., dysarthria, dysphagia, emotional incontinence)
- Focal deficits

Lewy Body/Parkinson's Dementia:
- Diffuse presence of Lewy body proteins in brain, including cerebral cortex
- Lewy bodies deplete dopamine
- Acetylcholine is depleted, causing disruption of perception, thinking, and behavior
- Resultant parkinsonian symptoms: stiff, shuffling gait, stiffness in arms and legs, tremors, frequent falls, mask-like facies with blank stare, flat affect, stooped posture, drooling, runny nose

Clinical Presentation:
- Parkinsonian signs
- Symptoms may fluctuate as often as moment to moment, hour to hour, or day to day
- Fluctuating cognition, varying degrees of alertness and attention
- Progressive memory loss
- Visual hallucinations
- Rapid eye movement (REM) sleep difficulties

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Frontotemporal Lobe Dementia/Pick's Disease:

- Gradual and progressive changes in behavior—socially inappropriate, disinhibition, easily frustrated, impulsive, compulsive behaviors
- Gradual and progressive language dysfunction—problems with expression of language, incorrect words, naming objects
- Difficulties with reading and writing

Mixed Dementia:

- More than one type of dementia (e.g., combination of AD and vascular dementia)

Treatment: A comprehensive, multidimensional treatment plan for dementia includes biological, psychotherapeutic, social, family, and pharmacological interventions (American Geriatrics Society, 2021).

Biological Interventions: Treat underlying medical disorders with medications, medical or surgical procedures, and ongoing evaluation and management as indicated.

Psychotherapeutic Interventions: Include behavioral management, reminiscence therapy, validation therapy, supportive psychotherapy, sensory integration, simulated presence therapy, reality orientation, skills training, recreation and art therapy, exercise, and aromatherapy.

Social Interventions: Include a functional and safety assessment, environmental modifications, assessment for abuse and neglect, provision of supervision and home health care, cleaning and meal services, assessment for appropriate level of care, financial and estate planning, and legal provisions for power of attorney.

Family Interventions: Include caregiver education, training and support, respite care, and support groups.

Pharmacotherapy: Cholinesterase inhibitors (ChEIs) are the cornerstone of pharmacological therapy, with the aim to enhance or preserve cognitive and behavioral status. Acetylcholine is important for the functioning of brain cells involved in memory, thought, and judgment, and brain levels are significantly decreased in those with AD. ChEIs inhibit breakdown of acetylcholine, which increases levels within the brain; this mechanism of action may improve or delay a decline in memory. ChEIs are effective in approximately 30% of patients and are not curative, preventive, or disease-reversing agents. The choice of ChEI is based on the patient's clinical presentation and comorbid conditions.

The three commonly prescribed ChEIs are donepezil, rivastigmine, and galantamine (NIA, 2018). Clinical and safety issues for ChEIs include medical and psychosocial factors before drug initiation, consideration of when to initiate the medication, and side effects, which are fewer with slower dose titration. Careful monitoring for efficacy and side effects is necessary. Common side effects of ChEIs are nausea, vomiting, dyspepsia, anorexia, diarrhea, insomnia, vivid dreams, fatigue, increased urination, and cramps. Uncommon side effects of ChEIs are syncope, bradycardia, confusion, depression, and agitation. Use cautiously in patients with liver or gastric disease, COPD, bradycardia, and inadequate supervision.

Considerations regarding when to stop ChEIs may include intolerable side effects, new medical contraindications, poor compliance, lack of supervision, and rapid cognitive and/or functional decline. Any benefits of treatment are rapidly lost upon discontinuation. Long-term treatment may continue to offer advantages such as slowing of cognitive decline, continued ability to perform ADLs, fewer noncognitive behavioral symptoms, and decreased caregiver burden (NIA, 2018).

Another medication approved to treat dementia is memantine (Namenda), an *N*-methyl-D-aspartate (NMDA) receptor antagonist. Memantine assists in regulating high levels of glutamate in the brain, typically found in AD. Common side effects include headache and constipation, and an uncommon side effect is confusion. Memantine is excreted through the kidneys, and caution is advised in patients with renal impairment. Combination therapy of memantine with a ChEI is a good strategy, because these medications work differently (NIA, 2018). Usually, medications are started when AD severity is moderate, but they can be initiated earlier depending on individual patient clinical presentations (see Table 20-6).

Management of Neuropsychiatric Symptoms: Includes determination and management of other potential or influencing factors, including (International Psychogeriatrics Association [IPA], 2015):

- Environmental: external (noise) or internal (UTI, constipation)
- Situational: time of day, unknown trigger
- Psychiatric: depression, anxiety, panic, fear
- Medical: medication, pain, metabolic, infection, sensory deficits, cardiopulmonary

Nonpharmacological Approaches Include (IPA, 2015):

- Ensure safety and provision of adequate supervision.
- Analyze behavior(s) for clues to potential causes.
- Use environmental interventions.
- Provide structure—usual routines and predictability are important to allay anxiety.
- Provide pleasurable experiences.
- Do not rely on learning or memory.
- Educate caregivers and other support systems.
- Use of physical or chemical restraint is discouraged and may be used only as a last resort in order to ensure safety to self and others.
- Provide caregiver education for managing agitation (see Table 20-7).

Treatment Strategies and Pharmacotherapy for Neuropsychiatric Symptoms and Psychiatric Comorbidities: It is estimated that up to 90% of patients living with dementia will experience neuropsychiatric symptoms during the course of the disease trajectory (Bessey & Walaszek, 2019). One observational study (Tori et al., 2020) estimated that 65.1% of long-term care residents have psychiatric diagnosis.

One systematic review (Leung et al., 2021) showed the prevalence of depression in persons living with dementia ranges from 10% to 78% with a pooled prevalence of 39%. The prevalence of depression in mild (38%), moderate (41% and severe (37%) dementia is very close (Leung et al., 2021). Depressive symptoms may present as initial manifestations of dementia and may fluctuate over time. There are more reports of decreased ability to concentrate and indecisiveness, and fewer reports of insomnia or hypersomnia, feelings of worthlessness and guilt, or thoughts of suicide and death. Diagnostic criteria for comorbid depression in dementia

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TABLE 20-6 FDA-Approved Medications for Alzheimer's Disease

	DONEPEZIL (ARICEPT) CHEI	RIVASTIGMINE (EXCELON) CHEI	GALANTAMINE (REMINYL) AND EXTENDED RELEASE (RAZADYNE) CHEI	MEMANTINE (NAMENDA) (NMDA RECEPTOR AGONIST)
FDA approval	1996; mild, moderate, severe AD	2000; mild, moderate AD	2001; mild, moderate AD	2004; moderate, severe AD
Benefit	Typically, well tolerated; improves cognitive and behavioral status, caregiver burden, and capacity for ADLs	Improves cognitive, behavioral, and functional impairments; is more selective for central processes and regions critical for cognition and memory	Significantly improves cognitive, behavioral, and functional symptoms of AD	Delays loss of daily functions, cognition, and global performance; decreases agitation
Dosage strengths (mg)	5, 10	1.5, 3, 4.5, 6	4, 8, 12 Extended Release: 8, 16, 24	Titrate to 10 mg bid over 4 wk
Oral solution	1 mg/mL	2 mg/mL	4 mg/mL	
Starting dose	5 mg qd	1.5 mg bid	4 mg bid	
Maximum recommended dose	10 mg qd	6 mg bid	8–10 mg bid Extended Release: 16–24 mg qd	10 mg bid
T1/2 (hours)	73	5	6–8	60–80
Plasma protein binding	96%	40%	18%	
CYP450 substrate of	2D63A4	NA	2D63A4	
CYP450 inhibitor of	NA	NA	NA	NA

TABLE 20-7 Managing Agitation: Caregiver Education

DO	DON'T	PREVENTION	SAFETY
Ask permission to approach/provide assistance.	Raise voice.	Create a calm environment.	Use alarms and/or locks on doors and gates.
Use a calm approach.	Take offense.	Follow a routine with set structure and tasks.	Remove or secure firearms.
Slow down (do not rush patient or self).	Corner or crowd.	Use verbal cueing.	
Use visual and verbal cues.	Rush or pressure.	Redirect attention.	
Provide time and space.	Criticize or condescend.	Use a clock and calendar.	
Limit stimuli.	Argue or attempt reason.	Monitor heat, cold, hunger, sleep, elimination, and comfort.	
	Shame or ignore.		
	Demand, force.		
	Make sudden movements.		
	Restrain.		

include the addition of irritability, social withdrawal, and isolation with frequent, concurrent apathy and anxiety.

The Cornell Scale for Depression in Dementia (CSDD) is a validated screening tool designed for use in the assessment of those who can communicate basic needs (Goodarzi et al., 2017). Other diagnostic instruments include the PHQ-9 and the Geriatric Depression Scale (GDS) (see Depression). First-line treatment strategies for comorbid depression include supportive psychotherapy and a selective serotonin reuptake inhibitor (SSRI) such as citalopram (Celexa), fluoxetine (Prozac), or sertraline (Zoloft). If interventions are ineffective and/or suffering is severe and persistent, patients may be referred to psychiatry for consideration of electroconvulsive therapy (ECT), a well-established and effective treatment option.

The prevalence of anxiety in persons living with dementia varies from 27.7% to 63.4% (Goodarzi et al., 2017). In one meta-analysis anxiety occurs in 5% ($N_{studies}$ = 9) of patients with AD and 14% ($N_{studies}$ = 4) in vascular dementia (Kuring

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et al., 2018). One meta-analysis (Leung et al., 2021) reports the prevalence of anxiety is 38% in mild dementia, 41% in moderate dementia and 37% in severe dementia. Manifestations of anxiety in dementia include restlessness, irritability, muscle tension, and fear. Respiratory symptoms, such as hyperventilation or difficulty catching one's breath, correlate with excessive anxiety and worry. Diagnostic instruments to assist in diagnosing anxiety in those with dementia include the Worry Scale and the Rating Anxiety in Dementia Scale. First-line treatment options include psychosocial interventions and an SSRI or buspirone (Buspar). Use of benzodiazepines (e.g., lorazepam) is discouraged due to sedating side effects and increased risk of falls.

Psychosis in AD is frequently present with other cognitive symptoms (global deficits, anosognosia), affective symptoms (depression, elevated mood), and behavioral symptoms (agitation and overt aggression). Approximately 18% of dementia patients present with delusions that typically manifest as persecutory and misidentification delusions (IOM, 2012). Hallucinations are present in approximately 14% of dementia patients, with the occurrence of visual hallucinations more than twice that of auditory hallucinations (IOM, 2012). Capgras syndrome (belief that a close relative or friend has been replaced by an impostor) and "phantom boarder syndrome" (belief that strangers are living in the home) may be associated with agnosia. Instruments to assist in diagnosing psychosis in dementia include the Behavioral Pathology in Alzheimer's Disease (BEHAVE-AD) Scale and the Dementia Psychosis Scale. Behavioral and environmental interventions are first-line treatment strategies.

Before initiating pharmacological treatment with antipsychotic medications, the clinician should carefully analyze the risks and benefits of the use of such medications for each patient. Based on studies demonstrating increased risk for stroke and mortality in older adults, the U.S. Food and Drug Administration (FDA) has issued multiple black box warnings for use of antipsychotic medications in this population (Maust et. al., 2015). Judicial and cautious use of antipsychotic medication should be reserved for hallucinations, delusions, aggression, agitation, hostility, and uncooperative behavior that significantly interferes with care. Antipsychotics effective at low doses include aripiprazole (Abilify), haloperidol (Haldol), olanzapine (Zyprexa), quetiapine (Seroquel), risperidone (Risperdal), and ziprasidone (Geodon). Research evidence, FDA warnings, and clinical guidelines recommend use of antipsychotic medication only when (1) behavioral symptoms are due to mania or psychosis, (2) symptoms present a danger to the patient or others, or (3) the patient is experiencing inconsolable or persistent distress, a significant decline in function, or substantial difficulty receiving needed care (Reus et al., 2016).

Antipsychotic medication should not be used for sedation or restraint and should be used at the minimum dosage for the minimum amount of time possible. Careful monitoring for efficacy and side effects is required (Reus et al., 2016).

Approximately 27% of dementia patients exhibit agitation and/or aggression. Prevalence increases as dementia progresses (13% in mild dementia, 24% in moderate dementia, and 29% in severe dementia). *Agitation* is defined as intermittent psychomotor hyperactivity, disinhibition, screaming, physical aggression, and combativeness. There are many potential causes for agitation, including the underlying pathophysiology of dementia (e.g., serotonergic deficiency) and an inability to communicate needs (e.g., hunger) or physical discomfort (e.g., pain, constipation). Psychosocial stressors that may induce agitation include changes in one's living situation, caregiver(s), or environment. Medical evaluation is needed to rule out occult medical problems, medication side effects, and delirium. Instruments that may assist in accurate diagnosis are the BEHAVE-AD Scale, and the Cohen-Mansfield Agitation Inventory (IPA, 2015).

Interventions include evaluation and management of antecedents and/or causes of agitation, behavioral approaches (e.g., distraction, pleasurable activities), and calming activities or gentle sensory stimulation (e.g., music, art, routine/known physical activities such as folding towels). Pharmacotherapy options might include off-label use of mood stabilizers, such as carbamazepine or Depakote, to effectively manage agitation. Antipsychotic medications are not considered to be first-line treatment, because they are less effective than first believed; however, they should be considered when behaviors present a safety risk to self or others (Reus et al., 2016). For sleep problems, low-dose doxepin may be effective and is FDA approved for insomnia.

Follow-Up: After the presumptive diagnosis of AD is made, the patient should be followed closely with pharmacotherapy initiation and following any adjustments for efficacy and side effects. Thereafter, follow-up visits every 3 to 6 months to assess physical, mental, and emotional status should be individualized to the patient. Reevaluation of cognitive function with the same scale used at diagnosis/baseline is useful to track cognitive stability or decline. The patient's functional status, ability to perform ADLs and instrumental ADLs, behavior, sleep, appetite, weight, elimination, communication, and signs of anxiety or depression should routinely be evaluated at follow-up visits. The physical examination is individualized to the patient and any episodic or chronic illnesses should be well managed to maintain optimum quality of life and avoid complications or worsening of cognitive function.

The ability to drive competently and safely is a frequent concern of family members, and clinicians are often asked to assist in making the difficult decision to revoke the patient's driver's license. Dementia exacerbates age-related changes in driving ability and poses a substantial risk to safe driving. The American Medical Association National Highway Safety Administration guidelines state that a dementia diagnosis is not sufficient to withdraw driving privileges and recommend basing decisions on an individual's driving ability. Determining whether a patient with mild dementia is fit to drive presents a challenge to the clinician and begins with discussion of driving history, safety, and cessation with the patient. Data from physical and cognitive assessments, family and caregiver reports, and, when available, on-road testing will assist in the decision-making process. For patients deemed to be safe, discuss the necessity of future driving cessation and suggest driving training and self-limitation. A history of significant traffic problems, inability to find the way home, inattention, and psychosis are indications of progressive cognitive decline and driving skill deterioration. When driving safety is uncertain and the patient wishes to continue driving, a referral for on-road driving evaluation is needed. Those with mild dementia who pass an on-road driving test should be reevaluated and retested at least every 6 months. If driving safety is uncertain and the patient decides to stop driving, or if the patient is deemed unsafe to drive, the

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Department of Motor Vehicles and the patient should be notified by letter, and a copy of the letter should be placed in the patient's medical record. International consensus groups agree that a diagnosis of moderate-to-severe dementia precludes driving, and the driver's license should be revoked. Driving is essential to autonomy, and the vast majority of older adults rely on driving as their primary mode of transportation. Although the clinician's recommendation for driving cessation is distressing to patients and families, it is critical for patient and public safety (Pomidor, 2019).

Caregiver burden regarding patient care, household and financial responsibilities, and ability to provide adequate supervision and care at home should be determined at each follow-up visit. When the patient loses bowel and/or bladder control, their behavior becomes too difficult to manage, or the patient's or caregiver's safety is compromised, institutional care should be discussed.

Sequelae: Complications from severe dementia include immobility, swallowing disorders, malnutrition, and significantly increased risk of developing pneumonia, which is the most commonly identified cause of death among the elderly with AD and other dementias. Although there is a blurred distinction between death *with dementia* and death *from dementia*, since 2000 the AD mortality rate has been on the rise. AD is the sixth leading cause of death in the United States and the fifth leading cause of death among those 65 years of age and older. Death due to AD increased 16% with the COVID-19 pandemic (Alzheimer's Association, 2021b).

Prevention/Prophylaxis: A comprehensive evidence review commissioned by the Agency for Healthcare Research and Quality (AHRQ) included 25 systematic reviews and 250 primary research studies, both observational and randomized clinical trials (RCTs) on preventive interventions for AD. The primary conclusion was that there was a dearth of evidence for any strong recommendations for preventive interventions for AD (Williams et al., 2010). Physical activity and cognitive engagement were factors that demonstrated fairly constant association with prevention of cognitive decline and AD; diabetes, depression, smoking, and APOE e4 were associated with increased risk of cognitive impairment and AD. The National Academies of Sciences, Engineering, and Medicine (2017) conducted a follow-up study using RCTs, the gold standard for evidence. In spite of using RCTs, there remains inconclusive evidence for interventions including cognitive training, blood pressure management and increasing physical exercise to delay or prevent cognitive decline of dementia. Instead, multimodal interventions are thought to hold promise for preventing cognitive impairment and dementia.

Referral: Neurology, geriatric psychiatrist, geriatric nurse practitioner, psychiatric mental health nurse practitioner or clinical nurse specialist, psychology, support groups for patients and caregivers.

Education: The impact of AD on caregivers expands as the course of illness progresses. Caregivers, family, and friends of those with AD experience new or changing responsibilities such as shopping, meal preparation, cleaning, financial management, provision of ADLs, and managing behavioral issues. Caregivers also experience financial burden, physical and emotional stress, fatigue, and depression. It is estimated that 34% of caregivers are 65 years or older (Alzheimer's Association, 2015), and 23% are within the "sandwich" generation, providing care for family members (Alzheimer's Association, 2021b).

Patient and caregiver education and support needs include:

- Disease process, course of illness, staging
- Anticipatory guidance, life planning, advance directives, power of attorney (POA)

Preservation of the following:

- Safety at all times
- Dignity, respect, and self-esteem
- Independence and autonomy for as long as possible/practical/safe
- Daily schedules and routines
- Least restrictive environment
- Cognitive, behavioral, and pharmacological therapies

Clinical Recommendation	Evidence Rating	References
Amyloid and fluorodeoxyglucose positron emission tomography may increase accuracy when differentiating between AD and non-AD when added to a clinical evaluation.	C	Fink et al., 2020
Laboratory evaluation should include CBC, TSH, serum calcium and electrolytes, vitamin B_{12}, and fasting glucose levels to examine for treatable causes of cognitive decline. Consider serum folate, tests for syphilis, and HIV serology if patient is at risk for those conditions.	C	American Geriatrics Society, 2021
There is currently no adequate, robust evidence to recommend the use of any nonpharmacological intervention to reduce wandering in dementia.	C	MacAndrew et al., 2018
The use of atypical antipsychotics for behavioral and psychological symptoms of dementia is associated with increased mortality.	A	Maust et al., 2015 Reus et al., 2016
Memantine has a small, beneficial effect on moderate-to-severe AD and no better than placebo in mild AD	C	McShane et al., 2019
ChEIs, donepezil, galantamine, and rivastigmine produced small improvements in cognition and function compared with placebo for moderate to severe AD.	C	Fink et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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DEPRESSION

Signal Symptoms: Depression in older adults may be manifested by pervasive and sustained depressed mood, discouragement, lack of pleasure in usual activities, guilt, loss of motivation, low energy, and sleep and/or appetite disturbances (American Psychiatric Association [APA], 2013).

Description: Transient symptoms of depression are expected and healthy responses to life stressors and disappointments. Pathological depression manifests when a patient's coping skills are inadequate for adaptation to stressful life events or loss. Depression in older adults can be life threatening and associated with increased risk of suicide (Van Orden & Deming, 2018). Depression is characterized by a pervasive feeling of sadness or a lack of interest or pleasure in previously enjoyed or usual activities (APA, 2013). Feelings of guilt, low self-esteem, sleep and appetite disturbances, psychomotor changes, low energy, and decreased concentration are common symptoms (APA, 2013). Late-life depression involves new onset of depression occurring after age 60. Depression may be categorized as a single episode or recurrent, and further qualified as mild, moderate, or severe, with or without features such as melancholy, mood congruence, catatonia, peripartum onset, or with a seasonal pattern (APA, 2013).

Etiology: Although depression is common among older adults, depression is not a normal result of the aging process. Late-life depression involves combinations of physiological, environmental, and psychosocial risk factors (Van Damme et al., 2018).

Psychosocial factors contributing to late-life depression can include unemployment, loss of a spouse or partner, pain, social isolation, poverty, and limited access to mental health care (Alexopoulos, 2019; Van Damme et al., 2018). Difficulty accomplishing developmental tasks associated with life stages may contribute to and/or be a consequence of depression. Depression in older adults could be triggered by a single major life event or a combination of events and stressors. Loss of any kind may contribute to depression, and in the older adult, loss may include loss of a loved one or loss of functional abilities, relationships, mobility, independence, one's home, and financial security, along with social isolation and deterioration of physical health.

Biological risk factors are theorized to include genetic vulnerabilities, frailty, nutritional deficiencies, neurodegenerative disease, neuroplasticity problems, dysregulation of hypothalamic-pituitary-adrenocortical axis, deficiencies or dysregulation of monoamines (particularly serotonin, norepinephrine, and dopamine), stress, and vascular disease (Liu et al., 2017; Van Damme et al., 2018). Researchers discovered that genetic components that impact hippocampal plasticity and stress reactivity may be related to late-life depression (Tsang et al., 2017).

Occurrence: Depression is one of the most common psychiatric illnesses experienced by older adults, but prevalence data are not certain due to undertreatment, misdiagnosis, or underdiagnosis of depression in this population. Older adults may experience comorbidities and somatic symptoms that could prevent the diagnosis of depression in this population. Older adults may encounter help-seeking barriers related to stigma, access to care, self-motivation, and ageism (Polacsek et al., 2019). Researchers found that cognitive symptoms are common among older adults, but these problems are not frequently recognized or treated, and depression could have a key role in misdiagnosis of dementia (Voros et al., 2020). Higher depression prevalence is associated with impaired physical functioning, lack of a spouse or partner, and dementia (Sjöberg et al., 2017). Late-life depression in long-term care may be more prevalent than late-life depression in community settings, but prevalence data vary greatly, and depression is believed to be underrecognized among older adults in both settings (Simning & Simons, 2017). Older adults in long-term care are at particularly high risk of depression, especially when experiencing pain, sleep disturbance, lack of social support, and problems with person-environment fit (Chau et al., 2021). Researchers observed that high rates of depressive symptoms may occur in the last year of life, especially during the last 4 months (Kozlov et al., 2020).

Age: Depression occurring initially after age 60 is classified as late-life depression. In the United States, older adults aged 65 years and older were more likely than adults in other age-groups to experience mild depression symptoms in 2019 (Villarroel & Terlizzi, 2020).

Ethnicity: According to the National Institute of Mental Health (2019), prevalence of major depressive disorders (MDD) was highest among adults reporting two or more races. Researchers found that non-Hispanic White and non-Hispanic Black adults were most likely to experience mild depression symptoms when compared to Hispanic and non-Hispanic Asian adults (Villarroel & Terlizzi (2020). Non-Hispanic Asian adults were least likely to experience mild to severe depression symptoms when compared with Hispanic, non-Hispanic White, and non-Hispanic Black adults (Villarroel & Terlizzi, 2020). When considering older adults as a population, the chance of screening positively for depression was higher among study participants self-reporting as Mexican, Puerto Rican, Cuban, another Hispanic/Latino, multiple Hispanic/Latino ethnicities, Black/African American, Asian Indian, Filipino, Native Hawaiian/Pacific Islander, and two or more races, when compared with non-Hispanic White adults (Hooker et al., 2019).

Contributing Factors:

Genetics: Gene studies revealed that *APOE, BDNF*, and *SLC6A4* are associated with late-life depression (Tsang et al., 2017).

Psychosocial: Researchers identified unemployment, loss of spouse, pain, social isolation or loneliness, poverty, and limited access to mental health care as psychosocial risk factors for late-life depression (Alexopoulos, 2019; Van Damme et al., 2018). Persistent sleep disturbances in older adults were found to increase risk of depression development, recurrence, and worsening (Bao et al., 2017).

Biological/Physical Illnesses: Researchers discovered that frailty and depression had a reciprocal relationship, with each increasing prevalence and incidence of the other (Soysal et al., 2017). Multiple comorbidities, multiple medications,

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poor nutritional status, vitamin deficiencies (vitamin D, vitamin B_{12}, and folate), neurodegenerative disease, and cardiovascular disease are potential biological risk factors (Van Damme et al., 2018).

Signs and Symptoms: Depression among older adults may be manifested by depressed mood, anhedonia, apathy, helplessness, hopelessness, worthlessness, and loneliness as affective symptoms. Potential cognitive symptoms include ambivalence, uncertainty, inability to concentrate, confusion, poor memory, slowed speech, lack of motivation, a pessimistic outlook, negative thoughts, self-criticism, and poor self-esteem. Assess for perceptual disturbances, such as hallucinations, illusions, and delusions, to determine whether psychotic features are present.

Physiological changes may include sleep, appetite, and energy disturbances, weight change, constipation, pain, headache, decreased libido, multiple unexplained somatic complaints, or refusal to eat or drink (Kok & Reynolds, 2017). Assess for behavioral symptoms, such as psychomotor retardation or agitation, irritability, poor personal hygiene, tearfulness, and social withdrawal. It is vitally important to question the patient about suicidal ideation and/or plans, as well as assess for access to lethal weapons. Some patients experience excessive worry, preoccupation, and generalized anxiety. Major depression involving anxiety and somatic symptoms could increase disability (Morin et al., 2020). Some older adults may not associate behavioral or physiological symptoms with depression, so it is important for clinicians to suspect depression as an underlying cause (Kok & Reynolds, 2017).

The *DSM*-5 (APA, 2013) diagnostic criteria for MDD include sustained, disruptive, and pervasive depressed mood or loss of interest or pleasure. With the exception of suicidal ideation and weight change, five or more of the following symptoms must be present for most of the day, on most days, over a 2-week period:

- Depressed mood as reported in subjective report or as observed by others
- Obsessive rumination or worry
- Change in appetite and significant change in weight
- Change in sleep pattern: insomnia (difficulty falling asleep or staying asleep, waking earlier than necessary, inability to fall back asleep), hypersomnia, frequent napping
- Psychomotor agitation or retardation (including as observed by others)
- Fatigue or loss of energy
- Feelings of hopelessness
- Feelings of worthlessness, excessive guilt
- Diminished concentration, indecisiveness
- Recurrent thoughts of death, suicidal ideation or gestures, suicide attempt, suicide plan

Distinct clinical manifestations in older adults include:

- Report of lack of emotions (versus depressed mood)
- Excessive concern with bodily functions
- Seeking reassurance and support
- Isolative, withdrawn behavior
- Change in previous level of function, decline in activities of daily living (ADLs)
- Feeling overwhelmed, easily frustrated, excessive crying
- Irritability, fearfulness, agitation, anxiety
- Transient, recurring symptoms; diurnal fluctuations or pattern
- Minimizing expressed death wishes or passive suicidal behavior

If possible, at the first encounter, the patient should be interviewed individually. Goals of the interaction should include establishing a therapeutic, trusting alliance, which can then enhance the discussion of potentially sensitive topics, such as abuse and suicidal thoughts. The subjective history could begin with open-ended questions, which could then be followed by specific and focused questions. The history should include present illness, past psychiatric history, family history including mental health, medical history, prescription and over-the-counter (OTC) medication use, social history (education, work history, important relationships, sexual activity, spirituality, and current living arrangements), and functional assessment. Assessment should include a comprehensive physical examination to look for secondary causes of depressive symptoms, a full mental health assessment, and a mental status examination if confusion or cognitive impairment are present.

Diagnostic Tests: Diagnostic tests to assess for underlying or undiagnosed medical causes of depressive symptoms should be ordered. Standard blood work includes complete blood count with differential, comprehensive metabolic panel, lipid panel, thyroid function studies (thyroid-stimulating hormone [TSH] with reflex T_4), and serum vitamin B_{12} and vitamin D levels. Clinical evaluation instruments and scales are useful in assessing symptoms and severity of depression, cognitive impairment, and disability. Such instruments provide objective measures of signs and symptoms of illness and help in establishing baseline information with which future assessments can be compared in evaluating efficacy of treatment and interventions. Instruments also provide guides to dialogue, and they allow the practitioner to further discuss key concerns with the patient. Researchers found that the Geriatric Depression Scale, especially shorter versions, had high sensitivity and specificity for detecting depression in older adults (Krishnamoorthy et al., 2020),

Depression Scales:

- Geriatric Depression Scale (GDS, long and short forms)
- Beck Depression Inventory (BDI)
- Patient Health Questionnaire (PHQ–9)
- Hamilton Depression Scale (HAM-D)
- Two-Question Screen

Overall Cognitive Functioning:

- Montreal Cognitive Assessment (MoCA)

Differential Diagnosis:

- Mood disorder due to general medical condition such as thyroid disease, diabetes, cancer, epilepsy, stroke, multiple sclerosis, Parkinson's disease, cardiac disease, acute illness, or injury
- Substance-induced or medication-induced mood disorder related to alcohol use, illicit drug use, cardiac medications, steroids, sedatives, or other medications or substances
- Dysthymic disorder that manifests symptoms of mild depression and may have an early or late onset, is chronic in nature, and lasts more than 2 years

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- Bipolar affective disorder, in which bipolar depression may be misdiagnosed as unipolar depression
- Delirium
- Dementia
- Life circumstances, grief, bereavement, loss, financial challenges
- Somatization disorder
- Sleep disorder, obstructive sleep apnea

Treatment: Goals of treating late-life depression include preventing or reducing relapse or recurrence, improving quality of life and functioning, improving medical health, and reducing mortality. Compassion, therapeutic communication approaches, active listening, and respect can help to improve the therapeutic relationship during treatment of depression. It is important to evaluate the present medication regimen and remove or change any medications that may contribute to depression symptoms. Treat any medical condition that may have predisposed the patient to depression. Provide education or treatment for sleep disturbances and nutritional or vitamin deficiencies that may contribute to depression symptoms. A stepped-care approach based upon patient preference, severity of late-life depression, and functional impairment can improve treatment outcomes, especially in rural areas that may lack access to mental health care (Meuldijk & Wuthrich, 2019; Van Damme et al., 2018). Researchers found that depression severity, comorbid anxiety, executive dysfunction, episode duration, early improvement, physical illnesses, and age were predictors of treatment outcomes for depression in older adults (Tunvirachaisakul et al., 2018). In addition to treatment with pharmacotherapy, evidence-based psychotherapy may also be effective for late-life depression (Kok & Reynolds, 2017).

TABLE 20-8 First-Line Treatment with Antidepressant Medications

TYPE OF ANTIDEPRESSANT	MEDICATION—GENERIC NAME (TRADE NAME)
Selective serotonin reuptake inhibitor	citalopram (Celexa)
	escitalopram (Lexapro)
	fluoxetine (Prozac, Sarafem)
	fluvoxamine (Luvox)
	paroxetine (Paxil, Pexeva, Brisdelle)
	sertraline (Zoloft)
Serotonin and norepinephrine reuptake inhibitor	desvenlafaxine (Pristiq, Khedezla)
	duloxetine (Cymbalta)
	milnacipran (Savella)
	levomilnacipran (Fetzima)
	venlaxafine (Effexor, Effexor XR)
Norepinephrine-dopamine reuptake inhibitors	bupropion (Wellbutrin)
Serotonin modulator	nefazodone (Serzone)
	trazodone (Desyrel, Oleptro)
Norepinephrine-serotonin modulator	mirtazapine (Remeron)

Pharmacotherapy: The strategy for pharmacological management of late-life depression is to achieve complete and sustained relief or remission of depressive symptoms with the least amount of distressing adverse effects. If utilizing pharmacological interventions for older adults with depression, it is important to initiate pharmacotherapy with a "start low and go slow" approach to avoid risks of adverse effects in this population. The most widely prescribed antidepressants and with greatest evidence for achieving remission are selective serotonin reuptake inhibitors (SSRIs) (Gutsmiedl et al., 2020). Other types of antidepressants that are recommended treatment for late-life depression include serotonin-norepinephrine reuptake inhibitors (SNRIs), serotonin partial agonist/reuptake inhibitors, norepinephrine-dopamine reuptake inhibitors, selective norepinephrine reuptake inhibitors, and alpha-2 antagonists (see Table 20-8). SNRIs can be helpful when treating both depression and peripheral neuropathic pain in older adults (Van Damme et al., 2018). Mirtazapine can be effective for treating depression, insomnia, and appetite loss (Van Damme et al., 2018).

Although tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) are available, they are no longer considered first-line recommendations due to increased risk of adverse effects compared to SSRIs. TCAs should be used with caution in older adults due to risk of anticholinergic effects, confusion, arrhythmias (Beyer & Johnson, 2018). Frequent adverse effects for older adults with depression who are taking SSRIs include gastrointestinal disturbances, sexual dysfunction, insomnia, and hyponatremia (Kok & Reynolds, 2017; Van Damme et al., 2018). QT interval prolongation may occur with doses of citalopram above 40 mg (U.S. Food and Drug Administration [FDA], 2017; Van Damme et al., 2018). The SNRIs, including venlafaxine and duloxetine, have been shown to be effective in older adults with depression, but blood pressure may be increased when taking SNRIs (Van Damme et al., 2018). Considerations when choosing an antidepressant for treatment of late-life depression include short- and long-term adverse effects, least-desirable adverse effects, safety, comorbid conditions, and cognition. Additional factors in antidepressant selection include the patient's primary symptoms, symptom clusters, current medications, history of medications used, efficacy and adverse effect tolerance, and family history of effective medication use.

It is important to monitor and evaluate therapeutic response to antidepressant therapy, as well as observe for side effects, tolerance, and unremitting symptoms of depression. Researchers estimate that approximately half of older adults with MDD taking antidepressants for 4- to 12-week trials experience improvement in depression symptoms (Gutsmiedl et al., 2020). For older adults, 2 to 3 months may be required to achieve the full benefit of antidepressant treatment (Avasthi & Grover, 2018). For patients who do not respond adequately to monotherapy after 4 to 8 weeks, consider reevaluating the diagnosis, evaluating treatment adherence, and assessing for other medical or psychosocial factors that could impact pharmacotherapy treatment (Avasthi & Grover, 2018). If monotherapy is not effective, consider maximizing the antidepressant, switching to a different antidepressant (of the same or different class), or augmenting an antidepressant with another medication, psychotherapy, or electroconvulsive therapy (ECT) (Avasthi & Grover, 2018).

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Second generation antipsychotics, such as aripiprazole, quetiapine, and olanzapine, can be effective in low doses and for short-term treatment when augmented with antidepressants for treatment-resistant depression (Cakir & Senkal, 2016). However, second generation antipsychotics should be used with caution in older adults because there is risk of cerebrovascular events and other adverse effects with these medications (Cakir & Senkal, 2016).

Partnering with the patient through inquiry into prior antidepressant use, shared decision making, and education regarding expected therapeutic response time could positively affect patient adherence to the therapeutic regimen. Discussion regarding common and potentially bothersome side effects, as well as the likelihood that they will wane over time, can promote medication adherence. Educate patients about serious or potentially dangerous effects of antidepressant medication and instruct them when it is necessary to notify their prescriber (see Table 20-9). As patients begin to feel better, advise them to continue taking the medication, and explain the risk of stopping medication abruptly or too early. Patients should be educated about the dangers of combining herbal remedies such as St. John's wort (hypericum) with SSRIs, because this combination raises the risk of serotonin syndrome.

Length of Pharmacotherapy Treatment and Follow-Up: When initiating or changing the dose of antidepressant medication, it is critical to monitor the patient closely for efficacy and adverse effects. Observe for worsening of depression, suicidal thoughts or actions, unusual changes in behavior, agitation, and irritability. Educate patients, families, and caregivers to pay close attention to sudden changes in mood, behaviors, thoughts, or feelings, as well as suicidal thoughts, and to report these concerns immediately to the provider. As depression symptoms begin to decrease, patients may become more energized and may be able to follow through on prevailing suicidal ideation and plans. Factors that increase risk for suicide in late life include cognitive control deficits, current depression, and impulsivity (Szanto et al., 2020). Patients should be screened for suicidal thoughts during pharmacological initiation, at dosing phases, and at every subsequent follow-up visit.

Length of antidepressant treatment varies depending on whether it is a first or recurrent episode. With each recurrence, there is an increased risk of future recurrence if medication is discontinued, and as a result, antidepressant therapy must be maintained for longer periods of time. The *acute phase* of treatment lasts up to 3 months after the start of medication, with the goal to achieve remission. Close follow-up is critical and highly individualized; however, there should be patient contact within the first month and additional contact every four weeks or sooner with dosage adjustments, switching, combination, or augmentation. Researchers concluded that in older adults with major depression and dementia, adherence to antidepressant treatment during the acute phase was associated with decreased all-cause hospitalization risk (Bhattacharjee et al., 2020). The *continuation phase* of treatment begins once remission is achieved, and medication should be continued for at least another 4 to 12 months. Patients in the continuation phase of treatment should be seen every 6 months or earlier. The *maintenance phase* of antidepressant therapy is specifically for patients with two or more lifetime episodes of major depressive disorder. These patients should be maintained on medication at the same dosage for another 15 months to 5 years. Patients in the maintenance phase of treatment should be seen every 6 to 12 months or earlier.

TABLE 20-9 Common Side Effects and Potentially Serious/Dangerous Side Effects of Antidepressants

SSRIs, NDRIs, SNRIs: common side effects	Mild nausea, loose bowel movements, anxiety, headache, insomnia, increased sweating, weight gain/loss, sexual dysfunction, vivid dreams, rash, SIADH
Serotonin modulators: side effects	Sedation, weight gain, mild anticholinergic symptoms; priapism, a side effect of trazodone, is a medical emergency
Serotonin syndrome (excessive serotonin)	Agitation, restlessness, diarrhea, diaphoresis, muscle twitching or rigidity, confusion, hyperpyrexia, seizures, tachycardia, death
SSRI discontinuation syndrome	Dizziness, headache, paresthesia, nausea, diarrhea, insomnia, and irritability; seen with missed doses and abrupt discontinuation of antidepressants with a short half-life

Abbreviations: NDRIs = norepinephrine-dopamine reuptake inhibitors; SSRIs = selective serotonin reuptake inhibitors; SNRIs= serotonin–norepinephrine reuptake inhibitors. SIADH = syndrome of inappropriate antidiuretic hormone secretion

Psychotherapy and Nonpharmacological Interventions: Research studies demonstrated that psychotherapeutic approaches, including cognitive behavioral therapy, problem-solving therapy, interpersonal psychotherapy, and life review therapy, could decrease depression symptoms in older adults (Kok & Reynolds, 2017; Renn & Areán, 2017; Van Damme et al., 2018). For patients with mild to moderate depression, psychotherapy may be sufficient as a treatment strategy, especially if the patient prefers to participate in psychotherapy instead of pharmacotherapy, or experiences nonadherence or adverse effects with medications (Renn & Areán, 2017). Combined psychotherapy and pharmacotherapy for older adults with depression may be more effective than use of monotherapy (Avasthi & Grover, 2018).

Older adults with severe depression or depression with psychotic features may benefit from ECT (Van Dierman et al., 2018). Most older adults with depression can tolerate treatment with ECT, but cognitive adverse effects are possible in this population (Obbels et al., 2018).

Activities that promote physical and mental wellness, including exercise and mindfulness-based activities, can reduce depression symptoms for some older adults. Mind-body, resistance, and aerobic exercises, especially when self-selected by patients according to preference, can improve outcomes for older adults participating in pharmacological treatment for depression (Miller et al., 2020). Although evidence is limited, mindfulness-based stress reduction has been found to reduce depression symptoms in older adults immediately after the intervention (Ho Li & Bressington, 2019). Some older adults may prefer or benefit from spiritual or religious support.

Integrated Care: Integrating mental health care into primary care has been found to increase quality of treatment for

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depression in older adults (Bruce & Sirey, 2018). Effective integrated care interventions include multidisciplinary care coordination, monitoring and screening for depression, treatment teams that include primary care and mental healthcare providers, and the use of guidelines for depression treatment in older adults (Bruce & Sirey, 2018).

Follow-Up:

- Use diagnostic scales/instruments (symptom and severity tools) to objectively assess progress compared to baseline evaluation.
- Assess for therapy and medication adherence, response, and adverse effects.
- Assess for suicidal ideation.
- Titrate medication dose for total remission.
- If medication trial is discontinued, then taper over 2 to 4 weeks.
- Monitor for early signs of recurrence.

Sequelae: Depression that is not identified and treated appropriately in older adults can be life threatening and debilitating. Late-life depression can increase risk of mortality in older adults, especially with older age, physical disability, and impairment in ability to perform activities of daily living (Cai et al., 2020). Complications of depression include impaired interpersonal relationships, interpersonal problems, increased medical comorbidity and medical risk factors over time, worsening of cognitive impairment, self-neglect, decreased mobility, increased disability, and increased mortality from suicide and interactions with medical conditions, such as cardiovascular and cerebrovascular disease. Depression can diminish health and overall life span.

Prevention/Prophylaxis: Minimizing risk factors can help to prevent incidence or exacerbation of late-life depression symptoms. Modifiable risk factors include nutritional deficiencies and cardiovascular disease (Van Damme et al., 2018). Interventions for these modifiable risk factors may include improvements in diet, exercise, sleep hygiene, nutritional supplementation, and smoking cessation (Van Damme et al., 2018). Stress reduction, strengthening support systems, and treatment of underlying medical conditions may also minimize depression risk in older adults.

Referral: Patients who should be referred to psychiatric providers include those experiencing prominent suicidal/self-harm thoughts or previous suicide attempts, a questionable diagnosis, suspected bipolar disorder or comorbid psychiatric conditions, persistent residual symptoms, and partial or no response to monotherapy, combination, augmentation, or adjunctive medications. For counseling, consider referring the patient to a psychiatric mental health nurse practitioner, a psychiatric clinical nurse specialist, licensed clinical psychologist, or other licensed therapist, and provide resources for support groups and appropriate service professionals and agencies.

Education: Patient and family education should include information about the disease process, risk factors, heritability, risk of relapse or recurrence, suicide risk, treatment strategies and recommendations, psychotropic medication use, side effects, length of time for medication efficacy, and use of herbs, vitamins, and supplements.

Clinical Recommendation	Evidence Rating	References
Effective screening tools for depression include evidence-based instruments, such as Geriatric Depression Scale and Two-Question Screen.	B	Krishnamoorthy et al., 2020 Tsoi et al., 2017
First-line treatments for depression in older adults include SSRIs and SNRIs.	A	Beyer & Johnson, 2018 Gutsmiedl et al., 2020
Second generation antipsychotics, such as aripiprazole and quetiapine, can be effective in low doses and for short-term treatment when augmented with antidepressants for treatment-resistant depression.	B	Cakir & Senkal, 2016
Psychotherapeutic approaches, including cognitive behavioral therapy, problem-solving therapy, interpersonal psychotherapy, and life review therapy, can decrease depression symptoms in older adults.	A	Kok & Reynolds, 2017 Renn & Areán, 2017 Van Damme et al., 2018
Older adults with severe depression or depression with psychotic features may benefit from electroconvulsive therapy.	B	Van Dierman et al., 2018

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DIOGENES SYNDROME

Signal Symptoms: Social withdrawal, hoarding, neglected self-care and refusal of help

Description: Named after Greek philosopher Diogenes, known for his cynicism and contempt for social organization and his lack of shame, this complex syndrome occurs primarily in older adults. It is a constellation of symptoms that includes poor insight or understanding of self-hygiene and public health and safety; distrust of society and strangers, paranoia,

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or general suspiciousness; aloofness or detachment; extreme social anxiety; excessive hoarding; unsafe living conditions; poor nutrition; unwillingness to accept outside help; fear or distrust of medical professionals; hostility and aggression toward others; distorted concept of reality; and dermatitis passivate (Cipriani et al., 2012; Sacchi et al., 2021).

Occurrence: Fifteen percent of the population; 36% of those with Diogenes syndrome have frontotemporal dementia (Irvine & Nwachukwu, 2014;; Sacchi et al., 2021).

Age: Older than 60 years; average 79 years of age

Ethnicity: No significant difference.

Contributing Factors: Living alone, death of a spouse. Often initially confused for abuse or neglect, dementia, hoarding disorder, or severe depression (Sacchi et al., 2021).

Etiology: The pathogenesis is hypothetical. It does contain elements of acquired hoarding disorder. There does appear to be a higher incidence in those with frontotemporal dementia. This is believed to be a result of vascular lesions in the medial prefrontal or bilateral orbitofrontal cortex. Left lateral temporal lobe atrophy in frontotemporal dementia and obsessive-compulsive disorder may impair categorization of objects as unique and predispose individual to hoarding behavior (Sacchi et al., 2021).

Signs and Symptoms: Social withdrawal, depression, hoarding, self-neglect, and exacerbation of underlying medical conditions due to lack of care. Skin lesions and dermatitis passivate due to lack of washing, which forms a horny crust on the torso and extremities (Biswas et al., 2013; Cipriani et al., 2012; Irvine & Nwachukwu, 2014; Sacchi et al., 2021).

Diagnostic Tests: General panel of complete blood count (CBC), comprehensive metabolic panel (CMP) to rule out underlying medical problems. No specific tests for this syndrome because it primarily involves psychological conditions.

Differential Diagnosis:

- Dementia
- Paranoia
- Mood disorder
- Schizophrenia
- Hoarding disorder

Treatment: Medications for depression and hoarding have been found to be helpful. Paroxetine in doses of 20 to 40 mg has shown results in decreasing obsessive-compulsive disorder (OCD) symptoms. Recent studies have shown high-dose sertraline (100 to 150 mg) has decreased mood and behavioral symptoms. If psychotic symptoms are present, risperidone and quetiapine have shown positive results. Counseling and care management are recommended to deal with hoarding behavior. Skin lesions need to be manually removed. The patient may need to be treated for secondary cellulitis (Sacchi et al., 2021).

Follow-Up: As indicated for treatment of underlying medical conditions and skin management. Monitoring of medications and follow-up with referrals.

Prevention/Prophylaxis: None known because this is a complex and misdiagnosed condition.

Referral: Psychological counseling, cleaning and biohazard services, care management.

Clinical Recommendation	Evidence Rating	References
Absence of normal skin cleansing can cause keratin and dirty debris to accumulate and with time form a thick shell.	A	Biswas et al., 2013
The frequent presence of Diogenes syndrome in frontotemporal dementia may contribute to the symptoms. Initial treatment should be a behavioral program.	A	Cipriani et al., 2012
It is hypothesized that it may occur as the result of response to various stress factors, such as the death of a spouse or a medical illness in those with subclinical personality disorder.	A	Eren et al., 2015
The approximate annual incidence of Diogenes is 0.03% in people over 60. Affected individuals come from any socioeconomic status, but are usually of average or above average intelligence. Mortality is increased with a 40% 5-year death rate.	A	Irvine & Nwachukwu, 2014
A neurobehavioral syndrome characterized by severe domestic squalor, pathological hoarding, and lack of insight into their condition. Associated with psychosis, alcohol-induced disorder, affective disorder, or OCD in younger patients where it is frequently associated with dementia in the elderly.	A	Sacchi et al., 2021

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ELDER ABUSE

Signal Symptoms: Tell-tale signs indicative of abuse may include bruises, broken bones, poor personal hygiene, abrupt changes in finances, sudden withdrawal in normal activities, unexplained weight loss, and excessive power or control by a close family member or friend (Friedman et al., 2017).

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Description: The National Adult Protective Services Association identifies elder abuse as a form of mistreatment resulting in harm to a vulnerable person (Ejaz et al., 2022). It is a global public health problem that can be difficult to detect (Dong, 2015). *Elder abuse* is defined as any knowing, intentional, or negligent act performed by a caregiver or another person that may cause harm or risk of harm to an older adult who is vulnerable (NAPSA, 2021). Types of abuse include:

- Physical abuse: causing physical pain or injuring a vulnerable elder
- Sexual abuse: sexual contact with a vulnerable elder without their consent
- Neglect: failing to provide food, shelter, health care, or protection for a vulnerable elder
- Exploitation: the taking of funds, property, or any assets of a vulnerable elder without legal consent and not for the benefit of the elder
- Emotional abuse: using verbal or nonverbal means to cause mental pain, anguish, or distress in an elder
- Abandonment: deserting the vulnerable elder after someone has assumed responsibility for that individual
- Self-neglect: the elder fails to perform the needed activities to protect their own health and safety (lacks food/utilities, refuses medications, hoards, lives in unsafe conditions, neglects their grooming/appearance, is unable to handle finances, is isolated, is disoriented, develops a dependence on drugs and/or alcohol) (Pickens et al., 2021)

Elder abuse is highly underreported to authorities and is more common in the community setting compared to institutional settings. It is estimated that 0.6% to 5.2% of the older adult population experiences some form of abuse (U.S. Department of Justice, n.d.).

Etiology: Abuse of vulnerable older adults can happen in many settings, from private homes to long-term care facilities and hospital settings. The days when the family lived close by and took responsibility for its members are dwindling. Families are spread out and lack the close communication of past years. This separation leaves loved ones in closest proximity to older adults to be fully responsible for their oversight and care thus creating unforeseen stressors to the responsible family member. A lack of adequate support in these situations hampers individual's efforts in providing care and may play a role in perpetrating elder abuse. Common features of perpetrators committing elder abuse are partners or spouses living with the victim, history of alcohol or drug abuse, history of mental illness, history of unemployment, and being socially isolated (Amstadter et al., 2011).

Storey (2020) suggest that the abused older adult is more likely an older female. She generally has a physical impairment and is in poor health. She may either live alone, with the abuser, or in a household with many members. The perpetrator is generally found to be a male who has a history of past or current substance abuse, has mental health issues, is socially isolated, and has a history of past trouble with law enforcement. He may be financially dependent on the older adult and be under major stress.. According to Weissberger and colleagues, family members were the most common perpetrators in cases of elder abuse reported to National Center on Elder Abuse (2020). These cases result in an increased risk of death for the vulnerable older adult involved in the abusive situation.

Occurrence: The actual numbers of cases of elder abuse are difficult to quantify due to the variance in mandatory state reporting laws. Estimates include 1 in 10 Americans 60 years of age and older have experienced abuse, although others estimate the number to be 5 million. One study reported only 1 in 24 cases of elder abuse are reported to authorities (World Health Organization, n.d.). The National Elder Abuse Incidence Study states that for every one reported case of abuse there are about five that go unreported (Administration for Community Living, 1998). These numbers are expected to increase with the burgeoning of the older population.

Age: One out of every 10 older adults older than 60 years is a victim of elder abuse. Sixty percent of abusers are close family members.

Ethnicity: Occurs in all ethnic groups and socioeconomic classes.

Contributing Factors: Social isolation, frailty, physical or mental disability, and dependency are some of the contributing factors. Living with others can also be a risk factor for elder abuse.

Signs and Symptoms: The Administration on Aging provides several examples of potential abuse to observe in older patients. Physical signs include slap marks and unexplained burns or blisters, especially circular, as from a cigarette or other familiar object. Unusual bruising in areas that are not usually thought to be accidental can raise suspicion of possible abuse. Any bruising around breasts or genital area and/or unexplained sexually transmitted infections might indicate sexual abuse. Emotional abuse can be suspected if a patient withdraws from their normal activities or has an unusual change in their level of alertness or any other change in behavior that has not been previously observed. Furthermore, the inability to interview the individual alone may provide suspicion of elder abuse. Often, the affected victim fears placement in long-term care or being abandoned and, thus, tolerates the abuse (Powers, 2014).

The National Institute of Justice warns sudden changes in finances, unexplained changes to wills or trusts, unexplained bank withdrawals, and loss of property may indicate financial exploitation of an older adult. Signs of caregiver or self-neglect can be decubiti that are untreated, evidence of restraint use, suspicious bruising, medication nonadherence, lack of medical devices such as hearing aids or dentures, missed medical appointments, untreated medical conditions, unkempt appearance, refusal of care, and unusual weight loss (Boyle, 2020). These are all concerns that need to be followed up as possible signs of caregiver neglect or in cases of self-neglect, when no caregiver is involved (Ayalon, 2015; Pickens, 2021; Wong & Waite, 2017).

Diagnostic Tests: The basis to establishing a baseline of health is a head-to-toe examination of the patient in question. Having the patient unclothe to a patient gown will allow full examination of areas that may otherwise be hidden by clothing, socks, or shoes. It is important to examine the patient alone without the caregiver present. This individual time allows the practitioner to ask indirect and nonthreatening questions regarding abuse (because most older adults do not self-report abuse) followed by more direct questioning (Burnett et al., 2014; Lachs & Pillemer, 2015). Interviewing the caregiver separately may provide clues to

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differences in the victim and the alleged perpetrator's story regarding suspicious physical findings. The baseline examination will dictate the needed adjunct laboratory and imaging tests required to establish a diagnosis. If impairment in memory or alertness is suspected, a formal assessment of cognition and mood needs to be performed (Lachs & Pillemer, 2015; Pickens, 2021). In complex cases of suspected elder abuse, a referral to a geriatric team for a comprehensive geriatric assessment may be warranted (Burnett et al., 2014).

Differential Diagnosis:

- Unintentional injury
- Falls
  - Alcohol or substance abuse
  - Cancer
- Thin, friable skin with easy bruising

Treatment: If elder abuse is suspected, it is the health-care professional's responsibility—and in most cases a legal obligation—to report this to either 911 or the state elder abuse hotline (Boyle, 2020). Carefully collect information regarding the patient, using physical findings, cognitive screening, patient's functional abilities, testing results, and verbal information from the patient and their caregivers. Use an interdisciplinary team and speak with social workers, nursing staff, and others who may have interacted with the patient and caregiver (Ejaz et al., 2020; Rosen et al., 2019). Document all findings because they may be required to be presented in court later. Especially document any differences in verbal accounts between the patient and their caregiver. It is also prudent to photograph suspicious injuries, as well as measure or compare size of an injury with a familiar object if a ruler is not available (Cooper et al., 2009; Yonashiro-Cho et al., 2019). When a patient has dementia, a history can be difficult to evaluate. This collection of information will assist the adult protective services case workers in their case investigation. The information may protect the patient from further exploitation, neglect, or abuse. Be sure to follow up with the case workers to determine the outcome of the case. It sometimes takes several reports before the true picture of neglect, exploitation, or abuse can be investigated thoroughly, and the elder individual moved to a safe environment.

Follow-Up: After the elder abuse is reported, adult protective services will become involved and take action to protect the patient from further abuse. Contact them to obtain information on the outcome.

Sequelae: The older adult may need to be moved to a safe environment, such as a long-term care setting or the residence of another family member. There may be legal proceedings that can involve the health-care professional's testimony based on the observations and findings that have been carefully documented. The abuser may be incarcerated for their acts. Sometimes what is required is an evaluation of support in resources to assist the caregiver in improving their knowledge of the caregiving role. This requires education and counseling from community resources (Mosqueda et al., 2020). Unfortunately, risk of death increases in elder abuse cases (Lachs & Pillemer, 2015).

Prevention/Prophylaxis: Prevention can come in the form of education at multiple levels. The caregiver especially requires education on the patient's care. This can be done in part on regular clinical visits with the primary care provider, in community offerings, at Area Agency on Aging seminars, and with other local resources. In some communities, there are social workers and nurses who provide support services to families through private agencies. Respite programs can be accessed to lessen the stress on the caregiver by providing much-needed time for themselves. Adult day-care services are available in larger communities, as are meal services and other resources that can assist the caregiver in lessening the burden of providing care.

Health-care professionals need to incorporate routine screening of elder abuse in at-risk populations (Dong, 2015).

Referral: See Treatment for immediate referral. Access to information on National Adult Protective Services Association and resources available in your community can be found at NAPSA-Now.org.

Education: Education of health-care professionals also needed so that there is an understanding of those responsible for the care of older adults. Providing education on normal aging body expectations found in the older patient and what to do when there are red flags that require further investigation can help professionals provide better care for older adults.

Clinical Recommendation	Evidence Rating	References
Findings of this systematic review of elder abuse suggest elder abuse is common, particularly in underrepresented community-dwelling older adults. This review also confirms knowledge gaps, inconsistent definitions, and insufficient findings regarding intervention and prevention research in cases of elder abuse.	A	Dong, 2015
The state of current elder abuse research is comprised primarily of descriptive, observational case studies, no meta-analyses, and a few intervention trials. Little evidence is available that supports any intervention to prevent elder abuse. More rigorous elder abuse research and more investigators are needed.	A	Baker et al., 2016

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GRIEF AND BEREAVEMENT

Signal Symptoms: Societal and cultural terms of grief vary and must be taken into consideration when determining appropriate length of time for one to grieve. This is not standard for everyone, every culture, or every society; even though diagnostic criteria give a time frame, it should be used only as a guide. Most people will go through Elisabeth Kübler-Ross's five stages of grief: (1) denial, (2) anger, (3) bargaining, (4) depression, and (5) acceptance (Corr, 2020). The stages are not always linear, and a person can emotionally be in two stages at the same time; however, this has become widely accepted as the grief process. Deviations from this lasting longer than 6 months are considered abnormal (Meichsner et al., 2020).

Description: Unfortunately, grief is encountered frequently for older adults and is a natural response emotionally, behaviorally, and cognitively to a loss (Bui & Robert, 2020; Meichsner et al., 2020). According to the most recent edition of the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; American Psychiatric Association [APA], 2013), bereavement is an intense sorrow and yearning for the deceased that can cause emotional pain. Complicated grief refers to the inability to cope with the loss or becoming "stuck" in the grief process. When the patient is unable to work through their grief, it intensifies and physical or psychological illness may occur; this type of grief is more intense and prolonged (Diolaiuti et al., 2021). Persistent complex bereavement, also known as prolonged grief disorder, can be diagnosed after more than 6 months of bereavement with persistent symptoms (APA, 2013).

Etiology: Loss or a significant change perceived as a loss. For older adults, the loss of a spouse or life partner is the most common and significant event (Diolaiuti et al., 2021). Other losses include loss of a parent, child, sibling, or close friend.

Occurrence: Almost one-third (32.5%) of persons aged 65 and older have been widowed (Medicine Encyclopedia, 2021). Among older adults aged 75 and older, 58% of women and 28% of men have been widowed at some point (Gurrentz & Mayol-Garcia, 2021). Grief and bereavement affect more women than men because life expectancy for women is higher (at 81.4 years prior to the COVID-19 pandemic and 80.2 years after 2020). It stands to reason that the longer one lives, the more loss one will endure.

Age: May occur at any age but becomes more repetitive as we age.

Ethnicity: The Hispanic population has a life expectancy of 78.8 years after 2020. The non-Hispanic White population has a life expectancy of 77.6 years after 2020. The non-Hispanic Black population has a life expectancy of 71.8 years after 2020 (Arias et al., 2021).

Contributing Factors: Length of illness, amount of suffering, relationship quality, survivor guilt, financial burden of illness, caregiver burden, personality attributes of deceased and survivor, and religious and cultural expectations all may be related to the variety of grief responses (Diolaiuti et al., 2021). Losing a loved one during the COVID-19 pandemic has caused increased grief symptoms in the bereaved individuals (Diolaiuti et al., 2021; Szuhany et al., 2021). When an older adult loses a family member that they were a caregiver for, their grief may be twofold, not only of the loss of a loved one but grieve the loss of the role of caregiver (Mason et. al., 2022).

The provider needs to inquire about substance use such as alcohol or marijuana. Alcohol is the most commonly used and abused substance among older adults and the use of marijuana is significantly increasing among older adults (National Institute on Drug Abuse [NIDA], 2020). Sometimes, grief turns into addiction when the grieving person uses a substance to avoid or distract them from feeling the severity of a loss (Juergens, 2020). Providers must be aware of this possibility and be able to pick up on signs and symptoms.

Signs and Symptoms: Grief is characterized by anxious and depressive symptoms including the inability to relax, feelings of impending doom, poor appetite and weight loss or compulsive eating and weight gain, sleep disturbance, tearfulness, anhedonia, avolition, difficulty concentrating, withdrawal and isolation, emptiness, indecisiveness, guilt feelings, and possibly suicidal ideation.

Diagnostic Tests: Patient interview and obtaining collateral information form sources who know the patient best, if possible. The Generalized Anxiety Disorder – 7 Scale and the Patient Health Questionnaire – 9 (PHQ-9) should be used to assess symptoms of anxiety and depression. The Brief Grief Questionnaire (BGQ) is a very quick and easy tool to use to assess for complicated grief and can be found at https://complicatedgrief.columbia.edu/professionals/complicated-grief-professionals/overview/. The Grief Intensity Scale is a free online tool that is diagnostic for prolonged grief disorder and can be found at https://endoflife.weill.cornell.edu/research/grief-intensity-scale.

Differential Diagnosis:

- Generalized anxiety disorder (GAD)
- Major depressive disorder (MDD)
- Adjustment disorder
- Post-traumatic stress disorder (PTSD)
- Persistent complex bereavement disorder

Treatment: If the person meets diagnostic criteria for any of the above, then starting appropriate medications is warranted. The provider and patient should have a discussion and determine whether medications are needed and decide on the best medication for the individual person. Appropriate classes of medications to consider are selective serotonin reuptake inhibitors (SSRIs), serotonin-norephinephrine reuptake inhibitors (SNRIs), or buspirone. Tricyclic antidepressants (TCAs) are fatal in overdose and should not be used in these cases.

Referral: Provide emotional support and refer for therapy. Patients should understand therapy and medications together have the best outcomes (Szuhany et al., 2021). Referral to support groups should be considered. A card or letter from

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professionals who cared for the deceased is also recommended. Reaching out to the surviving spouse in the early bereavement period is also helpful. Complicated grief treatment is an evidenced-based treatment that has seven themes focused on adaption to loss and resolving impediments. The themes are "accepting grief, managing emotional pain, thinking about the future, strengthening relationships, telling the story of the death, living with reminders, and connecting with memories" (Meichsner et al., 2020, p. 564). Encourage patients to return to their normal routine as soon as possible. Daily physical exercise can help patients cope with the depression that accompanies grief. If the primary care provider does not feel comfortable in treating the grieving older adult, then a referral to a psychiatric mental health nurse practitioner or psychiatrist should happen sooner rather than later.

Follow-Up: This person needs close and careful monitoring with weekly to monthly visits and phone calls in between visits.

Sequelae: In the first 3 months after the death of a spouse, older adults are prone to the *widowhood effect*, which is the increased mortality risk of being a widow. Some studies show men having a higher mortality risk and some show women having a higher mortality risk, but a systematic review indicated the risk of mortality to be between 19.2% and 48% regardless of the cause of death. Mortality can be as high as 90% immediately following bereavement. Men are at a higher risk of cardiovascular issues, and men with preexisting cardiac conditions have an even higher mortality rate (Ennis & Majid, 2021). Persons with mental health conditions may experience a relapse of symptoms during bereavement (Meichsner et al., 2020).

Prevention/Prophylaxis: If the loss can be anticipated, the goal is to encourage and support the patient in the normal grieving process and prevent dysfunctional grieving. Activation of social and spiritual support networks, discussion of anticipated loss, and involvement in support group activities or volunteerism may be helpful. If the patient was in palliative care, bereavement support and grief counseling are available to the family for 13 months. Often, this process begins before the death of the loved one.

Education: Make patients and their support networks aware of the variability of normal grieving; alert them to signs of dysfunctional grieving and resources for help. A helpful resource for survivors and families is www.nlm.nih.gov/medlineplus/bereavement.html. This site has information on usual and complicated grief written for the general public.

Clinical Recommendation	Evidence Rating	References
At the time of admission to a hospice or palliative care program, an initial, developmentally appropriate professional assessment is completed to identify patients and families at risk for complicated grief, bereavement, or comorbid complications, particularly among older adults.	A	National Consensus Project for Quality Palliative Care, 2018
Following the death of the patient, it is essential to allow the patient's loved ones to perform any customs or rituals that are important to them, within the policy guidelines of the facility. Clinicians should be available to answer questions and offer support.	A	National Consensus Project for Quality Palliative Care, 2018
Some older adults may take substances to cope with grief and loss.	A	National Institute on Drug Abuse, 2020
Losing a loved one during the COVID-19 pandemic has caused increased grief symptoms in the bereaved individuals.	C	Diolaiuti et al., 2021 Szuhany et al., 2021
Acute grief typically does not require treatment.	B	Shear et al., 2021
Receiving Complicated Grief Treatment and citalopram, a selective serotonin reuptake inhibitor, improved bereavement symptoms compared to either alone	C	Szuhany et al., 2021

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

INSOMNIA

Signal Symptoms: Patient report of not sleeping, excessive daytime sleepiness, loud snoring (potential sleep apnea), restless legs, difficulty falling asleep, difficulty staying asleep, early morning awakening, sleep that is not refreshing and restful (Winkleman et al., 2021).

Description: Normal age-related changes have significant effects on sleep. Sleeping states and sleep schedules change with age. For example, peak sleepiness happens earlier in the evening for the older adult, but this time for bed does not fit societal norms, so the person often ignores this. In older adults, sleep during early morning hours is reduced. As we age, time to sleep, sleep efficiency, rapid eye movement (REM) sleep, slow-wave sleep (the deepest, most restorative sleep), and REM latency are all reduced. Sleep latency is slightly increased, and wake after sleep onset is increased in older adults. Sleep efficiency (time sleeping versus time in bed) is less than 80% in older adults, and time to fall asleep is extended (Feinsilver, 2021).

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Etiology: Insomnia can have several etiologies, including medical conditions, side effects of medications, substance use disorders, circadian rhythm disorders, or psychiatric conditions. Chronic insomnia lasts more than 1 month and results from age-related changes in sleep and chronic stressors (Bonnet & Arand, 2021).

Occurrence: Sleep disturbances increase with age (Feinsilver, 2021). Insomnia symptoms are present in as much as 65% of people aged 65 and older (Matheson & Hainer, 2017). Approximately 30% to 48% of older adults have insomnia (Patel et al., 2018) and 57% are affected by chronic insomnia (Abad & Guilleminault, 2018). Insomnia is more prevalent in women; older adults; those who have lost a family member; those who are unemployed, divorced, widowed, or separated; those of lower socioeconomic status or no higher education; or in those going through withdrawal from alcohol or opiates (Matheson & Hainer, 2017; Tsaras et al., 2021). Additionally, researchers have already linked the COVID-19 pandemic to insomnia and sleep-related disorders in older adults. It is also plausible that decreased sleep may increase one's vulnerability to be infected with SARS-COV-2 and for them to have a poorer prognosis (Pires et al., 2021).

Age: More common in older adults than any other age-group and continues to increase as one ages from the 65+ age-group to the 85+ age-group (Matheson & Hainer, 2017; Pires et al., 2021). Persons with chronic comorbidities (medical and psychiatric) are also at higher risk (Matheson & Hainer, 2017; Pires et al., 2021). Women are more likely to have insomnia and twice as likely to be diagnosed (Matheson & Hainer, 2017) but men have more insomnia in the over-85-years age-group (Bonnet & Arand, 2021).

Ethnicity: Starting with the least amount of sleep per night is Native Hawaiian/Pacific Islanders then Black, multiracial, American Indian/Alaskan Native, then Hispanic. Individuals who are White report having the most amount of sleep per night (Centers for Disease Control [CDC], 2017).

Contributing Factors:

- Sleep disorders such as restless legs syndrome or periodic limb movement disorder
- Sleep apnea
- Dementia
- Mood disorders (depression, anxiety)
- Bipolar disorders
- Substances such as caffeine, alcohol, nicotine, and stimulants
- Medications such as stimulants, antidepressants, glucocorticoids, NSAIDs, opioids, and diuretics can affect sleep (Murphy et al., 1994; Winkleman et al., 2021)
- Comorbid chronic medical conditions
- Poor sleep habits and poor sleep hygiene (Winkleman et al., 2021).
- Screen time: stop using electronic devices at least 30 minutes before bedtime (National Sleep Foundation, 2021)

Signs and Symptoms: A complete history should reveal a full description of the problems. Questions to be included include how often has the patient experienced insomnia (number of nights a week and for how long?). Patients may complain about difficulty falling asleep (a sign of anxiety) and staying asleep, frequent awakenings, early morning awakening (a sign of depression) and inability to return to sleep, daytime fatigue with unwanted naps, irritability, or difficulty concentrating. Patients should be questioned about their use of caffeine to include amount of caffeine consumed and time of day. Medications should be reviewed to determine whether insomnia could be medication related, especially if a new medication was prescribed or there has been an adjustment in dosage. Additionally, an older adult may spend 10 to 12 hours in bed at night trying to sleep. A pertinent physical examination should evaluate the systems associated with any medical conditions listed here. Falling may be a sign of insomnia. A mental status examination is useful in detecting cognitive or psychiatric disease (Bonnet & Arand, 2021).

Diagnostic Tests: Diagnosis is usually made on patient interview and obtaining sleep history. The sleep history should include an assessment of daytime sleepiness, fatigue, or sleep disturbance; the sleep environment; and the duration of symptoms. Additionally, information on frequency and duration of awakenings, sleep times, nap times, and lengths is important (Bonnet & Arand, 2021). Insomnia is a clinical diagnosis (Patel et al., 2018), verified by a sleep log. The Epworth Sleepiness Questionnaire can be used for patient's complaining of daytime sleepiness; however, it is not well validated in older adults (Feinsilver, 2021). The University of Pittsburgh has five different validated sleep questionnaires that a provider must obtain permission to use (https://www.sleep.pitt.edu/instruments/). The American Thoracic Society also has the insomnia severity index, which also requires permission to use. The Patient-Reported Outcomes Information System (PROMIS) sleep disturbance tool is a free and validated self-report tool for sleep–wake function (Northwestern University, 2021).

Wrist actigraphy monitors and stores data for up to 28 days and can be used to assess treatment response (Patel et al., 2018). Persons with insomnia tend to overestimate the time it takes them to get to sleep and underestimate their total sleep time (Bonnet & Arand, 2021). Polysomnography is not needed in the evaluation and diagnosis of insomnia, but it is used in the evaluation of sleep apnea or parasomnias (Patel et al., 2018).

Differential Diagnosis:

- Mood disorders such as depression and/or anxiety
- Inadequate sleep hygiene
- Medical problems
- Medication-related sleep disorder
- Substance-related sleep disorder

Treatment: Treat underlying or coexisting disorders. Changes in one's sleep habits and maintaining good sleep hygiene is the first step. Then, cognitive behavioral therapy for insomnia is considered first-line treatment (Pires et al., 2021). Mindfulness meditation is a successful treatment in motivated patients (Perini et al., 2021).

Medications for insomnia should be considered the last resort, not the first option. Melatonin, which is over the counter, is the safest medication to begin with and should be tried first. Over-the-counter (OTC) antihistamines are not considered safe for older adults due to their anticholinergic effects. They are also on the potentially inappropriate medication (PIM) list and should not be used for insomnia. Ramelteon (Rozerem), a melatonin receptor agonist, should be used for sleep onset insomnia (Neubauer, 2021). Lemborexant and suvorexant are

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orexin-receptor antagonists and should be used for sleep onset and sleep maintenance (Neubauer, 2021). Antidepressants are listed on the PIM list (Roux et al., 2020); however, low-dose mirtazapine is known to be sedating, but it may also increase appetite. Trazodone is used for insomnia, and it works for sleep onset and maintenance. Doxepin works on sleep maintenance. In older adults, avoid benzodiazepine hypnotics (estazolam, flurazepam, temazepam, triazolam, and quazepam) if possible because these have significant side effects in the older adult, are addictive, and are on the PIM list (Neubauer, 2021; Roux et al., 2020). The benzodiazepine receptor agonists (eszopiclone, zaleplon, and zolpidem in all forms) also have adverse risks for older adults, are also on the PIM list, and should not be used unless necessary (Neubauer, 2021; Roux et al., 2020). All these medications have interactions among substrate systems and the provider must be aware of that prior to prescribing.

Safe prescribing practices include (Neubauer, 2021):

- Prescribe the lowest possible effective dose.
- Do not prescribe more than the maximum dose.
- Educate the patient on not combining with substances such as alcohol or other sedatives.
- Do not provide refills until continued use has been deemed necessary.
- In older adults, use all these medications with caution.
- Assess for suicidal ideation in persons with comorbid depression.
- Educate the patient on proper timing of medication and half-life properties and when not to use.
- Discuss risk of next day impairment.
- Discuss risks of taking these types of medications and driving.
- Know the substrate systems and any potential interaction.

Follow-Up: Patients should return in 2 weeks. If the patient has a bed partner, this person should be interviewed as well. Examine the patient's sleep diary and evaluate the effectiveness of the treatment. If indicated, reevaluate the diagnosis and restructure the treatment. Pharmacological therapy should be considered a last choice and every effort should be made to wean the patient from these as soon as possible and/or avoid long-term use.

Sequelae: Includes reduced quality of life, depression, increased risk for falls/injury, and potential for drug dependence or drug interactions resulting from use of OTC sleep aids.

Prevention/Prophylaxis: The tips for better sleep from World Sleep Society (2020) include:

- Establish a regular bedtime and wake-up time.
- Avoid napping in excess of 45 minutes.
- Avoid alcohol and nicotine.
- Avoid caffeine 6 hours before bedtime.
- Exercise on a regular basis but not right before bed.
- Create an optimal sleep environment: temperature between 60°F and 67°F, comfortable bedding, turn off all lights and distracting noises, charge phones outside of the bedroom.
- Reserve your bed for sleep and sex.
- Avoid heavy, spicy, or sugary foods 4 hours before bedtime. A light snack is preferred.
- Maximize daytime exposure to bright light.
- Set aside a time each evening for relaxation and thinking.
- Maintain a sleep log or diary if having difficulty with sleep.

Referral: If therapy brings no improvement and other underlying causes have been eliminated, refer the patient to a sleep laboratory for evaluation.

Education: The National Sleep Foundation recommends 7 to 8 hours of sleep being optimal for older adults with a range of 5 to 9 hours being acceptable (2021). Explain age-related sleep changes to the patient and their family. Teach the patient to follow the guidelines listed under prevention/prophylaxis.

Clinical Recommendation	Evidence Rating	References
Cognitive behavioral therapy for insomnia is considered first-line treatment.	A	Pires et al., 2021
Mindfulness-based interventions are also first-line treatment.	B	Perini et al., 2021
Avoid use of benzodiazepine hypnotics in older adults.	A	Roux et al., 2020

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

SUBSTANCE-RELATED AND ADDICTIVE DISORDERS

Signal Symptoms: Variable due to the substance-related disorders, craving, pinpoint pupils, constipation, confusion, drowsiness, anxiety, behavioral changes, impulsivity, personality changes

Description: These disorders, gambling disorder (GD), alcohol use disorder (AUD), and substance use disorder (SUD), commonly occur together.

According to the general criteria put forth by the *Diagnostic and Statistical Manual of Mental Disorders* (5th ed.; *DSM-5*; American Psychiatric Association [APA], 2013), diagnoses of SUD, AUD, and GD are closely related and include impaired control, social impairment, and risky use. The individual may drink more than intended, use substances more often than intended, or spend more money

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than intended. The individual may have tried to cut down or stop using substances or stop gambling without success. They spend an inordinate amount of time obtaining access to the substances or behaviors, using, and recovering from using or participating in these behaviors. Sometimes, when the cravings are so intense and the use disorder is severe, all activities in the day are directed at obtaining the substances or the gambling applications. All these disorders also manifest as a social impairment in one way or another, either isolation or entering relationships that are uncommon for that person. Risky use implies that use of the substance, alcohol, or gambling causes the individual discomfort in some way, either physically, socially, mentally, or financially. Cravings are defined as intense desire for the substance, alcohol, or gambling behavior and may occur anytime, but generally occur where the behavior usually occurs.

SUBSTANCE USE DISORDER

The *DSM*-5 definition (APA, 2013) of SUD includes the following substances: amphetamines, cocaine and other stimulants and combined stimulants, caffeine (intoxication and withdrawal), cannabis (with withdrawal symptoms), phencyclidine and other hallucinogens, inhalants (no withdrawal syndrome), tobacco, opioids, sedatives, hypnotics, and anxiolytics. Other substances included in this category include psilocybin, MDMA (Ecstasy/Molly), ketamine, Kratom, synthetic cathinone (bath salts), and synthetic cannabinoids. The use of prescription medications for reasons other than intended and "borrowing" a medication or other substance such as loperamide (used as an opioid alternative and has been linked to overdose) for pain or insomnia, are also included in SUD (Bulloch, 2018).

Substance use disorder in older adults is increasing, in part because many substances were not classified as dangerous or addicting in older generations. For example, heroin, whose name came from the sense of feeling "heroic," was used in the civil war and used in cough preparations and over-the-counter (OTC) products until it was clear that the product was addictive. It became a Class I controlled substance in 1924. Benzodiazepines were widely prescribed in the 1960s to help women cope with the stressors of raising children (Pyle, 2020). Until the addiction potential was discovered and the *DSM*-5 included Sedative, Hypnotic and Anxiolytic Use Disorder DSM-5 304.1 F13.1 (APA, 2013), which identified substance use resulting in distress or functional impairment, specified by the drug, and graded on a continuum from mild to severe, benzodiazepines have been considered a useful and commonly used treatment.

Cannabis is now a legalized entity for recreational use in many states, and many have changed their attitudes toward its use. Prior to that, use of medical marijuana was legalized in most states for multiple issues including chronic pain, seizure disorders, cancer, multiple sclerosis, fibromyalgia, and other chronic pain issues that would be anticipated to last a significant period. According to the National Survey on Drug Use and Health (NSDUH), use of marijuana among older adults is on the increase since over a decade ago (Han & Palamar, 2020).

GAMBLING DISORDER

Frequent trips to the casino, gambling on smartphones and online, the need to bet higher amounts of money, believing that the next bet will be "the winner" (also known as chasing one's losses) are some symptoms of GD. Other characteristics identified in the *DSM*-5 include preoccupation with gambling, persistent thoughts about past experiences, planning the next trip or how to download an app, gambling when feeling distressed, lying to conceal the extent of involvement with gambling, and jeopardizing or losing a significant relationship, job, or career opportunity because of gambling. Relying on others to provide money to relieve a difficult financial situation because of gambling is also part of the criterion for GD.

Individuals older than the age of 65 tend to have a lifelong history of problem gambling. The population at risk for GD is heterogenous and is at risk secondary to multiple motivations for beginning or maintaining gambling. Laws regarding gambling have loosened in the past 5 to 10 years in multiple states. Gambling programs can be accessed online and, in some states, advertisements for gambling programs are prevalent. Risks for gambling behaviors include retirement, social isolation, reduced social contact, physical-mental disease, or the loss of a partner.

Abbott and associates (2018) looked at the two types of gambling preferences. Nonstrategic games involve little or no decision making or skill and where the participant cannot influence the outcome. These include slot machines, bingo, scratch tickets, keno, and lottery games. The second game type includes those in which gamblers attempt to use their knowledge to influence the outcome. Some examples include poker, sports betting, craps, and blackjack.

Granero and associates (2020) identified two clusters of gamblers. Cluster 1 had a low risk of problem gambling and participated in nonstrategic games of chance or did not gamble at all. This group included women: older, lower education and income levels, fewer total number of life events, better psychopathological state, and lower prevalence of substance use. Cluster 2 included the higher proportion of men: married, higher levels of education, higher incomes, higher mean number of cumulative events, worse psychopathological states, and higher prevalence of substance use. All the members of cluster 2 met criteria for GD. Members of cluster 2 also had a higher propensity for AUD and SUD.

ALCOHOL USE DISORDER

A common controversy in AUD is the claim that moderate consumption of alcohol is healthy and is associated with decreases in mortality and morbidity. Yet studies have shown that the risk of mortality increases with heavier drinking (Hartz et al., 2018). The definition of moderate alcohol use is usually ≤1 drink per day (Kueber et al. 2014).

Etiology: Dopamine is a key chemical in the pleasure center of the brain. Substances, rewards, even sitting down at a screen can stimulate the release of dopamine, which then stimulates the reward center in the brain. The frontal lobes of the brain are involved in executive functioning and oversee voluntary actions such as reasoning, thinking, movement, decision making and planning. The amygdala is a cluster of cells involved in the limbic system of the brain that is responsible for the emotional and behavioral responses to stressors and events as well substances. The amygdala is responsible for preserving memories and specific emotions. It is also responsible for initiating the fight-or-flight response. On occasion, the frontal lobes are disabled in an event called an "amygdala hijack" where reasoning and executive function is diminished.

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Occurrence: According to the National Institutes of Health (NIH, 2020), nearly 1 million adults aged 65 and older live with SUD as reported in the 2018 data. The number of older adults who engage in unhealthy behaviors is expected to increase significantly as Baby Boomers age. Alcohol is the most used drug among older adults, with about 65% of people 65 and older reporting high-risk drinking, defined as exceeding daily guidelines at least weekly in the past year (NIH, 2020). Binge drinking is also of concern. More than a tenth of adults aged 65 and older currently binge drink (NIH, 2020). During the early months of the COVID-19 pandemic, 1 in 10 older adults reported an increase in their drinking (Eastman et al., 2021).

Smoking cigarettes is still the most common form of tobacco use. The highest rates of smoking occur for those 45 to 65 years old. In those persons older than 65, only 8.2% reported smoking in 2020. Currently, LGBTQ+ adults were more likely to be current smokers than heterosexual adults. Current smoking by adults is higher in the Midwest and lowest in the West (Centers for Disease Control and Prevention [CDC], 2020).

The prevalence of problem gambling among older people ranges from 0.3% to 10.4% in studies of those older than 55 years of age (Guillou Landreat et al., 2019).

Age: An evaluation of death certificates in the United States (White et al., 2020) reveals that the overall rates of alcohol-related deaths are more than four times higher among middle-aged and older adults aged 45 to 74 than those in an age bracket of 25 to 34. The baby boomer generation (those born between 1946 and 1964) has significant differences in attitudes and uses of alcohol and recreational use of illicit substances (Han & Moore, 2018).

Contributing Factors: Being male, being a woman who identifies as lesbian or as a woman who has sex with women, major life changes, and losses are contributing factors to AUD and SUD (Selix et al., 2020). Additionally, aging itself is often associated with an increased risk of medical conditions involving pain, and alcohol and other substances are often used to cope with pain. This practice itself results in poorer health outcomes. Other contributing factors include:

- Cultural attitudes toward drinking and intoxication
- Happy hour
- Free casino bus trips
- The availability of alcohol and substances
- Acquired personal experiences with alcohol
- Exaggerated positive expectations of the effects of alcohol and substances
- Persistent stress levels
- LGBTQ+

It is unclear whether risky drinking in older people represents a pattern of continued use, a return to use after a period of abstinence, new onset of use, or a combination of all these patterns. As adults move into the retirement years, many life changes occur. For instance, stressful late-life events, loss of productive social roles, loneliness, and the absence of supportive social relationships, to name a few. Additionally, drinking habits acquired in early life continue to be maintained through the life span. Several genetic markers have been studied, and a clear case for biological heritability has been established as one factor. Neurotransmitter effects from alcohol and alterations in brain anatomy in patients with alcohol use disorders as well as genetic makeup serve to reinforce the biological connection (Setka, 2018). Consistent with the complexity of substance use disorders, multiple pathways appear to contribute to substance use disorder.

Concerns about alcohol consumption in the older adult are directed primarily toward the physiological changes that accompany aging and the problems posed by regular alcohol consumption. Chemical breakdown of alcohol does not seem to change with aging; however, the changes associated with aging may increase the concentration of alcohol in the blood. These age-related changes include decreased lean muscle mass, decreased amount of body water, changes in liver function, and increased nervous system sensitivity to alcohol. After drinking one ounce of 80-proof alcohol, a 60-year-old would have a 20% higher blood alcohol level than a 20-year-old, and a 90-year-old would have a 50% higher blood alcohol level than a 20-year-old (Gilbertson et al., 2009). Patterns of AUD in older adults have been divided into two categories: early onset and late onset. See Table 20-10 for a comparison of the two categories.

Lower socioeconomic status is a frequently associated with gambling. Additionally, alcohol use, living in a neighborhood with limited resources, and being African American or Native American are common contributing factors in those with GD (Barnes et al., 2017). Pathological gambling has been observed in patients with Parkinson's disease, particularly those who are younger and that have a personal or family history of alcohol abuse (Heiden et al., 2017). Case reports have described patients diagnosed with frontotemporal dementia as exhibiting pathological gambling behaviors (Battista et al., 2019; Tondo et al., 2017).

Signs and Symptoms:

SUD: Many older adults are solitary, so problematic use is hidden. One way that substance misuse comes to light is when older adults are brought to the emergency department due to events related to their problem behavior. Other

TABLE 20-10 Patterns of Alcohol Use Disorder

VARIABLE	EARLY ONSET	LATE ONSET
Age at onset	Teens and twenties	Later life
Sex	Male	Female
Socioeconomic status	Low	High
Family history of alcoholism	Yes	Less likely
Physical dependence and withdrawal	Typically, have	May never become physically dependent
Cognitive damage	Less reversible	More reversible
Death related to alcohol	More likely	Less likely

Adapted from: SAMHSA: TIP 26 – Substance Abuse among older adults. U.S. Department of health and human services. *(1998). Public Health Service: Substance Abuse and Mental Health Services Administration, Center for Substance Abuse Treatment: HHS Publication No. (SMA) 12-3918.*

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symptoms possibly related to substance misuse include falls, confusion, anxiety, insomnia, paranoid ideation, stroke, pneumonia, pancreatitis without stones, respiratory depression, hypotension, and delirium (National Institute on Alcohol Abuse and Alcoholism [NIAAA], n.d.).

GD: Symptoms may include suicide attempts, homelessness, depression, anxiety, paranoia, and other psychiatric disturbances. Physical signs that may be present on examination include tachycardia, atrial fibrillation, peripheral neuropathy, physical trauma, tremulousness, hepatosplenomegaly, rhinophyma, inconsistent or mild hypertension, and telangiectasias.

AUD: For older adults with AUD, physical examination findings may include hepatomegaly, ascites (late stage), jaundice (with pancreatitis), anemia, electrolyte imbalance, tremors, tachycardia, nausea, vomiting, insomnia, and spider angiomas; men may have gynecomastia, testicular atrophy, and loss of pubic and axillary hair. A complete neurological examination that includes cranial nerves, gait, sensory, motor, reflexes, Romberg sign, and tandem walking should be included.

Diagnostic Tests: The contemporary approach to the screening and intervention with individuals who may have at-risk, or problem use of substances is called Screening, Brief Interventions, and Referral to Treatment (SBIRT), which is an evidence-based practice used to identify, reduce, and prevent problematic use, abuse, and dependence on alcohol and illicit drugs (Hargraves et al., 2017). Diagnostic assessment depends on a thorough history.

As a part of screening, several tools can be used. Probably the most familiar screening test is the CAGE questionnaire originally developed, tested, and reported in 2001 by Hinkin and colleagues. This questionnaire has excellent sensitivity but poor specificity. However, the ease of use in the older adult for both alcohol and drug abuse make this a valuable screening tool. Primary prevention also includes the use of the Michigan Alcoholism Screening Test – Geriatric version (MAST-G). The MAST-G varies from the MAST in that questions are modified in relation to social and retirement situations. The MAST-G has a sensitivity of 93% and a specificity of 65%. Use of this tool can then direct the clinician in the screening, brief intervention, and referral to treatment also known as SBIRT. A GD tool has been developed by Molander and colleagues (2019). Labeled the G-DIT, the screening test is based on 47 gambling measures and is being tested clinically.

A psychosocial assessment that includes a mental status examination and a geriatric depression scale should also be performed. Additionally, consider a cultural assessment if appropriate.

Drug screening has evolved significantly over the years. Drug testing can not only identify the presence or absence of the drug and metabolite, but drug screening can also be used to monitor success in treatment programs. A broad definition is used to confirm the recent use of a substance and various sources can be used such as hair, nails, blood, breath, and saliva. Confirmatory assays have matured to increase confidence in the result of the testing.

Differential Diagnosis:

- Nonpathological use of alcohol; drinking, even daily, in low doses and occasional intoxication does not by itself identify misuse.
- Recreational use of marijuana in states where it is legal
- Misuse or a use disorder of other psychoactive substances such as opiates, benzodiazepines, or other psychoactive drugs
- Dementia
- Cerebrovascular accident
- Urinary tract infection
- Gastritis
- Pancreatitis also should be considered

Treatment: According to the USDA and HHS Dietary Guidelines for Americans 2020-2025, healthy adults older than the age of 65 (who do not take medications) should limit their daily alcohol consumption to one drink a day or less for women and two drinks or less for men in older adults. Older adults with health problems or who take medications that may interact with alcohol or substances should abstain from using alcohol or substances altogether. Going to casinos should be limited and attending events where liberal use of alcohol may be an issue should be of concern. The level and severity of alcohol use and misuse as well as substance use and misuse determine the treatment. Patients in physical distress such as alcohol withdrawal, respiratory depression or those who are hemodynamically unstable should be admitted to the hospital. Uncomplicated or mild alcohol use disorder can be treated in the outpatient setting.

The Substance Abuse and Mental Health Services Administration (SAMHSA) provides an in-depth guide to treating SUD in older adults with evidence-based interventions. It is available for download at https://store.samhsa.gov/sites/default/files/SAMHSA_Digital_Download/PEP20-02-01-011%20PDF%20508c.pdf

Alcoholics Anonymous (AA) and Narcotics Anonymous (NA) are the most successful groups in encouraging ongoing sobriety; however, the self-sufficient spirit, often characteristic of older adults, reduces the probability of participation. An AA/NA volunteer of the same gender and of an age comparable to the patient's age is usually available to meet with an individual at the clinic site and can assume the role of the patient's sponsor, reducing fear and providing the support that may encourage group participation. For older adults, people who are important in their lives need to be instructed by counselors in ways to encourage the treatment process and decrease behaviors that enable the older adult to misuse alcohol.

After consultation with an addiction specialist, naltrexone may be given to help maintain abstinence in healthy patients; naltrexone can be used in patients with opioid use disorder, not currently using opioids, and requires proper supervision, and intensive therapies. For chronic alcoholism, the diet should be supplemented with multivitamins containing folic acid and thiamine, 100 mg/day. The patient should also be evaluated for electrolyte problems and anemia.

Opioid use disorder is a frequent problem after years of prescription of opioid use for the management of chronic pain. Dalal and colleagues report that buprenorphine is an effective treatment for chronic pain in patients aged 65 to 84 years (2021). Buprenorphine also decreased sleep disturbances but was associated with constipation, nausea, dizziness, vomiting and in some more frail patients, respiratory depression.

Follow-Up: Alcohol diminishes the effect of many medications and unpredictably strengthens the effects of sedatives. Certain medications are known as alcohol-interactive (AI) drugs that can be problematic: benzodiazepines, antidepressants, sleep

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medications, muscle relaxants, antipsychotics, anticholinergics, prescription narcotics, antihypertensives, antidiabetic, and cholesterol medications (Weathermon & Crabb, 1999). It is critical that patients with AUD are aware of these potential interactions and avoid the use of alcohol if prescribed these medications.

Following when treatment has begun for the substance related and addictive disorder, the older adult should be seen weekly to provide continuity in the practitioner–patient relationship and to monitor treatment effectiveness. When the patient is participating in the treatment protocol, monthly visits should be adequate to monitor progress.

Sequelae: A major concern associated with SUD in the older adult is the increased occurrence of drug-alcohol and drug-drug interactions. The decreased metabolism of drugs by the liver in older adults yields significantly higher-than-normal drug levels, and alcohol increases this effect. Alcohol is metabolized by the CYP2E1 enzyme. Consequently, drugs metabolized by that enzyme pathway will be affected. Alcohol also blocks an enzyme in the liver known as CYP2C9 (Lu & Cederbaum, 2018). Alcohol misuse can lead to gastrointestinal bleeding, especially if the patient is taking aspirin or arthritis medications. More than two alcoholic drinks daily can contribute to hypertension. Gait disturbances, peripheral neuropathy, and decreased functional ability are consequences of alcohol misuse. Malnutrition, cirrhosis, urinary incontinence, decline in cognitive status, insomnia, anxiety, addiction, and tolerance with concomitant withdrawal symptoms may occur. Substance misuse is very serious in that many forms of heroin and narcotics are mixed with manufactured fentanyl which is extremely dangerous secondary to overdose.

Suicide is associated with self-destructive behaviors at any point in the trajectory of SUD, AUD, and GD. Frequently, alcohol and substances are used to self-medicate for depression, anxiety, and other mental health issues. Gambling can contribute to the depression and can worsen anxiety and depression.

Prevention/Prophylaxis: Older adults have age-related risks for continued use that should be considered. Several risk factors have already been identified in this section. Alcohol and substance use/misuse as well as risky behaviors such as gambling are frequently used to combat feelings of loss, grief, depression, and social isolation. On the other hand, social interactions, happy hour, and group activities that also incorporate alcohol and substance use may not be negative. The severity of the implications of substance use/misuse in a person's life dictates the treatment.

Referral: Referral must be completed thoughtfully. Referral to AA or NA is common. The SAMHSA national hotline is 1-800-662-HELP and is a way to explain to families and patients how substance and alcohol treatment works. Refer to in-person or virtual counseling. Gamblers Anonymous is a newer organization to help men and women deal with gambling. Like AA, they have a 20-question survey to identify problem gambling. It is critical for the practitioner to be familiar with these services as well as services in the community so that referral is appropriate and functional.

Education: Education regarding substance use and abuse, alcohol use and abuse, and gambling behaviors all have similar challenges. It is crucial to use a nonjudgmental attitude and avoid stigmatizing terms. Treat people with substance use disorders with respect, caring and compassion. When people with addiction are stigmatized and rejected, it only contributes to the vicious cycle of substance abuse (Volkow, 2020).

Clinical Recommendation	Evidence Rating	References
The U.S. Preventive Services Task Force (USPSTF) Screening for Unhealthy Drug Use recommends screening by asking questions about unhealthy drug use in adults aged 18 years or older. Screening should be implemented when services for accurate diagnosis, effective treatment, and appropriate care can be offered or referred.	B	USPSTF, 2020
The USPSTF recommends screening for unhealthy alcohol use in primary care settings in adults 18 years or older, including pregnant women, and providing persons engaged in risky or hazardous drinking with brief behavioral counseling interventions to reduce unhealthy alcohol use.	B	USPSTF, 2020
APA recommends that patients be assessed for co-occurring conditions (including substance use disorders, other psychiatric disorders, and other medical disorders) that may influence the selection of pharmacotherapy for alcohol use disorder.	C	Reus et al., 2019
APA recommends that patients with alcohol use disorder have a documented comprehensive and person-centered treatment plan that includes evidence-based nonpharmacological and pharmacological treatments.	C	Reus et al., 2019
For patients with opioid use disorder, recommendations are buprenorphine/naloxone in any setting or methadone or buprenorphine/naloxone provided through an accredited opioid treatment program.	A	Management of Substance Use Disorders Work Group, 2021
Cognitive behavioral therapy has been shown to be especially effective for gambling disorder; however, there is a lack of research to associate a grade.	C	Menchon et al., 2018

A consistent, good-quality, patient-oriented evidence; B inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

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CASE STUDY

Mrs. C. is a 69-year-old married woman who presents to your practice with a chief complaint of fatigue. She tells you that she is tired all the time, despite sleeping through the night. She is concerned she may be coming down with something. You ask her about other symptoms, and she confesses that she is under a lot of stress. Her husband has terminal cancer and is also depressed. He is still functional but has refused all interventions. Mrs. C. relates that she quit her job to take care of him, but it is "dragging her down" because he is so depressed. She has four children, three of whom are close by, but she feels she is bearing the burden herself, and the children do not realize what is happening. She tells you tearfully, "I want to have a life, too, before it is all over."

Review of her chart shows recent CBC and chemistry profiles that are normal, normal TSH, and normal EKG. There is a family history of alcohol abuse (her father) and suicide (a sibling).

1. What additional subjective data are you seeking?
2. What additional objective data will you be assessing for?
3. What national guidelines are appropriate to consider?
4. What tests will you order?
5. Are there any screening tools that you want to use?
6. What are the differential diagnoses that you are considering?
7. What is your plan of care?
8. Are there any *Healthy People 2020* objectives that you should consider?
9. What additional patient teaching may be needed?
10. Will you be looking for a consultation?

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unit IV

Complex Illness

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CHAPTER 21

Polypharmacy

Lori Martin Plank

Most experts agree that polypharmacy is an imprecise term that is utilized to describe the prescribing of many medications (five or more), as well as the prescribing of potentially inappropriate medications (PIMs), failing to prescribe necessary medications, and overprescribing (Chou et al, 2021; Khezrian et al., 2020; Pazan & Wehling, 2020). Older adults, particularly those with multiple chronic health conditions, most frequently experience polypharmacy. Polypharmacy is a global problem and occurs in a variety of health-care settings, including communities, hospitals, and long-term care settings (Chou et al., 2019; Gazarin et al., 2020; Jordan et al., 2021; Schneider et al., 2021; Sluggett et al., 2020).

Polypharmacy appears to be an unexpected consequence of advancing medical and pharmaceutical sciences, the development of clinical guidelines and evidence-based medicine, a rapid increase in the older adult population, and the desire to support those with chronic health conditions, especially older adults. Despite the recognition of the prevalence of prescribing PIMS to older adults over the past 40 years, many of the same problems remain because, especially near end of life (Ouslander, 2020). Currently, there is no shortage of research and publications on the dangers of polypharmacy, but change in the practice arena is slow. Research to date has not focused on demonstrating positive outcomes when polypharmacy is addressed (Baumgartner et al., 2020; Cross et al., 2020; Khezrian et al., 2020; Pazan & Wehling, 2020). A Cochrane review (Cross et al., 2020) found mixed results with using behavioral and educational measures to promote adherence in older adults with multiple medications.

Polypharmacy contributes to increased health-care costs and utilization (Clark et al., 2020). In addition to multimorbidity, obesity and metabolic syndrome and history of smoking are factors associated with polypharmacy (Khezrian et al., 2020). Clinical outcomes associated with polypharmacy include falls, frailty, functional and cognitive decline, hospitalization, and even mortality (Pazan & Wehling, 2020).

This chapter will examine polypharmacy trends and consequences in older adults, including underprescribing, overprescribing, and misprescribing; adverse drug reactions (ADRs) as an outcome of polypharmacy; iatrogenic illness related to drugs; specific areas of concern in prescribing for older adults; pharmacodynamics and pharmacokinetics that may affect safe prescribing in older adults; recommendations for safe prescribing in older adults; and recommendations for deprescribing, including tools.

PHARMACOKINETICS AND PHARMACODYNAMICS IN OLDER ADULTS

Certain changes occurring with the aging process alter the dynamic processes that drugs undergo to produce therapeutic effects. These changes involve the activities of pharmacokinetics (what the body does with the drug) and pharmacodynamics (what the drug does to the body). While all older adults will experience aging changes, the timing and extent will vary individually and are driven by biological mechanisms unique to the person, not chronological aging (Khan et al., 2019; Tam, 2016). Because of this individual response, close monitoring is required when prescribing pharmacotherapy for older adults.

Absorption

Absorption is the least affected pharmacokinetic change in older adults. Individual factors such as concurrent consumption of over-the-counter (OTC) drugs, including antacids, laxatives, and supplements, may alter the gastric pH, resulting in a less-favorable environment for the absorption of certain drugs. Calcium supplements or calcium-based antacids interfere with the absorption of iron products, whereas orange juice facilitates iron absorption—both by altering the acidity of the gastric pH. Some drugs are best absorbed when taken with food whereas others, such as levothyroxine, require an empty stomach for optimal absorption. Other factors in older adults that influence absorption include altered nutritional status and delayed gastric emptying, especially in those with diabetes (Andres et al., 2019; DiPiro et al., 2020; Katzung, 2021; Tam, 2016).

Distribution

Three physiological changes in older adults cause them to be more sensitive to the effects of drugs and more vulnerable to adverse reactions. Older adults generally have less lean body mass and more body fat; they have less total body water than younger adults. Serum albumin also tends to decline (Andres et al., 2019; DiPiro et al., 2020; Katzung, 2021). Body fat

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serves as a storage depot for lipophilic drugs, thus reducing the amount of circulating free drug available to act; this can also prolong the action of the drug as it is released over time. The decrease in lean body mass and total water volume cause hydrophilic drugs to be distributed in a smaller volume of water, so they are more concentrated than in younger adults. The decrease in serum albumin impedes the protein binding of drugs, so levels of free circulating drug are higher, intensifying the intended effect of the drug. Poor nutrition and dehydration also impact distribution.

Metabolism

The liver plays an important role in the biotransformation of many drugs. Whereas liver size is decreased in older adults, liver function tests are usually normal unless there is pathology such as hepatitis, liver cancer, nonalcoholic fatty liver disease (NAFLD), or cirrhosis—all of which affect drug metabolism (Katzung, 2021; Perumpail et al, 2017). Clinical studies suggest that certain drugs, including barbiturates, some benzodiazepines, and many psychotropics, are metabolized more slowly, prolonging their effect. Metabolism via the cytochrome P450 enzyme system is also less effective. Comorbid diseases affecting blood flow to the liver, such as heart failure, affect the ability of the hepatic system to metabolize drugs, as does severe malnutrition, which is common in older adults. Acetaminophen, an OTC analgesic, can cause severe liver injury and death when used in excess; this is important to note because many older adults use acetaminophen daily, and it is also contained in multiple cold and flu preparations, leading to unintentional overdose (Yan et al, 2018).

Elimination

The most profound pharmacokinetic change is reduced elimination of drugs. Most drugs are excreted in the urine via the renal system, although some are excreted in the feces via the biliary system and inhaled drugs via the lungs. Water-soluble drugs are excreted directly by the kidneys, and fat-soluble drugs are converted to water-soluble drugs by the liver first. Changes in kidney function begin in the fourth decade of life and continue to decline with each subsequent decade (Katzung, 2021). Therefore, by age 70 years an individual might reasonably have a 40% to 50% decrease in renal function, even in the absence of disease. These kidney function changes may prolong the half-lives of drugs. This is particularly important for drugs that are excreted unchanged in the urine and for drug categories known to be particularly nephrotoxic in older persons (e.g., radiocontrast materials, aminoglycosides, angiotensin-converting enzyme inhibitors, and NSAIDs). Drug accumulation resulting from decreased renal excretion is the most significant factor in adverse drug reactions in older adults (Triantafylidis et al., 2018). Serum creatinine is tied to lean muscle mass; because this muscle mass is significantly decreased in older adults, serum creatinine is not a valid indicator of renal function in older adults. Creatinine clearance should be used to evaluate kidney function in older adults when prescribing drugs (Andres et al., 2019; DiPiro, et al., 2020; Katzung, 2021).

Pharmacodynamics

Although some researchers believe that older adults are more "sensitive" to certain drugs, causing interactions between receptor and drug, evolving evidence shows that pharmacokinetic reactions and alterations in homeostatic mechanisms are responsible for these interactions. Drug responsiveness may vary depending on the patient's activity and stress levels and on the environment. For the most part, pharmacokinetic data from drug manufacturers demonstrates that older adults have higher plasma levels of a drug than younger adults, given the same dosage (Katzung, 2021), hence the directive to "start low, go slow" in prescribing for older adults. An exception to this is the blunted response of older adults to β-adrenoceptor agonists. Research continues in this area.

Adverse Drug Reactions

Studies have shown that adverse drug reactions (ADRs) are more common in older adults with polypharmacy (Scott et al., 2015). Multimorbidity, changes in pharmacokinetics, frailty, poor adherence to prescribed drug regime, and self-prescribing also contribute to ADRs (Zazzara et al., 2021). Some of the most frequent drugs implicated in ADRs include anticoagulants, antiplatelets, insulins, digoxin, oral hypoglycemics, NSAIDs, anti-epileptic agents, psychotropics, antipsychotics, diuretics, antibiotics, and drugs with anticholinergic activity (Pazan & Wehling, 2020). ADRs account for a significant number of emergency department visits by older adults worldwide, often requiring hospitalization. Failure to accurately diagnose an ADR can result in a prescribing cascade, where another drug is ordered to treat the side effect of one drug or the ADR, or the ADR is mistakenly diagnosed as another illness to be treated (Katzung, 2021). Providers treating older adults with polypharmacy need to have a high level of suspicion for ADRs when new symptoms present. Use of brown bag medication reviews, electronic medical record software alerts, and comprehensive and holistic geriatric assessment are helpful in preventing ADRs in community-based settings. Medication reconciliation upon discharge can detect any PIMs and correct them prior to hospital discharge; failure to do this can result in further ADRs after discharge (Weir et al., 2020).

COMPLEMENTARY AND ALTERNATIVE REMEDIES

Supplements including complementary and alternative remedies (CAM) are frequently implicated in ADRs in older adults. St. John's wort is one of the most used supplements, and studies have found some efficacy when it's taken for mild depression. However, it interacts with several other drugs, including warfarin, selective serotonin reuptake inhibitors (SSRIs [potential for serotonin syndrome]), benzodiazepines, statins, contraceptives, cyclosporine, and multiple drugs metabolized by the CYP450 enzyme system (Davies & O'Mahony, 2015; National Center for Complementary and Integrated Health [NCCIH], 2020).

Ginkgo is used for memory issues; it interacts with warfarin, heparin, and NSAIDs, leading to increased bleeding tendencies. Kava is used for anxiety. Kava interacts with dopamine agonists and antagonists as well as central nervous system (CNS) depressants. Valerian is used for insomnia; there are multiple drug-drug interactions, particularly with benzodiazepines, barbiturates, opioids, and other CNS drugs (Davies & O'Mahony, 2015; NCCIH, 2020). These are only a few complementary and alternative remedies, but clearly they are not benign substances, and their risk of drug-drug interaction is high. It is essential to elicit information on whether the older

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adult patient is taking any CAM or other OTC drugs during the initial encounter and all subsequent ones.

SEROTONIN SYNDROME

Serotonin syndrome is a serious, sometimes fatal ADR that occurs when two or more drugs with serotonergic activity are prescribed simultaneously or in such close succession that the initial drug has not been eliminated from the body (Scotton et al., 2019; Zazzara et al., 2021). A wide variety of drugs are potentially impacted including SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), monoamine oxidase inhibitors (MAOIs), tricyclic antidepressants (TCAs), antihistamines, drugs of abuse, opioids, atypical antipsychotics, dietary and herbal supplements, and cold remedies (Scotton et al., 2019). Symptoms focus on three areas: altered mental status, ranging from insomnia, anxiety, and agitation to confusion; neuromuscular, including hyperreflexia, tremor, sustained clonus to rigidity with respiratory failure; and autonomic system from nausea, diarrhea, tachycardia, and hypertension to severe hyperthermia (Scotton et al., 2019). The combination of drugs along with altered pharmacokinetics in older adults are contributory factors; clinicians need to be alert to the possibility of serotonin syndrome when prescribing psychotropic drugs.

TARDIVE DYSKINESIA

Tardive dyskinesia (TD) is another ADR seen primarily with dopaminergic antagonist drugs, including first- and second-generation antipsychotic drugs and some gastrointestinal motility agents, usually after long-term use of these agents. Symptoms manifest as involuntary facial grimace and abnormal movements of the lips, tongue, face, and trunk. They are commonly seen in older adults, particularly females, with a history of schizophrenia, bipolar disorder, or schizoaffective disorder who have been prescribed dopamine antagonist agents. Symptoms are also seen less frequently in older patients with diabetes who are on metoclopramide for gastrointestinal dysmotility (Brasic et al., 2018). Best practices include patient education and consent prior to prescribing, prescribing the lowest possible dose that is effective, and considering alternative neuroleptics if symptoms of TD manifest. In many cases it is irreversible; however, changing to clozapine can decrease symptoms. Treatment of symptoms with valbenazine or botulinum toxin is successful in modulating symptoms in some cases (Caroff, 2020).

DRUG-INDUCED LUPUS ERYTHEMATOSUS AND DRUG-INDUCED SUBACUTE CUTANEOUS LUPUS ERYTHEMATOSUS

Drug-induced lupus erythematosus (DILE) and drug-induced subacute cutaneous lupus erythematosus (DSCLE) are iatrogenic illnesses occurring due to consumption of specific drugs over an extended timeline, usually years. DILE is an autoimmune disorder like systemic lupus erythematosus (SLE); however, it does not usually result in organ damage. Once the suspect drug is discontinued, DILE usually resolves within 6 months. Hydralazine, used in hypertension management, and procainamide, an antidysrhythmic are considered high risk drugs for DILE, with isoniazid as medium risk (He & Sawalha, 2018); the use of hydralazine and procainamide have declined as more efficacious drugs have been introduced. More recently, anti-tumor necrosis factor drugs (anti-TNF) used for rheumatoid arthritis, psoriatic arthritis, and inflammatory bowel disease have been implicated in DILE (He & Sawalha, 2018; Pan et al., 2021; Vaglio et al., 2018). DILE tends to produce higher autoimmune antibodies, particularly anti-nuclear antibodies (ANA), than known autoimmune diseases (Ferro et al., 2021; He & Sawalha, 2018; Pan et al., 2021; Vaglio et al., 2018; Yoshikawa et al., 2020). Symptoms of DILE include myalgia and arthralgia, sometimes with joint swelling, serositis, and fatigue. Proton pump inhibitors (PPIs), anti-TNF, chemotherapeutic agents, thiazide diuretics, anti-epileptics, terfenabine, calcium channel blockers (CCBs), and angiotensin-converting enzyme inhibitors (ACE-I) have resulted in DSCLE at lower levels than the DILE agents. Older adults are the primary patient population who are prescribed most of these drugs, so clinicians need to maintain a level of awareness about DILE and DSCLE (He & Sawalha, 2018; Pan et al., 2021; Vaglio et al., 2018; Yoshikawa et al., 2021).

ANTICHOLINERGIC BURDEN

The term *anticholinergic* refers to a wide variety of drugs that inhibit the action of the neurotransmitter acetylcholine, preventing it from binding to receptors on specific nerve cells, centrally and peripherally. As a result of this, involuntary muscle movement, mucus secretion, and digestion are reduced. Anticholinergic drugs are used therapeutically by older adults in the treatment of chronic obstructive pulmonary disease (COPD), asthma, overactive bladder, urinary incontinence, depression, psychosis, allergic rhinitis, Parkinson's disease, and gastrointestinal (GI) dysmotility and are given during surgery (Egberts et al., 2021; Green et al., 2019; Lisibach et al., 2021; O'Donnell et al., 2017; Stewart et al., 2021). Adverse effects of anticholinergic activity in drugs include dry mouth, dry eyes, constipation, blurred vision, urinary retention, heat intolerance, decreased sweating, cognitive impairment, delirium, confusion, increased heart rate, drowsiness, and dizziness (O'Donnell et al., 2017). A combination of factors, including altered pharmacokinetics in older adults, dosing and number of drugs with anticholinergic activity used by older adults, and extent of anticholinergic drug properties, results in an anticholinergic burden for many older adults. Several instruments have been developed by researchers to assess and quantify this anticholinergic burden (Egberts et al., 2021; Green et al., 2019; Lisibach et al., 2021; O'Donnell et al., 2017; Stewart et al., 2021); however, translation to clinical use is challenging. Drugs with strong anticholinergic qualities should be avoided or minimized in older adults due to safety (falls, cognitive changes), adverse effects, and quality of life issues. The Beers List and STOPP/START are two tools that recommend avoidance of anticholinergic drugs and list specific drugs with high anticholinergic activity. Two drugs frequently encountered with older adults include diphenhydramine (Benadryl®) and oxybutynin (Detrol®).

TOOLS TO ASSIST PROVIDERS TO AVOID PIMS AND POLYPHARMACY

As awareness of the dangers of polypharmacy evolve, the number of tools to prevent or alleviate it are proliferating. Several of the tools are focused on deprescribing. Two of the most widely used tools include the STOPP/START, Version 2 and the 2019

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BEERS list (American Geriatrics Society [AGS] Expert Panel, 2019; O'Mahony et al., 2015). STOPP/START (O'Mahony et al., 2015) is a tool designed to detect prescribing of PIMs. This screening tool of older persons' potentially inappropriate prescriptions (STOPP) consists of 80 clinically important criteria that relate to PIMs and can contribute to hospitalization for ADRs, including a brief explanation of each. This is used in conjunction with the screening tool to alert doctors to right treatment (START), which contains 34 criteria, supported by evidence, to remind prescribers to consider certain drugs that are appropriate for specific conditions but may be omitted. The expansion of the original STOPP/START added criteria on antiplatelet/anticoagulant drugs, drugs increasing anticholinergic burden, drugs impacting renal function, vaccines, analgesics, and urogenital drugs (Earl et al., 2020).

The Beers Criteria® (AGS Expert Panel, 2019) lists PIMs to be avoided in older adults; they are listed by drug category and by diagnosis. The 2019 update has several important revisions. Important additions among the nearly 70 modifications to the 2015 AGS Beers Criteria® were new medications, clarifications of criteria language and rationale, and the addition of selected drug-drug interactions. There is an additional article from the 2015 update (Hanlon et al., 2015) that details potential alternative drugs to those listed in the Beers Criteria®, which can be safely used in older adults. This is recommended to be used along with the 2019 update. The 2019 revisions include holistic information on nonpharmacological measures that are effective for specific conditions in older adults. The Beers Criteria® is not appropriate for patients on palliative care or hospice (AGS Expert Panel, 2019).

The STOPP/START and the Beers Criteria® are both valuable tools for prescribers, but they are not meant to be mandates for prescribing. Clinical judgment, knowledge of the patient who has the disease, clinician and patient shared goals, risk–benefit considerations, and quality of life all factor into decision making for individual patients. There may be times when drugs on these lists need to be prescribed; however, this should be done with full awareness of the aforementioned factors and the need for monitoring. Additional tools for deprescribing are listed in Table 21-1.

PREVENTING POLYPHARMACY/ ADDRESSING POLYPHARMACY

One of the first requirements for clinicians in preventing polypharmacy is awareness of the problem. The Centers for Medicare and Medicaid (CMS) is permitting longer visit times with patients; this extra time can help providers carefully review and discuss the patient's health conditions and medications. Goals of care should be jointly identified and agreed upon by the patient and the provider; doing so will drive the plan of care, which should be holistic and evidence-based and include lifestyle and other nonpharmaceutical interventions as well as pharmacotherapy (AGS Expert Panel, 2012). Once the goals are established, medications are reviewed and discussed, including how they "fit" with the goals, and then a plan to meet the goals is devised. Communication with any specialty providers is essential for clarity and consistency. Programs such as the patient-centered health-care home

TABLE 21-1 Deprescribing Tools

RESOURCE	DESCRIPTION
Choosing Wisely https://www.choosingwisely.org/	A campaign from the American Board of Internal Medicine encouraging consumers and clinicians to think carefully and avoid unnecessary tests and procedures
Fit for the Aged (FORTA)	Designed by a pharmacy professor from Germany, provides a scheme for evaluating drug fitness for older adults (Wehling, 2016)
The American Geriatrics Society's Guiding Principles for the Care of Older Adults with Multimorbidity	Offers a comprehensive and evidence-based guide for the management of these older adults (AGS Expert Panel, 2012; Reeve, 2020).
Deprescribing.org https://deprescribing.org	Canadian deprescribing resources
Medstopper https://medstopper.com	
PrescQIPP https://www.prescqipp.info/our-resources/webkits/polypharmacy-and-deprescribing	Webkit from a community interest company based in England and Wales that focuses on medication optimization
Screening Tool of Older Persons Prescriptions in Frail Adults with Limited Life Expectancy (STOPPFrail) https://www.sunderlandccg.nhs.uk/wp-content/uploads/2018/11/Stoppfrail-v1.pdf	Criteria for potentially inappropriate medication use in this patient population published by the City Hospitals of Sunderland, United Kingdom
Managing Medicines https://www.primaryhealthtas.com.au/for-health-professionals/programs/managing-medicines/	Deprescribing resources from Tasmania, Australia

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(medical home) or the 4 Ms (mentation, medication, mobility, what matters) are helpful in providing structure (Fulmer, 2018). Staff and patients/families should be educated about the initiative, including the need to elicit/disclose all OTC, supplements, herbal preparations, and recreational drugs when interviewing for medication history. At every visit, medications should be reviewed and updated. The following script is helpful:

- "I'm going to review your medications as we have them on your chart. As I go through each one, please confirm or let me know if it has changed. If there are any additions—vitamins, supplements, herbal preparations, or anything that you use from the pharmacy without a prescription—please let me know."
- "Are there any medications that you have stopped taking?"
- "Are you taking your medications as ordered?"
- "Is there anything that you want to discuss about your medications?"

The Medicare Annual Wellness Visit (AWV) or annual physical examination is also an opportunity to revisit goals of care and medications.

Although some hospitals have medication reconciliation with a pharmacist prior to discharge, hospitalized patients should be seen within 48 hours of discharge to review discharge instructions and clarify medications to be taken. Encourage patients to bring in any drugs that they were taking prior to hospitalization to this appointment. A study by Weir et al. (2020) found that one out of two hospitalized older adults were discharged on at least one PIM, leading to increased risk of ADR and rehospitalization. It is not uncommon for older adults to misunderstand or misplace discharge instructions and resume taking "at home" medications, which might have been responsible for their hospitalization. Transition of care visits or calls by nursing can identify and intervene to prevent PIMs and decrease the risk of rehospitalization (Tomlinson et al., 2020).

Research in the areas of primary care delivery at home (Schneider et al., 2021) and in long-term care (Jordan et al., 2021) demonstrate that polypharmacy is rampant, resulting in poor quality of care, increased risk of ADRs, and hospitalization in some of the frailest older adults. The same strategies being used in primary care to address polypharmacy are available to providers and staff, but there is a strong need for education to increase awareness of the problem and potential solutions. In long-term care, consistency in provider and care staff contributes to person-centered care and promotes trust in patients and family members (Jordan et al., 2019; Jordan et al., 2021).

Deprescribing and Appropriate Prescribing

Deprescribing is one step in the continuum of good medication management. It is the systematic process of reducing or discontinuing a medication, initiated by a health-care professional in conjunction with the patient/family within the context of polypharmacy or PIM use. The goal of deprescribing is to optimize medication management and improve patient outcomes, considering patient preferences, safety, efficacy, and principles of multimorbidity. Presently there is global agreement about the need to deprescribe, but efforts have fallen short of demonstrating improved patient outcomes (Baumgartner et al., 2020). Deprescribing is a proactive, holistic endeavor that goes beyond the usual patient encounter and challenges clinical inertia. Health-care provider and the patient/family come together to discuss the patient's health trajectory and goals of care in the context of medication management. Scott et al. (2015) outline a 5-step process to deprescribing:

1. **Review all medications.** The initial step is review of all medications, including those prescribed by any prescriber, OTC drugs used on a frequent basis, herbal remedies, and dietary supplements. Recreational drugs and alcohol use should also be included because they impact the total picture. Medication reconciliation can be accomplished by the provider, pharmacist, nurse, or trained medical assistant. For outpatient visits, the "brown bag" review is frequently used. It is important to confirm what medications the patient is taking and, if there is nonadherence, to discuss the reason for nonadherence. Issues such as prohibitive costs of medications, side effects, pill burden, and misunderstanding about the rationale or purpose of a medication can be discussed at this point. Alcohol misuse or dependency on recreational drugs needs to be addressed.
2. **Assess ADR risks from individual medications.** Having all medications and related substances together facilitates the identification of drug-drug, drug-disease, or patient-related factors that can contribute to ADR risk. Using a deprescribing tool such as the Beers Criteria® or STOPP/START facilitates the identification of PIMs currently being used by the patient (Earl et. al., 2020). Is there a risk for falls related to a specific medication? What is the patient's functional and cognitive status? How complex is the medication regime? (Gazarin et al., 2020; Krishnaswami et al., 2019; Scott et al., 2015).
3. **Evaluate each drug's potential for elimination.** Begin by obtaining input from the patient/family because their commitment is critical to successful implementation. Is there a drug with no compelling indication? Using a drug/disease/indication table can be helpful in determining this—long-term use of PPIs is one example. Is there a drug prescribed for symptom control that is ineffective or no longer needed? Is there more than one drug ordered for the same indication? Is there a drug that is cost prohibitive or requires multiple daily doses? What is the anticholinergic drug burden for the patient, and can that be reduced (Scott et al., 2015)? Best practice is to discontinue one drug at a time.
4. **Prioritize which drug needs to be reduced or stopped.** Consultation with patient/family is essential to determine the drug and timeline for deprescribing. Patient/family education is important so that there is no misunderstanding about the rationale for deprescribing. If there is no compelling indication, start with a drug that is unlikely to cause adverse effects if deprescribed. In some cases, starting with dose reduction is prudent, then evaluating.
5. **Discontinue the drug and institute a monitoring plan.** Once the drug is stopped, instruct the patient/family to call with any concerns or changes, just as

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you would when making any change in medication regime for cause; for example, stopping an antihypertensive in a patient who is normotensive and experiencing dizziness. If possible, schedule a brief follow-up call in 7 to 10 days to reevaluate. For patients in long-term care settings, include health-care personnel in the plan and monitoring (Jordan et al., 2021).

Deprescribing at end of life is a special situation, sometimes referred to as deintensification (Curtin et al., 2020; Niznik et al., 2020; Ouslander, 2020; Thompson et al., 2019). The goal is to reduce or eliminate drugs that offer no therapeutic advantage at end of life while considering the individual person. Anticholinesterase inhibitors that have proven ineffective, statins, intensive treatment for diabetes that can lead to hypoglycemia, tight control of hypertension that can cause syncope, and anticoagulants that can lead to serious bleeding if the patient falls are frequently targeted in patients with a terminal illness. Close communication with family and staff is important to emphasize the rationale for deprescribing and to reassure that it will alleviate potential ADRs and improve patient quality of life at end of life (Ouslander, 2020).

Barriers to deprescribing include clinical inertia, provider time constraints, coordination of care with multiple prescribers, and resistance from patients or family members (AlRasheed et al., 2018; Jungo et al., 2021). However, a recent international study of family physicians in 31 countries demonstrated a willingness to deprescribe in the oldest-old and those with limited function or frailty (Jungo et al., 2021). Several studies of patients determined that they were receptive to having drugs deprescribed if they trusted their primary care provider (Achterhof et al., 2020; Holmes & Todd, 2017; Linsky et al., 2019). Interprofessional collaboration, including pharmacists and nurses, can support patients and prescribers in deprescribing.

Appropriate prescribing for older adults should be parsimonious in nature, person-centered and focused on patient goals for care, grounded in evidence, efficacious, cost-effective, safe, and easy to self-administer with minimal side effects. Tools such as the American Geriatrics Society's *Care for Patients with Multimorbidity* (AGS Expert Panel, 2012) provide guidance for busy clinicians about appropriate prescribing for older adults.

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CHAPTER 22

Chronic Illness and the APRN

Evelyn Duffy

Evidence-based management of common chronic diseases is an essential skill for advanced practice registered nurses (APRNs) in order to provide quality care for patients. It is also essential to understand and manage complex challenges of older adults with chronic disease. This chapter reviews the effect of chronic illness on older patients, their families, providers, and the overall health-care system. Specific topics include the demographics of chronic disease, lifestyle risk factors, the significance of multiple chronic conditions (MCCs), new models of care that reorganize health care to improve outcomes for complex patients with chronic disease, reimbursement mechanisms that support chronic disease, and the role of the APRN in chronic illness.

DEFINITIONS OF CHRONIC DISEASE AND CHRONIC ILLNESS

The literature does not support a single uniform definition for chronic disease, but the concept of chronicity includes the knowledge that patients experience persistent and recurring health problems. Definitions of chronic disease also reflect the pathophysiology of disease and, more importantly, consider the meaning of chronic illness and the experience of the patient, family, and provider as they struggle to cope with the range of mildly complicated to extreme challenges. A condition is defined as chronic if it lasts 1 year or more, requires ongoing medical attention, limits independent living, social interactions, or basic activities of daily living (ADLs) (Gulley et al., 2018).

DEMOGRAPHICS OF CHRONIC ILLNESS

Increased life expectancy and health-care advances are the main reasons for the overwhelming increase in numbers of patients with chronic illness. In 2019 the population of individuals aged 65 years and older was 54.1 million, 30 million women and 24.1 million men, which represents 16% of the population. That number is projected to increase to 21.7% of the population in 2040 (Administration on Aging (AOA), 2021).

Most older Americans have at least one chronic condition, and many have multiple chronic conditions (AOA, 2021). In 2019 the most common chronic diseases in the population age 65 years and older include arthritis (48%), cardiac disease (14%), myocardial infarction (9%), angina (4%), chronic lung diseases (10%), stroke (9%), and diagnosed and undiagnosed diabetes (29%). From 2015 to 2018 82% of men and 86% of women aged 75 years and older had hypertension (AOA, 2021).

More than 2/3 of all deaths in the United States are caused by one or more of these five chronic conditions: heart disease, cancer, stroke, chronic obstructive pulmonary disease (COPD), and diabetes (Raghupathi & Raghupathi, 2018). Heart disease is the number one cause of death among both men and women.

Notable Changes in Incidence and Prevalence of Chronic Disease

From 2008 to 2018, coronary heart disease (CHD) annual deaths declined by 27.9%, but the burden of disease remains high (Virani et al., 2021). The prevalence of diabetes in the United States remains high, affecting 34.2 million or 10.5% of the population—diagnosed and undiagnosed (ADA, 2022). The prevalence of chronic kidney disease (CKD) in the United States has stabilized in recent years (Vart et al., 2020).

Multiple studies indicate that the risk of Alzheimer's disease and other dementias in the United States and other developed Western countries may have declined in the past 25 years. That change is hypothesized to be due to increasing levels of education and improved control of cardiovascular risk factors. The total number of people in the United States with Alzheimer's disease and other dementias is still, however, expected to continue to increase dramatically because of the population's aging population. By 2050 the number of people aged 65 years and older with Alzheimer's disease is estimated to reach 13.8 million compared to the 5.8 million in 2020 (2020 Alzheimer's Disease Facts and Figures, 2020). Whereas between 2000 and 2018 deaths from heart disease, stroke, and HIV declined, deaths from Alzheimer's disease increased 146.2%.

The requirements of care for specific chronic diseases, such as heart failure (HF) or HIV, have changed dramatically

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in the last two decades. HIV has evolved from an untreatable and usually fatal disease to a chronic illness with a life expectancy of several decades. The prevalence of HF continues to rise with an estimated 6 million Americans diagnosed. Prevalence is higher in men than in women. Prevalence is expected to increase by 46% from 2012 to 2030 (Virani et al., 2021). From age 45 through 95 the overall lifetime risk for HF ranges from 20% to 45%. Most patients with HF are very old, with increasing debility and very complex health-care regimens.

Health Risk Behaviors

According to the Centers for Disease Control and Prevention (CDC), four health risk behaviors are responsible for the majority of chronic disease and death, including tobacco use, poor nutrition, lack of physical activity, and excessive use of alcohol. The American Heart Association adds health factors such as cholesterol, blood pressure, and glucose control. The prevalence of cigarette smoking is down; in 2019, 14% of adults were still smoking cigarettes (about 34.1 million adults). In those aged 65 and older the prevalence is much lower, 8.4% (Virani et al., 2021). The Surgeon General reported that in 2020 more than 480,000 Americans died as a result of cigarette smoking and more than 41,000 died due to secondhand smoke exposure (Virani et al., 2021).

Binge or heavy drinking can lead to high-risk sexual behavior, unintentional injuries (e.g., motor vehicle crashes), falls, violence, and suicide. Excessive alcohol consumption can also lead to development of high blood pressure, heart disease, stroke, liver disease, several cancers, and dementia. (CDC, 2022a).

The U.S. prevalence of obesity in 2017 to 2018 was 41.9% (CDC, 2022b). This represented an increase from the prevalence in 1999 to 2000 of 30.5%. Individuals who are obese can suffer serious health problems, face discrimination, and have a reduced life expectancy. The greater the body mass index (BMI) (and waist circumference), the greater the risk of heart disease, stroke, type 2 diabetes, and certain cancers (CDC Adult Obesity Facts, 2021). They are also at risk for sleep apnea, osteoarthritis, gallbladder disease, respiratory problems, and depression. It is known that 85.2% of people with type 2 diabetes are overweight or obese (American Diabetes Association (ADA), 2022). There is strong evidence that modest weight loss (5% to 15%) can greatly reduce the risk of these conditions.

Prevention

The goals of national health promotion and disease prevention are to prevent or delay disease, decrease premature mortality, and improve health-related quality of life. Modification of behavioral risk factors and using preventive services such as screenings and immunizations can substantially reduce morbidity and mortality.

The 2010 passage of the Patient Protection and Affordable Care Act (PPACA), or the ACA, increased the opportunities for disease prevention. Ongoing efforts are aimed at redesigning the health system to support overall population health. One successful prevention initiative removed out-of-pocket costs and increased access to evidence-based clinical preventive services recommended by the U.S. Preventive Services Task Force (USPSTF). Results have demonstrated increased use of those preventive services, including tobacco counseling, cervical cancer screenings, and colorectal cancer screenings (Koh et al., 2016).

In the United States, diabetes affects 34.2 million or 10.5% of the population and prevalence is projected to increase approximately twofold for all U.S. adults (ages 18 to 79 years) by 2050, if current trends continue (CDC, 2020). Another successful intervention is the Centers for Medicare and Medicaid Services (CMS) Diabetes Prevention Program (DPP), an evidence-based intervention targeted to individuals with prediabetes, with the primary goal of weight loss and behavior change. The DPP is public–private partnership that uses lifestyle coaches to deliver evidence-based counseling interventions to Medicare beneficiaries with prediabetes. The results of the program demonstrated that participants lost at least a modest amount of weight through dietary changes and increased physical activity, which reduced their chances of developing diabetes. A list of all organizations recognized to deliver the evidence-based programs is available online at https://dprp.cdc.gov/Registry. There are more than 2,089 options.

MULTIPLE CHRONIC CONDITIONS

The U.S. health system was created to manage and pay for acute illness with a focus on one disease or health-related problem at a time. As the number of chronic conditions in an individual increases, there is a parallel risk for poor outcomes, often related to the unintended consequences of a single-disease approach. Those outcomes include poor functional status, unnecessary hospitalization, adverse drug events, conflicting medical advice from multiple providers, and even death. There is an increasing awareness that the health system and health-care providers require a new paradigm of care that recognizes patients with MCCs. To explore the public health problem of MCCs, the USDHHS created the Multiple Chronic Conditions Interagency Workgroup in 2008, and in 2010 they published the *Multiple Chronic Conditions: A Strategic Framework*. One of the main goals of the framework is to generate research to bridge knowledge gaps about individuals with MCCs (USDHHS, 2010). This work has not been updated.

Data from the 2018 National Health Interview Survey (NHIS) were used to generate estimates of MCCs for U.S. adults. Over half, 51.8% (129 million), of noninstitutionalized U.S. adults have at least 1 of the 10 most common chronic conditions, which include hypertension, CHD, stroke, diabetes, cancer, arthritis, hepatitis, CKD, asthma, or COPD. In addition, one in four adults (27.2% [68 million]) had more than two or more chronic conditions (Boersma et al., 2020). There was a marked disparity among those aged 65 and older who were on both Medicare and Medicaid and those on Medicare only. The "dual eligibles" on both Medicare and Medicaid had the highest prevalence—76.9% compared to 58.5% of those on Medicare alone (Boersma et al., 2020). The numbers from the NHIS do not include mental health issues or institutionalized older adults, which would substantially increase the estimates.

MCCs can contribute to frailty and disability, and older adults who are frail or disabled typically have MCCs. Functional limitations can often complicate access to health

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care, interfere with self-management, necessitate reliance on caregivers, and produce high levels of spending. Older adults with MCCs often require long-term services and supports (LTSS). LTSS include the broad range of paid and unpaid medical and personal care assistance that people may need when they cannot complete self-care tasks because of aging, chronic illness, or disability (Lewis et al., 2018). The 2017 report on LTSS expenditures found great variation from state to state (Eiken et al., 2017). They also note that the growth in expenditures was almost completely due to the increase in cost of home- and community-based services with institutional service expenditures unchanged. There is a growing trend to use managed care plans to provide LTSS (Lewis et al., 2018). Medicaid spending for managed LTSS has more than doubled from 2012 to 2015.

With the potential for continued growth of older adults requiring LTSS, it is especially important to increase knowledge about the high-risk factors related to MCCs that can increase costs or the risk of hospitalizations.

Other high-risk individuals with MCC include those with serious mental illness or behavioral health problems. Co-occurrence of mental and medical disorders is a disabling combination and occurs in approximately 30% of individuals with MCCs. Those with depression and a chronic medical condition are more likely to experience greater severity of both conditions. Substance use in older adults, while lower than in younger adults, is complicated by the changes with aging that make them more likely to experience adverse events (Lehmann & Fingerhood, 2018). They are more likely to have MCC and be on multiple medications that can interact with alcohol and other substances. Many of the common red flags such as difficulty at work or driving issues are not relevant in the older adult (Lehmann & Fingerhood, 2018).

Self-Care Management

Patients coping with MCCs are especially vulnerable to a sense of burden with their treatment regimen because they are required to engage in a complex array of self-care activities on a daily basis. Treatment burden is the impact on patient functioning and well-being that results from the time and energy required of the patient and their caregiver to accomplish the work required to implement treatment plans, health monitoring, and diet and exercise requirements (Sheehan et al., 2019). That work might include medication management, self-monitoring of blood pressure or blood sugars, visits to providers, laboratory and radiology testing, and lifestyle changes. Treatment burden may add to the difficulties already imposed by the disease or diseases themselves. It is unique to each patient but may add to the physical and psychosocial stressors resulting from the chronic condition or conditions themselves (Sheehan et al., 2019)

Many chronic conditions share common challenges in self-care management. Most require daily management of symptoms, complex medication regimens, nutrition, diet, and exercise. APRNs should discuss with patients the ways in which they are managing, or failing to manage, the chronic conditions in their everyday lives. The resulting person-centered care will allow plans to be put into place to minimize the burden by adjusting treatment to the unique constraints of the patient. As noted in Chapter 6, including the question of what matters most to the patient can help in creating of the person-centered care plan.

New models of care are essential to provide tools to improve self-management and quality support systems. The National Institute of Nursing Research (NINR) at the National Institutes of Health (NIH) has promoted self-management science as one of its core areas of research to improve and manage symptoms of acute and chronic illness (NINR, 2016). Two of the most successful and well-known self-management programs are the Arthritis Self-Management Program (ASMP), developed by Margaret Grey, and the Chronic Disease Self-Management Program (CDSMP), developed by Kate Lorig.

The two programs are supported by the evidence that they improve the quality of life of those who participate. They address topics including dealing with problems resulting from chronic disease; exercise; use of medications; communicating with family, friends, and health-care providers; nutrition; and how to evaluate new treatments (Stanford Medicine, 2016). Programs are held in the community, meet weekly for two-and-a-half hours for 6 weeks. Detailed information and a link to locate a program in your area are available at https://www.cdc.gov/arthritis/interventions/self_manage.htm.

Caregivers

As older adults become more functionally limited, caregivers become central members of the care team and play a major role in supporting the daily self-care management and maintaining the health and well-being of the care recipient. The Caregiving in the U.S. 2020 report identifies the continued increase in Americans providing unpaid care as our population ages. The estimated prevalence of caring for an adult aged 50 or older is 16.8% of the population, or 41.8 million people. The majority of caregivers are female (61%) and most care for a relative (89%) and 40% live with their care recipient. Caregivers report that those adults receiving care have more health and functional needs than what was reported in 2015 and there is increasing comorbidity with the average recipient having 1.7 chronic conditions. The typical care recipient is female (61%), with an average age of 50.1 years (National Alliance for Caregiving [NAC] & AARP, 2020).

Caregivers' tasks can include assistance with ADLs and instrumental ADLs (IADLs), medication and treatment management, monitoring signs and symptoms, or navigating health-care appointments and health-care systems. The demands of caregiving can create additional stress in the caregiver's life, commonly referred to as caregiver burden. Caregiver burden is associated with anxiety, depression, insomnia, poor self-care management, poor self-rated health, and greater mortality (NAC & AARP, 2020). Caregiver burden also directly affects decisions to place care recipients in long-term care facilities. About 40% of caregivers report high burden, 16% report moderate burden, and 43% report a relatively low burden (NAC & AARP, 2020).

Caregiving has traditionally been seen as a family obligation, but little attention has been paid to the type of formal support, guidance, and skills needed to perform caregiving. There are a few sporadic programs that provide educational support for caregivers. The Web site programsforelderly.com offers access to multiple resources to support the care of older adults that are available across the United States. Because prevalence of burden is not specific to stage of illness and is relatively stable over time, health-care teams should assess caregiver burden and refer burdened caregivers to supportive resources early in the course of chronic illness. Ongoing

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caregiver education should be provided by multiple members of the health-care team and should include caregiver involvement in decision making and guidance prior to any potential health-care crisis. The American Geriatrics Society in 2019 introduced their *Guiding Principles for Care of Older Adults with Multimorbidity* (Boyd et al., 2019). They emphasize the need to include the patient and caregiver in medical decision making; recognize the limitations of the evidence regarding the older adult population; frame management decisions in the context of harms, burdens, benefits, and prognosis; consider treatment complexity and feasibility; and use strategies for choosing therapies that optimize benefit, minimize harm, and enhance quality of life.

Health Literacy

The ability to use and correctly interpret health information is important for anyone with one or more chronic diseases. Health literacy involves using reading, writing, verbal, and numerical skills in order to obtain, process, and understand basic health information to make appropriate decisions (Samerski, 2019). Ninety million Americans are identified as having low health literacy, with more prevalence in those with lower socioeconomic status or less education, in older adults, in those with low English proficiency, and those on Medicaid (Hickey et al., 2018).

Research indicates that low health literacy contributes to a number of health-related problems, including a poor understanding about health conditions and services, the inability to provide self-care, difficulty understanding medication instructions, poor medication adherence, and low use of preventive services (Chen et al., 2018; Hickey et al, 2018). Individuals with limited health literacy also experience more negative outcomes. Due to the limited knowledge of their health problems, they make more medication errors, use more inpatient and emergency department care, and have worse overall health status and higher health-care costs (Chen et al., 2018).

Clinicians have trouble identifying patients with limited health literacy, so it is suggested that universal precautions are used regardless of the complexity of any information. Universal precautions defined in the AHRQ *Health Literacy Universal Precautions Toolkit,* 2nd edition include simplifying communication with and confirming comprehension for all patients, making the office environment and health-care system easier to navigate, and supporting any and all patient efforts to improve their health. Studies have shown that 40% to 80% of the medical information patients are told during office visits is forgotten immediately, and nearly half of the information retained is incorrect. The teach-back method is a way of checking understanding by asking patients to state in their own words what they need to know or do about their health. *Teach-back is a way to confirm that the provider has explained things in a manner that the patient understands* (Brega et al., 2015, p. 18).

ECONOMIC BURDEN OF CHRONIC DISEASE

Patients with MCC account for a disproportionate use and cost of care. They account for 64% of provider visits, 70% of inpatient stays, 83% of prescriptions, 71% of all health-care spending and 93% of Medicare spending (Bierman et al., 2021). Ninety percent of the $4.1 trillion in health-care spending in 2020 was for people with one or more chronic medical conditions (National Center for Chronic Disease Prevention and Health Promotion [NCCDPHP], 2021). Heart disease and stroke alone are costing $214 billion a year and $138 billion in lost job productivity. These statistics preceded the current COVID pandemic.

According to the CMS, Medicare spending for fee-for-service (FFS) beneficiaries in 2019 was 799.4 billion dollars. The one-third of beneficiaries with zero or one chronic condition accounted for only 6% of Medicare spending, whereas the 18% with six or more chronic conditions accounted for 54% of Medicare spending (Centers for Medicare and Medicaid Services (CMS), 2021). Per capita costs were highest for those with stroke, CKD, and chronic obstructive pulmonary disease.

Cost and complexity of care are greater for individuals with multiple chronic diseases, who account for 75% of overall health-care spending. Additional costs of chronic disease result from multiple acute care hospitalizations experienced by the seriously chronically ill population and readmission within 30 days. In 2010 the Hospital Readmission Reduction Program (HRRP) was established by the ACA. The program has been successful in reducing readmissions and lowering the cost of health care, including this vulnerable population (Gai & Pachamanova, 2019)

CHRONIC DISEASE IN UNDERREPRESENTED POPULATIONS

The older population in the United States continues to be more racially and ethnically diverse as the population of people of color grows. Underrepresented racial and ethnic populations have increased from 7.8 million in 2009 (20% of older adults) to 12.9 million in 2019 (24% of older adults) and are projected to increase to 27.7 million in 2040 (34% of older adults) (Administration for Community Living, 2021).

Chronic conditions can be more common or severe for some populations. Non-Hispanic Blacks are 50% more likely to have high blood pressure and with poorer control than are non-Hispanic Whites (CDC, 2017). Non-Hispanic Blacks are more likely to be aware of their hypertension and to have it treated, than are non-Hispanic Whites. Diagnosed diabetes is 77% higher among non-Hispanic Blacks, 66% higher among Hispanics, and 18% higher among Asians than among non-Hispanic Whites. Black women are twice as likely to be severely obese as almost every other group. Native Americans and Alaskan Natives are 60% more likely to be obese than non-Hispanic Whites (Reeves & Smith, 2020). As a result, life expectancy for non-Hispanic Blacks is 75.1 years, compared to 78.9 years for non-Hispanic Whites. However, the death rate for non-Hispanic blacks has declined 25% over the past 17 years. Hispanics, despite lower incomes and migrant patterns outlive non-Hispanic Whites by 3 years on average.

There are noticeable racial/ethnic differences in the prevalence of many chronic conditions and treatment for those illnesses. CKD is more common in non-Hispanic Black adults (16%) than non-Hispanic White adults (13%) (CDC, 2021c). The literature shows consistent disparities among Blacks and Hispanics compared to non-Hispanic Whites in the

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prevalence and incidence of Alzheimer's disease, mortality, participation in clinical trials, use of medications and other interventions, use of LTSS, and quality of care (Quiñones et al., 2020). Blacks have the highest death rate and shortest survival of any racial/ethnic group in the United States for most cancers, although the gap is closing, particularly for non-Hispanic Black men (Zavala et al., 2021).

FUNCTION AND FRAILTY

Aging is a highly variable process that leaves some older adults with strength and vitality, and others with increased vulnerability to illness, injury, and disease. That reduced physiological capacity contributes to the development of geriatric syndromes such as falls, delirium, and frailty (Leff et al., 2015). Consideration and documentation of geriatric syndromes and overall function is as important in the care of older adults with chronic disease as a medical diagnosis. ADLs and IADLs are used to measure functional status. ADLs are measures of functions that people perform daily and include feeding, bathing, dressing, grooming, toileting, ambulating, and transferring. IADLs are indicators of more complex functions required on a regular basis, including use of the telephone, shopping, housekeeping, laundry, transportation, management of medications, and handling of finances.

Older adults are often more concerned about the impact of their illness on daily function than they are about the specific diagnosis. Despite the importance of function to alert providers to changes in health or prognosis and to determine appropriate interventions, mobility and function are not routinely measured or monitored in clinical practice. It is important to systematically include mobility and functional assessment in clinical documentation.

Frailty is not synonymous with comorbidity or disability, but comorbidity is a risk factor for frailty, and disability is an outcome of frailty. Precise definition of frailty has been elusive (Junius-Walker et al., 2018). In their comprehensive literature review Junius-Walker and colleagues attempt to more clearly define the concept to allow for the development of policies and interventions. Frailty has evolved as a concept over the past decades and is now viewed from a more holistic perspective. Awareness of frailty will help to develop accurate assessments, help patients and families with anticipatory planning, and make appropriate decisions about interventions and treatment. From their systematic review they identified core concepts: vulnerability, genesis, characteristics, phenotype and adverse health-related outcomes. They (as cited in Junius-Walker et al., 2018) conclude that the WHO definition best reflects their core concepts: "*a progressive age-related decline in physiological systems that results in decreased reserves of intrinsic capacity, which confers extreme vulnerability to stressors and increases the risk of a range of adverse health outcomes*" (WHO, 2015, p. 63).

A screening tool for frailty, FRAIL, was developed by Dr. Fried in 2001. Aprahamian et al., (2017) conducted a study to compare the properties of the FRAIL with Fried's phenotype. They conclude that the FRAIL scale is time- and cost-effective in screening for frailty.

The FRAIL tool asks five screening questions about fatigue, walking, number of chronic diseases, and weight loss of more than 5% in 6 months to identify those at high risk of being frail. Those who answer yes to at least three of the screening questions are likely to be frail with a score of 1 or 2 considered a measure of prefrailty (Aprahamian et al., 2017). Identification of frailty in older adults is important because a likelihood of poor outcomes is very high. In frail older adults there is a higher frequency of primary care visits, home care and nursing home services, and a higher likelihood of rehospitalization and death (Junius-Walker et al., 2018).

EVIDENCE-BASED PRACTICE AND CHRONIC DISEASE

Available evidence to manage chronic disease is found within clinical practice guidelines (CPGs). Guidelines, however, are almost exclusively focused on one specific disease. It is essential to evaluate those guidelines to determine whether they are appropriate for frail, older adults with MCCs. There is wide diversity in the older adult population in life expectancy, functional status, and individual priorities and preferences related to health care. Those characteristics limit the use of specific disease-oriented models of care. Complex comorbid conditions and geriatric syndromes are common, and usual signs and symptoms, such as fatigue, may be due to one or several chronic diseases, problems, or syndromes, and require different or multiple interventions.

When CPGs have been evaluated for content that considers unique issues of complex older adults with multiple comorbidities, it has been determined that only a few CPGs address those issues. In 2019, Dent and associates published the *Physical Frailty: ICFSR International Clinical Practice Guidelines for Identification and Management*, and while focused on frailty, includes much of the content that has been identified as missing in less comprehensive CPG. Muth et al (2019) conducted a systematic review of eight guidelines that addressed managing multimorbidity and polypharmacy. The neglected content identified by both includes patient and caregiver concerns, setting clinical priorities based on life expectancy, managing expectations around prognosis, maintaining communication, and considering patient, provider, or system barriers to implementation (Dent et al., 2019; Muth et al., 2019).

Older adults with MCCs have poorer outcomes when treated according to disease-specific guidelines. Those negative outcomes may be due to decreased benefit from therapy directed at any one chronic disease, the presence of polypharmacy, or the increased likelihood that the high-risk older adult will have a poor response to any specific intervention. To improve decision making, clinicians require unique data about the frail older adults and alternative approaches that include patient and family values; communication and coordination with specialty providers, and other members of the team; and a restructured reimbursement system (Dent et al., 2019; Muth et al., 2019).

Experts continue to study the complex relationship between patients with MCCs and available evidence. To guide understanding about CPGs and MCCs, researchers developed a patient-centered and context-sensitive model of care called minimally disruptive medicine (MDM). MDM acknowledges the limitations of disease-centered treatment recommendations for patients with MCC. MDM suggests caveats to clinicians caring for complex patients. For example, following an evidence-based

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recommendation for a frail older adult with MCCs, especially when the recommendation is not strong, may do more harm than good (Trevena, 2018). Shared decision making and discussion regarding the burden of the treatment and the patient's ability to cope with the requirements address the need for a thoughtful approach to the application of the minimally disruptive medication approach.

LEGISLATION AND CHRONIC DISEASE

Accountable Care Organizations

The Patient Protection and Affordable Care Act included multiple payment and delivery system reforms with incentives for health systems to better manage the care of patients with chronic disease. Beginning in 2012, the law authorized Medicare to contract with accountable care organizations (ACOs) in a Medicare Shared Savings Program. ACOs provide financial incentives to improve the coordination and quality of care for Medicare beneficiaries while reducing costs. ACOs are groups of doctors, hospitals, and other health-care providers who come together voluntarily to give coordinated high-quality care to their Medicare patients. The primary goal of coordinated care is to ensure that patients with chronic disease receive quality care, while avoiding unnecessary duplication of services and preventing medical errors. When the ACO succeeds in delivering high-quality care and reduced spending, it will share in the savings it achieves (CMS, 2022a).

A key element of ACOs will relate to the effective discharge of patients from acute care settings and initiatives to reduce admissions. All members of the ACO are incentivized to coordinate care of patients across the continuum to achieve savings. In 2021 there are 512 Medicare ACOs serving over 12 million beneficiaries. They have demonstrated positive trends in savings, but with major variation in performance (Herrel et al., 2017). Organizations require time to create major transformation and determine new paths to affect positive changes in health-care delivery.

Hospital Readmission Reduction Program

A major provision of the ACA is the Hospital Readmissions Reduction Program (HRRP) that financially penalizes hospitals for excess readmissions within 30 days of discharge. The HRRP motivates hospitals to conduct interventions that reduce the likelihood of readmission and has drastically changed how hospitals manage complex patients at high risk for readmission (CMS, 2022a).

Before 2012, hospitals had little direct financial incentive to reduce readmission. The HRRP requires CMS to reduce payments to hospitals who experience excess readmissions. The HRRP initially targeted select diagnoses of HF, pneumonia, and acute myocardial infarction. In 2015, the additional diagnoses of COPD, total hip arthroplasty, and total knee arthroplasty were added (CMS, 2022a). As of 2015, penalties for excess hospitalizations increased to 3% of base payments by Medicare, and readmissions for these diagnoses are also treated as an indicator of the quality of a hospital's care and are publicly reported and available to consumers.

High rates of preventable hospitalizations and emergency department visits are still frequent poor outcomes. At least in part due to the financial incentives, the 30-day rehospitalization rates for Medicare beneficiaries decreased 7% from 2010 to 2016, from 18.3% to 17.1% (AHRQ, 2019). Many hospital readmissions are not preventable, but evidence and model programs are available to assist hospitals with system-wide changes that will decrease readmission rates. The HRRP has helped create collaborative relationships within hospitals, between medical institutions, and with surrounding communities that focus on improving the overall patient experience through hospitalization and post-discharge.

Patient-Centered Medical Home

The National Committee for Quality Assurance (NCQA) (2019) defined standards for the patient-centered medical home (PCMH), which reinforce the central components of primary care. Those core components include an ongoing relationship with a provider, person-centered care, enhanced access to care, coordinated care, quality and safety, and a payment structure. Additional requirements for PCMH designation include patient tracking and registry, a care management component, patient self-management support, advanced electronic communication (including electronic prescribing), and performance reporting and improvement. Outcome measures include patient and family satisfaction, decreased emergency department use, decreased hospitalization, improved health parameters (e.g., blood pressure, hemoglobin [Hb] A1c), provider satisfaction, decreased cost, improved preventive care, and patient language preference.

The 2019 Benefits of NCQA Patient-Centered Medical Home Recognition reported improved outcomes for PCMHs, including reduction in emergency department visits and hospitalizations, improved patient satisfaction, and increased use of measures such as recommended diabetes services, and decreased overall health-care costs (NCQA, 2019). APRNs are involved in PCMHs by providing primary care, care coordination, and health system navigation and serving as community team members.

TRANSITIONS OF CARE

Coordination of Care

Improving care coordination has been identified by payers and policymakers as a priority to improve quality and lower costs of health care. The National Quality Forum (2010) identified important performance measures of care coordination, including prevention of hospital admissions and readmissions, care transitions, the patient experience of care coordination, the importance of cultural and linguistically appropriate resources and services, and communication to support patient self-management. Others have identified continuity of care as an important measure of care coordination. The PCMH was developed in response to this identified need.

Transitional Care Models

Medicare's attention to preventing hospital readmissions places a high premium on care continuity and coordination, with a central focus on transitions across providers and sites of care. Transitional care is defined as a set of actions necessary to ensure the coordination and continuity of care as patients transfer between different sites of care or from one level of care to another within the same site. Health-care

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services for older adults exist on a complex continuum that includes primary care, acute care, post-acute care, long-term care, home health care, and community-based services. Each of the care settings along the continuum serves a specific purpose and meets the needs of specific patients, but also generates health-care transitions that occur as patients move across multiple providers, payers, and settings for different acute episodes or for the same episode of care. Efforts to improve care transitions are intended to improve patient safety and quality of care; decrease significant burden on patients, families, and caregivers; and decrease costs to patients, providers, and payers.

The transitional care model (TCM) defines transitional care as a "broad range of time-limited services designed to ensure health-care continuity, avoid preventable poor outcomes among at-risk populations, and promote the safe and timely transfer of patients from one level of care to another or from one type of setting to another." Transitional care functions in a complementary role to other health services, is time-limited, and has a specific focus on managing adverse outcomes of transitions (Naylor, et al., 2011, p. 747).

As a response to challenges facing the health-care system, APRNs were the first to develop and study transitional care, an empirically supported method to reduce readmissions post-hospitalization. The TCM has consistently shown reductions in readmissions, emergency department visits, and costs of care (Naylor et al., 2018).

Technology plays a significant role in communication and coordination of care to improve access to care and quality, especially with the implementation of electronic medical records (EMRs). Because hospital readmission is a common and costly problem and a target of recent health-care system reform, efforts to use technology to advance knowledge of high-risk patients and standardize evidence-based discharge information are priorities. The ability for timely follow-up in primary care after hospitalization motivated CMS to add financial incentive to provide for that follow-up. Reimbursement is now provided for the follow-up after hospital or post-acute care discharge.

Palliative Care

Chronic illnesses are marked by fluctuations over time, with the potential for worsening symptoms, decrease in function, and caregiver burden. Palliative care consists of specialized care for people living with serious illness. It focuses on providing relief from the symptoms and the stress of the serious illness, with the goal is to improve quality of life for both the patient and the family. Palliative care can serve as an intervention to manage chronic illness, not just at the end of life, but also in the early phases of illness to support patients and caregivers. Patients who receive early palliative care show significant improvements in quality of life and mood and may survive longer (Zhuang et al, 2018).

The Center to Advance Palliative Care emphasizes that palliative care is commonly used among people living with serious, complex, and chronic illnesses. The most common clinical conditions relevant to this discussion include cancer, congestive HF, COPD, and CKD and/or end-stage renal disease. Palliative care should be considered for close to half (45%) of all Medicare beneficiaries who have four or more chronic conditions for which palliative care services may be clinically indicated. Palliative care is used to alleviate symptoms, either in combination with or instead of curative treatment. For a thorough discussion of palliative care, review Chapter 23.

Interprofessional Education and Interprofessional Teams

Prevention and management of complex older adults with chronic illness are best implemented by interdisciplinary teams in primary care and in most other sites of care. It is suggested that a larger interdisciplinary workforce is needed, and payment for primary care should reward practices that incorporate interdisciplinary teams. Interprofessional education (IPE) occurs when learners of two or more health and/or social care professions engage in learning with, from, and about each other to improve collaboration and the delivery of care (Institute of Medicine, 2015).

Researchers and educators continue to evaluate the impact of IPE on outcomes, including patient safety, patient and provider satisfaction, quality of care, health promotion, population health, and the cost of care. Core competencies for interprofessional practice were updated in 2016 by the Interprofessional Education Collaborative, which is now comprised of 16 health-care professional groups. Those competencies relate to values and ethics for interprofessional practice, roles, and responsibilities; interprofessional communication; and teams and teamwork (Interprofessional Education Collaborative, 2016).

Interprofessional practice continues to validate approaches to complex patient management. In one study, using a team consisting of a physician, nurse practitioner, clinical pharmacist, nurse, dietary specialist, and behaviorist, clinical outcomes were optimized in a low-income diabetic population. Interprofessional diabetic care improved outcomes related to the Hb A1c, triglycerides, and blood pressure values (Madsen et al., 2021). Improved interprofessional teamwork and team-based care play critical roles in many of the new primary care approaches, including the PCMH, chronic care coordination, and transitions of care.

PROVIDER REIMBURSEMENT FOR CHRONIC ILLNESS CARE

Chronic Care Management Services

There is widespread awareness that frail, older adult patients, and others with complex physical and functional problems often experience worsening disease, decreased function, unwanted transfers to skilled nursing facilities, and potentially costly emergency department visits or preventable hospital admissions or readmissions. Typically, those complex issues are not well addressed within the traditional outpatient office visit. As previously discussed, strategies and programs that include care coordination are known to lower the rates of adverse outcomes.

As of January 2015, Medicare started reimbursing physicians, nurse practitioners, and other non-physician providers for non–face-to-face care coordination for patients with two or more chronic conditions associated with significant risk of exacerbation, decompensation, functional decline, or death. Those services are known as chronic care management (CCM) services (CMS, 2022b).

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CMS stipulates that the clinician must provide at least 20 minutes of coordination for each 30-day billing period and lists seven components of CCM. Three components involve the patient and clinician, including continuous access to care management (including use of EMRs and 24/7 telephone coverage); continuous care with a designated health-care professional; and multiple ways for the patient or caregiver to communicate with that clinician (Agarwal et al., 2018). The next two requirements relate to the clinician's plan of care. Initially, there must be a comprehensive assessment and management of the patient's medical, cognitive, functional, and psychosocial needs, as well as the patient's environment, resources, and support. The second requirement requires creation of a comprehensive care plan. The third and fourth requirements include the management of transitions among clinicians and settings, and coordination with home- and community-based health-care professionals (Agarwal et al., 2018).

Incorporating all of the requirements for CCM can be challenging in many practices. It may be necessary to make additional investments in technology, staff training, and the care management protocols. Patient care benefits of CCM services include increased round-the-clock access to providers, enhanced care continuity across settings, stronger community support services, and the ability to develop a patient-centered care plan with providers.

Transitional Care Management Services

Reimbursement for intentional Transitional Care Management has been an incentive for a practice to make contact with the patient immediately after discharge from a hospital or post-acute setting (CMS, 2021). Within 2 business days of discharge, you or staff in your office must contact the patient by phone or document two or more unsuccessful attempts to contact the patient. You cannot bill for the service without the face-to-face visit. At least one face-to-face visit must occur within the time frame of the appropriate code. CPT Code 99495 requires communication in 2 business days, moderate complex decision making and face-to-face within 14 days of discharge. CPT Code 99496 requires the call within 2 business days, high complexity of decision making, and face-to-face within 7 days. CMS allows for concurrent billing of select additional codes—for example, codes for chronic care management.

The Annual Wellness Visit

The annual wellness visit (AWV) is a yearly preventive care visit offered at no cost to all Medicare Part B beneficiaries and separate from any physical examination. The purpose of the visit is to identify patient risk factors and plan for future preventive service needs. The visit is well reimbursed and can be conducted by a provider or another supervised professional. There are significant patient care benefits, including a yearly opportunity for a health-risk assessment, which includes psychosocial and behavioral risks, functional and cognitive assessments, as well as a general safety check. Older adults can also work with providers to update a preventive care plan and be connected to necessary community resources. You may bill for other medically necessary services on the same date as the AWV, but those services are subject to the deductible and coinsurance. Many patients come in for the AWV with the understanding that it is at no cost to them, so any additional service should be discussed.

Advance Care Planning Discussions

In 2016, Medicare began covering advance care planning discussions as a separate and billable service. Physicians, APRNs, and other health professionals are encouraged to have discussions with patients regarding end-of-life care preferences. Communication about serious illness care goals is now an intervention that is systematically integrated into our clinical care structures and processes. The CPT codes allow the clinician to explain and discuss advance directives and assist with the completion of approved forms. The codes are time-based and allow for a basic code, as well as an add-on code for each additional 30 minutes of time spent with patients (CMS, 2020).

End-of-life conversations are associated with better quality of life, reduced use of life-sustaining treatments near death, earlier hospice referrals, and care that is more consistent with patient preferences. Patients who engage in advance care planning are more likely to have their wishes known and followed. Best practice in communication about advance care planning should include discussions about individual goals of care, prognosis, decision-making preferences, and wishes for family involvement.

THE ROLE OF APRNS IN CHRONIC DISEASE

The effect of health-care reform as part of the ACA of 2010, the rise in complex chronic diseases, and the continuing growth of the aging population combine to create a huge demand for health-care services. Individuals with multiple chronic disease, including frail older adults, will interact frequently with the health-care system. APRNs will continue to play an essential role in individual patient quality of care, as well as health system reform.

National attention has been placed on the removal of all scope-of-practice restrictions on APRNs to drive down costs and increasing high-quality access to primary health care. Numerous studies have shown the importance of APRNs as key components of an overall health-care system strategy to address chronic disease (Buerhaus et al., 2018).

APRNs are ideally suited to incorporate elements of the CCM into practice because they excel in patient education and patient empowerment, with the goal of supporting the patient's self-management skills. APRNs are involved in technology and clinical information systems by using shared medical appointments, telehealth, electronic documentation and developing and maintaining data for quality improvement. APRNs embrace evidence-based care that is maximized with decision support tools and algorithms.

APRNs appreciate the diversity of the older population, including diversity of health trajectory, functional ability, cultural background, support systems, and individual values and preferences. The APRN's holistic approach to care includes prevention and support of healthy aging, education, care coordination, management and monitoring of complex medication and treatment regimens, counseling for family issues related to caregiving and finances, access to community resources, advance care planning, and the vigilant management of all comorbid conditions.

New health-care models and alternatives to traditional care address discontinuities in health care. APRNs are presently

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involved in unique strategies that target high-risk older adults across systems of care, partnerships with families and caregivers, identification of resources for individuals with chronic disease, and involvement in key policy decisions that affect those populations. APRNs are committed to providing affordable, accessible, and high-quality care through clinical practice, education, leadership, and research.

Clinical Recommendation	Evidence Rating	References
The Frail Scale can be used as a time and cost-effective screening tool for frailty.	B	Aprahamian et al., 2017
The Transitional Care Model has consistently shown reductions in readmissions, emergency department visits, and costs of care.	B	Naylor et al., 2018
Hospital Readmission Reduction Program has been successful in reducing readmissions and lowering the cost of health care including in this vulnerable population.	B	Gai & Pachamanova, 2019
Older adults with MCCs have poorer outcomes when treated according to disease-specific guidelines. Improved decision making requires alternative approaches, including patient and family values; communication and coordination with specialty providers, and other members of the team; and a restructured reimbursement system.	A	Muth et al., 2019 Dent et al., 2019

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/afp/2004/0201/p548.html.

CASE STUDY

Mrs. A. is an 82-year-old woman. She lives with her 86-year-old husband, who has mild-to-moderate dementia. Mrs. A. has a primary care provider, endocrinologist, cardiologist, ophthalmologist, and podiatrist. She has a daughter nearby who assists with shopping and housekeeping. Mrs. A. is overweight and has hypertension, type 2 diabetes, CKD, macular degeneration, incontinence, and peripheral neuropathy with chronic pain. She has trouble sleeping, complains of chronic fatigue, and has fallen twice in the past 2 months. She is on nine prescription medications. Her self-care regimen includes monitoring her glucose, weighing herself daily, taking medications twice daily, and managing her nutrition and exercise. She is also responsible for managing her husband's meals and medications.

Additional comprehensive assessment is critical to developing a person-centered plan of care for Mrs. A. A multidisciplinary and continuity-of-care focus will prevent poor outcomes.

1. What multiple factors place Mrs. A. at high risk for poor outcomes?
2. What additional assessment data are essential to determine whether Mrs. A. can safely manage her complex health-care regimen at home?
3. How do Mrs. A.'s multiple chronic diseases contribute to the complexity of her care?
4. Are there caveats when using evidence for individual chronic diseases in light of her MCCs?
5. What communication is necessary to provide ongoing coordination of care?
6. What community resources may be available to support Mrs. A.?
7. What additional team members would be appropriate to contribute to a safe and person-centered plan of care?
8. What new models of care can potentially contribute to Mrs. A.'s quality of care while she is at home or in the event of a hospitalization?

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CHAPTER 23

Palliative Care and End-of-Life Care

Joshua Borders, Freda Cowan

OVERVIEW OF PALLIATIVE CARE AND HOSPICE

Description: Palliative care is an interdisciplinary approach to care aimed at improving the quality of life of patients and their families facing a life-threatening illness. The goal of palliative care is the prevention and relief of suffering by means of early identification, assessment, and treatment of physical, psychosocial, and spiritual problems. Palliative care is provided in a variety of settings including hospitals, primary care and specialty clinics, patient homes, and nursing facilities. Palliative care:

- Provides relief from pain and other distressing symptoms
- Affirms life and regards dying as a normal process
- Intends to neither hasten nor postpone death
- Integrates the psychological and spiritual aspects of patient care
- Offers a support system to help patients live as actively as possible until death
- Offers a support system to help the family cope during the patient's illness and in their own bereavement
- Uses a team approach to address the needs of patients and their families, including bereavement counseling, if indicated
- Enhances quality of life, and may also positively influence the course of illness
- Is applicable early in the course of illness, in conjunction with other therapies that are intended to prolong life, such as chemotherapy or radiation therapy, and includes those investigations needed to better understand and manage distressing clinical complications (World Health Organization, 2018).

There are several well-described barriers to patients receiving palliative care, including provider reluctance to refer due to fear of upsetting patients or not understanding the benefits, confusion of terminology (hospice versus palliative care), and a lack of palliative care resources (Hawley, 2017). There are many potential benefits of palliative care, including improved end-of-life communication, reduction in distressing symptoms, and improved patient quality of life (Temel et al., 2017). Patients and families benefit from the availability of palliative care services early in the disease process, particularly when symptoms affect quality of life. Palliative care has also been shown to reduce health-care costs and lessen emergency department and hospital utilization (Cassel et al., 2018). In some cases, patients that receive palliative care services may actually live longer than those that do not receive palliative care (Temel et al., 2017).

As the disease advances and end of life nears, hospice care becomes an option. The National Hospice and Palliative Care Organization (NHPCO, 2020) defines hospice as "the model for quality, compassionate care for people facing a life-limiting illness, hospice provides expert medical care, pain management, and emotional and spiritual support expressly tailored to the patient's needs and wishes." Hospice uses the principles of palliative care, focusing on quality of life, but whereas palliative care is appropriate at the time of diagnosis with a life-limiting illness, patients are eligible for hospice when their prognosis is expected to be 6 months or less. Another important difference between hospice and palliative care are the goals of treatment. Palliative care is appropriate for patients receiving ongoing curative and aggressive medical treatments. However, most patients discontinue aggressive treatments when they opt to receive hospice. Hospice services are covered by Medicare, Medicaid, and most private insurance providers. Hospice is provided in a variety of settings including patient homes, nursing facilities, hospitals, and inpatient hospice facilities. Hospice provides the following services:

- An interdisciplinary team to facilitate the management of distressing symptoms at end of life
- Assists the patient and family with emotional, psychosocial, and spiritual care
- Provides grief and bereavement counseling to the family for at least a year following the death of the patient
- Provides short-term inpatient care when pain or symptoms become too difficult to manage at home or if the caregiver needs respite time

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- Delivers specialized services such as speech and physical therapy when needed
- Provides medications and medical equipment to facilitate the care of the patient (NHPCO, 2020)

Etiology: In the United States, the five leading causes of death in 2019 were heart disease, cancer, unintentional injuries, stroke, and chronic lower respiratory diseases. In 2020, because of the global coronavirus pandemic (COVID-19), COVID-19 deaths displaced unintentional injuries as the third leading cause of death in the United States (Ahmad & Anderson, 2021).

Numerous medical advances in the management of these illnesses have led to people living longer with chronic health conditions. Accurate prognostication of chronic illnesses is difficult, and the difficulty of prognostication can result in overuse of acute care interventions at the end of life and delays in referral to hospice care. In 2018, the median length of stay in a hospice program was 18 days, meaning one-half of patients died within 2.5 weeks of enrollment in a hospice program. The average length of stay in a hospice program was 89.6 days (NHPCO, 2020). Thus, most people are not benefiting fully from the Hospice Medicare Benefit, which is designed to provide care for patients in the last 6 months of life.

Occurrence: In 2017, for the first time, deaths of Americans at home (30.7%) surpassed those in the hospital (29.8%). The same year 20.8% of Americans died at nursing facilities and 8.3% of Americans died at a hospice facility (Cross & Warraich, 2019). It is important to provide access to hospice and palliative care services in all settings. The goal is to ensure a peaceful, dignified death with symptoms well-managed and support for the family and caregivers. Establishing the goals of care in treating older adults with life-limiting illnesses is essential.

Age: In 2018, average life expectancy was 78.7 years in the United States (Xu et al., 2020). The United States has an aging population with an expectation that by 2034, older adults (aged 65 and over) will outnumber children (Vespa et al., 2020). Palliative care is beneficial for frail older adults because there is limited data to suggest improved outcomes from aggressive medical interventions in this population (Lazris, 2019).

Caregiving needs increase with advanced age and are typically met by the family. Caregivers are at risk for physical and psychological distress, including depression, insomnia, fatigue, and anxiety, as well as physiological effects and financial burden (Sun et al., 2019). Palliative care can have a role in supporting families and improving caregiver outcomes (Hui et al., 2018).

Ethnicity: In the United States, Hispanic females have the longest life expectancy (84.3 years), followed by non-Hispanic females (81.1), Hispanic males (79.1), non-Hispanic black females (78), non-Hispanic White males (76.2), and non-Hispanic Black males (71.3) (Arias, 2020). Cultural influences affect how people define health and illness and shape their beliefs and practices in end-of-life care (Cain et al., 2018).

Contributing Factors: Contributing factors include advanced age and multiple comorbidities. The average overall life expectancy for females is 81.2 years; the average life expectancy for males is 76.2 years (Xu et al., 2020).

Signs and Symptoms: See Symptom Management.

Differential Diagnosis: Not applicable.

SYMPTOM MANAGEMENT

A few of the most prevalent symptoms in end-of-life care in the geriatric population are delirium, dyspnea, and pain. Additional symptoms such as nausea and vomiting, constipation, diarrhea, fatigue, depression, anxiety, and insomnia are common. These latter symptoms are described in detail elsewhere in this book. When addressing pharmacological symptom management in older adults, it is important to consider physiological changes, such as decreased renal and hepatic function and altered body fat distribution, that may alter drug metabolism, leading to higher serum drug levels. Older adults are more susceptible to adverse reactions, thus, begin with lower initial doses and titrate cautiously (American Association of Colleges of Nursing & City of Hope, 2019).

DELIRIUM

Description: Delirium is disturbance of attention and awareness accompanied by a change in baseline cognition, developing over a short period of time, fluctuating during the course of a day, and often worsening at night (Hshieh et al., 2020). Those with delirium have:

- A reduced awareness of their environment
- Disturbance of consciousness with impaired ability to focus, sustain, or shift attention
- Cognitive changes involving memory impairment, disorientation, and language disturbance
- Perceptual disturbances, including delusions and hallucinations

Delirium can be hyperactive with symptoms of hyperalertness, hypervigilance, and agitation, or delirium may be hypoactive and characterized by somnolence (Mattison, 2020).

Etiology: There are numerous potential causes of delirium in the dying patient related to the terminal disease itself, treatment of the disease, metabolic effects of organ failure, and electrolyte imbalance, including hypoglycemia, infection, hematological disorders, nutritional deficiencies, dehydration, hypoxia, uncontrolled pain, sensory deprivation, sleep disturbance, alcohol or drug withdrawal, diarrhea, constipation, and urinary retention. Many medications, particularly benzodiazepines and anticholinergic medications, can cause delirium. Opioids, particularly meperidine, may increase risk for delirium as well (Kates, 2020).

Occurrence: Delirium is common at end of life and can be very distressing to the family, as well as to the patient. Prevalence ranges from 13% to 93%. It is often unrecognized, particularly hypoactive delirium (Mattison, 2020). Terminal delirium is common as death approaches, affecting

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up to 90% (Hshieh et al., 2020; Mattison, 2020; Rieck et al., 2020).

Age: Advancing age is a risk factor for delirium (Li et al., 2020). Older patients presenting with delirium have up to 50% mortality at 1 year (Mattison, 2020).

Ethnicity: Delirium can affect all people. Utilize culturally sensitive screening tools.

Contributing Factors: The frail older adult with less physiological reserve, multiple comorbidities, polypharmacy, pre-existing dementia, previous history of delirium, and/or sensory impairment who is in an unfamiliar environment is more vulnerable to delirium. Patients admitted to the hospital, in particular to an intensive care unit, are at increased risk for delirium (Gravante et al., 2021; Li et al., 2020).

Signs and Symptoms: Acute onset and fluctuating course of inattention, altered level of consciousness, and disorganized thinking are signs of delirium. Disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, emotional instability, and impaired sleep–wake cycle are common findings (Hshieh et al., 2020; Mattison, 2020; Rieck et al., 2020).

Diagnostic Tests: Patient history and assessment, including a review of the patient's medications, are the first steps in diagnosing delirium. Disorientation, memory impairment, perceptual disturbances, psychomotor agitation or retardation, and impaired sleep–wake cycle are common findings. The Confusion Assessment Method (CAM) has been validated as an effective tool to diagnose delirium (Helfand et al., 2021). CAM assesses for the presence of acute onset and fluctuating course, as well as inattention and either disorganized thinking or altered levels of consciousness. These findings are diagnostic of delirium. Other tools include the Memorial Delirium Assessment Scale and the Delirium Rating Scale (Helfand et al., 2021). More invasive diagnostic tools may be indicated to determine the etiology if further evaluation is consistent with goals of care. In the terminally ill, the most common cause of delirium is medications, including opioids, anticholinergics, and benzodiazepines. The second most common cause of delirium is metabolic insufficiency due to organ failure (Klankluang et al., 2021).

Differential Diagnosis: Consider the possibility of dementia, depression, or the coexistence of either of these with delirium (Mattison, 2020).

Treatment: The first step in treating delirium is to identify the cause(s) if possible. Make appropriate changes to the plan of care based on the etiology. Perform regular medication reviews to eliminate unnecessary agents. Consider inadequate pain control as a cause of delirium; remember, however, that opiates can cause delirium and dose reduction may be necessary (Mattison, 2020). Deprescribing of psychoactive medications is also important (Hshieh et al., 2020). Evaluate fluid and electrolyte imbalances, infections, organ failure, hypoglycemia, drug toxicity, as well as withdrawal from alcohol and sedatives (Mattison, 2020). Attention should also be paid to providing a therapeutic environment, as well as a supportive and safe environment focusing on clear communication and a structured daily routine with consistent caregivers and a structured sleep–wake cycle, avoiding sensory overstimulation and providing for glasses and hearing aids if indicated, and providing physical activity and attention to oral intake and elimination (Hshieh et al., 2020). Frequent reassurance, touch, and verbal orientation may lessen behavior disturbances (Bush et al., 2017).

Nonpharmacological interventions are the mainstay of managing delirium. However, in the acutely agitated patient, a trial of pharmacological agents may be indicated. Neuroleptic agents are generally used, but there continues to be limited data to support their use (Rieck et al., 2020). Atypical antipsychotics, such as olanzapine, risperidone, quetiapine, and ziprasidone, can be considered for the agitated patient. However, these agents carry an increased risk of QT prolongation, with increased risk for cardiovascular events and death in the elderly with dementia (Bush et al., 2017; Hshieh et al., 2020). In the palliative care literature, haloperidol is considered the mainstay of delirium management, beginning with low doses, 0.5 mg intravenously or subcutaneously, or 1 mg orally (Hshieh et al., 2020). Titrate slowly in older adults. Chlorpromazine 25 to 50 mg is an alternative if more sedation is needed, but it may cause hypotension (Bush et al., 2017).

Benzodiazepines, such as lorazepam, may benefit patients with a seizure disorder or alcohol withdrawal and those who cannot tolerate antipsychotic medications. However, benzodiazepines may lead to paradoxical agitation, causing symptoms of delirium to worsen. Therefore, these agents should be used cautiously (Klankluang et al., 2021).

Anticholinergic medications should be avoided. Cholinesterase inhibitors have recently been found to aid delirium. In a double-blinded randomized study comparing rivastigmine patch 4.6 mg and melatonin 7 mg patch in 180 adults aged 60 to 85 years concluded that both were comparable in reducing severity of delirium (Hussien & Shoukry, 2020). Also, the melatonin agonist ramelteon is showing promise in the reduction and prevention of delirium (Khaing & Nair, 2021).

Follow-Up: Provide adequate treatment of underlying cause. Due to multimodal causes, an interdisciplinary approach is preferred.

Sequelae: Prompt evaluation and treatment can improve outcomes. Delirium is distressing to patients, their families, and health-care providers. Delirium contributes to increased morbidity and mortality. Older patients presenting with delirium have up to 50% mortality at 1 year (Mattison, 2020). Patients are at risk for falls and potential injury. In end-of-life care, the goal is supportive care to promote a peaceful, dignified death.

Prevention/Prophylaxis: Avoid polypharmacy. Discontinue unnecessary medications and use high-risk medications cautiously. Maintain adequate hydration and nutrition, as appropriate, with prompt attention to elimination needs. Minimize invasive devices such as catheters. Correct sensory deficits. Promote normal sleep patterns. Avoid physical restraints. Use music and massage. Provide a therapeutic milieu with appropriate environmental stimulation (Hshieh et al., 2020).

Referral: Refer the patient to a geriatric psychiatrist, geriatrician, geriatric nurse practitioner, and/or palliative medicine practitioner as needed.

Education: Teach the patient's family signs of delirium and ask that they report the signs promptly to the medical team. Teach nonpharmacological methods of providing a supportive environment. Avoid over-the-counter (OTC) medications (Mattison, 2020).

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DYSPNEA

Description: Dyspnea, also called breathlessness, shortness of breath, or air hunger, has been defined by the American Thoracic Society as a subjective experience of breathing sensations that vary in intensity (Hui et al., 2021; Parshall et al., 2012). The patient's experience of dyspnea is derived from the complex interplay of emotional, physical, social, and spiritual factors that may induce secondary physiological and behavioral responses. It is a distressing symptom at end of life and affects quality of life (Crombeen & Lilly, 2020).

Etiology: Dyspnea can have multiple causes, such as infection, cancer, heart failure, chronic obstructive pulmonary disease (COPD), obstructive sleep apnea (OSA), asthma, pulmonary fibrosis, interstitial lung disease, thrombotic events, pneumothorax, pleural effusion, anemia, amyotrophic lateral sclerosis, and anxiety. Dyspnea is physiologically complex, stemming from activation of receptors in the airway, lung parenchyma, chest wall, and peripheral or central chemoreceptors (Pisani et al., 2018).

Occurrence: Dyspnea is one of the most common symptoms experienced by patients as they approach the end of life. It is commonly reported in patients with advanced cardiovascular disease, pulmonary disease, and cancer (Stevens et al., 2018). Together, these diagnoses account for over 50% of all deaths in the United States (Ahmad & Anderson, 2021). An estimated 43% of patients with respiratory diagnoses and 25% of patients with cardiovascular diagnoses report dyspnea in the 24 hours prior to hospitalization (Stevens et al., 2018). In cancer patients, prevalence of dyspnea can be greater than 50%, with symptoms affecting treatment and frequently leading to hospitalization (Crombeen & Lilly, 2020).

Age: Certain causes, such as heart failure, cancer, and chronic lung disease, are more common in older adults.

Ethnicity: Not applicable.

Contributing Factors: Smoking and comorbidities can contribute to the development of dyspnea.

Signs and Symptoms: Shortness of breath at rest and/or exertion, tachypnea, use of accessory muscles, hypoxia, adventitious breath sounds, cyanosis, and pursed-lip breathing are all signs of dyspnea.

Diagnostic Tests: The first step in diagnosing dyspnea is the clinical patient interview and physical examination. The physical examination should include respiratory rate, oxygen saturation, and assessment of breath sounds, heart rate, heart sounds, presence or absence of jugular venous distension, pallor, cyanosis, or ascites (Budhwar & Syed, 2020). The clinical interview should at a minimum include lifestyle assessment (such as smoke or irritant exposure), modifying factors or self-interventions, and use of a dyspnea assessment tool (American Association of Colleges of Nursing & City of Hope, 2019). Multiple dyspnea assessment tools are validated; however, many are one-dimensional, disease-specific, or do not address the affective component in dyspnea in advanced disease. The American Thoracic Society and American College of Chest Physicians do not endorse one specific tool (Parshall et al., 2012). However, use of these tools in combination with the clinical interview, physical examination, and diagnostic testing, if warranted, while keeping in mind the patient's goals for care, can help determine the appropriate course of dyspnea treatment (Birkholz & Haney, 2018).

Examples of dyspnea assessment tools are the Modified Borg Scale, Visual Analog Scale, Numeric Rating Scale, Memorial Symptom Assessment Scale, Edmonton Symptom Assessment Scale, Dyspnea-12 (for congestive heart failure [CHF], COPD, interstitial lung disease [ILD]), Cancer Dyspnea Scale (cancer-specific and addresses the affective component of dyspnea as well), and Respiratory Distress Observation Scale for those patients who are unable to self-report (Aslakson et al., 2017).

Diagnostic tools should be used as appropriate, considering the patient's goals of care. Diagnostic tests include laboratory tests, such as complete blood count to determine anemia, basic metabolic panel to evaluate renal function, chest x-ray, and electrocardiogram (EKG). Computed tomography (CT) scan to evaluate for malignancy and/or pulmonary embolism may be indicated. Echocardiogram may also be performed to evaluate for poor cardiac ejection fraction or pericardial effusion (Budhwar & Syed, 2020).

Differential Diagnosis: Consider all etiologies as outlined previously. If cough is present, consider pneumonia; pleural effusion; side effects of medications, such as angiotensin-converting enzyme inhibitors; and gastroesophageal reflux disease (Budhwar & Syed, 2020; Crombeen & Lilly, 2020).

Treatment: Treatments should be aimed at the underlying etiology. Pharmacological interventions might include diuretics, bronchodilators, vasodilators, steroids, antibiotics, opioids, and/or sedatives (Budhwar & Syed, 2020; Crombeen & Lilly, 2020) (Table 23-1). Opioids remain the mainstay for treatment of dyspnea at end of life (Arya et al., 2020; Budhwar & Syed, 2020; Hui et al., 2018; Pisani et al., 2018; Slawnych, 2020). Similar to when used for the treatment of pain, opioids act on receptors in the central cortex and thereby affect the neurological perception of dyspnea. Opioids are likely underutilized for management of dyspnea due to fear that they will lead to respiratory depression. However, evidence suggests that when used judiciously ("start low and go slow"), opioids are safe for use in the management of dyspnea and do not hasten death (Pisani et al., 2018; Slawnych, 2020). There is no consensus on which opioid medication or dose is the most efficacious for the management of dyspnea. One author recommends that for hospitalized patients, clinicians start with morphine at low doses (1 to 2 mg IV) and titrate up every 15 minutes until patients are more comfortable (Pisani et al., 2018). Some authors suggest utilizing hydromorphone as the opioid of choice either in oral, IV, or subcutaneous formulations. For hospitalized patients at end of life, clinicians can use hydromorphone 0.5 mg IV or subcutaneously every 30 minutes as needed (Arya et al., 2020; Slawnych, 2020). In the case of severe dyspnea, particularly in patients that are at end of life, clinicians may opt to start a continuous opioid infusion.

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TABLE 23-1 Pharmacological Interventions for Dyspnea

Opioids	Morphine 0.5 to 10 mg orally every 3–4 hours prn SOB
Nebulized opioids	Further research is needed
Benzodiazepines	Studies reveal no significant benefit
Nebulized furosemide	Potential benefit, further research is needed
Bronchodilators, diuretics, steroids, antibiotics, vasodilators	As indicated based on etiology

For patients that are at end of life and for which IV access is limited, clinicians can use a butterfly needle inserted into the subcutaneous tissue as a method for opioid delivery (Slawnych, 2020).

Oral morphine can be used safely and effectively and may be a good choice for nonhospitalized patients. For patients who are opioid naïve, clinicians can start oral morphine 2.5 mg to 5 mg every 4 to 6 hours (Crombeen & Lilly, 2020). Oral morphine can then be titrated up to achieve comfort. Patients may require around-the-clock dosing or conversion to a long-acting formulation once symptoms are stable (Crombeen & Lilly, 2020). Morphine in an elixir formulation is often utilized by hospice for the management of pain/dyspnea even in patients that are no longer able to effectively swallow.

Some guidelines suggest trial of a benzodiazepines for dyspnea refractory to opioids or in the case of concurrent anxiety (Hui et al., 2018; Slawnych, 2020). Inhaled/nebulized opioids and anesthetics have not proved to effectively treat dyspnea (Crombeen & Lilly, 2020). It is also recommended to reduce excessive secretions with anticholinergics such as scopolamine, hyoscyamine, atropine, or glycopyrrolate. There is usually little benefit from suction, particularly in patients that are at end of life (Slawnych, 2020).

Diuretics may help improve dyspnea in patients who are volume overloaded due to heart failure or in the case of lymphangitic carcinomatosis. Nebulized furosemide has been used as a novel intervention to help with dyspnea, although its mechanism of action is unknown (Pisani et al., 2018). Corticosteroids are often used to reduce airway inflammation in a variety of terminal diseases (Hui et al., 2018; Pisani et al., 2018).

Nonpharmacological interventions include the use of a fan directed at the cheek or face, oxygen if hypoxic, elevation of the head of the patient's bed, relaxation and breathing exercises, cooler room temperatures, acupuncture, and stress reduction techniques (Hui et al., 2018; Pisani et al., 2018). Temporary ventilator support can be explored if clinically indicated for severe reversible conditions. The routine application of oxygen to patients who are near death is not supported. Oxygen therapy for those who are hypoxic has shown to be beneficial for managing dyspnea (Pisani et al., 2018). Implement oxygen therapy if there is a subjective report of relief. Interventional therapies to be considered for dyspnea management related to refractory pleural effusions include thoracentesis, pleurodesis, and tunneled catheter to drainage. Other interventional options for refractory dyspnea related to obstruction can be bronchoscopy or stenting (Budhwar & Syed, 2020; Hui et al., 2018).

Follow-Up: Follow-up is dependent on etiology. Ongoing assessment, reevaluation, and adjustment of plan of care should be used as needed. Monitor for therapeutic effect, as well as adverse effects from interventions.

Sequelae: Dependent on etiology and goals of care, dyspnea should improve when the cause is treated. However, dyspnea is also common in the dying person, and the goal is comfort measures when death is an anticipated outcome.

Prevention/Prophylaxis: Preventive measures are dependent on the cause. Smoking cessation is beneficial, as is the avoidance of smoke exposure. Use energy conservation and durable medical equipment for the severely dyspneic patient with advanced illness. If the patient is an aspiration risk, modifying food textures and a speech therapy consult may be beneficial.

Referral: Referral may be indicated based on etiology and goals of care. Appropriate referrals may include visits to a palliative care specialist, cardiologist, pulmonologist, and/or oncologist.

Education: Smoking cessation; the proper use of medications, including inhalers and nebulizers; the use of fans; energy conservation; and potential adverse effects of medications.

PAIN

Description: "Pain is an aversive sensory and emotional experience typically caused by, or resembling that caused by, actual or potential tissue injury" (Sukel, 2019). The prevalence of cancer pain is high with less optimal treatment reported by patients (Fee Voon Ho, et al., 2020). The patient's own report is the best indicator of pain (Schwan et al., 2019). Most older adults, including those with dementia, can effectively communicate pain, but a more detailed assessment of pain can be challenging. Several pain assessment tools are available, including the Visual Analogue Scale (VAS), Numerical Analogue Scale (NAS), Wong-Baker FACES Pain Rating Scale, Pain Assessment in Advanced Dementia (PAIN-AD) Scale, NOPPAIN, and Checklist of Non-Verbal Pain Indicators (Lukas, 2019: Resnick et al., 2019; Sirsch et al., 2020).

Etiology: Pain is categorized as somatic, visceral, neuropathic, or mixed (American Association of Colleges of Nursing & City of Hope [AACN & COH], 2020). Somatic pain originates from cutaneous, bone, and musculoskeletal tissues. Examples include muscle pain, such as fibromyalgia or myofascial pain; inflammatory pain, such as an acute injury or chronic

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inflammatory pain, including arthritis; and mechanical pain related to fractures or dislocations or compression of tissue by bony structures. Somatic pain is typically well localized and described as aching. Visceral pain originates in the thoracic, abdominal, and pelvic viscera. It is diffuse pain and often radiates. Neuropathic pain is nerve pain due to dysfunction of the nervous system. Examples include diabetic neuropathy, neuropathy due to herpes zoster, and peripheral vascular disease (Schwan et al., 2019). Psychological pain should be considered as well, related to depression, anxiety, personality disorders, somatization disorders, and post-traumatic stress disorder. Common causes of pain in older adults are low back pain, cancer pain, and neurogenic pain syndromes (Schwan et al., 2019). Patients also experience nonmalignant pain from cardiac, renal, pulmonary, hepatic, neurological, or immune disorders (AACN & COH, 2020).

Occurrence: Pain is a common end-of-life symptom in older adults. Fifty percent of older adults report chronic pain, and it is not alarming that up to 70% report pain in more than one site of the body (Schwan et al., 2019). About 53% of patients with cancer experience pain (Sirsch et al., 2020), and about 45% to 80% of nursing home residents experience pain (Sirsch et al., 2020). Women and men are at equal risk for undertreatment of pain (American Association of Colleges and Nursing & City of Hope, 2020).

Age: The comorbidities experienced with aging make pain more likely. Older adults, particularly those with dementia, are at risk for undertreatment of pain (American Association of Colleges and Nursing & City of Hope, 2020). Many of the interventions to treat these challenging symptoms are pharmacological interventions. It is important to consider geriatric pharmacology when formulating treatment plans. Several physiological factors affect drug distribution, including cardiac output, regional blood flow, body mass and composition (which affect hydrophilic and lipophilic drug distribution), and plasma protein concentration. These changes make an older adult person more susceptible to adverse drug effects. Drug metabolism and clearance in an older adult is often slowed due to declining renal and liver function. Drug interactions, particularly with drugs metabolized through the P450 enzyme system, also put an older adult at risk. The health-care provider needs to be mindful of these effects when prescribing. Begin with low doses and titrate carefully, with frequent reassessment, to optimize pain relief and minimize adverse effects (Yang et al., 2020).

Ethnicity: Nondominant cultures are at risk for undertreatment of pain; biases exist in pain assessment and management. Culture impacts access to medical care, including access to medications (American Association of Colleges and Nursing & City of Hope, 2020).

Contributing Factors: Multiple comorbidities, as stated earlier in the text.

Signs and Symptoms: Complete a thorough pain assessment, including history, location, intensity (using an appropriate pain assessment tool), quality, pattern, aggravating/relieving factors, temporal pattern medication history, and cultural influences (Portenoy, 2020). Clinicians conducting the comprehensive pain assessment should utilize one of the validated pain tools and also assess the holistic impact of pain, including physical, psychological, social, and spiritual factors, as well as capturing medical diagnoses, comorbid conditions, psychiatric history (including substance abuse history), and prior treatments for pain (Sirsch et al., 2020).

Diagnostic Tests: Patient history and physical examination should direct appropriate diagnostic testing to assess the underlying cause.

Differential Diagnosis: Determine somatic, visceral, and/or neuropathic pain, or treatment-related pain.

Treatment: Treatment of pain should include a multidimensional approach consisting of both pharmacological (see Table 23-2) and nonpharmacological interventions. The World Health Organization (WHO) analgesic ladder has been revised to include integrative therapies at each stage of opioid medication escalation. The previous analgesic ladder has been found not to be effective for noncancer chronic pain syndromes (Yang et al., 2020). The addition of integrative therapies is an attempt to reduce the overuse of opioids while utilizing the holistic approach of evidence-based alternative and complementary modalities (Yang et. al., 2020). The first step of the WHO ladder recommendation is the use of NSAIDs and acetaminophen for mild pain. Acetaminophen is still considered an effective agent for pain associated with osteoarthritis and low back pain. Many experts recommend limiting intake of acetaminophen to 3,000 mg per 24 hours to prevent overdose and decrease liver risks associated with its use (Portenoy, 2020). In those with hepatic insufficiency or alcohol abuse, acetaminophen dose should be reduced by 50% to 75%. Liver failure is an absolute contraindication.

Recent guidelines from the American Geriatrics Society advise against the routine use of NSAIDs in older adults for several reasons (Yang et al., 2020). These include gastrointestinal (GI) toxicity, renal toxicity, and platelet dysfunction, as well as adverse effects on blood pressure control and heart failure management. The risk of myocardial infarction or stroke is increased with the use of NSAIDs (Portenoy, 2020). The risk increases with concurrent use of corticosteroids. Concurrent use of daily acetylsalicylic acid (ASA) and/or selective serotonin reuptake inhibitors (SSRIs) also may pose additional risk for GI bleeding. Administering NSAIDs with food, proton pump inhibitors, or histamine-2 blockers can help prevent

TABLE 23-2 Pharmacological Interventions for Pain Management

Acetaminophen	Limit to 3,000 mg or less in older adults
NSAIDs	Avoid routine use in older adults
Opioids: morphine, oxycodone, hydromorphone, fentanyl	Severe pain, start low go slow
Tramadol	Weak opioid antagonist and selective norepinephrine reuptake inhibitor (SNRI)
Methadone	Opioid agonist and NMDA antagonist
Buprenorphine	Opioid agonist-antagonist

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GI challenges (Portenoy, 2020). The COX-2 inhibitors may place a person at greater risk for cardiovascular events, including myocardial infarction (Portenoy, 2020). When using NSAIDs, the maximum daily doses (MDDs) for specific NSAIDs are ASA, 4,000 mg/day; ibuprofen, 2,400 mg/day; Naprosyn, 1,375 mg/day; and Toradol, 120 mg/day in 24 hours (Portenoy, 2020).

Patients with moderate-to-severe pain with functional impairment and/or decreased quality of life due to pain can be considered for opioid therapy (Davis et al., 2020). The WHO ladder adds opioids, typically in combination with acetaminophen, which should limit the number of total opioids. Examples include codeine, hydrocodone with acetaminophen, and oxycodone with acetaminophen. These are used for moderate pain (Davis et al, 2020).

For severe pain, the WHO ladder includes opioid pain medications. Opioid administration in the older adult population should consist of a "start low and go slow" approach. Consider long-term opioids in those patients who do not respond to more conservative management and who continue to experience pain-related distress or functional impairment and demonstrate benefit from the opioid medication. Clinicians may prescribe a trial of opioids in cancer survivors with chronic pain (Davis et al., 2020). The only absolute contraindication to the use of opioids is if there is a history of rash, wheezing, or edema (Schwan et al., 2019). Common opioids include morphine, oxycodone, and hydromorphone. Tramadol is a weak opioid agonist and a serotonin-norepinephrine reuptake inhibitor. It has a ceiling dose and can lower the seizure threshold, as well as contribute to hypoglycemia, and can lead to serotonin syndrome (Davis et al., 2020). Monitor the patient on short-acting pain medication. If the patient requires regular dosing every 4 to 6 hours, consider a long-acting formulation, but monitor closely for adverse effects (including altered mental status). Patients with continuous pain may be treated with around-the-clock dosing to achieve steady state (Davis et al., 2020).

Controlled-release opiates are appropriate for chronic pain (Prommer et al., 2021). Examples of long-acting opioids for pain control include morphine sulfate sustained release, oxycodone sustained release, hydromorphone sustained release, fentanyl patch, and the Butrans patch (Davis et al., 2020). Methadone is a unique opioid in that it appears to also act as an *N*-methyl-D-aspartate (NMDA) antagonist in addition to opioid receptor bonding. This unique element helps in the treatment of neuropathic pain management (Davis et al., 2020; Portenoy et. al., 2020). Methadone is also a long-acting pain medication, but it requires careful dosing and monitoring due to its variable half-life, potential prolongation of QT interval, and numerous drug interactions (Davis et al., 2020).

Be cautious with opioid rotation and use an appropriate equianalgesic dosing chart (Davis et al., 2020). Pay attention to renal and hepatic impairment. Choose an opioid with less active metabolites (fentanyl, hydromorphone, methadone) if renal function is declining (Portenoy, 2020). Monitor for signs of drug accumulation, which can include delirium, sedation, and myoclonus. Also monitor polypharmacy due to potential for drug interactions. If opioids are no longer necessary, they should not be stopped abruptly. They should be tapered because abrupt withdrawal could potentiate withdrawal symptoms (Davis et al., 2020).

Anticipate, assess for, and identify potential adverse effects (Resnick et al., 2019). Common adverse effects include constipation, nausea, sedation, urinary retention, and pruritis (Resnick et al., 2019). Long-term adverse effects include constipation, mental clouding, fatigue, osteoporosis, osteopenia, reduced libido, risk of myoclonus, mood changes, risk of opioid-induced hyperalgesia, and increased risk of sleep-disordered breathing (Resnick et al., 2019).

Unless a patient is in the dying process, if a patient becomes unarousable or experiences opioid-induced respiratory depression, the opioid can be reversed by using an opioid antagonist such as naloxone (Resnick et al., 2019). Sedation precedes respiratory depression, so monitor closely, particularly in the opioid-naïve patient. Begin with short-acting medications before adding a long-acting formulation (Portenoy, 2020). Sedation can occur during the inception of opioid treatment, yet tolerance generally develops to the effect. If sedation persists, consider rotating to another opioid. Methylphenidate can also be used to counteract sedation (Portenoy, 2020).

Most people develop a tolerance to all of the adverse effects, except for constipation, which typically requires an aggressive bowel regimen with regular dosing of a laxative and stool softener and/or osmotic agent. Most often this regimen is started while the opioid is prescribed (Portenoy, 2020). Methylnaltrexone is approved for severe opioid-induced constipation, and naloxone given orally has also demonstrated effectiveness (Portenoy, 2020). In addition, lubiprostone is approved for treating opioid-induced constipation (Resnick et al., 2019). Monitor bowel function closely to avoid obstipation, but if fecal impaction occurs, administer a lubricant, such as a glycerin suppository or mineral oil enema, and disimpact manually. Suppositories and enemas should be avoided in patients with neutropenia and thrombocytopenia. Because disimpaction can be a painful procedure, the patient may require premedication with an appropriate analgesic (Resnick et al, 2019).

Clinicians should educate patients and families about potential risks and benefits when initiating treatment, including adopting a universal precautions approach to minimize abuse, addiction, diversion, as well as clarify myths and misconceptions about opioid therapy. Clinicians should educate patients and families regarding safe storage, use, and disposal of controlled substances, as well as caution with using alcohol or sedating over-the-counter (OTC) medications (Portenoy, 2020).

Adjuvant medications may improve pain control and can be added at any step of the WHO step ladder (Forbes, 2011) (see Table 23-3). Tricyclic antidepressants may improve neuropathic pain. Adverse effects due to anticholinergic activity need to be considered. Nortriptyline and desipramine may be better tolerated in the older adult (Portenoy, 2020). Duloxetine, an inhibitor of norepinephrine and serotonin reuptake, is another option, indicated for diabetic neuropathy and chronic musculoskeletal pain, as well as for fibromyalgia (Portenoy, 2020). Anticonvulsants can be beneficial for lancinating neuropathic pain, which is often described as burning, shooting, and electrical. Gabapentin and pregabalin are commonly used (Schwan et al., 2019). Topical analgesics, such as lidocaine 5% patch, can be beneficial for postherpetic neuropathy. Capsaicin cream has shown benefit in neuropathic and non-neuropathic pain syndromes; however, about 30% of

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people do not tolerate the adverse burning sensation when treatment is initiated (Schwan et al, 2019). The use of topical agents, such as anti-inflammatories, anesthetics, compounded creams or gels with baclofen, tricarboxylic acids (TCAs), ketamine, or other combinations, show evidence that benefits outweigh harms; evidence quality is intermediate, and strength of recommendation is moderate (Portenoy, 2020). The effectiveness of ketamine is insufficient to make a recommendation for routine clinical use although it has proven to be acceptable with close monitoring (Portenoy, 2020).

Corticosteroids improve the pain of nerve or spinal cord compression. They also reduce edema and inflammation, resulting in improved pain control (Hardy et al., 2021). Corticosteroids also may improve pain management related to bowel obstruction and headaches caused by increased intracranial pressure (Hardy et al., 2021). Caution is advised due to the adverse effects of corticosteroids and therefore the use of long-term corticosteroids for chronic pain is usually reserved for end-of-life use (Portenoy, 2020). Clinicians can follow state-specific regulations to allow access to medical cannabis or cannabinoids for patients with chronic pain after consideration of the potential benefits and risks of available formulations (evidence-based benefits outweigh harms; evidence quality intermediate, strength of recommendation moderate) (Yang et al., 2020). A study by Yang and associates (2020) revealed that the majority of participants used cannabis for medical purposes, with the most common symptoms being pain/arthritis, followed by insomnia, anxiety, and depression. Calcitonin may be beneficial for bone pain due to vertebral compression fracture, pelvic fractures, and pain due to bony metastatic disease (Hardy et al., 2021). Baclofen, a muscle relaxant, can be used for spasticity due to central nervous system injury and neuromuscular disorders. Start with a low dose and increase slowly to minimize dizziness, sedation, and GI disorders. Baclofen should be tapered slowly to avoid potential delirium and seizure (Hardy et al., 2021).

Nonpharmacological approaches include behavioral therapies such as relaxation, mindfulness, distraction, imagery, prayer, and cognitive reframing (Sandvik et al., 2020). Physical measures include heat and/or cold application, repositioning, massage, and other complementary therapies such as acupuncture (Sandvik et al., 2020).

Radiation therapy is effective in the relief of pain related to tumor or masses. Radionucleotides also can be used for bone pain related to bone cancer. Chemotherapy, biological response modifiers, hormone therapy, and bisphosphonates all can reduce pain in patients with malignancies (Henson et al., 2020). Interventional procedures such as neuroablation, nerve blocks, celiac-plexus block, implantable drug delivery systems, vertebroplasty, and kyphoplasty can also help in the treatment of chronic pain (Henson et al., 2020).

TABLE 23-3 Adjuvant Pain Medications

Tricyclic antidepressants: desipramine, nortriptyline, amitriptyline	Neuropathic pain
SNRI: duloxetine	Diabetic peripheral neuropathy, fibromyalgia, and musculoskeletal pain
Anticonvulsants: gabapentin, pregabalin	Neuropathic pain
Capsaicin topical	Neuropathic and non-neuropathic pain
Lidocaine topical	Postherpetic neuralgia
Corticosteroids	Pain due to nerve compression; anti-inflammatory
Cannabinoids	State-specific regulations

Follow-Up: Perform ongoing assessment, reevaluation, and adjustment of plan of care as needed. Monitor for therapeutic effect, as well as adverse effects. Older adults are more susceptible to the adverse effects of opioids and other nonopioid analgesics and adjuvant medications and, thus, require close follow-up (Portenoy, 2020).

Sequelae: Unrelieved pain is associated with functional impairment, falls, mood disorders (including depression and anxiety), sleep and appetite disturbances, and decreased socialization (Hardy et. al., 2020). Improved pain control improves function and quality of life. Potential negative outcomes of opioids can include sedation, respiratory depression, coma, and death. These adverse events can typically be avoided by choosing the appropriate medication for the patient, starting at a low dose, and titrating slowly to effect while monitoring for adverse effects. Addiction can occur and should be monitored (Sirsch et al., 2020).

Prevention/Prophylaxis: Prevention/prophylaxis is dependent on etiology. Pain escalation may indicate advancing disease, particularly in the cancer patient; a new clinical finding; or tolerance to current opioid drug dose. Monitor with ongoing assessment. Anticipate painful procedures, such as wound care, and treat appropriately. Clinicians should incorporate a universal precautions approach to minimize abuse, addiction, and adverse consequences of opioid use, and should be cautious in coprescribing other centrally acting drugs (Resnick et al., 2019).

Referral: Refer the patient to a palliative care or pain management specialist for complicated pain syndromes or intolerance to common analgesics.

Education: Explain causes of pain syndromes, treatment strategies, and importance of regular follow-up for reassessment of pain and possible adverse effects. Educate patient and family about the risks of opioids and appropriate interventions for common adverse effects such as nausea and constipation. Advise the patient, family, and staff that sedation precedes respiratory depression and to report excessive sedation promptly. Educate the patient and family on the risk also of drug diversion and stress safe keeping of opioids. Educate patients and families on risks and benefits of nonopioid analgesics and the need to report to the clinician any changes regarding their pain management needs. Also instruct the patient and family on safe disposal of opioid medications after they are discontinued.

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THE DYING PATIENT

Description: Death and dying are mostly considered medical events today, but there is growing acceptance of hospice and palliative care as creating a more natural dying experience. According to the *NHPCO Facts and Figures* (National Hospice and Palliative Care Organization [NHPCO], 2020), in 2018, the percentage of Medicare patients to die under hospice care varied significantly by state with a low of 22.8% (Alaska) to a high of 60.5% (Utah). Of the patients enrolled in hospice care, 51.5% died at home, 17.4% in a nursing facility, 12.8% died in a hospice inpatient facility, 12.3% died in an assisted living facility, and 6% died in "other" locations including the hospital (NHPCO, 2020).

Etiology: Physiological changes of aging and multiple comorbidities influence the dying process.

Occurrence: Mortality rate is 100%. All people will die.

Age: Risk of death increases with advancing age.

Ethnicity: The meaning and experience of death are often influenced by one's culture and ethnicity. Honor the patient's cultural beliefs, traditions, rights, and rituals (Cain et al., 2018; National Consensus Project for Quality Palliative Care & National Coalition for Hospice and Palliative Care, 2018).

Contributing Factors: Advancing age, terminal illness, and comorbidities.

Signs and Symptoms: End-of-life symptoms commonly include pain, delirium, dyspnea, nausea and vomiting, constipation, noisy secretions, and fever (Albert, 2017). Other symptoms observed in the actively dying are disorientation, agitation, restlessness, generalized weakness, drowsiness, sleeping more, decreased oral intake, dysphagia, fever, bowel changes, and incontinence (Table 23-4). Although most people sleep more as death approaches with only brief periods of interactions, some experience a surge of energy. A dying person may also

TABLE 23-4 Quick Reference Guide for Symptom Management

SYMPTOM	TREATMENT
Fatigue	• The most prevalent of symptoms reported in advanced disease • Rule out possible causative factors and evaluate which might be treatable given goals of care: anemia, iron deficiency, electrolyte imbalances, hypothyroidism, hypoxia, nutrition deficiencies, medications, anxiety/depression, sleep abnormalities • Exercise, physical therapy, occupational therapy • Assistive devices, caregiving support (hygiene, cleaning, meals) • Stimulants such as methylphenidate (Ritalin®) 2.5–5 mg PO QD or bid to start, then titrate prn • Dexamethasone (Decadron®) 2–8 mg PO QD, do not give in the evening • Mirtazapine (Remeron®) 15 mg PO QHS to enhance sleep, also improves appetite and mood
Insomnia/Sleep Disorders	• Evaluate sleep patterns current and prior to diagnosis • Suggest sleep hygiene measures: reduce caffeine in afternoon/evening, do not watch TV/computer/cellphone/tablets in bed, limit alcohol intake, cool room, warm bath before bed • Relaxation therapy such as mindfulness exercises, meditation, guided imagery • For some, pharmacological therapies ineffective if used daily • Zolpidem (Ambien®) 5–10 mg PO QHS; lower doses for women; safety concerns–sleep walking/eating • Mirtazapine (Remeron®) 15 mg PO QHS to enhance sleep, also improves appetite and mood • Buspirone (Buspar®) 5–20 mg PO tid • Trazodone (Desyrel®) 25–50 mg PO QHS • Avoid antihistamines (diphenhydramine) for sleeping aid, especially in elderly or frail

Constipation [Acute]	• Assess frequency, volume, consistency, and normal patterns of bowel movements
	• Diarrhea may be due to impaction; rectal examination indicated
	• Goal ≈3/week without straining, pain, tenesmus
	• Identify potential causative factors that can be addressed: opioids, anticholinergics, antihistamines, phenothiazines, tricyclic antidepressants, diuretics, iron, chemotherapy, ondansetron, antacids, dehydration, inactivity, hypercalcemia, hypokalemia, partial bowel obstruction, spinal cord compression, autonomic neuropathy, depression, anorexia, hypothyroidism
	• Encourage varied diet
	• First evacuate bowel: magnesium hydroxide (Milk of Magnesia) 30 mL PO QD, magnesium citrate 150–300 mL per day, bisacodyl 2–3 tabs PO QD or 10 mg suppository or Fleet's Enema® (nothing per rectum if patient thrombocytopenic [<50,000 platelets] or neutropenic [ANC <500–1,000]); limit Fleet's and other sodium phosphate agents in renal dysfunction; if these are ineffective, give:
	  • Methylnaltrexone (Relistor®) SQ (for opioid-induced constipation only); dosing is weight based; contraindicated in obstruction
	  • Naloxegol (Movantik®) 12.5 or 25 mg PO Q AM [for opioid-induced constipation only]
	  • Naldemedine (Symproic®) 0.2 mg PO QD [for opioid-induced constipation for patients with chronic noncancer pain]

Continued

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TABLE 23-4 Quick Reference Guide for Symptom Management—cont'd

SYMPTOM	TREATMENT
Constipation [Ongoing Prevention]	• All patients on opioids should have an order for a bowel regimen • Add stimulant and softener combination (e.g., senna/docusate) and titrate to effect (max 8 tabs/day) • Increase with upward titration of opioid dose • If persistent, consider adding bisacodyl 2–3 tabs PO QD or 1 rectal suppository QD; lactulose 30–60 mL PO QD; metoclopramide (Reglan®) 10–20 mg PO QID; magnesium hydroxide (Milk of Magnesia) 30 mL PO QD • When constipation is related to opioids or in debilitated patient, changing the diet or adding fiber supplements is rarely helpful • Educate patients/families; there is much stigma about discussing bowel function *Even when not eating, patients should have bowel movements every 1–2 days. Untreated constipation can lead to discomfort and increased pain, as well as agitation in the cognitively impaired patient.*
Diarrhea	• Evaluate for potential causes of diarrhea common in palliative care and correct/treat when feasible: medications (overuse of laxatives, antibiotics, magnesium, chemotherapy, immunotherapy), infection, diet, herbal products (e.g., milk thistle, cayenne, ginger), fecal impaction, malabsorption syndromes from surgery or tumor, radiotherapy that includes abdomen in treatment field, inflammatory bowel disease, and other comorbid disorders • Loperamide (Imodium®) 2 mg PO; start with 4 mg, followed by 2 mg after each bowel movement, not to exceed 8 capsules/24 hours • Diphenoxylate/atropine (Lomotil®) 1–2 tabs PO QID, maximum 8 per 24 hours • Tincture of opium: 0.6 mL PO q 4–6 hours prn • Methylcellulose (e.g., Metamucil®) or pectin can help provide bulk to liquid stools • Octreotide (Sandostatin®) 50 mcg SQ/IV q 8 hours, maximum 1,500 mcg/day • Cholestyramine: 2–4 g PO/day before meals (especially for *Clostridioides difficile* diarrhea) • Pancrelipase (Creon®, Pancreaze®) 500–2,500 lipase units/kg PO with meals
Dyspnea [Shortness of Breath; Air Hunger]	• Identify and treat reversible causes: airway obstruction (e.g., bronchodilators and/or corticosteroids), infection (e.g., antibiotics), CHF or fluid overload (e.g., diuretics), anxiety (e.g., anxiolytics) • Opioids are first-line therapy; start with morphine 2.5–5 mg PO every hour (any opioid can be used); titrate upward aggressively 25%–50% if unrelieved • Liquids may be easier to swallow or can be placed sublingually [although absorbed enterally]: morphine liquid; oxycodone liquid • Parenteral (IV or SQ) opioids can be used if patient unable to swallow • Add anxiolytics (benzodiazepines) if anxiety is present [e.g., lorazepam every 4 hours as needed] or opioids fail to provide relief • Elevate head of bed [can use a fan for comfort]; pursed lip breathing • Consider oxygen only if patient is hypoxemic • Distraction, relaxation, mindfulness, create calm environment
Anorexia	• Educate and counsel patient/family regarding anorexia as a natural response to disease; interventions below only when loss of appetite bothersome to patient • Environmental alterations: small, frequent meals; moist foods or those with sauce/gravy take less energy to eat; assistance with meal preparation to improve energy for eating • Dexamethasone (Decadron®) 4 mg PO QD or prednisone 20 mg PO QD, especially when prognosis <6 weeks • Dronabinol (Marinol®) 2–10 mg PO every 4 hours, use with caution in the older adult • Mirtazapine (Remeron®) 15 mg PO QHS to enhance sleep, also improves appetite
Nausea and Vomiting *Not intended to prevent or treat chemotherapy-induced nausea and vomiting*	• Rule out potentially reversible causes: constipation, central nervous system disease, pain, altered electrolytes, ↑ICP, obstruction, antibiotics, chemotherapy, radiation therapy, opioids, digoxin *If nausea and vomiting due to activation of chemoreceptor trigger zone (CTZ) (e.g., medication-induced):* • Prochlorperazine (Compazine®) 10 mg PO q 6 hours or 25 mg PR q 8 hours • Haloperidol (Haldol®) 0.5–4 mg PO or IV/SQ q 6 hours • Ondansetron (Zofran®) 4–8 mg PO or IV q 8 hours (best when used for chemotherapy or radiation-induced nausea/vomiting; less effective when treating opioid-induced nausea and vomiting) • Olanzapine (Zyprexa®) 2.5–10 mg PO QD–bid • Promethazine (Phenergan®) 12.5–25 mg IV q 6 hours or 25 mg PO or PR q 6 hours *If nausea and vomiting due to gastric stasis causing early satiety, GI tract spasm:* • Metoclopramide (Reglan®) 10–20 mg PO or IV tid AC & HS [not with bowel obstruction] • Hyoscyamine (Levsin®) 0.125–0.25 mg PO/SL q 4 hours prn *If nausea and vomiting due to vestibular effects (nausea exacerbated by movement):* • Scopolamine transdermal patch 1.5 mg q 3 days (especially if underlying mechanism is vestibular; increased nausea or dizziness with ambulation) • Cyclizine (Meclizine®) 25–50 mg PO every 8 hours; best for motion sickness or increased intracranial pressure *If mechanism of nausea and vomiting is unclear, or unresponsive to other therapies:* • Dexamethasone (Decadron®) 4–8 mg PO/IV daily • Dronabinol (Marinol®) 2–10 mg PO every 4 hours *Administer antiemetics around the clock (scheduled). If nausea is controlled, then try reducing after 2–3 days.*

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TABLE 23-4 Quick Reference Guide for Symptom Management—cont'd

SYMPTOM	TREATMENT
Pain in the Final Hours of Life	• Observe for escalating pain and increase medications accordingly • May need to change route if swallowing is diminished; alternatives include transdermal, concentrated liquids taken orally in small volumes, parenteral • Abruptly discontinuing opioids or benzodiazepines may precipitate withdrawal syndrome; reduce dose 25% daily if no sign of pain in comatose patient; return to previous dose if any sign of return of pain • Myoclonus may occur; treat with clonazepam (Klonopin®) 0.5 mg PO tid, MAX 20 mg/day or lorazepam (Ativan®) 0.5–2.0 mg PO/IV q 4 hours if patient unable to swallow; may require midazolam (Versed®); IV/SQ; rotate opioids
Delirium and Agitation	• Identify and treat reversible causes: full bladder, fecal impaction, pain, dyspnea (hypoxemia, secretions, pulmonary edema), severe anxiety, nausea, pruritus, medications (e.g., corticosteroids, neuroleptics, anticholinergics), dehydration, infection • Reduce noise, orient gently, reduce nighttime interruptions to promote sleep/wake cycle • Haloperidol (Haldol®) 0.5–2 mg PO every 2–4 hours prn or IV/SQ 50% of oral dose (may repeat q 1 hour prn in severe delirium) • Olanzapine (Zyprexa®) 2.5–5 mg PO QHS; to start, increase to 10 mg after one week • Risperidone (Risperdal®) 1–2 mg PO q PM, increase by 0.5–1 mg q 2–7 days • Quetiapine (Seroquel®) 12.5–25 mg PO q 12–24 hours; to start, increase up to 50 mg bid • Chlorpromazine (Thorazine®) 12.5–25 mg PO/SQ q 4–12 hours, or 25 mg per rectum q 4–12 hours (IV can cause hypotension; avoid unless other agents ineffective and oral/rectal route unavailable) • Buspirone 5–20 mg PO tid
Excessive Secretions ["Death Rattle"]	• Atropine 0.4 mg SQ q 15 minutes prn • Scopolamine transdermal patch 1.5 mg topical, start with 1 mg (about 4-hour onset), increase to 2 mg after 24 hours. If insufficient, begin scopolamine 50 mcg/hour IV or SQ; double every hour to maximum of 200 mcg/hour • Glycopyrrolate (Robinul®) 1–2 mg PO or 0.1 mg–0.2 mg IV/SQ q 4 hours prn or 0.4–1.2 mg/day continuous IV/SQ infusion (this agent does not cross the blood brain barrier; less likely to cause confusion) • Hyoscyamine (Levsin®) 0.125–0.25 mg PO q 4 hours (liquid can be placed sublingually) • Change patient's position • D/C IV and/or enteral fluids as they may increase discomfort (e.g., cough, pulmonary congestion, sensations of choking/drowning, vomiting, edema, pleural effusions, ascites) • If fluids not discontinued, IV or SQ rate ought not exceed 500 mL/24 hours • Furosemide (Lasix®) prn to control overhydration. • Control thirst by moistening lips and mouth with substitute saliva (Oral Balance Moisture Gel® or Salivart®, at bedside; apply as frequently as needed) *Patients may be too weak to expectorate. This is not painful but distressing to family. Suctioning is traumatic, can cause bleeding and is painful. Do not suction beyond the oral cavity.*

References (and for more details): Dahlin et al., 2016; Ferrell et al., 2019.

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experience near-death awareness (American Association of Colleges of Nursing & City of Hope, 2019).

Diagnostic Tests: Usually not appropriate in the dying patient.

Differential Diagnosis: Not applicable.

Treatment: Assess the dying person frequently for objective signs of distress, such as grimacing and moaning, and treat distressing symptoms as follows: morphine liquid concentrate for pain and/or shortness of breath/air hunger; oxygen may be beneficial if the person is hypoxic; lorazepam liquid concentrate for restlessness and anxiety; haloperidol liquid concentrate for agitation/delirium or nausea; glycopyrrolate, or hyoscyamine for upper airway secretions; acetaminophen suppository for fever; and haloperidol liquid concentrate or prochlorperazine suppository for nausea and vomiting. For seizures, lorazepam can be given subcutaneously or IV, and diazepam or phenobarbital rectally. In the dying patient, glucocorticoids such as dexamethasone are often effective adjunctive medications for pain, anorexia, nausea, and asthenia (Albert, 2017; American Association of Colleges of Nursing & City of Hope, 2019). Focus on comfort measures such as oral care, skin care, continence care, and repositioning as appropriate; provide a calm environment (American Association of Colleges of Nursing & City of Hope, 2019).

Include the interdisciplinary team when addressing the spiritual, psychosocial, and emotional needs of the patient and the family. For most people, being "fully present" with the dying person is important. When death is inevitable, the dying person's attention shifts to the spiritual process of withdrawing from life. This process can create fear of abandonment, fear of the unknown, and fear of the dying process itself. Thus, it is essential for active involvement of the interdisciplinary team to support the patient and family through this process (American Association of Colleges of Nursing & City of Hope, 2019; National Consensus Project for Quality Palliative Care & National Coalition for Hospice and Palliative Care, 2018).

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Follow-Up: Ensure 24-hour access to care for the dying patient and their family. Provide bereavement care for the family (National Consensus Project for Quality Palliative Care & National Coalition for Hospice and Palliative Care, 2018).

Sequelae: Death of the patient; bereavement follow-up for the family. Ensure adequate symptom management and family support during the terminal phase (National Consensus Project for Quality Palliative Care & National Coalition for Hospice and Palliative Care, 2018).

Prevention/Prophylaxis: Effective communication of the patient's end-of-life wishes and advance care planning are essential. Too often these discussions are held when death is imminent. Rather, these discussions should occur at a time in the person's life when they can clearly express their essential wishes (Rietjens et al., 2017).

The delivery of bad news can have a profound and lasting impact (De Leo et al., 2020). An established model for the delivery of bad news is the A-B-C-D-E method, which encourages use of advanced preparation, building of a therapeutic environment, communication, dealing with patient/family reactions, and encouraging/validating emotions (Rabow & McPhee, 1999). Another useful tool is the S-P-I-K-E-S protocol, with its focus on Setting, Perception, Invitation, Knowledge, Empathy, and Strategy/Summary (Baile et al., 2000). Ensure that the setting of the meeting is private and free from interruptions. Ask about the patient's perception of their illness. This can be done by using open-ended questions to assess understanding. It is then helpful to obtain the patient's invitation/permission to provide the bad news. Understand that the amount of information desired from the patient can vary based on situation and culture. Use of a warning prior to the actual delivery of bad news can lessen the emotional impact. Avoid use of medical jargon. Use silence and empathetically validate any emotions that arise. It is helpful to have tissues available in advance. Summarize the news and facilitate questions. Establish a plan and "next steps." Ensure that the patient and family can contact you later if any further questions arise (Berkey et al., 2018).

Education: Teach the patient's family the signs of impending death and ask them to notify the medical team of distressing symptoms. Educate on comfort measures such as oral care, repositioning, and incontinence care. Prepare the family for the patient's possible near-death experience. Educate the patient's family on the signs of death and care at the time of death. Educate on bereavement resources (American Association of Colleges of Nursing & City of Hope, 2019).

GRIEF AND BEREAVEMENT

Description: Experiencing the loss of a loved one is a universal human experience. Bereavement is the condition of having experienced the death of a loved one and adjusting to a world without the deceased. Grief is the emotional response experienced by those who are bereaved. Grief is a normal response to loss and mourning which has both biological and psychological adaptive processes (Rabins, 2019; Riordan et al., 2020). Grief and bereavement are affected by the circumstances at the time of death. There are three primary types of grief: anticipatory, normal, and prolonged grief (Riordan et al., 2020). Originally, anticipatory grief was used to describe an increased detachment by family prior to the death of a loved one. This detachment was felt to be protective and aided in the emotional recovery of the bereaved. Use of the term anticipatory grief evolved to include all forms of pre-death grief and can be experienced by everyone involved, including the patient. Normal grief encompasses the typical emotional, physical, cognitive, and spiritual reactions to a loss (Riordan et al., 2020).

Prolonged grief (formerly referred to as complicated grief) is prolonged, intense, and disabling, with troubling thoughts, dysfunctional behaviors, dysregulated emotions, and/or serious psychosocial problems impeding adaptation to the loss (Boelen & Smid, 2017; Lundorff et al., 2017). Prolonged grief disorder (PGD) is a proposed ICD-11 diagnostic category to classify those individuals who experience prolonged disfunction (6 months or greater) related to loss (Boelen & Smid, 2017). In prolonged grief, individuals experience pervasive yearning, preoccupation with the deceased, and severe emotional pain (Lundorff et al., 2017). Delayed grief occurs when the normal grief reaction is suppressed or postponed, with the survivor avoiding the pain of loss either consciously or unconsciously. Exaggerated grief consists of intense reactions such as nightmares, delinquent behavior, phobias, and suicidal thoughts. Masked grief occurs when the survivor is unaware that behaviors interfering with normal functioning are the result of loss.

Etiology: Death of a loved one as experienced by family and caregivers.

Occurrence: Grief is very subjective, but some component of normal grief is experienced by most (90%) bereaved individuals. Anticipatory grief is estimated to occur in up to 15% of caregivers (Riordan et al., 2020). Prolonged grief is estimated to occur in 10% of survivors (Lundorff et al., 2017).

Age: Affects people of all ages. Consider multiple cumulative losses in older adults. Consider developmental stages of children in bereavement care. Bereaved older adults are more likely to suffer complications (see Sequelae).

Ethnicity: Grief is influenced by one's culture, ethnicity, and religion (Rabins, 2019; Sadak & Weiser, 2017).

Contributing Factors: Contributing factors that increase risk of prolonged grief include older age, violent or unnatural death, psychiatric comorbidities, social isolation, and previous losses (Riordan et al., 2020).

Signs and Symptoms: Normal grieving includes physical, emotional, cognitive, and behavioral responses. Common grief reactions include somatic symptoms; sleep and appetite

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disturbances; memory loss and impaired concentration; social withdrawal and disinterest in prior activities; a sense of the presence of the deceased person, and auditory or visual hallucinations; questioning of spiritual and religious beliefs; and emotional reactions, which may include relief, numbness, helplessness, self-reproach, sadness, guilt, and despair (Riordan et al., 2020).

Prolonged grief typically includes intense shock, anger and denial, feelings of numbness or hopelessness, a blunted emotional expression and anxiety, panic, and chronic depression, as well as a risk for self-harm, such as suicide or substance abuse. Those with complicated grief often have ruminating thoughts, excessive avoidance of reminders of the loss, and difficulty regulating emotion. Symptoms often persist for at least 6 months and interfere with functioning (Riordan et al., 2020).

Diagnostic Tests: Screening for depression with patient health questionnaire (PHQ-9) may be indicated. The Prolonged Grief Disorder-13 (PG-13) Questionnaire can be used as a diagnostic screening tool to measure prolonged grief.

Differential Diagnosis: Depression, including risk of suicide.

Treatment: Most people that experience grief will have no need for treatment or clinical intervention. However, active listening, validation of feelings, discussion of support systems, anticipatory guidance of what to expect through loss, and psychoeducation are techniques that can be used universally in management of bereaved individuals (Fields et al., 2018; Riordan et al., 2020). In the case of prolonged grief, psychotherapy has been shown to improve symptoms (Fields et al., 2018). Antidepressants may have limited efficacy in managing prolonged grief but can be used as a second-line treatment (Fields et al., 2018; Riordan et al., 2020). Complicated grief therapy is a specialized type of psychotherapy that uses motivational interviewing and cognitive behavioral therapy to help improve adaptation (Riordan et al., 2020). Hospice enrollment of the deceased has also been shown to significantly reduce depression and grief of those left behind (Riordan et al., 2020). It should also be noted that many hospice organizations offer bereavement counseling that may be available even if the deceased was not enrolled in hospice care.

Interventions to support grief work include (American Association of Colleges of Nursing & City of Hope, 2019):

- Support grieving as a normal experience. Being present and actively listening are essential. Allow the person to tell their story.
- Assist with identifying support systems such as extended family, friends, and support groups, such as local hospice bereavement support groups.
- Provide emotional and spiritual support. Consider referral for bereavement support groups and pastoral counseling. Provide written materials about grief. Encourage expression of feelings and encourage reminiscence and life review. Journal writing, letter writing, and drawing pictures can be beneficial.
- For complicated grief, refer to a bereavement specialist, health-care provider, and/or psychologist/psychiatrist.
- Caregivers can support the bereaved by sending a note, attending the funeral or memorial service, or making a supportive phone call.
- Staff bereavement may include encouraging staff to express their grief, reviewing deaths and their effects on staff, enabling staff to attend memorial services, creating staff mourning rituals, and encouraging self-care.

Follow-Up: Bereavement is associated with increased morbidity and mortality (see Sequelae). Ensure regular health-care appointments with the primary care provider for appropriate assessment, screening, and interventions.

Sequelae: Bereaved older adults aged 60 to 89 are more than twice as likely to suffer cardiovascular events or stroke within 30 days of the death of a partner. Widowed men have a 77% higher risk of death within 3 years following loss compared with married men (Riordan et al., 2020). Of those bereaved with prolonged grief, a majority (88%) meet criteria for other psychiatric diagnoses including major depression, posttraumatic stress disorder, or anxiety (Kristensen et al., 2017; Riordan et al., 2020). Screen and treat appropriately.

Prevention: Grief assessment begins at the time of a patient's admission to a hospital, long-term care facility, or hospice, as well as at the time of diagnosis of an acute, chronic, or terminal illness. Assess grief frequently during the bereavement period. Allow expression of grief through appropriate support (Fields et al., 2018; Riordan et al., 2020).

Referral: Refer surviving family and friends to bereavement support groups, grief counseling, and psychiatric care, if indicated. Follow-up with the health-care provider is essential as well.

Education: Instruct on normal grief reactions, bereavement resources in the community, and awareness of signs of complicated grief and depression.

CASE STUDY

Mrs. M. is an 85-year-old woman with breast cancer with metastasis to the lungs and bone. She is receiving palliative chemotherapy. Her husband died 5 years ago, and she is currently living with her daughter, who works outside the home. A private caregiver has been hired through a community agency. Mrs. M. enjoys visits from her family and fellow church members. Mrs. M. is seen by the nurse practitioner when she comes to her follow-up appointment in the oncology clinic. She is experiencing moderate-to-severe right chest wall pain. She also is experiencing dyspnea on exertion, nausea, constipation, and fatigue. A recent CT scan revealed disease progression on third-line chemotherapy.

Her past medical history includes metastatic breast cancer, hypertension, and hypothyroidism. Current medications: hydrochlorothiazide 12.5 mg PO daily and

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CASE STUDY—cont'd

levothyroxine 50 mcg PO daily; and senna PO bid for constipation/APAP. She has no known allergies.

Exploring her symptoms: She rates her right chest wall pain at 7/10. It is a dull, aching pain and worsens with activity. The pain has been present for 2 weeks. Hydrocodone/APAP had initially helped but is no longer effective. Because of the pain and dyspnea, she spends most of her time sitting in a reclining chair or lying in bed. Her appetite has decreased. She has not moved her bowels in 2 days. She complains of anorexia, fatigue, and insomnia.

Focused physical examination: temperature 98.2°F, heart rate (HR) 75 beats per minute, respiratory rate (RR) 22 breaths per minute, blood pressure (BP) 120/80 mm Hg, oxygen saturation 94%, weight 105 pounds, height 5 feet 4 inches, body mass index (BMI) 18 kg/m^2.

Mrs. M. is in moderate distress. She appears thin and frail. Her color is sallow, and her heart sounds reveal regular rate and rhythm, no murmur, rub, or gallop. Her lungs have bibasilar crackles, greater on the right, no wheezing. Her abdomen is soft with active bowel sounds, nontender to palpation.

1. What would you recommend for her symptom management?

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appendix A

Physiological Influences of the Aging Process

AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
	Integumentary System	
Loss of dermal and epidermal thickness	Fragility of skin	Prone to skin tears
	Impaired nutrient transfer	Slower wound healing
Flattening of dermal papillae	Shearing and friction force more readily peels off the epidermis	Prone to skin breakdown and injury
	Diminished cell-mediated immunity in the skin	Increased risk of dermatological infections
Atrophy of the sebaceous glands	Decreased production of oil and cerumen	Frequent pruritus and xerosis
		Increased risk of cerumen impaction
Atrophy of the eccrine glands	Decreased sweating ability	Impaired thermoregulation
Decreased vascularity	Slower recruitment of sweat glands by thermal stimulation	Alteration in thermoregularity response; diminished ability to adapt to temperature changes
		Fluid requirements may change seasonally
	Decreased body odor	Loss of skin water
	Decreased heat loss	Increased risk of heat stroke
	Dryness	Increased prevalence of pruritus
Collagen cross-linking	Collagen production reduced	Increased wrinkling of skin
Elastin regression	Laxity of skin	Increase risk for pressure injury
Loss of subcutaneous fat	Intraosseous atrophy, especially to the back of hands and to the face	Loss of fat tissue on soles of feet—trauma of walking increases foot problems
Decreased elasticity	Skin is slack and hangs loosely	Difficulty assessing skin turgor
Loss of subcutaneous tissue	Purpuric patches after minor surgery	Evaluate why injury is occurring; be alert for potential abuse or falls
Decreased number of melanocytes	Loss of pigment	Teach the importance of using sun block creams; refer to a dermatologist as needed
	Pigment plaque appears	Presence of lentigo or "liver spots"
Decreased turnover rate of keratinocytes	Increased exposure of the epidermal cells to the environment to include UV radiation	Increased risk of neoplastic skin cancers and malignant melanoma
Decline in fibroblast proliferation	Decreased epidermal growth rate	Decreased tissue repair response
	Slower re-epithelialization	
	Decreased vitamin D production and synthesis	Increased risk for developing osteoporosis and other conditions associated with vitamin D deficiency

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AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
Decreased hair follicle density	Loss of body hair	Reduces the body's ability to sweat and regulate body temperature
Decreased growth phase of individual fibers	Thin, short villus hairs predominate	Senescent alopecia
	Slower hair growth	
Loss of melanocytes from the hair bulb	Graying of the hair	Potential effect on self-esteem
Alternating hyperplasia and hypoplasia of nail matrix	Longitudinal ridges	Nails prone to splitting
	Thinner nails of the fingers	Advise patient to wear gloves, keep nails short, and avoid nail polish remover (causes dryness)
	Thickened, curled toenails or claw-like nails known as onychogryphosis	Painful ambulation. Impaired or restricted activities; refer patient to podiatrist
	Respiratory System	
Decreased lung tissue elasticity	Decreased vital capacity	Reduced overall efficiency of ventilatory exchange
	Increased residual volume	Diminished ventilatory response to hypoxia and hypercapnia
	Decreased maximum breath capacity	Decreased sensation of dyspnea
Thoracic wall calcification	Increased anteroposterior diameter of chest	Obscuration of heart and lung sounds
Cilia atrophy	Change in mucociliary transport; mucous-producing cells increase	Increased susceptibility to infection
Decreased respiratory muscle strength	Reduced ability to handle secretions and reduced effectiveness against noxious foreign particles	Prone to atelectasis
	Partial inflation of lungs at rest	
Less sensitivity to hypoxia; impaired ability to recognize bronchoconstriction	Increased respiratory distress	Increased risk of mortality from acute respiratory conditions
	Cardiovascular System	
Heart valves fibrose and thicken	Reduced stroke volume: cardiac output may be altered	Decreased responsiveness to stress; heart rate and blood pressure take longer to return to normal resting rate following exertion
	Slight left ventricular hypertrophy	Increased incidence of murmurs, particularly aortic stenosis, and mitral regurgitation
Mucoid degeneration of mitral valve	S_4 sound commonly heard	Increased risk for mitral valve prolapse
	Valve less dense; mitral leaflet stretches with intrathoracic pressure	Potential for rupture of the chordae tendineae, which leads to acute mitral regurgitation or the enhancement of pre-existing insufficiency
Fibroelastic thickening of the sinoatrial node; decreased number of pacemaker cells	Slower heart rate	Potential for oxygen deprivation; risk of syncope, potential need for pacemaker
	Irregular heart rate	Increased prevalence of atrial fibrillation and extra heartbeats become more common (S_4)
Collagen accumulation around heart muscle	Cardiac fibrosis	Heart chamber dilatation, or even infarct rupture.
Elongation of tortuosity and calcification of arteries	Increased rigidity of arterial wall	Aneurysms may form
Elastin and collagen cause progressive thickening and loss of arterial wall resiliency	Increased peripheral vascular resistance	Decreased blood flow to body organs
Loss of elasticity of the aorta dilation	Increase pulse pressure	Increased systolic blood pressure, contributing to coronary artery disease; aortic aneurysm
Increased lipid content in artery wall	Lipid deposits form	Increased incidence of atherosclerotic events such as angina pectoris and stroke

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AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
Decreased baroreceptor sensitivity (stretch receptors)	Decreased sensitivity to change in blood pressure	Prone to loss of balance with the potential for falls
	Decreased baroreceptor mediation to straining	Valsalva maneuver may cause sudden drop in blood pressure, orthostatic hypotension, and dizziness when the patient changes from a lying or sitting position to standing
	Gastrointestinal System	
Atrophy of muscles and bones of the jaw	Difficulty with mastication	Ability to thoroughly chew food is impaired and can contribute to dysphagia with solid foods
Dental enamel thins	Staining of tooth surface occurs	Tooth and gum decay; tooth loss
Gums recede	Teeth deprived of nutrients	Gingivitis
Fibrosis and atrophy of salivary glands	Prone to dry mucous membranes	Shift to mouth breathing is common; frequent complaints of dry mouth are expressed
	Decreased salivary ptyalin	Membrane more susceptible to injury and infection
		May interfere with breakdown of starches
Atrophy and decrease in number of taste buds	Decreased taste sensation	Altered ability to taste sweet, sour, and bitter
		Change in nutritional intake
		Excessive seasoning of foods
Presbyesophagus (aging esophagus)	Decline in esophageal peristalsis	Occasional discomfort as food stays in esophagus longer
	Delay in esophageal emptying	
	Subtle decrease in lower esophageal and upper esophageal pressures	
	Stiffening of the esophageal wall	Increase in dysphagia and aspiration
Decreased hydrochloric acid secretion	Reduction in amount of iron, vitamin B_{12} and calcium that can be absorbed	Possible delay in vitamin and drug absorption, especially calcium and iron
Decreased gastric blood flow	Compromised repair mechanism in the stomach	Increase susceptibility to gastric ulcer, atrophic gastritis, peptic ulcer disease and gastrointestinal medication side effects
Decreased abdominal muscle tone	Altered motility	Prone to constipation, functional bowel syndrome, esophageal spasm, diverticular disease
	Decreased colonic peristalsis	Prone to constipation and obstipation, fecal impaction
Partial loss of gastric glands in the mucosa of the stomach	Hypochlorhydria	Chronic atrophic gastritis
	Achlorhydria	
Decreased proportion of dietary calcium absorbed	Altered bone formation, muscle contractility, hormone activity, enzyme activation, clotting time, immune response	Symptoms more marked in women than in men
Decrease in hepatic mass and hepatic blood flow	Decreased storage capacity	Decreased efficiency in metabolizing drugs that pass through the liver
	Decrease in the activity of Cytochrome P450 enzyme system	
Less efficient cholesterol stabilization absorption	Increased evidence of gallstones	Atypical presentation of acute cholecystitis
	Genitourinary and Reproductive Systems	
Reduced renal mass	Decreased sodium-conserving ability	Administration and dosage of drugs may need to be modified
Loss of glomeruli	Decreased glomerular filtration rate	Susceptibility to develop acute kidney injury
	Decreased creatinine clearance	Progression of chronic kidney disease
	Increased blood urea nitrogen concentration	Increase risk for developing kidney injury

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AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
Histological changes in small vessel walls	Decreased renal blood flow	Changes in drug levels with ↑ risk of adverse drug effects
Decline in number of functioning nephrons	Decreased ability to dilute urine concentrate	Altered response to reduced fluid load or increased fluid volume
		Susceptibility of nocturia especially if fluids consumed before bedtime
Reduced bladder muscular tone	Decreased bladder capacity or increased residual urine	Sensation of urge to urinate may not occur until bladder is full
	Decreased detrusor contraction strength	Increased risk of urinary tract infections
	Age-related post void residual	Episodes of urinary incontinence may develop
Atrophy and fibrosis of cervical and uterine walls	Loss of rugosity in the vaginal rugal folds	Potential for vaginal prolapse
Reduced number and viability of oocytes in the aging ovary	Menopause	Decline in fertility
Structural change in the vulva	Reduction in pubic hair	Increased risk of developing genitourinary syndrome of menopause
	Decreased fat in the labia majora,	
	Decrease size of labia minora and vestibular bulbs	Increased risk for itching and burning of the vulva
Decreased vaginal wall elasticity	Vaginal lining thin, pale, friable	Post-coital bleeding
	Altered mucosal immune response	Increased risk for genital infections
		Atrophic vaginitis
	Narrowing of vaginal canal	Dyspareunia
	Loss of vaginal rugae	
Decreased levels of circulating hormones	Reduced lubrication during arousal state	Increased frequency of sexual dysfunction
		Decreased arousal and orgasm
Degeneration of seminiferous tubules with a selective loss of germ cells	Decreased seminal fluid volume	Decreased sperm concentration; decrease fertility
	Decreased force of ejaculation	Decreased percentage of sperm progressive motility
	Reduced elevation of testes	Alteration in sexual arousal
Decreased sperm production	Decreased concentration	Increased sperm DNA fragmentation and mutation
	Decrease total sperm count	
		Impairment in fertility
Proliferation of prostatic stromal and glandular tissue	Prostatic hypertrophy	Potentially compromised genitourinary function; urinary frequency and increased risk of malignancy
Narrowing of urethral lumen in males	Alteration in urinary flow and pressure	Increased risk for lower urinary tract dysfunction
Testicular volume decreases	Decrease in the number of Leydig cells	Decreased testicular function
	Increased secretion of gonadotropins	Biofunctional sperm parameters worsen, decreasing (seminal fluid volume, sperm concentration, percentage of progressive motility, and percentage of spermatozoa with normal form)
Involution of mammary gland tissue	Connective tissue replaced by adipose tissue	Easier to assess breast lesions
	Neuromuscular System	
Decreased muscle mass	Decreased muscle strength	Increased muscle cramping
		Increased risk for developing sarcopenia
	Tendons shrink and sclerose	Slight decreased tendon reflexes especially the Achilles' tendon

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AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
Decreased myosin adenosine triphosphatase activity	Prolonged contraction time, latency period, relaxation period	Decreased motor function and overall strength
Deterioration of joint cartilage	Joint space narrowing	Potential for pain, crepitation, and limitation of movement; osteoarthritis
Loss of water from the cartilage	Narrowing of joint spaces	Loss of height
Decreased bone mass	Decreased bone formation and increased bone resorption, leading to osteoporosis	More rapid and earlier changes in women
Decreased osteoblastic activity and increased osteoclast activity	Decreased bone mineral density	Greater risk of fractures
Osteoclasts resorb bone	Hormonal changes	Gait and posture accommodate to changes
Increased proportion of body fat	Centripetal distribution of fat and invasion of fat in large muscle groups	Anthropometric measurements required
Regional changes in fat distribution		Increased relative adiposity
Thickened leptomeninges in spinal cord	Loss of anterior horn cells in the lumbosacral area	Leg weakness may be correlated
Accumulation of lipofuscin	Altered RNA function and resultant cell death	Increased risk for developing macular degeneration
	Cellular degeneration	
Loss of neurons and nerve fibers	Decreased processing speed and vibratory sensation	Increased time to perform and learn
	Altered pain response	
	Decreased deep tendon reflexes, especially Achilles' tendon	Safety hazard
Decreased conduction of nerve fibers	Decreased psychomotor performance	Alteration in pain response
Neurofibrillary tangles in hippocampal neurons	Disrupts the synaptic communication between neurons	Heavy tangle formation and neuritic plaques in cortex of patients with Alzheimer's disease
Changes in sleep-wake cycle	Decreased stage 4, stage 3, and rapid eye movement phases	Increased or decreased time spent sleeping
	Deterioration of circadian organization	Increased nighttime awakenings
	Decrease in melatonin production	Changed hormonal activity
Slower stimulus identification and registration	Delayed reaction time	Prone to falls
Decline in proprioception function	Impaired balance	Higher propensity for falls
Decreased brain weight and volume	Cerebral atrophy	May be present in absence of cognitive impairments
		Also increases risk of subdural hematoma
Sensory System		
Morphological changes in choroid, epithelium, retina	Decreased visual acuity	Corrective lenses required
		Decreased mobility
		Slower walking speed
		Increased depression due to change in quality of life because of limited vision
		Impairment in instrumental activities of daily living
	Visual field narrows	Increased possibility of disorientation and social isolation
Decreased rod and cone function	Slower light and dark adaption	Increased risk for falls and injury
Pigment accumulation	Pigment dispersion syndrome	Blurred vision or halos may alter vision
Decreased speed of eye movements	Difficulty in gazing upward and maintaining convergence	Limitation in locating/reading objects that are above the level of the eye (i.e., road signage, items on shelves)

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AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
Sclerosis of pupil sphincter	Difficulty in adapting to lighting changes	Glare may pose an environmental hazard
	Increased threshold for light perception	Dark rooms may be hazardous without availability of accessible lighting
Increased intraocular pressure	Increased incidence of glaucoma	Decreased vision due to decline in peripheral vision and increased glare.
Decreased contrast sensitivity	Distorted depth perception	Incorrect assessment of height of curbs and steps; potential for falls
Ciliary muscle atrophy	Altered refractive powers	Corrective lenses often required
Nuclear sclerosis (lens)	Presbyopia	Near work and reading may become difficult
		There is a continuous loss of the ability of the eye to change its focus on objects at close distances.
		Glare, especially at nighttime driving, because of light scattering.
Deposit of calcium and cholesterol salts	Arcus senilis	Does not affect vision.
Senile miosis due to dilator muscles atrophy	Decrease in the size of the pupils	Pupils are less responsive to changes in ambient lighting.
Lens yellows	Color vision may be impaired	Less able to differentiate low color tones: blues, greens, violets
Reduction in number of cones at the fovea		Difficulty in distinguishing amongst pills and tablets in these low color tones
Diminished tear secretion	Dullness and dryness of the eyes	Irritation and discomfort may result
	Intactness of corneal surface jeopardized	Increased risk of corneal abrasion
Loss of auditory neurons	Decreased tone discrimination and voice localization	Suspiciousness may be increased because of paranoid dimensions secondary to hearing loss
	High-frequency sounds lost first	Social isolation
Angiosclerosis calcification of inner ear membrane	Progressive hearing loss, especially at high frequency	Difficulty hearing, particularly under certain conditions such as background noise, rapid speech, poor acoustics
	Presbycusis	Can result in loneliness, isolation, dependence
Decreased number of olfactory nerve fibers	Decreased sensitivity to odors	May not detect harmful odors such as rancid foods or noxious gases
	Affects flavor of food which is a combination of taste and smell	Potential safety hazard
		Loss of appetite
Number of taste buds diminished	Alteration in taste sensation	Possible changes in food preferences and eating patterns
Reduced tactile sensation	Decreased ability to sense pressure, pain, temperature	Misperceptions of environment and safety risk
	Endocrine System	
Decline in secretion of testosterone, growth hormone, insulin, adrenal androgens, aldosterone, thyroid hormone	Decreased hormone clearance rates	Increased mortality associated with certain stresses (burns, surgery); increased prevalence of hormonal disease
Defects in thermoregulation	Shivering less intense	Susceptibility to temperature extremes (hypothermia/ hyperthermia)
Reduction of febrile responses	Poor perceptions of changes in ambient temperature	Unrecognized infectious process operative
	Reduced sweating; increased threshold for the onset of sweating	Delayed healing of the skin
		Hyperthermia
	Fever not always present with infectious process	Delay in diagnosis of infectious, inflammatory, or neoplastic disease

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AGE-RELATED CHANGE	APPEARANCE OR FUNCTIONAL CHANGE	IMPLICATION
Alteration in tissue sensitivity to hormones	Increased insulin resistance and glucose intolerance	Increased incidence of type 2 diabetes
Dysregulation of mineralocorticoid receptor	Vasoconstriction	Increase in blood pressure
Nodularity and fibrosis of thyroid	Increase in the development of thyroid nodules	Increased frequency of thyroid disease
Decreased basal metabolic rate	Alteration in carbohydrate tolerance	Increased incidence of obesity
Hematological System		
Decreased percentage of marrow space occupied by hematopoietic tissue	Ineffective erythropoiesis	Stem cell proliferation and maturation however is preserved.
	Decrease in trabecular bone in the marrow.	
Immune System		
Thymic involution and decreased serum thymic hormone activity	Decreased number of T cells	Less vigorous and/or delayed hypersensitivity reactions
	Production of anti–self-reactive T cells	
Decreased T-cell function	Impairment in cell-mediated immune responses	Increased risk of mortality
Decreased B-cell function		
Appearance of autoantibodies	Decreased cyclic adenosine monophosphate and glucose monophosphate	Increased incidence of infection
	Decreased ability to reject foreign tissue	Reactivation of latent infectious diseases. Increase risk for developing herpes zoster
	Increased laboratory autoimmune parameters	Increased prevalence of autoimmune disorders
Redistribution of lymphocytes	Impaired immune reactivity	Increased risk for developing sepsis
	Slowed inflammatory process	
Changes in serum immunoglobulin	Increased immunoglobulin A levels	Increased prevalence of infection
	Decreased immunoglobulin G levels	Slowed wound healing

Sources: Abdullah & Abbas, 2011; Aversa et al., 2019; Binkley et al., 2017; Breining et al., 2018; Condorelli et al., 2013; Cowling et al., 2019; Ferlinc et al., 2019; Gibson & Wagg 2017; Gunes et al., 2016; Hofman et al., 2017; Jones & Boelaert, 2015; Joosten, 2018; Kaya et al., 2017; Lipa et al., 2020; Liu et al, 2019; Mander et al., 2017; Neto et al., 2018; O'Sullivan et al., 2017; Salvi et al., 2006; Schott, 2017; Sharma & Goodwin, 2006; Swenor et al., 2020; Stott et al., 2017; Tay & Harwood, 2020; Trüeb et al., 2018; Umpierrez & Pasquel, 2017; van den Beld et al., 2018.

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appendix B

Laboratory Values in the Older Adult

LABORATORY TEST	NORMAL VALUES	CHANGES WITH AGE	COMMENTS
		Urinalysis	
Protein	0–5 mg/100 mL	Rises slightly	May be due to kidney changes with age, urinary tract infection, or renal pathology.
Protein-to-creatinine ratio	≤0.2 mg/mg	May increase	Ratio value >3.5 mg/mg confirms nephrotic proteinuria.
Glucose	0–15 mg/100 mL	Declines slightly	Glycosuria appears after high plasma level; unreliable.
Specific gravity	1.005–1.020	Lower maximum in elderly, 1.016–1.022	Decline in nephrons impairs ability to concentrate urine.
		Hematology	
Erythrocyte sedimentation rate	Male: 0–20 mm/hour Female: 0–30 mm/hour	Slight increase in normal aging. Elevated in inflammatory conditions. May be decreased during heart failure. Upper limit of reference range in males 40 mm/hour and 45 mm/hour in females	Neither sensitive nor specific in the aged. ESR should not be used alone to diagnose an inflammatory process in older adults. Levels above 50 are considered significant for disease and mortality risk.
Iron	50–160 mcg/dL	Slight decrease due to impaired production of gastric acid	Decrease is due to impaired production of gastric acid
Iron binding	230–410 mcg/dL	Decrease	
Hemoglobin	Male: 13 gdL	Male: 11.5 gm/dL	Anemia common in the elderly but not a normal change with aging. In males a decline in testosterone production results in a decline in hemoglobin, but not below that of a normal female.
	Female: 11.0 g/dL	Female: 11.0 gm/dL	
Hematocrit	Male: 40%–54% Female: 36%–46%	Slight decrease speculated	Decrease in anemias, multiple myeloma, protein malnutrition, CKD, rheumatoid arthritis. Increased in dehydration, severe diarrhea.
Leukocytes	4,300–10,800/mm^3	Drop to 3,100–9,000/mm^3	Decrease may be due to drugs or sepsis and should not be attributed immediately to age.
Lymphocytes	500–2,400 T cells/mm^3 50–200 B cells/mm^3	T-cell and B-cell levels fall	Risk of infection is higher; immunization is encouraged.
Platelets	150,000–350,000/mm^3	No change in number	
		Blood Chemistry	
Albumin	3.5–5.0 g/dL	Decline	Related to decrease in liver size and enzymes; protein-energy malnutrition common. Regardless of reason for decline if less than normal need to correct serum calcium as calcium is bound to albumin.

Continued

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LABORATORY TEST	NORMAL VALUES	CHANGES WITH AGE	COMMENTS
Globulin	2.3–3.5 g/100 mL	Slight increase	
Total serum protein	6.0–8.4 g/100 mL	No change	Decreases may indicate malnutrition, infection, liver disease.
Blood urea nitrogen	Men: 10–25 mg/100 mL Women: 8–20 mg/100 mL	8–28 mg or slightly higher	Increases with dehydration, GI bleeding, pre-renal failure. Decreases due to low protein diet, malnutrition, overhydration. Decline in glomerular filtration rate; decreased cardiac output. All electrolytes need to be evaluated when a concern for renal disease exists.
Creatinine	0.6–1.5 mg/100 mL	Increases to 0.6–1.2 mg/100 mL seen	Related to decreases in lean body mass. Unreliable indicator of abnormalities in renal function, especially in the frail older adult and/or those with sarcopenia.
Creatinine clearance	104–124 mL/min	Decreases 10%/decade after 40 years of age	Decreased renal impairment, hyperthyroidism, thiazides, increased hypothyroidism.
Glucose tolerance	62–100 mg/dL after fasting; <120 mg/dL after 2 hours postprandial	Slight increase of 10 mg/dL/decade after 30 years of age	Diabetes increasingly prevalent; drugs may cause glucose intolerance.
Triglycerides	40–150 mg/100 mL	20–200 mg/100 mL	Risk of coronary artery disease Elevated in non-fasting collection, hypothyroidism, alcoholism.
Cholesterol	120–200 mg/dL	Increases by 30–40 mg/dL by age 60	Risk of cardiovascular disease Goal for LDL cholesterol to be less than 100 mg/dL.
Thyroxine (T4)	4.5–13.5 mcg/dL	3.3–8.6 mcg/dL	Changes suggest thyroid disease; may be seen in euthyroid patients with acute or chronic illness or caloric deficiencies.
Triiodothyronine (T3)	90–220 ng/dL	Decrease 25%	May impact metabolism, body temperature, or heart rate.
Thyroid-stimulating hormone (TSH)	0.5–5.0 mcg/mL	Slight increase	Sensitive indicator for diagnosing thyroid disease.
Alkaline phosphatase	20–130 IU/L	Increase by 8–10 IU/L	Increases by 20% between the third and eighth decade. Elevations may be found with bone abnormalities, drugs (e.g., narcotics), and consumption of a fatty meal. For best results, this test should be ordered during fasting.
Serum alkaline aminotransferase (ALT)	M: 10–55 units/L F: 7–30 units/L	Overall increases can measure to 17–30 U/l	Increases can be due to cancer (liver, bone) leukemia, RA, multiple myeloma.
Serum aspartate aminotransferase (AST)	M: 10–40 units/L Female: 9–25 units/L	Overall increases can measure to 18–30 U/l	Increases can be due to MI, hepatitis, pancreatitis, liver cancer.

Sources: Dharmarajan & Pitchumoni, 2012; Edwards & Baird, 2005; Vásárhelyi & Debreczeni, 2017.

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CHAPTER 1: CHANGES WITH AGING

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CHAPTER 3: EXERCISE

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CHAPTER 8: DERMATOLOGIC DISORDERS

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CHAPTER 10: CARDIOVASCULAR DISORDERS

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CHAPTER 11: RESPIRATORY DISORDERS

Assessment

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CHAPTER 14: RENAL AND UROLOGIC DISORDERS

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CHAPTER 15: GYNECOLOGICAL DISORDERS

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CHAPTER 17: CENTRAL AND PERIPHERAL NERVOUS SYSTEM DISORDERS

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CHAPTER 18: ENDOCRINE AND METABOLIC DISORDERS

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CHAPTER 20: PSYCHOLOGICAL DISORDERS

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CHAPTER 21: POLYPHARMACY

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CHAPTER 22: CHRONIC ILLNESS AND THE APRN

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CHAPTER 23: PALLIATIVE CARE AND END-OF-LIFE CARE

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Bonus Chapter

COVID-19

Signal Symptoms: Coronavirus disease 2019 (COVID-19) affects different people in different ways. The symptoms are characterized mainly by cough, fever, fatigue, and dyspnea. Other common symptoms include a headache, sore throat, joint and muscle pain, and loss of the sense of smell and taste.

A Cochrane review found that at least one half of patients had a cough, sore throat, fever, myalgia/arthralgia, fatigue, and/or headache (Struyf et al., 2021). Anosmia and ageusia were also common features and may be useful as red flags for diagnosis. The presence of fever, myalgia/arthralgia, fatigue, and headache substantially increased the possibility of COVID-19 when present. Presentation may change based on the COVID variant. For example, for those affected by some of the more recent variants, symptoms have been similar to that of a sinus infection, but without many of its other classic signs.

Description: COVID-19 is caused by the severe acute respiratory syndrome (SARS) coronavirus (CoV) 2, which was first noted in Wuhan, China, in December 2019. After multiple cases were identified worldwide, it was officially designated as a pandemic by the World Health Organization (WHO) on March 11, 2020.

Etiology: Coronaviruses are a class of viruses that cause a variety of diseases from the common cold to more severe infections. *Corona*, meaning "crown," describes the spikes that cover the outer lipid layer of the virus. In each spike, there is a single strand of ribonucleic acid (RNA)-containing protein (Chorba, 2020). The main spike protein causing infection is the S protein. These spikes have been the target for the development of vaccines to combat viruses from influenza A to Ebola. Viruses are not living organisms; they depend on the host's DNA to replicate and cause disease. The SARS-CoV-2 virus enters the human cell by attaching to the angiotensin-converting enzyme 2 (ACE2) receptor. These receptors are primarily located in the upper and lower respiratory tracts, the gastrointestinal (GI) tract, and the kidneys.

Seven coronaviruses are known to infect humans. They primarily infect the upper respiratory and GI tracts. The coronavirus that causes the common cold was first identified in 1966. Several newly emerged viruses are zoonotic, meaning the infectious source originated in animals and mutated to novel viruses transmittable in humans. The SARS-CoV-1 emerged in China in 2003 and spread to four other countries before the infection was contained. In 2012, another novel coronavirus emerged, Middle East respiratory syndrome (MERS) CoV. Although very deadly, resulting in a 35% mortality rate, it was not very transmissible. When SARS-CoV-2 was first identified in 2019, it was not clear if it would result in a disease like SARS-CoV-1 (more transmissible but less deadly) or if it would be like MERS.

The median time of incubation after infection with SARS-CoV-2 is 5 days, but it can be up to 2 weeks during which the patient is contagious. How contagious a disease is can be described by the R0 (pronounced "R naught"), or reproduction number. The R0 describes how many people will contract a contagious disease from a person with the disease. The at-risk population are those who have not been vaccinated or have not previously contracted the disease. For COVID-19, the original estimates of the R0 underestimated the infectivity. In February 2020, the WHO estimated the R0 to be 2.0 to 2.5, whereas average R0 has been 5.7 to 5.9—more than double the original estimate. As more people are vaccinated or have had the disease, the R0 may drop, but the evolving variants and their susceptibility to the vaccines will make a difference. As a comparison, measles has an R0 of 12 to 18 among unvaccinated people.

Occurrence: The first cases of COVID-19 were identified in Wuhan city, Hubei province, Peoples Republic of China, in December 2019. The genome was published for the virus in January 2020. The WHO declared a Public Health Emergency of International Concern on January 30, 2020. The first confirmed case in the United States was identified in February 2020. On March 11, 2020, the WHO declared COVID-19 a pandemic. The numbers of infections and deaths from COVID-19 continue to rise. As of June 13, 2022, there were 545,226,550 cases reported worldwide with 6,334,728 deaths; more than 1,000,000 of these deaths

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occurred in the United States alone. More men than women are diagnosed with COVID-19 and men are more likely to die of the disease.

Occurrence: Individuals of any age are susceptible to COVID-19, but it commonly affects those who are middle-aged and older adults. The risk of developing dangerous symptoms increases with age. Those who are aged 85 and older are at the highest risk of serious symptoms. In the United States, nearly 81% of deaths from the disease have been in people aged 65 and older (Centers for Disease Control and Prevention [CDC], 2022a). Risks are even higher for older people when they have other existing comorbid conditions.

Ethnicity: The relationship between ethnicity and COVID-19 is unclear.

Contributing Factors: COVID-19 can affect anyone and can cause symptoms ranging from mild to very severe. Those with risk factors may be more likely to need hospitalization or intensive care, or they may be more likely to die of the infection. More men than women are diagnosed with COVID-19 and are more likely to die of the disease. Other contributing factors include:

- Residence in a long-term care facility
- Obesity
- Cardiovascular disease
- Diabetes
- Chronic respiratory disease
- Chronic kidney disease
- Chronic liver disease
- Smoking
- Malignancy
- Cerebrovascular disease
- Solid organ or blood stem cell transplant
- Hypertension
- Dementia
- Immunosuppression
- HIV infection
- Substance use disorders.

Signs and Symptoms: A Cochrane review found that at least one-half of patients had a cough, sore throat, fever, myalgia/arthralgia, fatigue, or headache (Struyf et al., 2021). Anosmia and ageusia was also common feature in some COVID variants. The presence of fever, myalgia/arthralgia, fatigue, and headache substantially increased the possibility of COVID-19 when present. Cough and sore throat were common in those without COVID-19, so these symptoms alone were less useful for diagnosis (Struyf et al., 2021).

In contrast to SARS-CoV-1, patients with COVID-19 were noted to have more thrombo-embolic pathologies and an increased risk of developing coagulopathy similar to disseminated intravascular coagulation and venous and arterial thrombosis and resulting pulmonary embolism.

Mild to moderate hepatic injury has also been observed as signs of acute phase inflammation or direct viral infection causing hepatitis. Acute kidney injury (AKI) has been associated with higher disease severity and is an adverse prognostic sign for survival. SARS-COV-2 may directly target the kidney parenchyma.

The neurologic system is also affected by COVID-19, causing headache, confusion, anosmia, dysgeusia, nausea, and vomiting. This neuroinvasion may be the cause of alterations in respiratory and cardiovascular regulation.

Diagnostic Tests: There are three types of diagnostic tests used in identifying SARS-CoV-2 infection.

Nucleic Acid Amplification Testing (NAAT): NAAT testing is a reverse transcriptase polymerase chain reaction (RT-PCR) diagnostic test that is considered the gold standard for detecting SARS-CoV-2 infection for people who are symptomatic and asymptomatic. The RT-PCR test amplifies and detects the presence of SARS-CoV-2 genetic material. RT-PCR tests look for the genetic material of the SARS-CoV-2 virus in the nose, throat, or other areas in the respiratory tract. A nasopharyngeal, oropharyngeal, or nasal swab; saliva; or a lower respiratory tract specimen is obtained and sent to the laboratory for testing. A positive result occurs when the SARS-CoV-2 primers match the DNA in the sample and the sequence is amplified, creating millions of copies from an infected individual (Bustin & Nolan, 2020). The primers only amplify genetic material from the virus, so it is unlikely a sample will be positive if viral RNA is not present. If it does, it is called a false positive. A negative result happens when the SARS-CoV-2 primers do not match the genetic material in the sample and there is no amplification or virus (Kucirka et al., 2020). A false-negative result happens when a person is infected, but there is not enough viral genetic material in the sample for the RT-PCR test to detect it. This can happen early after a person is exposed. Overall, false-negative results are more likely than false-positive results.

Conventional RT-PCR tests must be processed in a laboratory, which result in waiting a day or more before getting a result. Errors in test preparation or sample collection may result in false negatives in both asymptomatic and symptomatic people. The RT-PCR test has been found to be 87% sensitive and 97% specific (Blessen et al., 2020).

In patients who have had a recent SARS-CoV-2 infection, NAATs can detect SARS-CoV-2 RNA in specimens obtained weeks to months after the onset of COVID-19 symptoms (Rhee et al., 2020; Xiao et al., 2020). Currently molecular diagnostic assays are unable to differentiate between the presence of remnant viral RNA (noninfectious) and replication-competent (infectious) virus (Rhee et al., 2020). The probability of recovering infectious virus more than 10 days from the onset of symptoms in those with mild disease and more than 20 days in those with severe disease is very low (Arons et al., 2020; Bullard et al., 2020). The CDC (2021) recommends that NAATs should not be repeated in asymptomatic persons within 90 days of a previous SARS-CoV-2 infection unless the individual experiences new symptoms consistent with COVID-19. If reinfection is suspected, then the individual should follow isolation protocol pending test results. Results should be interpreted in consultation with an infectious disease specialist. Review of history, test results, and RT-PCR Ct value and presence of signs and symptoms of COVID-19 (CDC, 2021).

Antigen-Detection Rapid Diagnostic Tests (Ag-RDTs): An Ag-RDT detects viral antigens using a lateral flow immunoassay intended for the qualitative detection of nucleocapsid protein antigen from SARS-CoV-2. WHO (2021) recommends that Ag-RDTs meet the minimum performance requirements of ≥80% sensitivity and ≥97% specificity, which is comparable to the NAAT. Ag-RDTs are designed to directly identify SARS-CoV-2 proteins produced by replicating virus in respiratory secretions. Results are available within 15 minutes. Antigen is usually detectable using an anterior nasal swab during the

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acute phase of infection. A positive result, indicating the presence of viral antigen, along with patient history and the presence of clinical signs and symptoms are consistent with a diagnosis of COVID-19. The test is most reliable in patients who are symptomatic and who test within the first 5 to 7 days of symptom onset when the viral load is higher (WHO, 2021). The reliability of the result is dependent on the sensitivity and specificity of the test, as well as the incidence of infection in the population tested. The results of antigen testing are most reliable in areas with a high pre-test probability of infection (those communities with transmission and a test positivity rate 5% or more) (WHO, 2021). When there is a high pre-test probability of infection, an Ag-RDT may be considered diagnostic without a confirmatory NAAT. Confirmation may be best when considering prescribing therapeutics. When there is no transmission or low transmission there is a lower pre-test probability of infection, and there will be more false positives. In such situations RT-PCR testing is preferred. For a patient who has a positive Ag-RDT in the setting of low pre-test probability, a confirmatory NAAT should be considered. Negative Ag-RDT results in a symptomatic patient should be treated as a probable case, and confirmation with NAAT should be considered.

Serology Tests: Serology tests look for antibodies against SARS-CoV-2 in the blood. Antibodies determine whether someone has been previously infected or vaccinated against a virus that causes a disease, but they cannot determine a current infection. When ordering antibody tests, it is important to know the type of information various tests provide and how to interpret test results. Antibody testing is not currently recommended to assess immunity to COVID-19 following vaccination.

Immunoglobulin M (IgM) is the first antibody that is formed against infection and is usually detectable within 1 to 2 weeks. The body then forms immunoglobulin G (IgG), which is usually detectable 2 weeks after the illness starts. IgM usually disappears from the blood within a few months, but IgG can last for years. Some antibody tests look for both IgM and IgG, and some only test for IgG. A positive antibody test means that the person being tested was likely infected with COVID-19 in the past. A negative antibody test means that the person may not have had COVID-19 in the past. However, the person could have a current infection, and the sample may have been collected too soon to give a positive result. In fact, there may be a lag of up to 21 days before antibodies are detectable, meaning the diagnosis of an active case of COVID-19 may be missed (CDC, 2021). Antibody levels decrease over time, so those who had COVID in the past may not have detectable levels of antibodies. It is not known if a positive antibody test means you are protected against getting infected in the future (CDC, 2021).

Other Diagnostic Tests:

- Pulse oximetry
- Arterial blood gas
- Complete blood count
  - Leukopenia
  - Lymphopenia (A low absolute lymphocyte count can be a marker of severe COVID-19.)
  - Thrombocytopenia
- Comprehensive metabolic panel
  - Electrolytes
  - Glucose
  - Blood urea nitrogen (BUN)
  - Creatinine
  - Estimated glomerular filtration rate (eGFR)
  - Elevated aminotransferase levels
  - Lactate dehydrogenase
  - Total bilirubin
- Clotting factors
  - Partial thromboplastin time
  - Prothrombin time/International Normalization Ratio
  - D-dimer
- Inflammatory markers
  - C-reactive protein
  - Ferritin
  - Albumin
  - Sedimentation rate
- Cardiovascular markers
  - Troponin
  - Brain natriuretic peptide
- Imaging
  - Chest x-ray
  - Chest computed tomography

Differential Diagnosis:

- Acute pulmonary edema
- Acute respiratory distress syndrome
- Chronic obstructive pulmonary disease exacerbation
- Community-acquired pneumonia (bacterial or viral)
- Influenza
- Interstitial lung disease
- Nonspecific viral upper respiratory tract infection
- Opportunistic pulmonary infection
- Pulmonary embolism
- Streptococcal pharyngitis

Treatment: Approximately 80% of patients with COVID-19 have mild illness that does not warrant medical intervention or hospitalization (Stokes et al., 2020). Health-care providers must identify patients who may be at high risk for progression to severe COVID-19 because these patients may be candidates for antivirals or anti-SARS-CoV-2 monoclonal antibody treatment.

Options available for the treatment of nonhospitalized adults with mild to moderate COVID-19 who are at high risk of disease progression have increased. Factors that play a role in selection of the best treatment option for an individual patient include:

- Clinical effectiveness and availability of the specific treatment option
- Likelihood of administering parenteral medications
- Potential for significant drug–drug interactions
- The local prevalence of variants of concern (National Institutes of Health [NIH], 2022).

The COVID-19 Treatment Guidelines Panel made recommendations for using the following therapeutic interventions for patients outside the hospital setting. These are listed in order of the panels preferred therapies.

Nirmatrelvir/ritonavir (Paxlovid) 100 mg PO is a SARS-CoV-2 protease inhibitor antiviral combination medication given U.S. Food and Drug Administration (FDA) Emergency Use Authorization (EUA) in December 2021 for adults and children (age 12 years and older weighing at least 40 kg) with mild to moderate COVID-19 symptoms and at high risk

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for progression to severe COVID-19. It is not approved for pre-exposure or post-exposure prophylaxis. In the EPIC-HR trial, ritonavir-boosted nirmatrelvir reduced the risk of hospitalization or death by 88% compared to placebo in nonhospitalized adults with laboratory-confirmed SARS-CoV-2 infection (Hammond et al., 2022; Mahase, 2021).

Nirmatrelvir blocks the activity of an enzyme that SARS-CoV-2 needs to replicate. Ritonavir acts as a booster to increase nirmatrelvir drug levels, slowing the metabolism of nirmatrelvir to maintain plasma levels (NIH, 2022). The approved dose is 300 mg nirmatrelvir (two 150 mg tablets) with 100 mg of ritonavir (one 100 mg tablet), with all three tablets taken together twice daily for 5 days. Doses should not be chewed, broken, or crushed and must be initiated within 5 days of symptom onset. Dose adjustment is needed in patients with eGFR of 30 to less than 60 mL/min. Avoid using this medication if eGFR is below 30 mL/min.

Ritonavir has many drug–drug and drug–herbal interactions of clinical significance that may limit its use. The COVID-19 Treatment Guidelines Panel recommended careful review of each patient's concurrent medications, including over-the-counter medications and herbal supplements, to evaluate for potential drug–drug interactions. Each clinician should determine whether there are any potential strategies to minimize risk of drug–drug interactions. For example, consider adjusting the dose of concomitant medication, using an alternative, temporarily holding the medication, or increased monitoring for adverse reactions. Ritonavir is contraindicated in patients taking certain CYP-3A4 inducers or substrates (e.g., amiodarone, diltiazem, fluconazole) (Lemaitre et al., 2022). Serious adverse events may include hepatotoxicity and HIV-1 resistance in HIV-positive patients. Common medication side effects include dysgeusia, diarrhea, hypertension, and myalgia. Ritonavir-boosted nirmatrelvir has demonstrated antiviral activity against all coronaviruses that are known to infect humans (Owen et al., 2021).

Remdesivir (RDV) is an antiviral IV medication that was developed more than a decade ago to treat hepatitis C and respiratory syncytial virus (RSV). Unfortunately, RDV was not found to be effective in those diseases. Later, RDV was tested in clinical trials during an Ebola outbreak, but it was not found to be effective. Other studies suggested that RDV was effective against viruses in the coronavirus family, such as MERS and SARS.

RDV became the first drug to receive emergency use authorization from the FDA to treat people hospitalized with COVID-19 and in nonhospitalized patients with mild to moderate COVID-19 who are at high risk of disease progression. It is an antiviral medication that works by interrupting production of the virus. Coronaviruses have genomes made up RNA. RDV interferes with one of the enzymes the virus needs to replicate RNA. RDV has been studied in nonhospitalized patients with mild to moderate COVID-19 who were at high risk of progressing to severe disease. One trial showed that 3 consecutive days of IV RDV resulted in an 87% relative reduction in the risk of hospitalization or death compared to placebo (Gottlieb, 2022).

RDV should be initiated as soon as possible and within 7 days of symptom onset. In the nonhospitalized patient, RDV is a 3-day consecutive daily infusion. Patients should receive RDV in a setting where patients can be monitored and managed for potential allergic reactions. Patients should be monitored during the infusion and for at least 1 hour after infusion.

The COVID-19 Treatment Guidelines Panel recommends bebtelovimab and molnupiravir as alternative therapy options. These should only be used when neither of the preferred treatment options is clinically appropriate.

Molnupiravir is an oral antiviral medication that increases the frequency of mutations in the viral RNA that impairs SARS-CoV-2 replication in humans (Jayk Bernal et al., 2022). In the MOVe-OUT trial, molnupiravir reduced the rate of hospitalization or death by 30% compared to placebo in nonhospitalized patients with COVID-19 (Jayk Bernal et al., 2022). EUA was issued in December 2021 for its use in those older than 18 years. Patients must be COVID positive with mild to moderate symptoms. Molnupiravir is not authorized to initiate in hospitalized patients with severe or critical COVID-19 and is not authorized for use as pre-exposure or postexposure prophylaxis. Those who receive a prescription for molnupiravir take it for 5 days, and it must be initiated within 5 days of onset of symptoms. No renal or hepatic adjustments are necessary. Molnupiravir should not be crushed and may be taken with or without food. There are no known drug-to-drug interactions. The most common reported adverse reactions have been diarrhea, nausea, dizziness, and headache

Bebtelovimab is a monoclonal antibody given by infusion that targets against the spike protein of SARS-CoV-2. In February 2022, the FDA authorized emergency use to treat mild to moderate COVID-19 in adults and children with positive SARS CoV-2 test results who are at high risk for progressing to severe COVID-19. It is not recommended for use in those who are likely to be infected with a SARS-CoV-2 variant that is not able to be treated by bebtelovimab, those who are hospitalized with COVID-19, or those who require oxygen therapy and/or respiratory support due to COVID-19. Treatment should be initiated as soon as possible after a positive viral test for SARS-CoV-2 and within 7 days of symptom onset. Possible side effects include itching, rash, infusion-related reactions, nausea, and vomiting.

Symptom Management: Management of symptoms such as fever, cough and myalgias may be treated using over-the-counter antipyretics, analgesics, or antitussives. Patients should be advised to drink fluids frequently to avoid dehydration. Adequate rest is required during the acute phase of illness, and activity should be increased according to the patient's tolerance. Those who experience dyspnea may benefit from resting in the prone position rather than the supine position.

Other COVID-19 Treatment Guidelines Panel Recommendations: The panel recommends avoiding use of certain therapies. These therapies and rationales for avoiding them are discussed in Table BC-1. Use this information to educate patients who may ask about the effectiveness of these therapies.

Follow-Up: Follow-up is dictated by the severity of the disease and the organs affected. Patients with a history of AKI need follow-up renal function tests and may need to be comanaged with a nephrologist. Pulmonary damage may be severe and irreversible. Follow-up with pulmonary function tests, pulmonary rehabilitation, and comanagement with a

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TABLE BC-1 COVID-19 Treatments to Avoid

AGENT	RATIONALE
Chloroquine or hydroxychloroquine (HCQ) with or without azithromycin	• Several randomized trials have failed to show a clinical benefit for HCQ in nonhospitalized patients with early, asymptomatic, or mild COVID-19 (Mitja et al., 2020; Skipper et al., 2020). • In a large randomized controlled trial of hospitalized patients in the United Kingdom, HCQ did not decrease 28-day mortality when compared to the usual standard of care (RECOVERY Collaborative Group et al., 2020). • Chloroquine and HCQ have similar toxicity profiles. Cardiac adverse events have been reported in people who received hydroxychloroquine include QTc prolongation, Torsades de Pointes, ventricular arrythmia, and cardiac deaths (Nguyen et al., 2020). • Adding azithromycin and using it in combination with HCQ has been associated with a higher incidence of QTc prolongation and cardiac adverse events in patients with COVID-19 (Chorin et al., 2020; Mercuro et al., 2020).
Ivermectin	• This antiparasitic drug has not been approved by the U.S. Food and Drug Administration for treatment of any viral infection, including COVID-19. • Use should be avoided except in clinical trials. • Although ivermectin has been shown to inhibit replication of SARS-CoV-2 in some studies, other studies suggest that to achieve plasma concentrations necessary for efficacy against COVID it would require doses up to 100-fold higher than those approved for use in humans (Chaccour et al., 2020). • Studies had incomplete information and significant methodological limitations, which made excluding common causes of bias difficult. • Many of studies have not been peer reviewed, and some have now been retracted (COVID-19 Treatment Guidelines Panel, 2022).
Anticoagulants and antiplatelet therapy	• Avoid initiating therapy in the emergency department for the prevention of venous thromboembolism or arterial thrombosis unless the patient is being admitted to the hospital or has other indications for the therapy (Connors et al., 2021).
Dexamethasone or other systemic corticosteroids	• It is not recommended to treat outpatients with mild to moderate COVID-19 who do not require hospitalization and on supplemental oxygen (Clemency et al., 2022; Ezer et al., 2020). • Patients who take corticosteroids for other reasons should continue to do so unless directed by their provider.

pulmonologist may be needed. The return of taste and smell may take months to years and may not return at all.

Sequelae: The aftermath of COVID-19 is highly variable. New focus has been on the long-term effects that many patients experience after the acute phase of COVID-19 has resolved. These symptoms have been referred to by many names, including post-COVID conditions, long COVID, and post-acute COVID-19. Ongoing studies to evaluate the morbidity related to these long-term conditions are needed. Identifying changes in patients that persist after an acute infection with COVID-19 is an important role of the provider.

Cardiovascular complications were documented in a study by Xie et al. (2022). They found long-term effects in patients across the disease severity spectrum, with those with more severe disease experiencing more severe long-term effects. Similar findings were also noted by Satterfield et al. (2022). Dyspnea was one of the most prevalent symptoms and may be multifactorial due to pulmonary and cardiac complications.

In a systematic review and meta-analysis, Lopez-Leon and colleagues (2021) identified more than 50 long-term effects of COVID-19. In the older adult, the persistent fatigue, dyspnea, cognitive residual, effects on smell and taste, and joint pain all have the potential of directly and indirectly affecting functional ability and independence in activities of daily living and instrumental activities of daily living.

Prevention/Prophylaxis: The best prevention of COVID-19 disease is vaccination. The worldwide effort to develop a vaccine to prevent COVID-19 resulted in the fastest introduction of an effective vaccine ever realized to date. The effort was facilitated by advances in virology and the information from work done on other viral diseases such as hepatitis C and HIV. Initially, vaccines that demonstrated efficacy were granted EUA, and many applications continue to carry only that authorization, including boosters and vaccine forms used in children. Currently in the United States there are two vaccines approved by the FDA for use in adults. The first vaccine, from Pfizer-BioNTech, was approved on August 23, 2021, and will now be marketed as Comirnaty. The approval of the Moderna COVID-19 vaccine was granted in January 2022, and it will now be marketed as Spikevax. The Johnson & Johnson vaccine, brand name Janssen, was approved for emergency use in February 2021. The advantages of this vaccine are that it is a single injection and it is easier to store because it does not require the freezing temperatures necessary for the mRNA vaccines, so it was initially a popular choice. Since its EUA, however, it has faced a number

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of setbacks due to reported serious side effects, including blood clots and Guillain-Barré syndrome. To date, it has not received final FDA approval.

Types of COVID 19 Vaccines: Historically, vaccine development was a lengthy process involving much trial and error using a weakened or killed version of the targeted pathogen. The idea that a vaccine could be created that was affective against SARS-CoV-2 in less than a year was a daunting expectation. That historical perspective contributed to the vaccine skepticism that was and continues to be so rampant in the United States. Three types of vaccines are approved for use in the United States:

- *mRNA vaccines.* A new type of technology, mRNA technology, addresses the spike protein like the one on the coronavirus (Katella, 2022). This technology had been successfully used to develop a vaccine against the MERS virus, which is genetically like the SARS-CoV-2 virus (Glassman et al., 2022). The spike protein created by mRNA vaccines is recognized as foreign and activates the immune system to make antibodies that will recognize the SARS-CoV-2 spike protein and attack it if exposed. Both the Pfizer-BioNTech and Moderna are mRNA vaccines.
- *Carrier or virus vector vaccine.* This type of vaccine does not contain the antigen but uses a modified version of the virus to deliver the genetic code for the antigen (Katella, 2022). The resulting cellular immune response triggers the T cells and the production of antibodies by the B cells. The Johnson and Johnson vaccine used this type of technology. The Oxford-AstraZeneca vaccine also uses this type of technology. Although it is approved in the United Kingdom and used worldwide, it is not approved for use in the United States.
- *Protein adjuvant vaccines*. This type contains the spike protein of the coronavirus formulated as a non-disease-causing nanoparticle (Katella, 2022). When injected it also stimulates a cellular immune response. Produced by Novavax, this type of vaccine is not yet approved for use in the United States.

Healthy Habits: SARS-CoV-2 is primarily spread by respiratory droplets aerosolized by coughing, sneezing, talking, singing, or even just breathing. Wearing masks helps to prevent the spread especially when indoors. Although contact with droplets on surfaces is less likely to cause disease, surface decontamination, good hand hygiene, and avoiding touching the nose, mouth, or eyes if the hands are potentially contaminated are other commonsense measures to prevent illness.

Referral: Due to the unpredictable effects of COVID-19, which range from minor symptoms similar to the common cold to severe cardiopulmonary collapse, all patients must be evaluated thoroughly and referred for additional consultation if they are high risk or presenting with worrisome symptoms. There are many case examples of patients being evaluated in the emergency department and sent home to recover, only to return later needing intubation and intensive care. More recent variants have been less likely to result in hospitalization. Patients who are fully vaccinated and boosted are still susceptible to some of the more recent variants, but they are generally not becoming seriously ill.

Education: Patients need to understand the safety of the vaccines, and providers should utilize the technique of motivational interviewing to understand any hesitancy. Use shared decision making to come to a decision regarding protection against COVID 19. Encourage good hand hygiene and following the CDC recommendations for masking. Help patients understand their personal risk and the fact they may require a higher level of protection. Encourage testing for COVID when symptomatic or after exposure. For patients with long-term symptoms of COVID, provide support and up-to-date information as it becomes available.

Clinical Recommendation	Evidence Rating	References
The presence of fever, myalgia/arthralgia, fatigue, and headache substantially increased the possibility of COVID-19 when present.	A	Struyf et al., 2021
80% of patients who had COVID continue to complain of at least one long-term effect, with fatigue and headaches being the most frequently cited.	A	Lopez-Leon et al., 2021
Nirmatrelvir/ritonavir (Paxlovid), an oral SARS-CoV-2 protease inhibitor antiviral combination, reduced the risk of hospitalization or death by 88% compared to placebo in nonhospitalized adults with laboratory-confirmed SARS-CoV-2 infection.	A	Hammond et al., 2022
The mRNA vaccines, Spikevax (Moderna) and Comirnaty (Pfizer-BioNTech), have received full U.S. Food and Drug Administration (FDA) authorization for the primary series in individuals 18 years and older (Spikevax) and 16 years of age and older (Pfizer-BioNTech). Use in individuals below these ages and additional booster shots remain under FDA Emergency Use Authorization.	A	CDC, 2022d

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to https://www.aafp.org/pubs/afp/issues/2019/1101/p574.html

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HUMAN IMMUNODEFICIENCY VIRUS (HIV) AND ACQUIRED IMMUNE DEFICIENCY SYNDROME (AIDS)

Signal Symptoms: Acute infection presents with nonspecific symptoms often described as "flu-like symptoms" 2 to 4 weeks after infection. These symptoms include fever, chills, rash, night sweats, muscle aches, sore throat, fatigue, swollen lymph nodes, and/or mouth ulcers. Symptoms can last a few days or up to several weeks. Older adults usually present after they have been infected with HIV for several years. At this point, the virus is in the late stages and the presenting signs are those of an opportunistic infection, which indicates that the virus is more likely to have progressed to AIDS. This population presents with advanced infection, the signs and symptoms that include thrush, unintentional weight loss, unexplained anemia, unexplained thrombocytopenia, *Pneumocystis jirovecii* pneumonia, or other opportunistic infections (Centers for Disease Control and Prevention [CDC], 2021a; Chou et al., 2019; U.S. Department of Health and Human Services [USDHHS], 2021).

Description: HIV is classified as a retrovirus. This means the viral genetics consist of RNA rather than DNA. After entering the cytoplasm of a human lymphocyte, the viral RNA is transcribed by means of an enzyme called reverse transcriptase into DNA, which in turn integrates itself into human DNA in the cell's nucleus. This proviral genetic combination takes over the mechanism of the cell, producing new HIV virions, which in turn infect and destroy other T-lymphocytes. Understanding this cycle provided the pharmacological basis for antiretroviral medication used to treat HIV.

Untreated or poorly managed HIV results in progressive degradation of immune function. Profound immune compromise is designated as AIDS. AIDS is clinically defined as <200 CD4 cells/mm^3, subjecting the person to severe debilitating, sometimes fatal, concomitant or opportunistic infections. Although to date there is no cure, early detection and proper antiretroviral treatment can result in a normal life span.

Etiology: In the 1980s, medical anthropologists traced the origins of HIV to a zoonotic virus subsequently named Simian immunodeficiency virus (SIV). Direct exposure to the blood of an infected animal during hunting or eating seems the most plausible explanation for the crossover to human infection. The origin of HIV itself is believed to have occurred between 1884 and 1924 with the first documented case occurring in approximately 1931 in West Africa. There are two strains of HIV: HIV-1 and HIV-2. HIV-1, being the most virulent and most easily transmittable strain, accounts for the vast majority of worldwide cases.

HIV-1 was first introduced into the Americas via Haiti around 1966 and was sexually spread into the United States around 1972. The pandemic spread is overwhelmingly via heterosexual transmission. Dispersion has been facilitated by worldwide air travel, contamination of blood supplies before adequate testing, and contaminated needles and syringes used for injectable drugs. In the United States, localization of the disease in the gay, Haitian, and injectable drug–using communities accounts for the stigma that continues to negatively affect prevention, diagnosis, and care (Bailes et al., 2003).

Occurrence: The CDC published an updated national profile report of the diagnosis of HIV infection in the United States and dependent areas in 2019, which provides the most recent statistics available. At the end of 2019, an estimated 1,189,700 people age 13 and older had HIV in the United States, including an estimated 158,500 people who were undiagnosed (CDC, 2021b). In 2016, about 80% of new HIV infections in the United States were transmitted from the nearly 40% of infected people who have an unknown HIV-positive status or are not receiving HIV care (Li et al., 2019).

Age: In the United States in 2018, 51% of people diagnosed with HIV were age 50 and older. In the same year, the incidence of HIV among the same population was one in six new diagnoses (CDC, 2020a).

In the transgender community age greater than 55 years, during the period from 2015 to 2019, the CDC reported a 71% increase in the rate of new diagnoses (CDC, 2019, 2020a).

Gender

Please see Table BC-2 below for details.

Ethnicity: While anyone who is exposed bears the same risk of infection, some racial/ethnic communities have a higher percentage of HIV and thus there is increased risk of new infections with each sexual encounter or IV drug use.

At year-end 2019 in the United States, HIV prevalence was 1,044,977 people living with diagnosed HIV infection. The highest rate (1,027.5) and the largest percentage (40%) were for Black/African Americans, followed by rates of 673.1 for multiracial, 411.3 for Hispanic/Latino, 153.9 for White, 153.0 for Native Hawaiian/other Pacific Islander, 132.0 for American Indian/Alaska Native, and 82.3 for Asian persons. See Table BC-3 below.

Contributing Factors: Although the virus is found in multiple body fluids of HIV-positive persons with detectable serum viral loads, the concentrations necessary for human transmission are typically in blood, semen, vaginal fluid, and breast milk. The efficacy of transmission is predicated on the amount of virus present and the availability of target receptor sites (i.e., sites that are most plentiful) in the blood.

TABLE BC-2 Incidence and Prevalence of HIV by Gender

GENDER	% OF NEW HIV DIAGNOSES IN 2018	NUMBER OF HIV-INFECTED PERSONS WITHIN THE ESTIMATED 1.2 MILLION POPULATION OF THE UNITED STATES (2019)
Men	81%	912,100
Women	19%	261,800
Transgender	2%	—

Source: Centers for Disease Control and Prevention. (2020). Estimated HIV incidence and prevalence in the United States, 2014–2018. HIV Surveillance Supplemental Report, 25*(1)*.

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TABLE BC-3 Incidence of HIV by Race/Ethnicity (no prevalence here)

RACE/ ETHNICITY INCIDENCE	NUMBER OF NEW HIV DIAGNOSES IN 2019	INCIDENT RATES PER 100,000 IN 2019
Black/African American	15,334	37.3
Hispanic/Latino	10,120	16.7
White	9,013	4.6
Asians	737	3.9
American Indian/ Alaska Native	210	8.6
Native Hawaiians and other Pacific Islanders	66	11.1
Multiracial	918	12.6

Centers for Disease Control and Prevention. (2021c). HIV Surveillance Report, 32. *http://www.cdc.gov/hiv/library/reports/hiv-surveillance.html.*

Sex: HIV/AIDS is primarily transmitted by penile–vaginal or penile–anal sex, age of the participants notwithstanding. Anything compromising the integrity of mucous membranes, including preexisting inflammation, the presence of other sexually transmitted infections (STIs), or traumatic sexual practices, increases the risk of transmission. Because HIV is present in blood, semen, and preseminal fluid, anal sex that is unprotected by barriers such as latex condoms ranks as the highest transmission risk. The receptive partner is at most risk, although the insertive partner can also be infected by an HIV-positive receptive partner. These principles of risk also hold true for penile-vaginal sex. Circumcision has been demonstrated to significantly reduce the risk of HIV acquisition but not transmission.

Intravenous Drug Use: The use of HIV-contaminated needles and syringes is a significant mode of transmission. Eliminating the use of shared equipment, including cleaning practices and supplies, can mitigate risk. The use of a cleaning solution of 1:10 bleach to sterile water used to flush the needle and syringe can significantly reduce risk.

Pregnancy: Vertical transmission from mother to child can occur during pregnancy, delivery, or breastfeeding. Maternal testing should occur at first obstetrician (OB) visit, at third trimester, and at the onset of labor. Prompt and adequate antiretroviral treatment (that results in nondetectable viral loads), safe delivery practices, and access to infant feeding formula are likely to result in a seronegative child (Branson et al., 2006).

Occupational Transmission: The risk of occupational transmission is relatively small but has occurred in a variety of settings. There is no risk of HIV transmission with exposure of HIV-infected fluids to intact skin. Needle-stick injuries are the most common mode of occupational transmission in developed countries. The risk of this mode of transmission is estimated at 0.3% in an unprotected recipient but is mitigated by using latex gloves and minimizing the depth of the puncture (deeper punctures pose more risk). The risk can be further reduced to infinitesimal levels with prompt administration of a proper antiretroviral regimen to the person receiving the injury. An immediate referral should be made to an infectious disease specialist for comprehensive advice. In occupational exposures, bodily fluids in addition to blood, sexual fluids, and breast milk are also potentially infectious. These fluids include cerebrospinal fluid, synovial fluid, amniotic fluid, pleural fluid, peritoneal fluid, and pericardial fluid. Because semen and cervicovaginal secretions have been demonstrated to contain both virus and virus-infected cells, such secretions should be considered infectious. Urine, feces, and saliva are not considered infectious.

Stigma: Stigma has a profound effect on the ability to seek testing and to adhere to treatment. For the sake of community health and individual patients, primary care providers are ethically obligated to thoughtfully examine and carefully acknowledge their own biases to facilitate gaining trust from the patient for testing and for ensuring support needed to adhere to treatment.

Signs and Symptoms: The signs and symptoms of HIV/AIDS infection can be divided into acute presentation and chronic infection as follows:

Acute presentation is defined by the intact immune response to a pathogen: general malaise, myalgia, chills, low-grade fever, and fatigue. Occasionally a nonpruritic macular rash with a generalized distribution is present. This presentation can range from 3 days to 3 weeks and is consistent with a response to other viral illnesses. There are no HIV-specific presenting symptoms. Diagnosis is provided by HIV screening and testing.

Chronic disease in an untreated patient is marked by unexplained wasting, extreme fatigue, unexplained anemia or thrombocytopenia, and/or the presence of opportunistic infections such as thrush, disseminated lymphadenopathy, the presence of Kaposi's sarcoma, or *Pneumocystis jirovecii* pneumonia (formerly known as *Pneumocystis carinae* pneumonia or PCP). Because this is not an exhaustive list, HIV infection should be considered whenever an odd or difficult to treat infection is encountered.

The American Academy of HIV Medicine and the American Geriatrics Society agree that at age 50 years, an HIV-seropositive adult should be considered a geriatric patient. In providing primary care to these patients, it is important to recognize that the combination of the illnesses of aging and of HIV are considered "multimorbidity" or "polypathology." Unlike simple "comorbidity," in multimorbidity age plus debilitating conditions synergize to make morbidity and mortality worse than might otherwise be the case. The sum is greater than the parts (AAHIVM Provider Education Center, n.d.).

Diagnostic Tests: There are two groups of testing in HIV care: diagnostic tests and treatment tests. Primary care providers will use diagnostic tests and should be familiar with the testing used to guide HIV care.

Diagnostic testing can detect HIV infections but cannot tell how long a person has had HIV or if the person has AIDS. The CDC recommends that everyone ages 13 to 64 years be tested for HIV at least once in their lifetime. Diagnostic testing is also recommended for people with HIV risk factors such as vaginal or anal sex with an HIV-positive person or unknown HIV status person, before having sex with a new partner,

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having sex with many people, or sharing drug equipment with others.

Three types of screening and diagnostic tests are available: nucleic acid tests (NAT), antigen/antibody tests, and antibody tests. NAT identify HIV virus in the blood and can determine whether a person has HIV and how much of the HIV virus is present (viral load). NAT are accurate 10 to 33 days after an exposure. Antigen/antibody tests determine the presence of HIV antibodies and antigens in the blood and are available as a rapid test with a finger prick. Antigen/antibody tests are accurate 18 to 90 days after an exposure. HIV antibody tests are the most common rapid test and are currently the only approved self-test. Antibody tests are accurate 23 to 90 days after exposure. The HIV antibody test detects antibodies to HIV in blood or oral fluid. The error rate is higher for oral testing compared to blood testing (CDC, 2020b).

Differential Diagnoses: HIV infection should be considered in any person with unusual or recurrent infections. In the spectrum of HIV illness, AIDS is defined as a CD4 count <200 cells/mm^3 in an HIV-seropositive patient; the presence of opportunistic illness also meets the criteria. Opportunistic illness indicates severe immune decline. Such illnesses include:

- Pulmonary or disseminated tuberculosis (TB)
- Invasive cervical cancer
- Esophageal candidiasis
- Cryptococcosis
- Cryptosporidiosis
- Cytomegalovirus (CMV) retinitis, or infection outside of liver, spleen, or lymph nodes
- Herpes simplex virus (HSV)—chronic ulcers, bronchitis, pneumonitis, or esophagitis
- Kaposi's sarcoma
- Pruritic papular eruption of HIV
- Lymphoma—Burkitt's or primary brain
- Mycobacterium avium complex, disseminated or extrapulmonary
- PCP pneumonia
- Progressive multifocal leukoencephalopathy
- Brain toxoplasmosis
- HSV encephalitis
- HIV wasting syndrome
- Disseminated histoplasmosis
- Isosporiasis
- Recurrent salmonella septicemia
- Recurrent bacterial pneumonia
- (Waymack & Sundareshan, 2021)

Treatment: There is no effective cure for HIV. The goal of antiretroviral therapy (ART) is to reduce replication of the HIV virus so that the volume of virus is below the level of accurate detection, currently measured at less than 50 to 20 copies of virus/mL. In an untreated person, viral loads can be greater than 1 million copies/mL.

Advances in ART have made it possible for people with HIV to live a near-expected functional life span without progressing to AIDS and importantly, without transmitting HIV to sexual partners or fetuses (Thompson et al., 2021). Comprehensive evidence-based HIV primary care guidance is more important than ever as there is increasing emphasis on maintaining health throughout the life span. To achieve desired outcomes, people with HIV must be consistently engaged in care and be able to access uninterrupted treatment, including ART.

Immediate ART, also known as rapid ART and same-day ART, refers to starting HIV treatment medications as soon as possible, preferably the same day as the HIV diagnosis (Coffey & Bacon, 2021). Rapid ART initiation has been shown to reduce time to linkage to care and viral load suppression. Rapid ART is appropriate for nearly all people newly diagnosed with HIV, people with suspected acute HIV, and people with a positive rapid HIV antibody test before confirmatory tests results are available if the concern for HIV infection is high. While rare in the outpatient clinic setting, rapid ART is not appropriate for people with certain untreated opportunistic infections such as cryptococcal meningitis and central nervous system tuberculosis. To reduce the risk of immune reconstitution inflammatory syndrome (IRIS), there needs to be a short period of treatment for the opportunistic infection prior to starting ART. Another scenario that would not be appropriate for rapid ART involves those people with a preliminary positive rapid HIV test result but who have a low probability of HIV infection. In these cases, the preliminary result is more likely to be a false positive, and the confirmatory result should be obtained before starting ART. When an HIV test results are positive, a rapid referral to an HIV specialist should be made. If a specialist is not immediately available, guides to contacts are provided in the Referral Section of this chapter. Prior to giving a prescription to a patient, consider local accessibility of medications; this includes the patient's ability to meet the steep co-pay.

For a person who has chronic HIV and is looking to start or restart ART, a consultation with an HIV expert is needed. ART regimens should be selected based on resistance history as well as the person's comorbidities, tolerance of previous antiretrovirals, adherence challenges, and insurance status with respect to medication co-pays. Assistance may be provided through Ryan White funding. HIV specialists will be able to assist in accessing funding.

ART is heavily reliant on the cytochrome p450 pathway for metabolism; therefore, other medications commonly used in primary care such as statins, psychoactive medications, contraceptives, some antibiotics, antiepileptics, steroid injections, and vitamins carry the potential for serious drug–drug reactions. Primary care providers are urged to consult with an HIV specialist or HIV pharmacist before starting or stopping any medications.

When the CD4 count is measured at less than 200 cells/ mm^3 (AIDS), the patient is started on prophylactic medication for certain common opportunistic infections. The appropriate dosages for prophylaxis are suboptimal for treatment. Medication changes, and possibly resistance testing, are indicated in the instance of breakthrough infection. Consultation with the HIV specialist is recommended. If an HIV specialist is not immediately accessible, refer to the DHHS link https://clinicalinfo.hiv.gov/en/guidelines. This resource gives updated recommendations for ART. Up-to-date listings for HIV specialists are found at https://aidsetc.org/consultation.

Use of alternative therapies by the HIV seropositive population is very common. Despite this, reporting of these therapies is uncommon. Some herbal remedies have demonstrated potential for significant drug–drug interactions that either increase adverse ART effects or block intended effectiveness.

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Most herbal remedies and dietary supplements have not been adequately researched. Use of these agents should be continuously monitored and promptly reported to the HIV specialists by the primary care provider.

The rules of ART are rigid. Safe and effective therapy requires that agents be used in combination. Not all antiretrovirals work cooperatively. Regimens are carefully choreographed among the classes of antiretroviral agents and are coordinated with medications prescribed for comorbidities, alternative therapies, and occasionally diet. Failure to understand these principles can result in organ damage, resistance to ART, and failure to control HIV (Briggs & Narsavage, 2004; Coffey & Bacon 2021; Thompson et al., 2021).

Follow-Up: The HIV care continuum is a public health model that outlines the five steps that people with HIV go through from diagnosis to achieving and maintaining an undetectable viral load:

1. Diagnosis of HIV infection
2. Linkage to HIV medical care
3. Receipt of HIV medical care
4. Retention in medical care
5. Achievement and maintenance of viral suppression

The HIV care continuum is a tool to help identify gaps in services and develop strategies that better support a person with HIV to thereby achieve an undetectable viral load. Primary care is integral to this process by assuring that the patient is linked to and retained in HIV care and by establishing an ongoing relationship with the HIV team.

Testing: As was previously mentioned, there are two categories of testing: diagnostic testing, in which primary care providers have a significant role and testing is used to guide HIV treatment, which is primarily the purview of an HIV specialists, and treatment testing. This section defines use of treatment tests that facilitate the primary care team's understanding.

Basically, treatment tests are viral load tests that are used to measure the efficacy of ART, CD4 counts that roughly measure immune function, and viral genotypes and phenotypes that are used to individualize the selection of ART. People who have no documentation of HIV status should have an HIV antigen/antibody test at initiation into care. A CD4 cell count with percentage and a quantitative HIV RNA (viral load) level should be obtained on initiation of care.

In collaboration with HIV specialists, after ART is initiated, HIV RNA (viral load) should be rechecked in 2 to 4 weeks but no later than eight weeks, and then every 4 to 8 weeks until a viral load <50 copies/mL is achieved. If therapy is effective, this load reduction should occur within three months after which viral loads can be obtained in 3- to 4-month intervals. If nondetectable viral loads are not achieved within a 3-month interval, the patient should return to the HIV specialist for genetic testing of the virus. Viral load testing can be extended to every 6 months for adherent patients with stable CD4 counts who maintain an undetectable viral load for 2 years.

CD4 cell count should be checked every 3 to 6 months for the first 2 years after starting ART, or if viremia develops, or if CD4 cell count is $<300/mm^3$. After 2 years, CD4 cell count laboratory values can be extended to every 12 months if CD4 cell count is 300 to $500/ mm^3$ and HIV RNA is suppressed, or if CD4 cell count is $>500/mm^3$ with HIV RNA suppression, then CD4 cell counts are optional (Thompson et al., 2021).

Vaccines: Vaccines are recommended to prevent HIV-positive people from contracting infections that are vaccine preventable. To prevent herpes zoster, a two-dose series recombinant zoster vaccine should be given to people age greater than 50 years who are on ART and have CD4 cell counts greater than 200 cells/mm^3. For vaccination recommendations, consult current vaccination schedules. Live virus vaccines are contraindicated for HIV-positive people.

Cancer Screens: Cancers associated with smoking and infection are of particular risk in this population. Cancers associated with smoking that are common to these patients include lung, kidney, stomach, laryngeal, and oral. Cancers associated with infection include anal, vaginal, penile, nasopharyngeal, and Hodgkin's lymphoma associated with Epstein Barr virus. Hepatitis B and C viruses carry additional risk of cancer in the HIV-seropositive patient.

Dental examinations are of special importance, so an oral health examination should be performed semiannually due to increased risk of oral cancers. Smoking cessation should be emphasized, as well as cervical and anal Papanicolaou (PAP) testing. Screening for the following cancers should begin earlier than for the HIV-seronegative population and should be more frequent:

- Lung: Age 55 and 80 years who have 30 pack years of smoking and are current smokers or who have quit in the last 15 years should have an annual low-dose computed tomography (CT) scan of their chest until smoking has been discontinued for 15 years.
- Prostate: Follow U.S. Preventive Services Task Force or American Cancer Society guidelines and consider patient wishes.
- Colon: Age 50 to 75 years. Screen prior to age 50 if there is a family history of colon cancer. Colonoscopy every 10 years if normal, or more frequently if polyps are identified.
- Cervical: Begin within 1 year of sexual activity. Repeat at diagnosis of HIV and annually three times; if normal, reduce interval to every 3 years. Perform human papillomavirus (HPV) testing if PAP abnormalities are found. Continue screening past 65 years of age.
- Breast: Age 50 to 75 years. Perform mammography every 2 years.
- Anal: No current national recommendations. Some experts recommend anal cytology for males and females with HIV who have receptive anal sex, but only if high-resolution anoscopy is available.

Sexual History: Sexual history should be taken as a part of routine health care, as well as when signs or symptoms of an STI are present. A sexual history should include the "Five Ps": Partners, Practices, Protection from STIs, Past History of STIs, and Pregnancy Intention (Barrow et al., 2020, Thompson et al., 2021).

Sequelae: Special considerations for the >50-year-old HIV-infected population include:

- After initiation of ART, only plasma glucose criteria should be used to diagnose diabetes. Patients with diabetes mellitus should have an HbA1c level monitored every 6 months with an HbA1c goal of <7%, in accordance with the American Diabetes Association Guidelines. In the older and particularly frail person, studies indicate that overzealous glycemic control among type 2 diabetes

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is harmful and suggest a targeted glycosylated hemoglobin of 8%.
- Increased renal and hepatic monitoring should be implemented in older people with HIV that have multimorbidity and polypharmacy.

HIV infection accelerates age-related decline in pulmonary health—particularly with respect to chronic obstructive pulmonary disease (COPD)—independent of smoking histories, drug abuse, and opportunistic infections. This decline prompts increased attention to pneumonia, influenza, and COVID vaccinations as well as emphasis on smoking cessation.

Osteoporosis and bone fractures occur more commonly in the HIV infected, and these injuries increase with age. HIV-infected patients are at increased risk for vitamin D deficiency, thus requiring screening and replacement. The use of proton pump inhibitors may also contribute to osteoporosis. Post-menopausal HIV seropositive women require routine screening. Additional factors such as nutritional deficiency, smoking, physical inactivity, and androgen deficiency should also be addressed.

Treatment for hypertension remains the same in the HIV-infected population as in the HIV seronegative; however, the increased risk of renal and cardiovascular disease suggests that agents affecting the renin-angiotensin system may be especially helpful.

Despite effective antiretroviral treatment, neurocognitive disorders—particularly those affecting subcortical domains—remain a risk that increases with age. Because it does not test subcortical domains, the Mini-Mental State Examination is not an effective screening test. Valcour et al. (2011) recommend the Montreal Cognitive Assessment (free at http://www.mocatest.org) in addition to a routine neurological exam, screening for depression, and executive function testing (*Aging Report – AAHIVM*, n.d.).

Prevention/Prophylaxis: HIV is primarily sexually transmitted, with high serum viral loads being reflected in higher viral volume in genital secretions and tissue. In addition to adherence to ART, barrier protection (latex condoms) is an effective means of transmission prevention when used correctly. It has been said that it is easier to have sex than to talk about it; nevertheless, primary care providers should familiarize themselves with the variety and correct use of condoms and other barriers, as well as sex toys and sexual practices, in order to productively engage in open, frank, and useful risk-reduction discussions.

Pre-Exposure Prophylaxis (PrEP): PrEP is a medication for HIV at-risk people that prevents acquiring HIV from sex or IV drug use. PrEP is recommended for men or women with an HIV-positive partner or injecting partner, a recent bacterial STI, multiple sex partners, inconsistent condom use, or transactional sex. Before starting PrEP, a negative HIV test must be completed within 7 days of the start of PrEP medications. A PrEP prescribing provider can be located using https://preplocator.org/ (CDC, 2021d Update).

Nonoccupational Postexposure Prophylaxis (nPEP): Nonoccupational postexposure prophylaxis (nPEP) should be started within 72 hours of a sexual or injection-related substantial HIV risk exposure. If the exposure is not an isolated event such as sexual assault or infrequent condom failure, then the person is a candidate for ongoing HIV risk and should be evaluated for PrEP after completing nPEP. Nonoccupational postexposure prophylaxis is not recommended when the reported exposure is not a substantial risk of HIV transmission and/or when prevention is sought more than 72 hours after a potential exposure. All people who report behaviors or situations of recurring HIV exposures or who receive nPEP more than once per year should be provided risk-reduction counseling and PrEP (CDC, 2018, 2021d).

Referral:

- CDC–Clinician Recourses
  - Open 24/7 and has a search area on the left side of the page for PrEP and HIV testing
  - https://www.cdc.gov/hiv/clinicians/treatment/index.html
- HIV.gov
  - https://www.hiv.gov/
  - https://clinicalinfo.hiv.gov/en/guidelines
- AIDS Education and Training Center (AETC)
  - HIV Management Warmline that can help with ART, laboratory results interpretations, and clinical diagnosis: 800-933-3413
  - PrEPline: 855-448-7737 (855-HIV-PrEP)
  - https://aidsetc.org/consultation

Education:

National HIV Curriculum: https://www.hiv.uw.edu/
CDC: https://www.cdc.gov/hiv/basics/livingwithhiv/treatment.html
Association of Nurses in AIDS Care (ANAC): https://www.nursesinaidscare.org
American Academy of HIV Medicine (AAHIVM): https://aahivm.org/
University of Liverpool HIV Med Check: https://www.hiv-druginteractions.org/checker

Clinical Recommendation	Evidence Rating	References
Patients who are assessed as engaging in behaviors that are a risk for transmission should be encouraged to employ pre-exposure prophylaxis, including barrier protection.	A	Centers for Disease Control and Prevention (CDC), 2022d
Routine screenings should begin ~ 10 years earlier than those performed in the HIV seronegative Population	A	Thompson et al., 2021
Close monitoring of renal and hepatic functions is necessary for those who are prescribed antiretroviral therapy.	A	Thompson et al., 2021

A = consistent, good-quality, patient-oriented evidence B = inconsistent or limited-quality, patient-oriented evidence C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series For information about the SORT evidence rating system, go to www.aafp.org/afpsort.xml.

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MULTIDRUG-RESISTANT ORGANISMS (MDRO)

Signal Symptoms: Symptoms of infection with multidrug-resistant organisms (MDRO) vary depending on the part of the body that is infected. Infection can occur in any part of the body, including the skin, lungs, urinary tract, or bloodstream. The severity of these infections depends on the type of bacteria that causes the infection and the site of the body where the infection occurs.

Description: MDRO are defined as microorganisms, predominantly bacteria, that are resistant to one or more classes of antimicrobial agents.

Etiology: Microorganisms, such as bacteria, viruses, fungi, and parasites, are living organisms that evolve over time. Their primary function is to reproduce, thrive, and spread quickly and efficiently. Microorganisms adapt to their environments and change in ways that ensure their survival. If something stops their ability to grow, such as an antimicrobial, genetic changes can occur that enable the microbe to survive. There are several ways this occurs. The four major resistance mechanisms of microbes are to alter cell permeability to decreased drug uptake, modify the drug targets so antibiotics cannot act on them, efflux pumps to pump out the antibiotics, and modifying enzymes of the antibiotic to inactivate them (Sharma et al., 2019).

- Intrinsic or natural resistance is a result of the structural characteristics of the bacteria and not associated with previous use of antibiotics. *Pseudomonas aeruginosa* and *Klebsiella pneumoniae* are inherently resistant to ampicillin due to the permeability barrier provided by its gram-negative outer membrane (Reygaert, 2018).
- Acquired resistance occurs when bacteria generally susceptible to an antimicrobial change in a way that protects them from the antibiotics. These resistance mechanisms can be present together or in different combinations within the bacterial cell, allowing high level resistance to multiple antibiotics at the same time (Kapoor et al., 2017; Reygaert, 2018). The major resistant mechanisms of microbes are decreased drug uptake, efflux pumps, and enzymes that inactivate an antimicrobial chemical and target alterations by mutation.
- Modification of target sites often result from spontaneous mutation of a bacterial gene on the chromosome in the presence of the antibiotic (Kapoor et al., 2017; Reygaert, 2018). In the case of penicillin, the binding protein in the bacteria is altered, so penicillin can no longer bind to that protein, making penicillin ineffective (Kapoor et al., 2017). For example, methicillin-resistant *Staphylococcus aureus* (MRSA) developed resistance to methicillin and all other β-lactams.
- Enzymatic inactivation is the ability to destroy or inactivate the antibiotic resulting in antibacterial resistance (Kapoor et al., 2017; Reygaert, 2018). Beta-lactamases inactivate the β-lactam ring of penicillin, cephalosporins, and related drugs. The antibiotic is unable to bind to the penicillin-binding protein (PBP), which interferes with cell wall synthesis (Kapoor et al., 2017). *Neisseria* gonorrhea is now largely resistant to penicillin because of penicillinase activity.
- Decreased accumulation by decreased permeability or increased efflux occurs because the antibiotic is unable to access the site of action in enough concentrations to kill the organisms (Kapoor et al., 2017; Reygaert, 2018). Resistant organisms make their membrane less penetrable preventing the entry of antibiotics. Gram-negative organisms can limit the penetration of antibiotics because of an alteration in the number of outer membrane proteins (OMP) (Kapoor et al., 2017). The OMP change in number or character so that β-lactam uptake is substantially diminished contributes considerably to β-lactam resistance in gram-negative bacteria, e.g., *Pseudomonas aeruginosa* resistance to imipenem (Kapoor et al., 2017).
- Drug efflux occurs in some bacteria. The efflux pump is developed when antibiotic enters the cell, which throws out the antibiotics outside the cell limiting adequate drug levels (Reygaert, 2018). This type of resistance is seen in *Streptococcus pneumoniae* to macrolides.

Occurrence: The Centers for Disease Control and Prevention (CDC) (2019) reported more than 2.8 million antibiotic-resistant infections occur in the United States each year, and more than 35,000 people die. In a retrospective study by Nelson et al. (2021), the estimated national cost to treat these infections caused by six multidrug-resistant bacteria identified in the report was more than $4.6 billion annually. Conscientious infection prevention and control efforts in the United States reduced deaths from MDRO by 18% overall and by nearly 30% in hospitals (CDC, 2019a).

Age: Infection with an MDRO occurs most often in young children, older adults, or in people who have an existing severe illness or chronic health conditions. However, these organisms can infect anyone at any age. In 2017, older adults accounted for over one-third of the cost of care and deaths resulting from these antibiotic-resistant infections.

Gender: N/A

Ethnicity: The current literature describing racial and ethnic disparities in antibiotic-resistant infections in the United States is limited and inconsistent at best. Racial and ethnic data are not routinely collected or checked for accuracy (See et al., 2017). In one of the existing studies, it suggests that Black, Hispanic, and lower-income people are at higher risk of infection with community-acquired antibiotic-resistant pathogens such as methicillin-resistant *S. aureus* and drug-resistant *S. pneumoniae* (See et al., 2017).

In the review by See and colleagues (2017) using the CDC's Emerging Infections Program surveillance data for invasive community-associated (CA) MRSA cases from 2009 to 2011 in 33 counties of 9 states, they noted an incidence of 4.59 per 100,000 among Whites and 7.60 per 100,000 among Blacks (See et al., 2017). The racial disparity in CA-MRSA rates was primarily attributed to socioeconomic factors. This population has a higher rate of comorbidities and racial and ethnic minorities are hospitalized more often

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for preventable conditions, which puts them at increased risk for drug-resistant healthcare-acquired infections (See et al., 2017).

The newly established National Action Plan for Combating Antibiotic-Resistant Bacteria has not prioritized racial or ethnic disparities in antibiotic resistance-related outcomes for further research (CDC, 2021a). The COVID-19 pandemic has exposed the impacts of systemic health inequalities on racial and ethnic minorities in the United States. Black and Hispanic/Latino populations have been disproportionately impacted by COVID-19, accounting for nearly half of the cases and 37% of the deaths (CDC, 2020a). This disparity has highlighted the need to explore the role of racial and ethnic disparities in influencing health outcomes.

Contributing Factors:
Factors that increase risk for infection with MDRO

- Recent antibiotic therapy
- Immunosuppressed, chronic diseases, and inflammatory conditions
- Older age and frailty
- Surgery, invasive procedures, and/or dialysis
- Presence of an indwelling device
- Hospitalization or living in a long-term care facility

Diagnostic Tests: MDRO is identified by bacterial culture, antibiotic sensitivity testing, other specific laboratory tests, along with clinical signs and symptoms. The site for culture will depend on the signs and symptoms that the patient is exhibiting.

Individuals with MDRO may be colonized with the microorganism and not exhibit symptoms of infection but can still spread the MDRO into the environment. The colonized host may not be ill, though they have shed microorganisms to other people, and depending on the portal of entry and/or the immune system of the susceptible host, they may put the individual at risk for illness.

Differential Diagnosis: N/A

Treatment: The decision regarding treatment of MDROs is based on whether the patient has an active infection or if the patient is colonized with the organism. (See individual MDRO.)

Candida auris (C. auris)

- **Incidence:** The CDC (2020b) reported 746 cases of *Candida auris* across the United States. Worldwide, 46 countries reported cases of *C. auris*.
- **Threat:** Serious
- **Pathogen:** *C. auris* is a budding yeast, which almost never forms short pseudohyphae and does not form germ tubes (Ahmad & Alfouzan, 2021; CDC, 2020c; Černáková et al., 2021).
- **Types:** *C. auris* is a yeast species belonging to the genus *Candida*.
- **Common sites of infection:** It can cause invasive candidiasis and fungemia; the central nervous system, kidneys, liver, bones, muscles, joints, spleen, or eyes are invaded.
- **Populations affected:** Candidiasis is most often acquired in hospitals by patients with immunosuppressive states, presence of invasive catheters, chronic medical conditions, dialysis, recent exposure to antibiotics or antifungal agents, parenteral nutrition, and intensive care unit (ICU) admission.
- **Resistance patterns:** *C. auris* is often multidrug resistant, with some strains resistant to all three available classes of antifungals.
- **Transmission:** *C. auris* is efficiently transmitted person to person. *C. auris* can spread through contact with contaminated surfaces and fomites when shed from infected or colonized patients (CDC, 2021b; Lee et al., 2018). Shared multiuse patient equipment such as temperature probes and pulse oximeters may act as reservoirs of *C. auris*. *C. auris* can colonize skin and persist in the health-care environment, allowing for transmission between patients.
- **Treatment:** The choice of an agent should be based on local antimicrobial sensitivities, site of infection, cost, and comorbid conditions. CDC does not recommend treatment of *C. auris* identified from noninvasive sites (such as respiratory tract, urine, and skin colonization) when there is no evidence of infection (CDC, 2021b). Treatment is complicated because *C. auris* is easily mistaken as various other *Candida* species. Echinocandins are currently recommended as first-line therapy for the treatment of *C. auris* (Ostrowsky et al., 2020; Pappas et al., 2015). Agents approved by the U.S. Food and Drug Administration (FDA) in this class include anidulafungin, caspofungin, and micafungin (Ostrowsky et al., 2020; Pappas et al., 2015). Agents in this class are available for IV administration only. In patients who are unresponsive to echinocandin therapy or who have persistent fungemia for more than 5 days, the CDC recommends switching to liposomal amphotericin B (CDC, 2021b; Pappas et al., 2016)

Carbapenem-Resistant Enterobacterales (CRE)

- **Incidence:** Carbapenem-resistant Enterobacterales (CRE) accounts for more than 13,000 nosocomial infections and contribute to more than 1,000 deaths annually in the United States (CDC, 2019).
- **Threat:** Urgent
- **Pathogen:** Gram-negative bacilli
- **Types:** *Escherichia coli*, Enterobacter, *Klebsiella oxytoca*, and *K. pneumoniae*
  - **Common sites of infection:** These bacteria can cause pneumonia, urinary tract infections (UTIs), septicemia, endocarditis, meningitis, and severe intra-abdominal infections.
  - **Populations affected:** Prior and recent antibiotic use, residency in long-term acute care facilities, admission to an ICU, presence of indwelling medical devices, poor functional status, increased age, solid organ, or stem cell transplantation. Patients who need ventilators, urinary catheters, or IV catheters, and those who are immunocompromised are at risk for CRE infections.
  - **Resistance patterns:** Any isolate resistant to at least one of these: imipenem meropenem, doripenem, ertapenem, meropenem/vaborbactam, or imipenem/relebactam (Tamma et al., 2021; Tilahun et al., 2021).
  - **Transmission:** CRE transmits from person to person, often via the hands of health-care personnel or through contaminated medical equipment.

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- **Treatment:** The choice of an agent should be based on local antimicrobial sensitivities, site of infection, cost, and comorbid conditions.
  - Ciprofloxacin, levofloxacin, trimethoprim-sulfamethoxazole, nitrofurantoin, or a single dose of an aminoglycoside are preferred treatment options for uncomplicated cystitis caused by CRE (Tamma et al., 2021; Tilahun et al., 2021).
  - Ceftazidime-avibactam, meropenem-vaborbactam, imipenem-cilastatin-relebactam, and cefiderocol are preferred treatment options for pyelonephritis and complicated UTIs caused by CRE resistant to both ertapenem and meropenem. Extended infusion (lasting 3–4 hours) meropenem is a preferred treatment option for pyelonephritis and complicated UTIs caused by CRE resistant to ertapenem but susceptible to meropenem, when carbapenemase testing results are either not available or negative (Tamma et al., 2021; Tilahun et al., 2021).
  - Extended infusion (lasting 3–4 hours) meropenem is the preferred treatment for infections outside of the urinary tract caused by CRE resistant to ertapenem but susceptible to meropenem, when carbapenemase testing results are either not available or negative (Tamma et al., 2021; Tilahun et al., 2021).
  - Ceftazidime-avibactam is an alternative treatment for ertapenem-resistant, meropenem-susceptible CRE infections outside of the urinary tract (Tamma et al., 2021; Tilahun et al., 2021).

Pseudomonas aeruginosa with Difficult-to-Treat Resistance (DTR-P. aeruginosa)

- **Incidence:** The CDC (2019) reports that 32,600 cases of multidrug-resistant *P. aeruginosa* infection occurred in patients hospitalized in the United States in 2017, resulting in 2,700 deaths.
- **Threat:** Serious
- **Pathogen:** Gram-negative, strict aerobic, rod-shaped bacterium
- **Types:** *P. aeruginosa*
- **Common sites of infection:** Healthcare-associated infections including bloodstream infections, ventilator-associated pneumonia, catheter-associated UTIs, and surgical site infections.
- **Populations affected:** Common in individuals with an immunocompromised state such as cystic fibrosis, bronchiectasis, neutropenia, burns, cancer, AIDS, organ transplantation, uncontrolled diabetes mellitus, and ICU admissions. Individuals with invasive devices due to the ability to form biofilms.
- **Resistance patterns:** DTR-*P. aeruginosa* is defined as nonsusceptibility to at least one antibiotic in at least three classes for which *P. aeruginosa* susceptibility is generally expected: penicillin, cephalosporins, fluoroquinolones, aminoglycosides, and carbapenems (Tamma et al., 2021).
- **Transmission:** DTR-*P. aeruginosa* can spread in healthcare settings from one person to another through contaminated hands, equipment, or surfaces.
- **Treatment:** The choice of an agent should be based on local antimicrobial sensitivities, site of infection, cost, and comorbid conditions.
  - Ceftolozane-tazobactam, ceftazidime-avibactam, imipenem-cilastatin-relebactam, cefiderocol, or a single dose of an aminoglycoside is the preferred treatment for uncomplicated cystitis and pyelonephritis and complicated UTI.
  - Ceftolozane-tazobactam, ceftazidime-avibactam, and imipenem-cilastatin-relebactam, as monotherapy, are the preferred treatment options for the treatment of infections outside of the urinary tract (Tamma et al., 2021).

Extended-Spectrum β-Lactamase Producing Enterobacterales (ESBL-E)

- **Incidence:** ESBL-E infections in the United States have increased by 53% from 2012 through 2017, due to increased community-acquired infections (Jernigan et al., 2020).
- **Threat:** Serious
- **Pathogen:** Produced by both gram-positive and gram-negative bacteria.
- **Types:** *E. coli*, *K. pneumoniae*, *K. oxytoca*, *P. aeruginosa*, *Proteus mirabilis*
- **Common sites of infection:** ESBL-E can cause a variety of illnesses, including UTIs, pneumonia, blood infections, wound infections.
- **Populations affected:** ESBL-E infections occur more often in people who are older, immunocompromised, and those with chronic disease, previous antibiotic treatment, hospitalizations, and open wounds or drains.
- **Resistance patterns:** ESBL-E have a broad-spectrum β-lactamase enzyme that enables them to inactivate most penicillins, cephalosporins, and aztreonam (Tamma et al., 2021).
- **Transmission:** Direct contact with an infected person's bodily fluids and contact with equipment or surfaces that have been contaminated.
- **Treatment:** The choice of an agent should be based on local antimicrobial sensitivities, site of infection, cost, and comorbid conditions.
  - Nitrofurantoin and trimethoprim-sulfamethoxazole are preferred treatment options for uncomplicated cystitis caused by ESBL-E. Fluoroquinolones and carbapenems are also effective treatment options against ESBL-E cystitis, though discouraged when there are other safe and effective alternatives. Fluoroquinolones carry multiple black box warnings; the older adult is at higher risk for these adverse events when taking fluroquinolones.
  - Ertapenem, meropenem, imipenem-cilastatin, ciprofloxacin, levofloxacin, or trimethoprim sulfamethoxazole are preferred treatment options for pyelonephritis and complicated UTIs caused by ESBL-E.
  - Carbapenem antimicrobial is preferred for the treatment of infections outside of the urinary tract caused by ESBL-E (Tamma et al., 2021).

Methicillin-Resistant Staphylococcus Aureus (MRSA)

- **Incidence:** In 2017, 120,000 *S. aureus* bloodstream infections and 20,000 associated deaths occurred in the United States (Kourtis et al., 2019). After years of progress, the rate of decline of MRSA bloodstream infections has slowed, whereas bloodstream infections caused

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by methicillin-susceptible *S. aureus* are increasing slightly in the community (3.9% annually, 2012–2017) (Kourtis et al., 2019).

- **Threat:** Serious
- **Pathogen:** Gram-positive cocci in clusters, aerobic
- **Types:** There are two distinct types of MRSA. HA-MRSA (hospital acquired or healthcare acquired) and CA-MRSA (community acquired). Resistance in CA-MRSA may differ from HA-MRSA and is generally susceptible to more antibiotics than HA-MRSA. The definition of CA-MRSA has not been standardized. Attempts at definitions have focused on timing, infection that occurred within 48 to 72 hours of hospitalization, risk factors, those with no history of the following: hospitalization or surgery, permanent indwelling catheters or percutaneous medical devices, resident in long-term care facility, receiving dialysis.
- **Common sites of infection:** Skin and soft tissue infections most common in CA-MRSA. With HA-MRSA, infections often cause more severe illness: pneumonia, osteomyelitis, endocarditis, toxic shock, bacteremia and sepsis, and surgical and medical device site infections.
- **Populations affected:** HA-MRSA usually affects those with multiple comorbidities. CA-MRSA usually affect younger persons, that is, young adults, and athletes.
- **Resistance patterns:** HA-MRSA is multidrug resistant to broad-spectrum antibiotics such as methicillin, oxacillin, and cephalosporins. CA-MRSA is susceptible to many antibiotics except for β-lactam antibiotics.
- **Transmission:** Transmitted by direct and indirect contact.
- **Treatment:** The choice of an agent should be based on local antimicrobial sensitivities, site of infection, cost, and comorbid conditions. Uncomplicated MRSA infections may be treated with orally administered trimethoprim/sulfamethoxazole, tetracyclines, such as doxycycline or minocycline, and clindamycin (Kourtis et al., 2019). Newer agents, such as linezolid and tedizolid, and delafloxacin can be used though they can be cost prohibitive (Kourtis et al., 2019; See et al., 2017).
  - Complicated MRSA infections may be treated intravenously with vancomycin and daptomycin. Telavancin, ceftaroline, and quinupristin-dalfopritin may be used in certain circumstances, though they can be cost prohibitive (Kourtis et al., 2019; See et al., 2017). Decolonization for HA-MRSA should be based on the patient's medical condition and expected outcome (Liu et al., 2011). Decolonization therapy for CA-MRSA is not a recommended control measure for either individuals or outbreaks (Liu et al., 2011).

Vancomycin-Resistant Enterococci (VRE)

- **Incidence:** Enterococci ranked as the third most frequently reported pathogen across all types of adult healthcare–associated infections in 2015 to 2017 in the United States (Weiner-Lastinger et al., 2020) In 2017, there were an estimated 54,500 patients hospitalized for VRE infections and an estimated 5,400 VRE-associated deaths (CDC, 2019b).
- **Threat:** Serious
- **Pathogen:** Enterococci are facultative anaerobic gram-positive cocci in pairs. Enterococci is naturally present in the gastrointestinal tract.
- **Types:** *Escherichia faecalis* and *Escherichia faecium*
- **Common sites of infection:** VRE can cause bacteremia, urinary infection, intra-abdominal and pelvic infections, wound infections, pneumonia, endocarditis, or meningitis.
- **Populations affected:** Infection is more likely in people with chronic diseases, those who are immune compromised, those who have recently received antibiotics, or patients in long-term acute care hospitals or ICU settings. It is also more common in patients with indwelling devices such as IV lines or urinary catheters.
- **Resistance patterns:** Enterococci (*E. faecalis*, *E. faecium*) can become resistant to vancomycin by acquisition of genetic information from another organism**.** VRE has a minimum inhibitory concentration to vancomycin of greater than or equal to 32 mg/mL based on the Clinical and Laboratory Standard Institute 2020 *Performance Standards for Antimicrobial Susceptibility Testing*.
- **Transmission:** VRE spread indirectly from person to person on the hands of caregivers or contact with contaminated items or surfaces (CDC, 2019b). VRE can spread directly from person to person by contact with contaminated body fluids. VRE can remain alive for weeks unless the environment is cleaned and disinfected (CDC, 2019b).
- **Treatment:** The choice of an agent should be based on local antimicrobial sensitivities, site of infection, cost, and comorbid conditions. Antibiotics used include linezolid and quinupristin/dalfopristin, while the role of daptomycin and tigecycline requires further definition (Narayanan et al., 2019). Treatment for those colonized with VRE is not necessary (CDC, 2019b).

Follow-Up: N/A

Sequelae: MDRO infections place a substantial health and economic burden on the U.S. health-care system and population. In general, patients and those who reside in nursing homes with MDRO infections may experience prolonged illness and hospital stay, require more care, bear increased financial burden due to medical care, and are associated with significant morbidity and mortality.

Prevention/Prophylaxis: The risk of becoming colonized or infected with an MDRO infection is multifactorial, and advanced age, comorbid illnesses, invasive medical devices, frequent antibiotic exposure, and dependence on health-care workers all serve as contributing factors. There is no one-size-fits-all approach in optimizing antibiotic use for all settings.

The CDC (2019a) defines antibiotic stewardship as the effort to measure antibiotic prescribing; to improve antibiotic prescribing by clinicians and use by patients so that antibiotics are only prescribed and used when needed; to minimize misdiagnoses or delayed diagnoses leading to underuse of antibiotics; and to ensure that the 4Ds (see below) are utilized when an antibiotic is needed.

The goal of antimicrobial stewardship is to treat infection with minimal toxicity to the patient and minimal contribution to development of resistance. The 4Ds of antimicrobial

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Clinical Recommendation	Evidence Rating	References
Pseudomonas aeruginosa with difficult-to-treat resistance is defined as nonsusceptibility to at least one antibiotic in at least three classes for which *P. aeruginosa* susceptibility is generally expected: penicillin, cephalosporins, fluoroquinolones, aminoglycosides, and carbapenems.	A	Tamma et al., 2021
Extended-spectrum β-lactamase producing Enterobacterales have a broad-spectrum β-lactamase enzyme that enables them to inactivate most penicillin, cephalosporins, and aztreonam.	A	Tamma et al., 2021
Decolonization therapy for community acquired- methicillin-resistant *Staphylococcus aureus* is not a recommended control measure for either individuals or outbreaks.	A	Liu et al., 2011
Treatment for those colonized with vancomycin-resistant enterococci is not necessary,	A	Centers for Disease Control and Prevention (CDC), 2019b

A = consistent, good-quality, patient-oriented evidence; B = inconsistent or limited-quality, patient-oriented evidence; C = consensus, disease-oriented evidence, usual practice, expert opinion, or case series. For information about the SORT evidence rating system, go to www.aafp.org/afpsort.xml.

stewardship, initially described by Joseph and Rodvold (2008), are the following: (1) Choose the right drug that covers clinically suspected microorganisms, considering local resistance patterns. (2) Order the right dose by making sure each antimicrobial is dosed for source of infection and patient factors such as weight and renal function. (3) De-escalation to pathogen-directed therapy is achieved by following cultures closely and narrow coverage to microorganism isolated in culture. (4) Right duration of therapy antimicrobials must have a stop date consistent with current guidelines (Doron & Davidson, 2011) (i.e., community-acquired pneumonia: 5-day course of antibiotic treatment, Metlay et al., 2019).

Educate patients and their families about antibiotic use. Only prescribe antibiotics when they are needed. Antibiotics are not indicated for viral illness; they are treated through symptom management such as cough medication, acetaminophen, and so forth. Encourage them to seek care if they are not better or if their symptoms worsen. Educate them about possible harms from antibiotics such as allergic reaction, *Clostridioides difficile*, and antibiotic-resistant infections

Consider a consultation with an infectious disease specialist for advice about proper antibiotic therapy. Referencing local antibiograms is recommended to guide the clinician in selecting the best empiric antimicrobial treatment pending microbiology culture and susceptibility results. By carefully assessing every patient and making decisions using these principles, clinicians can promote safe and effective use of antimicrobials and ensure medicine stays on the winning side of the battle against antimicrobial resistance.

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