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CE for Kansas Nursing Professionals

Frequently Asked Questions

What are the requirements for license renewal?

Licenses Expire	Contact Hours Required
Every two years on the last day of your birth month.	30 (All hours are allowed through home-study)

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On-Line Submission: Go to ***nursing.elitecme.com*** and follow the prompts.You will be able to print your certificate immediately upon completion of the course.

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*Please note - providing a valid e-mail address is the quickest and most efficient way to receive your certificates when submitting via fax, e-mail or mail.

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How much will it cost?

Cost of Courses		
Course Title	**Contact Hours**	**Price**
Bugs and Drugs: Pharmacology of Infectious Disease Review	12	$29.00
Disorders of the Endocrine System: Anatomy, Physiology, and Current Treatment Initiatives	10	$29.00
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Kansas Board of Nursing Contact Information
Kansas Board of Nursing Landon State Office Building 900 SW Jackson Street, Suite 1051 Topeka, KS 66612 Phone: (785) 296-4929 | Fax: (785) 296-3929 Website: http://www.ksbn.org/

Bugs and Drugs: Pharmacology of Infectious Disease Review

12 Contact Hours

Release Date
12/2/2015

Expiration Date
12/2/2018

Faculty

Rachel R. Boersma, PhD., RN
Dr. Boersma is a recognized expert in nursing with many years of experience in clinical practice and higher education. She has taught and lectured internationally and has received numerous awards and grants for her work in nursing, human rights, and distance education. Dr. Boersma has taught nursing at the undergraduate, master's and doctoral levels and brings the same enthusiasm to teaching as she does to her work with the oppressed. She has taught a wide variety of courses including pharmacology, forensic toxicology, nursing research, nursing theory, healthcare ethics, and global health. Dr. Boersma earned her Bachelor of Science in Nursing and her PhD in Nursing from Boston College and her Master of Science in Forensic Nursing from Fitchburg State University.

Adrianne Avillion, D.Ed., RN
Adrianne E. Avillion, D.Ed., RN, is an accomplished nurse educator and published healthcare education author. Dr. Avillion earned her doctoral degree in adult education and her M. S. from Penn State University, along with a BSN from Bloomsburg University. Adrianne has served in various nursing roles over her career in both leadership roles and as a bedside clinical nurse. She has published extensively and is a frequent presenter at conferences and conventions devoted to the specialty of continuing education and nursing professional development. She currently owns and is the CEO of Strategic Nursing Professional Development, a business that specializes in continuing education for healthcare professionals and consulting services in nursing professional development.

Content reviewer
Katie Ingersoll, PharmD., RPh.

Audience

This course is intended for advanced practice nurses caring for patients with various infectious diseases. During this course, the learner will review basic principles of pharmacology and microbiology as well as prototype medications in the broad anti-infective class.

Purpose statement

This course is intended for advanced practice nurses caring for patients with various infectious diseases. During this course, the learner will review basic principles of pharmacology and microbiology as well as prototype medications in the broad anti-infective class. At the conclusion of this course, the learner will be able to approach the care of patients with infectious diseases with increased competence and with new tools to provide excellent clinical care.

Learning objectives

- Identify at least two examples of direct and indirect contact transmission of infectious disease.
- Identify the necessary core patient variables requiring assessment prior to prescribing anti-infective medications.
- Differentiate between the efficacy and effectiveness of a medication.
- Differentiate between an invading organism's pathogenicity and its virulence.
- Identify the prototype antibiotic that acts on the cell wall.
- Explain the meaning of "black box warnings."
- Explain how assessment of core patient variables can minimize the risk that a patient will experience one of the serious adverse events described in black box warnings.
- Identify the drugs of choice for the treatment of uncomplicated urinary tract infections.
- Distinguish between common mycobacterial infections and anti-fungal agents and identify the specific medication treatment for mycobacterial infections.
- Differentiate between medications for the treatment of the herpes viruses and medications for the treatment of influenza viruses.

How to receive credit

- Read the entire course online or in print which requires a 12 hour commitment of time.
- Depending on your state requirements you will asked to complete either:
  - An affirmation that you have completed the educational activity.
  - A mandatory test (a passing score of 70 percent is required). Test questions link content to learning objectives as a method to enhance individualized learning and material retention.
- Provide required personal information and payment information.
- Complete the MANDATORY Self-Assessment and Course Evaluation.
- Print your Certificate of Completion.

Accreditations and approvals

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Individual state nursing approvals

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Activity director

June D. Thompson, DrPH, MSN, RN, FAEN, Lead Nurse Planner

Disclosures

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Introduction

This course contains ten distinct modules designed to facilitate an understanding of pathogenic organisms, their infections processes, and the prototypical medications used to treat them. A review of basic pharmacotherapeutics (pharmacokinetics and pharmacodynamics) is included as well as links to some valuable resources related to pharmacology and infectious disease processes. The course concludes with a self-study section.

OVERVIEW

Role introduction and review

According to the American Association of Nurse Practitioners, there are over 205,000 licensed nurse practitioners (NPs) in the United States[1]. Standards set by the American Association of Colleges of Nursing delineate graduate level pharmacology as required content in Master's in Nursing educational programs[2].

NPs are registered nurses who received training after their initial nursing education in an NP program to provide care directly to patients. The profession originated in the mid-1960s in response to shortages of physicians. NP educational requirements, certification mechanisms, and legal scopes of practice are regulated at the state level and vary considerably[3].

Nurse practitioners (NP) are regulated by the state in which they are licensed. Regardless of the specialty they practice, NPs conduct physical examinations, diagnose, initiate treatment, and care for individuals with specific health/illness related problems. NPs also provide education to patients as well as referrals to other healthcare providers, clinics, hospitals, tertiary care settings, and community-based services as needed to promote the health and well-being of their patients.

In some states, NPs are completely independent practitioners; other states require a nurse practitioner to have a physician supervisor. This supervision may take several forms including the NP practicing in the same environment as the physician, or the NP providing care to patients under protocols established and approved by a physician. These protocols may be established through collaboration with the physician supervisor or adopted from other evidence-based sources. Prescriptive authority is governed by the state in which the NP practices. By 2014, NPs in all 50 states and the District of Columbia had achieved some degree of prescriptive authority. In 18 states, NPs may now prescribe drugs independently without physician involvement. The remaining states allow NPs to prescribe drugs with ranging levels of physician oversight[3].

Nurse practitioner clinical decision making

NPs integrate a large and diverse body of clinical data when presented with a patient's symptoms. They are under pressure to make accurate diagnostic assessments while balancing the economic realities of clinical practice with the risks to their patients. Data gathering, diagnostic testing, interpretation of diagnostic testing results, assessing the patient's clinical presentation, and integrating all of this information rapidly is demanding but crucial to making sound clinical and diagnostic decisions. This clinical decision-making process is the fundamental exercise necessary to determine which, if any, treatment regime should be undertaken.

In clinical situations when patient symptoms are clearly articulated and the NP recognizes a correlated clinical disease pattern, appropriate laboratory and/or radiological studies may be omitted and a prescription written to address the underlying infectious disease that the patient's symptoms appear to correlate with.

This pattern recognition may be an efficient method of clinical practice; however, errors may occur when other alternative explanations are not explored. For example, consider a patient presenting with the complaint of itching, redness in the affected area, rash, and a sensation of bugs crawling on her skin (formication), prickling, or tingling in the affected area, and uticaria for several days.

The patient explains that she is certain that it must be bugs, scabies, or fleas. Informal decision making on the part of the NP may lead to the patient being provided with a prescription for permethrin cream. However, an equally plausible explanation that may be overlooked is hyperthyroidism. Errors committed because of an over reliance on "rule of thumb" or "educated guesses" may result in poor patient outcomes and/or significant professional liability. It is imperative that NPs consider several other intellectual activities prior to initiating treatment plans involving medications because all medications have potential side effects and risks.

Nursing consideration: It is imperative that NPs obtain a detailed patient/family and consider possible diagnoses beyond the immediate "obvious" possibility.

Call for intent to change practice

These intellectual exercises include asking oneself, "If my initial diagnostic formulation is incorrect, what else could be causing this presentation? Is there anything in the patient's presentation that is incongruent with my initial diagnostic formulation? What are the potential morbidity and/or mortality outcomes of alternate diagnostic formulations?"

Leadership link

If rational prescribing is accepted as the ideal, practitioners should make decisions about treatment based on knowledge, reasoning, clear and logical thinking about the patient problem, and a plan of evidence-based care.

Inappropriate prescribing occurs when providers lack knowledge or allow external social or psychological pressures to shape their care instead of grounding their decisions in reason and known treatment efficacy. Decisions about treatment that are based on less rational thinking are more likely to result in suboptimal outcomes for the patient. Conversely, if the decisions about treatment are based more rationally, better outcomes are more likely[4].

To address the potential hazards of misdiagnosis and the subsequent undertaking of an erroneous treatment plan, the NP now has a large body of evidence-based medical and nursing practice information and clinical guidelines to consult. The benefit of this research is that the body of information found in these tools is based on the rigorous application of standards during evaluation of professional peer reviewed literature and research studies for inclusion in the best practice document or clinical guideline. Numerous databases are available to consult, freely available on the Internet and websites of specialty organizations. Below are some easily accessible resources that provide specific information regarding the diagnostics and treatments necessary when working with patients presenting with the possible symptoms of infectious disease:

- *http://www.cdc.gov/mmwr/mmwr_rr/rr_cvol.html*
- *http://www.cdc.gov/DiseasesConditions/*
- *http://www.guideline.gov/*
- *http://www.uspreventiveservicestaskforce.org/*

Beyond the traditional searches conducted with Google, Yahoo, or Bing, special search engines exist that will allow access to the areas of the Internet not traditionally searched with standard search engines. Less than 10% of the Internet is indexed by search engines. The remaining 90% of web content is what we call the invisible web. Use the resources identified in this guide to delve into the invisible web[5].

Overview of infectious disease

Infectious diseases have been a scourge throughout history. Epidemics or pandemics of infectious diseases have occurred frequently, decimating populations. Historical disease manifestations include smallpox, measles, bubonic plague, cholera, leprosy, and tuberculosis. The Egyptian pharaoh Ramses suffered from smallpox in 1157 BC and one half of the population of ancient Athens was killed during the 430-427 BC epidemic[6, 7].

Infectious diseases are caused by microorganisms that may be transmitted from one human to another, or from an animal to a human. These microorganisms include viruses, bacteria, fungi, parasites, and prions. The transmission of these microorganisms can occur directly, or through a vector. Direct transmission involves the transfer of a microorganism from human to human or from animal to human. Vector transmission commonly occurs through insect bites.

Infectious agents can be transmitted horizontally or vertically, and through direct and indirect contact. Horizontal transmission occurs when the infectious agent moves from one host to another. This can be from human to human or animal to human with direct or indirect contact.

Examples of direct contact include:

- Dermatological transmission (touching, licking).
- Respiratory secretions (air droplets).
- Via a break in the integumentary system resulting from a bite or wound (insect or animal bites, injury, surgical incisions).
- Sexual transmission.

Dermatological transmission via direct contact occurs in a variety of settings, especially in institutional and athletic contexts. Eliminating transmission of infection is a significant concern for healthcare providers in institutional settings, necessitating frequent hand washing.

The Centers for Disease Control and Prevention present the following information in part one of the self-study course on Principles of Epidemiology, and offer the following illustration [8]:

> …the traditional epidemiologic triad model holds that infectious diseases result from the interaction of agent, host, and environment. More specifically, transmission occurs when the agent leaves its reservoir or host through a portal of exit, is conveyed by some mode of transmission, and enters through

an appropriate portal of entry to infect a susceptible host. This sequence is sometimes called the chain of infection[9].

"The chain of infection has 3 main parts. A reservoir such as a human and an agent such as an amoeba. The mode of transmission can include direct contact, droplets, a vector (e.g., a mosquito), a vehicle (e.g., food), or the airborne route. The susceptible host has multiple portals of entry such as the mouth or a syringe[9]."

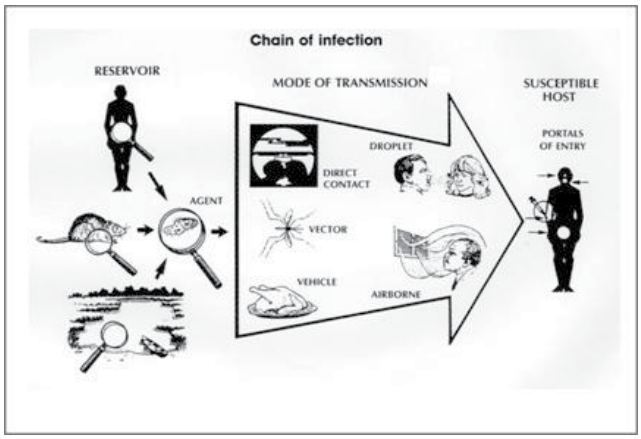

Figure 2
Source: Centers for Disease Control and Prevention. Principles of epidemiology, 2nd ed. Atlanta: U.S. Department of Health and Human Services; 1992.

Examples of indirect contact include:

- Oral or fecal transmission – foods, contaminated water, pica, mouthing of non-food items.
- Blood and other body fluids.
- Transplanted organs.
- Unsterilized equipment or poor sterile technique (institutional settings).

EBP alert! Research confirms the various methods of transmission via direct and indirect contact. It is imperative that all nurses know how infectious diseases are transmitted.

Healthcare-associated infections (HAI) remain a major cause of patient morbidity and mortality. Although the main source of nosocomial pathogens is likely the patient's endogenous flora, an estimated 20% to 40% of HAI have been attributed to cross-infection via the hands of healthcare personnel, who have become contaminated from direct contact with the patient or indirectly by touching contaminated environmental surfaces. Multiple studies strongly suggest that environmental contamination plays an important role in the transmission of methicillin-resistant Staphylococcus aureus and vancomycin-resistant Enterococcus species. More recently, evidence suggests that environmental contamination also plays a role in the nosocomial, or hospital-acquired, transmission of norovirus, Clostridium difficile, and Acinetobacter species. All three pathogens survive for prolonged periods in the environment, and infections have been associated with frequent surface contamination in hospital rooms and healthcare worker hands. In some cases, the extent of patient-to-patient transmission has been found to be directly proportional to the level of environmental contamination[10].

EBP alert! Research shows that environmental contamination may play a role in the nosocomial transmission of certain pathogens. It is essential that all healthcare professionals be aware of such research findings and implement preventive measures in their practice [10].

Vertical transmission occurs from mother to fetus primarily during the prenatal period; however, organisms can also be transmitted during delivery of the fetus and during breastfeeding. The acronym **CHEAPTORCHES** was introduced by Ford-Jones and Kellner[11] to highlight the various vertical transmission infectious risks:

C – Chickenpox and shingles.
H – Hepatitis B, C, (D), E.
E – Enteroviruses.
A – AIDS (HIV infection).
P – Parvovirus B19.
T – Toxoplasmosis / Toxoplasma gondii.
O – Other (Group B Streptococcus, Listeria, Candida, Lyme disease).
R – Rubella.
C – Cytomegalovirus.
H – Herpes simplex.
E – Everything else sexually transmitted (Gonorrhea, Chlamydia, ureaplasma urealyticum, Human papilloma virus).
S – Syphilis.

Viruses

Viruses are microscopic organisms or infective agents of genetic material (RNA or DNA). This core is surrounded by lipid, protein, or glycoprotein material [12]. Viruses require a host (cell) in order to reproduce.

On contact with a host, the virus inserts genetic material into the cell, resulting in the cell becoming infected and the cell functions hijacked. Outside of the host cell, viruses are generally inert.

Viruses that can infect humans include herpes, varicella, variola, influenza, HIV (human immunodeficiency virus), HPV (human papilloma virus), MCV (molluscum contagiosum virus), measles, mumps, rubella, and rabies [13].

These viruses cause significant illnesses including the common cold, influenza, gastroenteritis, warts, hepatitis, herpes, and rabies. There are a variety of transmission routes (see Table 1).

Table 1: Transmission routes[14]

Route	Examples
Skin contact	HPV (warts).
Respiratory	Cold viruses, influenza, measles, mumps, rubella.
Fecal-oral	Polio, Echo, Coxsackie, Hepatitis A, Rotavirus.
Milk	HIV, HTLV-1, CMV.
Transplacental	Rubella, CMV, HIV.
Sexually	Herpes 1 and 2, HIV, HPV, Hepatitis B.
Insect vector	Yellow fever, Dengue fever.
Animal bite	Rabies.

CMV, cytomegalovirus; HPV, Human Papilloma Virus; HTLV, Human T-Lymphotropic Virus.

Bacteria

Bacteria are among the oldest living organisms on Earth with fossilized examples dating back 3.5 billion years[15]. Bacteria are living one-cell organisms classified by several methods. Preliminary classification occurs according to the shape of the bacterium. Shapes include balls (cocci), rods (bacilli), or spirals.

The second major method of classifying bacteria is by the ability of the bacterial cell wall to absorb stain, typically crystal violet dye. This is often the first test performed in the laboratory to identify bacteria.

Based on this technique, bacteria are classified as either gram-negative or gram-positive. Gram-negative bacteria do not retain the crystal violet dye and stain pink or red, while gram-positive bacteria retain the crystal violet dye and stain purple. This classification has major implications in determining appropriate therapeutic agents to combat infection.

Below is a list of bacteria known to cause infections in humans:

- Staphylococci species.
- Streptococci species.
- Haemophilus influenzae.
- Streptococcus pneumonia (most prevalent cause of community-acquired pneumonia).
- Mycobacterium tuberculosis.
- Campylobacter jejuni.
- Salmonella species.
- Shigella species.
- Escherichia coli.
- Helicobacter pylori.
- Enterococcus faecium.
- Enterococcus faecalis.
- Enterobacter species.
- Pseudomonas aeruginosa (surgical wounds).

Fungi

Fungi are neither plants nor animals; they are in their own taxonomic kingdom. Taxonomists have classified more than 70,000 fungi, but not all fungi cause human illness. Some examples of fungi implicated in human illness or conditions include:

- Aspergillus.
- Candida.
- Coccidioides.
- Cryptococcus.
- Histoplasma capsulatum.
- Actinomycetes.
- Paracoccidioides brasiliensis.

Mycosis is a broad term used to describe an infection caused by a fungus. Fungi that cause infections are classified as pathogenic fungi to differentiate them from other fungi. Fungal infections may be opportunistic, hospital acquired, or community acquired. Opportunistic fungal infections occur when an individual's immune system is compromised from either another illness or medications.

Hospital-acquired fungal infections, especially blood stream infections caused by Candida, are very dangerous nosocomial infections.

The incidence of invasive mycoses is increasing, especially among patients who are immunocompromised or hospitalized with serious underlying diseases. These fungal infections may be broken into two broad categories: opportunistic and endemic. The most important agents of the opportunistic mycoses are Candida species, Cryptococcus neoformans, Pneumocystis jirovecii, and Aspergillus species (although the list of potential pathogens is ever expanding); while the most commonly encountered endemic mycoses are due to Histoplasma capsulatum, Coccidioides immitis/posadasii, and Blastomyces dermatitidis[17].

Community-acquired fungal infections are caused by common fungi found in the environment such as histoplasmosis, which caused by a fungus often found in bird or bat droppings. Other common community-acquired infections include tinea pedis (athlete's foot) and tinea cruris (jock itch).

Parasites

Parasites are organisms that live in or on a host and derive their nutrition from or at the expense of its host. Parasites may be internal to the human host, or cause illness from external contact. Internal parasites include various protozoa, worms, and flukes. Parasites can affect humans from all socioeconomic classes and are not found only in impoverished areas, though some parasitic infections such as Guinea worm disease are more common in rural parts of low income countries. Internal parasites in the general population that are of particular concern include[18]:

- Giardia (giardiasis).
- Ascaris (intestinal roundworms).
- Ancylostoma ceylanicum (hookworm).
- Plasmodium (malaria).

Common external parasites include:

- Sarcoptes scabiei (scabies).
- Pediculus (lice).
- Oxyuriasis (pinworms).
- Cimicidae (bedbugs).

Prions

Prions are proteins that can adopt two different forms: a normal form and a misfolded form. When they adopt the misfolded form, the misfolded prion causes other normal prions to misfold, potentially corrupting an entire population of normal prions. Prions are infectious and just a small number of misfolded prions can infect an entire organism. Prions cause rare progressive neurodegenerative diseases, as can be seen in mad cow disease, and often rapidly progresses once symptoms manifest. Prion infections can be fatal, however numerous studies are underway to develop treatments[19,20].

Nursing consideration: NPs must understand the action and pathogenesis of the various pathogens that affects their patients and how action and pathogenesis influence appropriate prescribing[17,18,19,20].

PHARMACOLOGY, NURSING PROCESS, DRUG PROTOTYPES, AND SPECIAL POPULATIONS

The nursing process

All registered nurses and advanced practice registered nurses utilize the nursing process as the framework for care of patients. The steps of the nursing process include assessment, nursing diagnosis, outcome identification, planning, intervention, and evaluation[21]. NPs utilize this framework routinely when providing care to patients presenting with a myriad of health problems, including infections or the potential for infections. To properly apply the steps of the nursing process to a patient's condition, the NP must maintain competence related to pharmacological management of care for patients[4]. Caring for patients with infections crosses multiple domains of practice, from acute care to correctional nursing. Infectious disease processes also occur across all professional practice specialties from neonatology to gerontology. All age groups and settings can experience infectious diseases.

Nursing consideration: Recognizing the varied and complex needs of this wide group of patients requires a fundamental knowledge and understanding of the basic principles of pharmacology. These principles are not dependent upon practice location, practice specialty or the age group of patients.

Overview of pharmacology

All nurses need to be familiar with the core drug knowledge of the medications a patient is taking in order to determine whether an interaction with core patient variables is likely to occur. This includes prescription drugs, over-the-counter drugs, or vitamin, herbal, of folk medicine preparations.

In addition, NPs applying the nursing process to the care of a patient with an existing or a potential infectious process must also consider the potential health outcomes (including interactions with core patient variables) for a patient to whom they are prescribing an anti-infectious agent. This is a significant responsibility for NPs with prescriptive authority.

Nursing consideration: Regardless of what class a drug falls into or whether it is an over-the-counter drug, a vitamin, an herb, a folk remedy or even an illicit drug, the basic principles of pharmacology remain the same.

General information about drugs

Drugs have generic and trade (brand) names. Chemical names of drugs are unique to a particular formulation and reflect the unique composition of the drug. Generic names of drugs are simpler than chemical names and are often required by institutions and organizations. The manufacturer assigns trade names to the drugs they produce. Generic formulations of particular drugs may be less expensive, but may differ in bioavailability when compared to a brand name formulation.

An anti-infective drug is any medication that is effective against infective, or pathogenic, organisms.Anti-infectives are broadly classified by susceptible pathogens (i.e., anti-bacterials fight bacteria, anti-fungals fight fungus). Anti-infectives are further classified by therapeutic properties, their mode of action, and/or by chemical similarities (aminoglycosides, sulfonamides, etc.).

The observed differences in drug effects between patients can be due to differences in drug metabolism caused by a variety of patient-specific factors.

Drug prototypes

There are thousands of medications available in the United States, making recollection of specific drug facts difficult for practitioners. Drug knowledge can be organized by a drug's therapeutic classification. Given the existence of so many drugs and the significant numbers of new drugs approved annually by the Food and Drug Administration (FDA), the initial study of pharmacology and subsequent pharmacology reviews must to provide a mechanism for understanding the pharmacology of a particular drug. The most common method is to focus on drug prototypes. A prototype drug is one that all other drugs in the same class are generally compared to, serving as a model drug.

Knowing the prototype drug will facilitate understanding the actions and any potential adverse effects that could occur with another drug in the same drug class. Studying drugs in this manner allows the practitioner to extrapolate knowledge of the prototype in a class of drugs to other drugs within the same class.

Nursing consideration: It would benefit all nurses, not just NPs, to become familiar with prototypes as much as possible. Those who administer drugs are accountable for their safe administration. This requires current knowledge of pharmacology.

Knowledge of the pharmacotherapeutics, pharmacokinetics, and pharmacodynamics of a drug prototype is critical.

Definitions pertinent to the study of pharmacology [22]

- **Pharmacotherapeutics** is the use of medications to treat, prevent, cure, or alleviate symptoms of a disease. It encompasses knowledge of the desired and therapeutic effect of the particular drug and requires an understanding of pharmacokinetics and pharmacodynamics.
- **Pharmacokinetics** is the study of changes that occurs to medications as they move through the human body (i.e., what the body does to a drug after it is administered).
- **Pharmacodynamics** is the effect of a particular drug on the human body.
- **Contraindications** are specific situations in which a drug may cause harm to an individual.
- **Precautions** are circumstances when a particular drug should not be used or should only be used carefully with monitoring.
- **Adverse effects** are unintended and usually undesired effects that may occur with a particular drug.
- **Drug interactions** are effects that may occur when a drug is given with another drug, certain foods, or other substances (e.g., alcohol).
- **Bioavailability** is the rate and extent to which the active ingredients are absorbed from a drug product and then available at the site of action, an important consideration when considering a drug's window of therapeutic range.
- **Core patient variables** are patient-specific conditions that should be considered when prescribing a medication to a patient and evaluating the efficacy of the treatment regime. See table 2: a table of core patient variables the NP should assess with all patients. Clinical judgment in prescribing considers all of these factors, as well as considering the costs associated with medications.

Table 2: Core patient variables

Core patient variables	
Medical history – past history of illness or injury.	History of present illness – onset, symptoms, duration.
Allergies.	Gender – if female, query patient regarding pregnancy.
Life span – Age/developmental level.	Diet.
Environment of care.	Culture/ethnicity.
Lifestyle.	Body mass (weight).
Genetics/ethnicity.	Drug/medication history.*

*During the assessment step of the nursing process, critical information about an individual's drug/medication history should be ascertained by the NP.

Nursing consideration: Medication hisotry must include information about prescription drugs, over-the-counter medications, herbal preparations, vitamins, minerals, dietary supplements, and the use of illegal drugs.

Elements of a comprehensive assessment of a drug/medication history

- Current medications, including dosages and routes.
- Time of last ingestion of each medication.
- Patient's perception about why each medication is prescribed.
- Other past medications and reason for discontinued use.
- Known drug, food or environmental allergies and intolerances, as well as a description of allergic/intolerant reactions.
- Over-the-counter medications, including frequency of use and time of last use.
- Use of any herbal products or folk remedies, including frequency of use and time of last use.
- Use of ethyl alcohol, including frequency of use and time of last use.
- Use of any other drugs (e.g., illicit, prescribed to others, street).

Table 3: Herb-drug (Anti-infective) Interactions

Herb	Source	Known or suspected interactions with anti-infective drugs
Astragalus	Astragalus membranaceus (root).	Cyclosporine, azathioprine, methotrexate (impairs intended immunosuppressive effects). Acyclovir, interleukin-2 (increased immunosupportive effects).
Bromelain	Ananas comosus (proteolytic enzymes of pineapple).	Antibiotics (increased effects). Tetracycline (increases serum levels of drug).
Cayenne	Capsicum minimum (fruit).	Increases biotransformation of drugs in general.
Echinacea	Echinacea purpurea (parts above ground).	Cyclosporine (reduces effectiveness).
Eleuthero (Siberian ginseng)	Eleutherococcus senticosus (root and/or rhizome).	Aminoglycoside antibiotics (increases effectiveness).
Kava kava	Piper methysticum (rhizomes).	Anti-fungals (increases risk for hepatotoxicity).
Garlic	Allium sativum (bulb).	Protease inhibitors (reduces serum levels).
St. John's wort or tianjihuang	Hypericum perforatum (tops).	Protease inhibitors(increased.bioavailability).
Other herbs may interact with anti-infective agents so if any patient acknowledges taking herbal remedies – consult a professional resource for potential interactions.		

Nursing consideration: All nurses must instruct patients and families about potential side effects and drug interactions of herbal preparations. Many people regard herbal preparations as "natural" and believe that they cannot cause harmful side effects or interactions with medications. Appropriate patient/family education is essential.

SPECIAL CONSIDERATIONS

The blood–brain barrier

The blood–brain barrier refers to a network of capillary endothelial cells that carry blood to the brain and spinal cord. These cells form a barrier that is impermeable to water-soluble drugs. This barrier can affect how medications, including certain anti-infective agents, access the central nervous system. This is of critical importance in infections of the central nervous system and brain, especially brain abscesses or fungal infections of the brain in immunocompromised patients.

The placental barrier

The placental barrier is a lipid membrane that allows passage of substances by simple diffusion. Lipid-soluble drugs pass across the placental barrier more easily than larger molecules or water-soluble medications. Placental transfer is responsible for many of the adverse effects of alcohol, cigarettes, narcotics, and other drugs. Some drugs may have teratogenic effects and result in physical defects in the developing fetus [24].

Pregnancy

The care of a woman who is pregnant or may become pregnant requires thoughtful and comprehensive assessment to minimize any risks to the mother or her fetus. Adherence to the principles of sound clinical decision-making is important at all times, and especially so when caring for both a mother and her unborn child.

Potentially almost any drug used by the mother during pregnancy could be deleterious to the fetus, causing an anatomic defect (teratogenic). Almost all lipid-soluble compounds readily cross the placenta. Water-soluble substances pass more easily when they are lower molecular weight. The degree to which a drug is bound to plasma protein also influences the amount of drug that is free to cross the placenta. Overall, most drugs cross the placenta to some degree, with the exception of large organic ions[24].

Many anti-infective drugs or medications carry significant risk to embryonic and/or fetal development so adequate precautions must be undertaken. Niebyl and Simpson presented documented risks to embryos and fetuses when a pregnant woman is treated with anti-infective agents[25]. The list is NOT comprehensive; NPs must seek appropriate, current prescriptive information prior to initiating antibiotic treatment of a pregnant woman.

EBP alert! Research shows that anti-infective drugs can pose significant risks to the health and well-being of the fetus. NPs must be particularly cautious when prescribing or thinking of prescribing such drugs to pregnant women [25].

Lactation

Just as pregnancy carries substantive risks when prescribing medications to an expectant mother, so does prescribing medications to a breast-feeding mother. The same judicious evaluation of risks and benefits to both mother and baby must be undertaken. Below is a summary of some risks associated with the administration of anti-infective agents to lactating mothers.

Table 4: Possible contraindications – maternal-fetal anti-infectives.

Anti-infective Safety During Lactation	
Penicillin V	Penicillin V is acceptable to use during breastfeeding. Limited information indicates that single maternal doses of penicillin V of 1320 mg produce low levels in milk that are not expected to cause adverse effects in breastfed infants. Occasionally, disruption of the infant's gastrointestinal flora, resulting in diarrhea or thrush, has been reported with penicillins, but these effects have not been adequately evaluated.
Penicillin G	Penicillin G is acceptable to use during breastfeeding. Limited information indicates that single maternal doses of penicillin G of 4 million units intramuscularly produce low levels in milk that these doses are not expected to cause adverse effects in breastfed infants. Occasionally, disruption of the infant's gastrointestinal flora, resulting in diarrhea or thrush, has been reported with penicillins, but these effects have not been adequately evaluated.
Ampicillin	Ampicillin is acceptable to use during breastfeeding. Substantial information indicates that maternal doses of ampicillin up to 4 grams daily produce low levels in milk that are not expected to cause adverse effects in breastfed infants. Occasionally, disruption of the infant's gastrointestinal flora, resulting in diarrhea or thrush, has been reported with penicillins, but these effects have not been adequately evaluated.
Amoxicillin	Amoxicillin is acceptable to use during breastfeeding [92]. Limited information indicates that single maternal doses of amoxicillin 1 gram produce low levels in milk that are not expected to cause adverse effects in breastfed infants. Occasionally, rash and disruption of the infant's gastrointestinal flora, resulting in diarrhea or thrush, have been reported, but these effects have not been adequately evaluated.
Gentamicin	Gentamicin is compatible with breastfeeding. It is excreted into breast milk in small amounts, but poorly absorbed by nursing infants [92]. Newborn infants apparently absorb small amounts of gentamicin, but serum levels with typical three times/day dosages are far below those attained when treating newborn infections and systemic effects of gentamicin are unlikely. Older infants would be expected to absorb even less gentamicin. Because there is little variability in the milk gentamicin levels during multiple daily dose regimens, timing breastfeeding with respect to the dose is of little or no benefit in reducing infant exposure. Data are not available with single daily dose regimens. Monitor the infant for possible effects on the gastrointestinal flora, such as diarrhea, candidiasis (e.g., thrush, diaper rash) or rarely, blood in the stool indicating possible antibiotic-associated colitis.
Cefazolin	Cefazolin is acceptable to use during breastfeeding despite low concentrations that are excreted in breast milk [92]. Limited information indicates that maternal doses of cefazolin up to 2 grams produce low levels in milk that are not expected to cause adverse effects in breastfed infants. Occasionally, disruption of the infant's gastrointestinal flora, resulting in diarrhea or thrush, has been reported with cephalosporins, but these effects have not been adequately evaluated.
Imipenem/Cilastatin	Imipenem/Cilastatin is excreted in the breast milk in low amounts. Effects on the nursing infant are unknown [92]. Acceptable to use during breastfeeding. Limited information indicates that single maternal doses of imipenem up to 500 mg produce low levels in milk that are not expected to cause adverse effects in breastfed infants. Occasionally, disruption of the infant's gastrointestinal flora, resulting in diarrhea or thrush, has been reported with beta-lactams, but these effects have not been adequately evaluated.
Vancomycin	Limited information indicates that vancomycin is excreted into breast milk. Since vancomycin is poorly absorbed from a normal, intact gastrointestinal tract, systemic absorption is not expected in nursing infants [92].

Tetracycline	Theoretically, tetracycline could stain a breastfeeding infants' dental enamel and inhibit bone growth. However, the possibility seems to be remote because infants exposed to tetracycline through breastfeeding have not developed detectable serum levels of tetracycline. The American Academy of Pediatrics classifies tetracycline as compatible with lactation [92].
Erythromycin	The American Academy of Pediatrics classifies tetracycline as compatible with lactation, despite its excretion in breast milk [92]. Because of the low levels of erythromycin in breast milk and safe administration directly to infants, it is acceptable in nursing mothers. The small amounts in milk are unlikely to cause adverse effects in the infant. Monitor the infant for irritability and possible effects on the gastrointestinal flora, including diarrhea, candidiasis (thrush, diaper rash). One case report and unconfirmed epidemiologic evidence indicates that the risk of hypertrophic pyloric stenosis in infants might be increased by maternal use of erythromycin during breastfeeding. Infant side effects are unlikely with topical application for acne, although topical application to the nipple may increase the risk of diarrhea in the infant. Only water-miscible cream or gel products should be applied to the breast because ointments may expose the infant to high levels of mineral paraffins via licking. Pyloric stenosis, vomiting, sedation, poor sucking and poor weight gain probably related to erythromycin in breast milk was reported in a 3-week-old infant. A cohort study of infants diagnosed with infantile hypertrophic pyloric stenosis found that affected infants were 2.3- to 3-times more likely to have a mother taking a macrolide antibiotic during the 90 days after delivery. Stratification of the infants found the odds ratio to be 10 for female infants and 2 for male infants. All of the mothers of affected infants nursed their infants. Seventy-two percent of the macrolide prescriptions were for erythromycin. However, the authors did not state which macrolide was taken by the mothers of the affected infants. "The use of macrolides during breast-feeding increases the risk of infantile hypertrophic pyloric stenosis" [26].
Gentamicin	Gentamicin is excreted into breast milk in small amounts and poorly absorbed by nursing infants, resulting in low levels of absorbed drug and unlikely clinical effects in the infant. The American Academy of Pediatrics classifies gentamicin as compatible with lactation [92]. Newborn infants apparently absorb small amounts of gentamicin, but serum levels with typical three times/day dosages are far below those attained when treating newborn infections and systemic effects of gentamicin are unlikely. Older infants would be expected to absorb even less gentamicin. Because there is little variability in the milk gentamicin levels during multiple daily dose regimens, timing breastfeeding with respect to the dose is of little or no benefit in reducing infant exposure. Data are not available with single daily dose regimens. Monitor the infant for possible effects on the gastrointestinal flora, such as diarrhea, candidiasis (e.g., thrush, diaper rash) or rarely, blood in the stool indicating possible antibiotic-associated colitis.
Ciprofloxacin	There is limited human data on the use of ciprofloxacin in breastfeeding, but the amount of drug that is excreted in breast milk does not seem to represent a significant risk to the infant. The American Academy of Pediatrics classifies ciprofloxacin as compatible with lactation [92]. Fluoroquinolones have traditionally not been used in infants because of concern about adverse effects on the infants' developing joints. However, recent studies indicate little risk. The calcium in milk might prevent absorption of the small amounts of fluoroquinolones in milk, but insufficient data exist to prove or disprove this assertion. Short-term use of moxifloxacin is acceptable in nursing mothers. However, it is preferable to use an alternate drug for which safety information is available. A case of pseudomembranous colitis in a 2-month-old breastfed infant was thought to be related to maternal self-treatment with ciprofloxacin [27].
Sulfamethoxazole-trimethoprim	There is conflicting evidence on the use of sulfamethoxazole-trimethoprim in breastfeeding women. The American Academy of Pediatrics classifies sulfamethoxazole-trimethoprim as compatible with lactation, while US and Canadian product labeling lists the drug as contraindicated in breastfeeding [92]. With healthy, full-term infants it appears acceptable to use sulfamethoxazole and trimethoprim during breastfeeding after the newborn period. Until further data are accumulated, alternate agents should probably be used in jaundiced, ill, stressed, or premature infants, because of the risk of bilirubin displacement and kernicterus. Sulfamethoxazole and trimethoprim should be avoided while breastfeeding a G6PD-deficient infant.
Isoniazid	The Centers for Disease Control and Prevention and other professional organizations state that breastfeeding should not be discouraged in women taking isoniazid. Nursing mothers who are taking isoniazid should take 25 mg of oral pyridoxine daily. Because of the low levels of isoniazid in breast milk and safe administration directly to infants, it is unlikely to cause adverse reactions in infants, but infants should be monitored for rare cases of jaundice [28,92].
Fluconazole	The American Academy of Pediatrics considers fluconazole to be acceptable in nursing mothers. No drug-induced toxicity has been observed in infants exposed to fluconazole through breastfeeding. Although no adequate clinical studies on fluconazole in Candida mastitis have been published, a survey of members of the Academy of Breastfeeding Medicine found that fluconazole is often prescribed for nursing mothers to treat breast candidiasis, especially with recurrent or persistent infections [30,92].
Nystatin	Although no information exists on the milk excretion of nystatin, it is virtually unabsorbed orally; therefore, most reviewers and clinicians consider it acceptable for use in nursing mothers. Excretion into breast milk is not expected. Only water-miscible cream or gel products should be applied to the breast because ointments may expose the infant to high levels of mineral paraffins via licking. Any excess cream should be removed from the nipples before nursing. Nystatin is less effective than other topical agents for the treatment of thrush [31,92].

Chloroquine	Very small amounts of chloroquine are excreted in breast milk. However, when given once weekly, the amount of drug is not sufficient to harm the infant nor is the quantity sufficient to protect the child from malaria. Breastfeeding infants should receive the recommended dosages of chloroquine for malaria prophylaxis. In HIV-infected women, elevated viral HIV loads in milk were decreased after treatment with chloroquine largely than other women who were treated with the combination of sulfadoxine and pyrimethamine. Because no information is available on the daily use of chloroquine during breastfeeding, hydroxychloroquine or another agent may be preferred in this situation, especially while nursing a newborn or preterm infant[32].
Metronidazole	With maternal intravenous and oral therapy, breastfed infants receive metronidazole in doses that are less than the dose used to treat infections in infants, although the active metabolite adds to the total infant exposure. Plasma levels of the drug and metabolite are measurable, but less than maternal plasma levels. Reports of Candidal infections and diarrhea have been reported, and a comparative trial suggested that oral and rectal colonization with Candida might be more common in infants exposed to metronidazole. Neither topical nor vaginal forms have been studied during breastfeeding. After vaginal administration, plasma levels are less than 2% of those after a 500 mg oral dose. Only water-miscible cream or gel products should be applied to the breast because ointments may expose the infant to levels of mineral paraffins via licking [33]. Because of the well-demonstrated mutagenicity and carcinogenicity in other species, concern has been raised about exposure of healthy infants to metronidazole via breast milk. Unnecessary esxposure to metronidazole should be avoided. It a single, two gram dose is needed for trichomoniasis, the American Academy of Pediatrics recommends holding breastfeeding for 12 to 24 hours to allow the medication to be excreted [92].
Acyclovir	Even with the highest maternal dosages, the dosage of acyclovir in milk is only about 1% of a typical infant dosage and would not be expected to cause any adverse effects in breastfed infants. Topical acyclovir applied to small areas of the mother's body away from the breast should pose no risk to the infant. Only water-miscible cream or gel products should be applied to the breast because ointments may expose the infant to high levels of mineral paraffins via licking[33].
Amantadine	It is probably best to avoid amantadine during breastfeeding because of its potential negative effect on lactation. Amantadine is a dopamine agonist. Clinical studies using amantadine dosages of 100 mg 2 or 3 times daily have demonstrated a decrease in serum prolactin and decreased galactorrhea in patients taking dopaminergic neuroleptic drugs such as phenothiazines, haloperidol and loxapine [35].
Lamivudine	In the United States and other developed countries, HIV-infected mothers should generally not breastfeed their infants. In countries in which no acceptable, feasible, sustainable, and safe replacement feeding is available, exclusive breastfeeding for 6 months is recommended for HIV-infected mothers to reduce the risk of HIV transmission from the mother to the infant compared with mixed feeding. In these settings, abrupt weaning at 4 months does not reduce the risk of HIV transmission or produce an overall health benefit compared to continued breastfeeding, and increases the risk of infant death in HIV-infected infants. Lamivudine is recommended by the World Health Organization to be given as part of a 3-drug combination to all antiretroviral-naive women who are breastfeeding their infants. Extended antiretroviral prophylaxis in breastfed infants with antiretroviral drugs appears to reduce the rate of HIV transmission during breastfeeding by about half, but the optimal regimen and duration of prophylaxis has not yet been defined. The infants who do become HIV infected during breastfeeding by mothers receiving a highly active antiretroviral therapy (HAART) regimen that includes lamivudine are often infected with multi-class resistant HIV. Lamivudine is often used as part of a regimen that decreases mother-to-child transmission of HIV and is generally well tolerated by the breastfed infant. Breastfed infants whose mothers receive HAART have higher rates of neutropenia during the first month and severe anemia during the first 6 months of life [36; 37]. A study compared the rates of severe anemia in 3 groups of infants who received postpartum prophylaxis with zidovudine for prevention of maternal-to-child transmission of HIV infection. Through 6 months of age, breastfed infants whose mothers received HAART had a higher rate of severe anemia (7.4%) than breastfed infants whose mothers received only zidovudine (5.3%). Formula-fed infants had the lowest rate of severe anemia (2.5%). The anemia generally responded well to iron and multivitamin supplementation, and discontinuation of zidovudine[38].

Age – Children

During childhood, changes occur rapidly as the child grows. The tissue to-fluid ratios change and the various organ systems change and mature. All of these factors have significant effects on a medication's pharmacokinetics. How these growth and development factors influence pharmacodynamics is much more difficult to determine, due to the continuously changing nature of growth.

We know that the capacity of the liver to metabolize drugs or medications is lower at birth, and the various pathways of metabolism mature at different rates making predictions of responses to specific substances quite variable. This variability can result in drugs being maintained in the child's body for longer periods and potentially reaching toxic effects.

Kidney function for neonates is immature. Therefore, dosages of medications need to be modified and often reduced. As the infant approaches a year of age, the immaturity of the renal system is resolved and quite similar to that of older children and adults. In fact, in many cases, it exceeds that of adults necessitating further modifications in dosages to account for the rapid renal clearance.

Developmental changes in both liver and kidney functioning during infancy and childhood may necessitate dose adjustments to achieve a therapeutic drug concentration and eliminate the risk of a toxic drug concentration. Additionally, we also know that some medications may exert deleterious effects on the growth and development of children. For example, tetracycline is contraindicated in young children because of the harmful effect that it has on bone growth and tooth enamel.

Age – The elderly patient

With advancing technology and improved healthcare, there is an increasing number of individuals aged 60 years and older in the United States, and these people need particular consideration in terms of pharmacology. With advancing age, there is typically an increased requirement for medication. Older people are more likely to have multiple disorders that will require multiple drug therapies, some of which may interact with one another. When older people receive drugs that could affect their balance or reduce their blood pressure, it could impact their risk of falls and fractures. As part of normal aging, the liver reduces in size, which can increase the time taken to metabolize or eliminate a medication. Consequently, in older people, medications can remain active for a longer period, resulting in a higher risk of side effects. Any prescribing should take into account the potential for toxicity; a patient assessment should be conducted. There is also an age-related reduction in kidney function, so the time it takes the kidneys to eliminate a drug is longer in the older patient, which also results in this population being more susceptible to side effects.

Antibiotic prescribing and administration in elderly patients places these patients at a risk of adverse events. The age-related physiological decline in kidney function, particularly when exacerbated by the adverse renal effects of comorbid conditions such as diabetes mellitus, congestive heart failure, and hypertension, substantially influences the excretion of numerous antibiotics. These comorbid conditions may predispose an elderly patient to the risk of an antibiotic-induced toxicity, requiring careful drug selection and clinical monitoring. Elderly patients often have multiple chronic disorders and receive numerous medications or poly-pharmacy with less than ideal coordination of care among multiple healthcare providers. Adding an antibiotic to the patient's regimen poses a risk for a drug–drug interaction [39].

Incidents of adverse antibiotic-related events appear to occur more frequently in elderly patients, and include aminoglycoside-induced nephrotoxicity and ototoxicity, antibiotic-associated pseudomembranous colitis, trimethoprim and sulfamethoxazole-induced blood dyscrasias and hyperkalemia, quinolone-related seizures, doxycycline- related esophageal ulcers and structures, and acute liver injury secondary to prolonged therapy with amoxicillin and clavulanic acid [40].

The penicillin family of drugs are generally well tolerated in most individuals, however a wide range of hypersensitivities have been reported including rash, fever, anaphylaxis, exfoliative dermatitis, and hemolytic anemia [41]. Some specific members of the penicillin family have been identified with particular adverse reactions. For example, ampicillin, amoxicillin, and amoxicillin/clavulanate are associated with diarrhea and C. difficile colitis, nafcillin is associated with neutropenia, ticarcillin is associated with hypokalemia, and methicillin and ampicillin are associated with interstitial nephritis [41].

The cephalosporin subclass has been shown to be fairly safe to use, partially explaining their widespread use, though they have been associated with diarrhea, pseudomembranous colitis, and rare hypersensitivity reactions including fever, rash, and interstitial nephritis [41].

Imipenem has caused phlebitis, gastrointestinal events, and rash, as well as development of seizures, which occur more commonly in elderly patients with renal impairment or underlying conditions of the central nervous system. Assessment of renal function should precede prescribing anti-infective agents to the elderly. Interactions may occur regardless of dosage adjustments or by the addition of other medications to interfere with the interaction [41].

The following conditions can influence the pharmacokinetics of a medication:

1. **Genetic influences**: Some acetylation and oxidative reactions have ethnic and familial patterns.
2. **Age**: Neonates and older adults may have reduced drug metabolism.
3. **Pregnancy**: Drug metabolism may be increased or decreased during pregnancy.
4. **Liver disease**: The rate of elimination of high-clearance drugs may be reduced.
5. **Time of day**: Circadian rhythm has some effect on drug metabolism.
6. **Environment**: Smoking, air pollution, and exposure to industrial chemicals may affect drug metabolism.
7. **Diet**: Drug metabolism may be affected by food – drug interactions or by malnutrition.
8. **Alcohol**: Alcohol may cause induction of drug metabolism.
9. **Drug interactions**: The concentration or function of various hepatic enzymes may change.

Nursing consideration: The age and general health status of patients have marked implications for safe and appropriate prescribing of drugs. It is essential that all nurses be aware of the impact of age and general health on the effectiveness of medications.

CALL FOR INTENT TO CHANGE PRACTICE

Ethnopharmacology

Ethnopharmacology, or the study of cultures and their use of traditional medicine, is a relatively new area of study [93]; however, current nursing students are taught that cultural competence is more than understanding different ethnic group beliefs and practices. Practitioners must be able to identify resources that describe variances in drug metabolism and excretion that may enhance or impede drug treatment outcomes. Also important are considerations of the potential for drug interactions with herbs or foods that may be part of culturally driven home remedies. Diversity is present in all healthcare settings, especially in primary care. Nurse practitioner prescribers (and all prescribers) must remain current in the area of ethnopharmacology and vigilant in prescriptive practices.

Genetics – Pharmacogenomics

An abundance of literature and recent studies describes the impact of the CYP enzyme system and its impact on patient pharmacokinetics and pharmacodynamics as more pharmaceutical companies are including CYP information on their products. This important information has not translated, however, in practice, resulting in under medicating patients, overmedicating patients, and treating patients with medications that simply do not work for those patients. In the absence of this information, or more accurately, not using or understanding the information that is available, clinicians prescribe medications in a trial-and-error approach, hoping for the desired outcome. Nurses

administering medications must be vigilant for common side effects and for evaluating the efficacy of the medication, which can vary tremendously. In current clinical practice, when the desired results are not achieved by a specific medication, a different medication is prescribed, and then another and another until a desired outcome is reached. Each time this occurs, the patient becomes an experiment[43].

Pharmacogenomics is an emerging field in healthcare. Many prescribers may have noted idiosyncratic responses to various medications in particular populations, increasing the study of personal differences in responses to medications. We know now that just as different age groups or genders respond differently to medications or drugs, so do individuals of the same age or gender that possess different genetic pedigrees.

All individuals with prescriptive privileges have the additional responsibility of considering genetic pedigree as a core patient variable in clinical decision-making. Pharmacogenetic investigation typically starts with an untoward response (or lack of response) to a medication or drug and examines possible genetic causes for this variability.

Pharmacogenomics is the study of how genes affect a person's response to drugs. This relatively new field combines pharmacology (the science of drugs) and genomics (the study of genes and their functions) to develop effective, safe medications and doses that will be tailored to a person's genetic makeup. Many drugs that are currently available are "one size fits all," but they do not work the same way for everyone. It can be difficult to predict who will benefit from a medication, who will not respond at all, and who will experience negative side effects (called adverse drug reactions). Adverse drug reactions are a significant cause of hospitalizations and deaths in the United States. With the knowledge gained from the Human Genome Project, researchers are learning how inherited differences in genes affect the body's response to medications. These genetic differences will be used to predict whether a medication will be effective for a particular person and to help prevent adverse drug reactions[44].

Variability can occur in drug targets (receptor sites), drug metabolism, and/or drug response. This variability can occur not only in the human patient but also in the organism that is causing the infection. Evidence of this variability in response to repeated exposure to certain anti-infective agents is readily apparent when we consider the various superbugs.

At least 2 million people in the United States each year become infected with bacteria that are resistant to antibiotics (superbugs) and more than 23,000 people die from these infections. Significant mortality is also associated with conditions that were further compromised by these concomitant antibiotic resistant infections [45]. These superbugs are now being classified according to their threat level. This model is now being applied to antibiotic resistant pathogens in urgent, serious, and concerning levels of threat [45].

The urgent category includes Clostridium difficile, carbapenem-resistant Enterobacteriaceae, and drug resistant and Neisseria gonorrhoeae. Multidrug-resistant Acinetobacter, drug resistant Campylobacter, fluconazole-resistant Candida, extended spectrum beta-lactamase-producing Enterobacteriaceae (ESBLs), vancomycin-resistant Enterococcus, multidrug resistant Pseudomonas aeruginosa, drug resistant non-typhoidal Salmonella, drug resistant Salmonella typhi, drug resistant Shigella, methicillin-resistant Staphylococcus aureus, drug resistant Streptococcus pneumoniae, and drug resistant tuberculosis are all rated as serious threats by the CDC. Vancomycin-resistant Staphylococcus aureus, erythromycin-resistant Group A Streptococcus, and clindamycin-resistant Group B Streptococcus are all rated by the CDC at the concerning threat level [45].

Practitioners are strongly encouraged to consult current peer reviewed literature and databases related to the pharmacogenomics of specific anti-infective medications. This information provide the practitioner with the knowledge to choose the right anti-infective for an individual's genetic pedigree and particular strains of pathogens. Below are several valuable genomic resources for nurse practitioners:

- *http://www.pharmgkb.org/index.jsp*
- *http://www.pacdb.org/*
- *http://www.fda.gov/drugs/scienceresearch/researchareas/pharmacogenetics/ucm083378.htm*
- *https://pharmacogenomics.ucsd.edu/*

SECTION III: PHARMACOKINETICS AND PHARMACODYNAMICS

Overview

No drug has only a single mode of action. In an ideal world, a particular drug would only have the expected and predictable action; however, this is not the case. Many drugs have the potential to affect and alter multiple systems of the body, some alterations resulting in no ill effect and others with potentially harmful or toxic effects. This leads to the development of side effects or adverse reactions. Prudent prescribing involves balancing the risks associated with side effects or adverse reactions with the potential benefit of drug therapy.

Nurse practitioners must know the therapeutic benefits, indications for use, contraindications in certain individuals or populations, potential adverse effects, and drug–drug interactions, especially in patients receiving poly-drug therapy, and the methods to determine if the drug prescribed is achieving the desired therapeutic effects. Selecting an appropriate medication for treatment may require choosing between many different drugs with similar actions and effects. This is especially true with anti-infective agents because of the cross-sensitivity or the cross-resistance of organisms to multiple different classes of anti-infective medications.

Choosing a particular medication from the myriad of options for any particular patient also requires the nurse practitioner to have knowledge of multiple disease processes, specific knowledge of any comorbid conditions a patient may have, knowledge of the pharmacodynamics properties and pharmacokinetic properties of a particular medication and the potential for any drug–drug interactions.

Ultimately, the primary role of the prescribing nurse practitioner is to choose the particular medication for the right patient, in the right dose so that an appropriate, therapeutic level of the medication is achieved at the appropriate site needed in the patient's body, and to minimize the risk of a toxic level of the drug.

Achieving this requires the nurse practitioner prescriber to have more than a basic understanding of drug action and effect. These factors are ultimately controlled by the absorption, distribution, metabolism, and excretion of the drug. This higher scientific knowledge is beyond that learned in basic nursing education. Hence, the need for advance pharmacology study and review.

Nursing consideration*:* In general, all drugs affect the biochemical and physiological functions in the living body. Understanding drug effects involves the relationship between the concentration of the medication achieved in the body and the pharmacodynamics properties of that particular medication.

When a drug acts at specific receptor, multiple effects may occur because the same or similar receptor sites may exist in multiple body locations or organs. Drug receptors are inherently tasked with responding to naturally occurring chemicals in the body so medications developed with similar qualities may subsequently affect the same receptors.

Pharmacokinetics and pharmacodynamics

It is important to recognize that pharmacokinetics and pharmacodynamics work in concert to determine virtually all choices in the selection of an appropriate drug, for an appropriate condition, to be administered to a specific individual. A clear understanding of this interaction is imperative for the prescribing nurse practitioner. Other general pharmacokinetic and pharmacodynamics principles include:

- How genetic influences may affect the metabolism of drugs and follow ethnic or familial patterns.
- How age influences these processes because the very young and the very old may have reduced or accelerated drug metabolism and/or excretion rates.
- How pregnancy may increase or decrease rates of drug metabolism and what risks are posed by in utero exposure to some medications.
- How liver disease can reduce the rate of metabolism and subsequently excretion of medications, potentially resulting in toxic accumulation in the tissues and body fluids.
- How the time of day of medication dosing can result in variability in medication response because of circadian differences among some individuals.
- How the environmental factors can affect drug metabolism, including smoking, pollution, and exposure to chemicals in the workplace.
- How an individual's diet can affect the metabolism of some medications either by increasing or decreasing bioavailability.
- How the consumption of alcohol can precipitate drug metabolism or interfere with metabolism due to the liver's exposure to alcohol.
- How drug–drug interactions can adversely affect certain necessary liver enzyme systems through competition.

Pharmacokinetics

The pharmacokinetics of a drug is a time-sensitive process. Knowledge of the ability of a drug to pass through cell walls and tissue membranes is fundamental to the understanding of how rapidly a drug may be absorbed and ultimately distributed to the areas of the body, particularly parts that are difficult to reach or pass through.

Drugs often move through the circulatory system to reach its intended site of action. This may result in either beneficial results or detrimental results. When a drug is metabolized by the liver before traveling to the site of action, it is considered first-pass metabolism.

As noted above, pharmacokinetics is the overall process that a drug undergoes while in the body, the changes that occur to the drug from ingestion to excretion. All drugs differ in their ability to produce an effect in the body, in the particular drug's ability to enter the location of desired activity, and in how the drug is removed from the site of desired activity. All of these pharmacokinetic properties predicate how a drug is administered, the frequency of administration, and the appropriate dosage for the desired effect.

Drugs use diffusion and active transport mechanisms to cross plasma membranes to reach their target cells where their actions will occur. The crossing of plasma membranes is predicated on various factors that may affect the movement of the drug including the size, the lipid solubility, and the molecular ionization. Pharmacokinetics involves several processes or phases.

Pharmacokinetics is the study and analysis of the time course of the drug in the body. The ease with which drugs pass through membranes is the key to assess the rates of absorption and extent of distribution throughout the many body compartments. Drugs are transported throughout the circulatory system and end up at tissues and organs where their presence is beneficial, in addition to areas where their presence may be detrimental. Drugs are usually metabolized in the liver either before they travel to the site of action ("first pass") or after they have been to the site of action. Drugs are eliminated from the body most commonly via the kidneys.

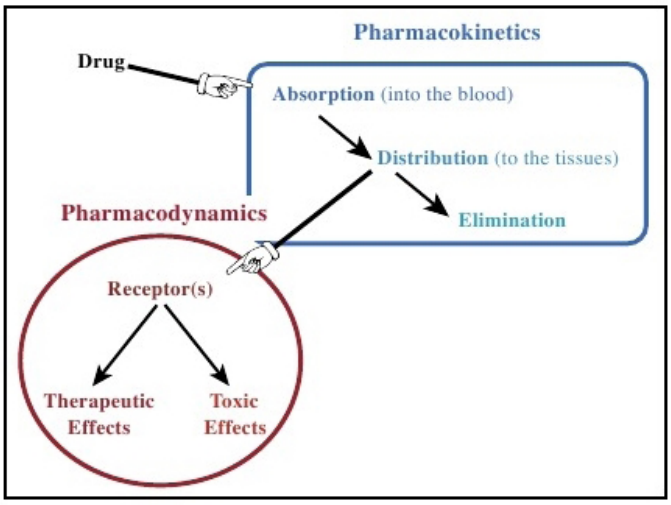

Figure 3.
Courtesy of Susan Masters, PhD.

Absorption phase

The first stage of pharmacokinetics is drug absorption. Most drugs need to be absorbed to produce an effect. The absorption phase is the process during which a drug moves from the site of the administration into the bloodstream or body fluids. Drug absorption includes all the chemical and biological processes during a drug molecule's transformation from the dosage form (tablet, liquid, etc.) to the circulatory system. For the drug to exert the desired effect and reach the intended body location, the form may need to be changed to one allowing absorption.

Several mechanisms facilitate drug absorption including diffusion and active transport. Passive diffusion refers to process of drug movement from an area of higher concentration to an area of lower concentration by passing through a membrane.

Another form of drug diffusion is facilitated diffusion, which occurs when the drug molecule combines with another molecule to facilitate absorption. An example of facilitated diffusion is the ability and process of hemoglobin binding with oxygen for delivery to tissues and organs.

Active transport occurs where a molecule is actively transported across a cell membrane requiring the expenditure of energy. Diffusion processes do not require the expenditure of energy.

The mechanism of absorption is a significant pharmacokinetic factor in determining the onset of a drug's action or efficacy. Parenteral drug delivery involves using a medication in a sterile liquid form to allow for direct injection. Absorption of parenteral products is simplified because the medication is already in liquid solution and when delivered intravenously (IV), and distribution occurs rapidly throughout the body. This is the clear advantage of IV drug delivery.

Although considered parenteral routes, intramuscular (IM) and subcutaneous (SC) drug delivery generally undergo absorption from the site of the injection. Although medications delivered via IM or SC routes may avoid having to dissolve and move through the membranes of the gastrointestinal system, thereby avoiding possible drug degradation in the intestinal-hepatic systems, blood flow to the injection site may affect absorption [94].

The form of delivery of certain drugs administered via the IM route may allow for an elongated period of absorption and drug effect [94]. For example, haloperidol decanoate is delivered in an oil-based solution when administered IM to allow for slower absorption. This facilitates increased compliance among some patients by allowing a higher dose to be administered with longer intervals between injections.

Physiological considerations in absorption are blood flow, total surface area, time for the drug to arrive at the site of action, and time needed for drug absorption at site of action. Other considerations for absorption are chemical stability and how soluble the drug is in lipids or water. Absorption varies with the route of drug administration. Most drugs must undergo this absorption phase except drugs that are administered directly to their site of action, such as some gastrointestinal antibiotics administered orally and certain topical medications. Various factors may affect this absorption phase.

Oral drug administration is the most common method of administration and the least invasive. To be absorbed, an orally administered solid dosage form such as a tablet must dissolve in liquid in the stomach or intestinal environment, because the body is unable to absorb a solid. This is quite similar to the process of food digestion to release necessary nutrients. It is critically important to understand that the ability of a drug to be diluted in the gastrointestinal system depends on the structural and functional workings of the GI tract, as well as the chemical conditions within the GI tract. The presence of fats, dairy products, and certain minerals can all affect absorption from the GI tract, hence the need for patient instruction about taking medication with or without foods or beverages. Absorption is also determined by the presence or absence of an adequate blood supply to the area.

Most absorption of orally administered medications occurs in the small intestine, so motility and length of the small intestine play a crucial role in this process. For example, the use of laxatives may increase the speed of movement of a medication through the small intestine, resulting in a lower rate of medication absorption and potentially sub-therapeutic levels of the drug.

The absorption of a medication depends on the blood flow surrounding the surface or site where the drug will be absorbed. Orally delivered medications and food stimulate the blood flow to the gastrointestinal system, thereby facilitating absorption; whereas, exercise may divert blood flow from the gastrointestinal system to the muscles, resulting in decreased absorption. Blood flow also plays a role in IM absorption, particularly when blood flow or volume is decreased due to heart disease, diminished circulating volume related to dehydration, or other circumstances. The blood flow to the skin may affect the absorption of medications delivered topically or trans-dermally, so in cases of vasoconstriction, the absorption of medications via these delivery routes may be affected.

In general, the more rapidly a solid drug dissolves, the faster the drug action occurs. Drugs may dissolve slowly or quickly, and solid dosage forms may be designed to dissolve more slowly to extend the effects of a medication. Knowledge of the particular drug and patient condition will determine which speed is more advantageous for an optimal outcome.

All of following variables may affect the absorption of a drug:

- The route of administration.
- The drug formulation (bioavailability may differ with generic formulations).
- The dosage of the drug.
- The motility of the digestive tract.
- The exposure of the drug to digestive enzymes in the GI tract.
- The blood flow to the site of the administration of the drug.
- The degree of ionization of a drug.
- The pH of local environment from which the drug is being absorbed.
- Any interactions with foods, beverages, or other drugs (drug–drug interactions).
- The surface area to which a topical drug is applied.

Metabolism phase

Biotransformation is the second phase of pharmacokinetics is drug metabolism. Biotransformation is the process of metabolizing drugs in the body. It commonly occurs in the liver and, therefore, is often called hepatic metabolism. Drug metabolism refers to the process of chemically changing a drug to a different compound called a metabolite to enhance its effects or facilitate excretion. When drugs are metabolized, the change can affect the drug's ability to permeate certain body tissues. Some drugs are activated by hepatic metabolism. These are called pro-drugs. Drug metabolism is divided into two phases in the liver.

Biotransformation is the chemical process of converting a drug into a form or compound that can be eliminated from the body. The human liver functions as the primary site for the metabolism of drugs. As a drug passes through the liver, several different chemical processes may occur, including hydrolysis, oxidation, and/or reduction. An example of phase one metabolism would be oxidation and example of phase two metabolism would be conjugation. Metabolism of drugs in the liver is often accomplished with the help of the hepatic microsomal enzyme system, the P-450 system. Genetic variants in the P-450 system can significantly affect drug metabolism. These variations can significantly affect the pharmacokinetics of a particular drug resulting in either under or over-medicating a patient [46]. Hence the need for the NP to assess the genetic background and ethnicity of the patient to prevent toxicity or lack of therapeutic response.

In most cases, the P-450 system functions to render a drug inactive and promote its excretion from the body. However, depending upon the individual's genetic heritage, this metabolism via the P-450 system may alter the drug's metabolism, resulting in decreased elimination or the chemically converted drug being more active than its original ingested form (increased bioavailability).

Neonates, infants, elderly patients, and patients with liver damage have decreased liver capacity to metabolize drugs. Drug dose adjustment may be necessary in these groups to prevent unintended effects related to drug accumulation.

The route of administration also affects drug metabolism. Drugs administered orally enter the hepatic metabolic system before distribution to other parts of the body. Drug metabolism via the liver is referred to as first pass metabolism. This metabolic step may activate the oral drug or result in a drug being rendered inactive, defeating the purpose of the drug's intended action. Under these circumstances, other routes of delivery are chosen (i.e., intravenous, sublingual, rectal, or topical).

When a specific therapeutic response or outcome occurs in 50% of patients, an effective dose is established. This is referred to as a drug's effective dose (ED50) for the average patient; however, many patients require dose adjustment based on the pharmacokinetics of the drug and the patient's biological constitution.

Regardless of the route of administration, drugs are generally distributed by the blood through the body; therefore, blood flow to a particular area of the body or organ predicates the concentration of drug in the region.

First pass metabolism

Orally administered medications, absorbed in either the stomach or small intestine, then move to the liver before passing into the general circulation of the body. Because the liver is heavily involved in drug elimination, drugs that are extensively metabolized in the liver can experience a significant loss of effect. Consequently, orally administered medications may require higher doses than parenterally-administered medications [94].

Other barriers to drug distribution include the affinity of some drugs to bind with plasma proteins, forming molecules that are too large to cross the blood capillary system walls, resulting in a lower distribution of drug. Drugs that bind to plasma proteins circulate until they are released from the drug-protein molecule. Binding sites of plasma protein may be occupied. Drugs bound to proteins circulate in the plasma until they are released or displaced from the drug–protein complex [94].

Drugs and other chemicals compete with each other for plasma–protein binding sites. Some agents have a greater affinity for the binding sites and displace other agents from the plasma proteins. The displaced drug can reach high levels and produce adverse effects[48].

Distribution

Drugs are distributed into major body fluids (i.e., blood and plasma). Specific tissues may also take up certain drugs. The distribution of a drug in the body is affected by the extent that the drug binds to plasma proteins. Drug distribution in the body is also affected by physiological barriers including the placenta and the blood–brain barrier [94].

Elimination or excretion phase

The drug elimination or excretion phase refers to the process by which drugs and their metabolites are removed from the body. Some drugs are excreted unchanged, and others are metabolized by the body. In excretion, a drug is removed from tissues and circulation. Most drugs and drug metabolites are excreted by the kidney through active and passive mechanisms [94]. The biliary system's route of excretion is important for many anti-infectives including ampicillin. Drugs are eliminated through the lungs, skin, saliva, tears, and, in lactating women, the mammary glands. Excretion through the respiratory system occurs commonly with drugs administered by inhalation or drugs in a vapor state.

Drugs can also be excreted by the skin, sweat, saliva, and tears. Although these routes seldom result in significant loss of drug concentration, they may be important to some patients if an adverse drug reaction occurs, including skin rash caused by skin excretion. Excretion in the saliva is the reason patients will experience a metallic taste with some medications.

Drugs are removed from the body by the process of elimination or excretion (pathway) and this process affects the ultimate action the drug has on the body. This pathway affects the amount or concentration of a drug in the patient's bloodstream and tissues.

The kidneys are the primary organ involved in this process of elimination; however, other factors affect this process, including liver or kidney illness, the health and the state of the patient's circulatory system, the patient's unique metabolism, and the affinity of the chemical compound to bind with circulating proteins. A patient experiencing diminished renal capacity or renal failure will retain drugs and medications for longer periods than patients without health impairments, hence drug and medication dosages must be reduced [94].

Other organs of the body may also excrete metabolized medications and drugs. These excretion systems include the respiratory system and bodily secretions, including saliva, sweat, and breast milk. Some drugs are eliminated through pancreatic excretion in conjunction with the liver.

Other important factors that medication prescribers must consider when determining a dosage for a patient are a patient's activity/exercise level and if a patient is receiving physical therapy. According to Ciccone, "Physical therapy interventions seem to have the greatest potential to affect absorption and distribution of drugs that are administered by transdermal techniques or by subcutaneous and intramuscular injections[49]."

Concept of half-life

The half-life of a drug is the amount of time it takes to eliminate one-half of the drug from the body. The half-life of a drug ultimately determines how often a drug needs to be administered and what the proper dosing schedule is. The half-life is usually not dose dependent; therefore, doubling the dose does not double the half-life.

The half-life of a drug or medication is the length of time necessary for a medication's concentration in the plasma to be reduced by one-half after administration of the drug. The rate of reduction to one-half in the circulating plasma may predict the duration of therapeutic action of the medication. The half-life of a drug or medication may be short or long and are referred to as short-acting drug or long-acting drug. This measurement of half-life is determined by the rate of excretion of the drug i.e. the shorter the half-life the more rapidly it is excreted. Half-life is an important consideration in the timing and amount of medication dosages to optimize the therapeutic effect on the target system or organ. To prevent toxic levels of drugs in the body, patients with liver or kidney disease may require less frequent dosing or a reduction in dosages.

Nursing consideration: It is critically important to communicate to patients that doubling the dose does not double the half-life so they do not function under the erroneous belief that more is better.

The half-life for a given drug generally remains the same for a given patient, but a patient with kidney or liver disease may result in a drug having an extended half-life. Generally, it takes 4 to 5 half-lives for a drug to reach a steady state of concentration when given continuously and 4 to 5 half-lives to be considered eliminated from the body when a drug is discontinued.

Half-life is an important principle not only for your patient but for you to consider as well. It can be useful for:

- Predicting the plasma levels following the start of drug treatment.
- Calculating how long will it take your patient to reach a steady-state plasma concentration.
- Determining the dose interval needed to provide a desired fluctuation in plasma concentration during that interval.
- Estimating the time required to eliminate all or a portion of a drug from the body upon your patient finishing a prescription or discontinuing it.
- Determining the fluctuation in plasma concentrations your patient may experience when given a specific dosing interval.

Efficacy

The amount of time it takes a drug or medication to reach a therapeutic level/response is the therapeutic effect. This therapeutic effect does not always correlate with the level of medication circulating in the bloodstream (plasma level) because the target of the medication intervention may be an organ or tissue with limited accessibility (for example a patient with a brain infection may have a peak plasma level but limited distribution in the brain tissue due to the blood-brain barrier.) The peak plasma level occurs when the medication has reached its highest concentration in the bloodstream. Loading doses may facilitate arriving at the therapeutic range.

Repeated doses and specific intervals are typically necessary for a drug or medication to reach and maintain the desired therapeutic level. This allows a drug to reach a steady state or balance between the amount of medication being administered and the amount being excreted optimizing delivery to the affected organ or tissue. For example, a short-acting drug such as tetracycline may need to be given more frequently for optimal effect than a long acting antibiotic such as doxycycline [50].

The effective dose in 50 percent of the population is called the ED50 of a given medication. The toxic dose in 50 percent of patients is the TD50 [94]. The TD50 is determined by the average lethal dose determined in tests and extrapolated to human beings. The ED50 and TD50 must be interpreted by the NP in the context of the assessment phase of the nursing process – knowledge and understanding of an individual patient's functional health status, etc.

A loading dose may facilitate arriving at a therapeutic concentration of a drug for a patient more rapidly. This loading dose may be given at the beginning of therapy to achieve higher plasma concentrations more rapidly, producing a more rapid therapeutic response. The loading dose is followed by maintenance doses at prescribed intervals to maintain a steady-state concentration in the circulating plasma.

Efficacy vs. effectiveness

Efficacy is the capacity to produce an effect (e.g., lower blood pressure). Efficacy can be assessed accurately only in ideal conditions (i.e., when patients are selected by proper criteria and strictly adhere to the dosing schedule). Thus, efficacy is measured under expert supervision in a group of patients most likely to have a response to a drug, such as in a controlled clinical trial.

Effectiveness differs from efficacy in that it takes into account how well a drug works in real-world use; often, a drug that is efficacious in clinical trials is not very effective in actual use[51].

Nursing consideration: It is essential that all nurses be able to differentiate between efficacy and effectiveness as part of their safe and appropriate administration (and in the case of NPs, the prescribing of) medications [51].

Pharmacodynamics

Pharmacodynamics is the effect that a drug or medication has on the body. This process involves the mechanism of action and the effect that particular drug concentrations have of human body responses. This process may involve both desired therapeutic effects as well as adverse effects. The key is balancing the positive therapeutic outcome against the risk of adverse side effects.

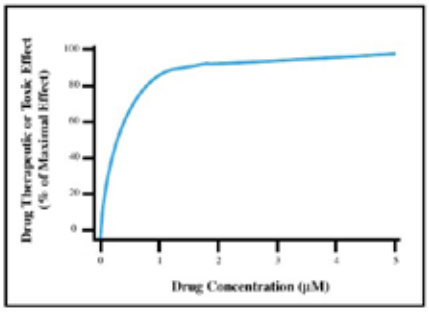

Figure 4.
Courtesy of Susan Masters, PhD.

There is great variability in patient responses to medications or drug administration. The responses are related to several factors including the dose-response relationship, the therapeutic index for a drug, and the interactions that occur between the drug and a receptor site. When considering a dosage to prescribe to a patient, it is important to consider that an average dose indicates that in 50% of cases a therapeutic response will be the outcome. That leaves another 50% of cases lacking a therapeutic response (serum level too low [sub-therapeutic] or high [toxic]). Therefore, monitoring of the drugs effect on a patient is imperative to adjust the dose or length/course of treatment.

The therapeutic index describes a drug's margin of safety. According to the National Institutes of Health, a drug's therapeutic index is "A ratio that compares the blood concentration at which a drug becomes toxic and the concentration at which the drug is effective. The larger the therapeutic index (TI), the safer the drug is. If the TI is small (the difference between the two concentrations is very small), the drug must be dosed carefully and the person receiving the drug should be monitored closely for any signs of drug toxicity" [52]. Further, some foods and/or co-prescribed medications may affect the therapeutic index of a drug.

The dose-response relationship of a drug

The dose-response relationship of a drug describes how the actions of that particular drug may change with dosage increases or decreases. This is best conceptualized as occurring in phases. Phase 1 occurs at the lowest dosage and indicates that too little an effect occurs in the affected tissue or organ. Phase 2 occurs when the dose of a medication is doubled resulting in twice as much response in the tissue or organ. This is the target range of dose for most medications because giving more medication results in a proportionate increase in effect and conversely a decreased dose of drug results in a proportionate decrease in effect. Phase 3 occurs when giving an increased dose does not result in an increased effect. This is referred to as the plateau, typically occurring because all of the binding sites are occupied by the drug or because the symptoms have been completely eliminated, therefore no further increase is necessary.

Potency

The response to a dose of a drug has two important characteristics - potency and efficacy. Potency of a drug expresses a drug's activity in terms of the concentration needed to produce a desired effect [53]. Potency is determined by assessing the level of desired activity at low doses and a drug's potency is affected by the absorption, distribution to the tissues, metabolism into inert compounds, and ultimately elimination from the body. The concept of potency is intrinsically linked to the concept of therapeutic equivalents (i.e. different medications at different doses or different frequencies resulting in similar optimal effects). An example to consider is the equivalent effect of the various benzodiazepines at different dosages.

Nursing consideration: Nurses should be able to differentiate between potency and efficacy.

In clinical practice, a medication's potency is certainly useful to consider; however, clinical effectiveness may not be dependent on potency exclusively, rather the efficiency of the drug to provide the maximum therapeutic effect by reaching the desired drug receptor sites. When faced with the dilemma of which drug to prescribe, the NP must consider this effectiveness rather than potency exclusively. Two drugs may be equipotent but have dissimilar target efficiencies. "Potency is an expression of the activity of a drug in terms of the concentration or amount of the drug required to produce a defined effect, whereas clinical efficacy judges the therapeutic effectiveness of the drug in humans." [53] There may be significant confusion about these processes, because not all drugs have equal efficacy despite being in the same larger class of drugs or they may be effective at quite different doses.

Consider the following example of antibiotic medications that could be prescribed to treat a wound infection. The organisms responsible for the wound infection are sensitive to both antibiotics. The recommendation for antibiotic A is that the patient should receive 10 mg/kg of body weight and for antibiotic B the recommendation is to prescribe 100 mg/kg of body weight. Potency is a concept critical to this phenomenon reflecting the strength of a drug at a particular concentration or dosage. Potency compares the dosages of two different drugs. A more potent drug will have the desired therapeutic effect on a tissue or organ at a lower dose compared to another drug in the same class. This is especially important when considering antibiotic treatment so in the above example, antibiotic A is more potent than antibiotic B; however, both may have the same desired effect.

Efficacy

Efficacy assesses the therapeutic effectiveness of a drug administered to humans [53]. Efficacy compares the therapeutic effect of two drugs with the goal of determining which will produce the maximum therapeutic effect.

Nursing consideration: Efficacy is usually the more significant factor when comparing different drugs or medications, because it reflects the outcome for the patient in treating the condition for which medication was prescribed.

The therapeutic window or therapeutic index

We know that the relationship between a medication's therapeutic effect and its potential for adverse consequences can be wide or narrow. The therapeutic window or therapeutic index is the ratio or difference in the medication dose (as measure by the circulating concentration) that will produce the intended effect or ultimately produce toxicity. If this index or window is wide, a drug is typically considered safe and close monitoring of serum concentration levels is not necessary. If this window is narrow, then close serum drug level monitoring will be necessary to prevent adverse reactions. An excellent example of this concept is the medication lithium carbonate. LiCO3 has a very narrow therapeutic window and frequent serum concentration monitoring is critically necessary to prevent lithium toxicity and possible patient mortality.

One goal in drug development is to have a large difference between the dose that is efficacious and the dose that causes adverse effects. This is a wide therapeutic index, therapeutic ratio, or therapeutic window. If the therapeutic index is narrow (e.g., <2), factors that are usually clinically inconsequential (e.g., food–drug interactions, drug–drug interactions, small errors in dosing) can have harmful clinical effects [51].

Receptor sites

Receptor sites are located on cellular membranes or within the cell itself and composed of proteins. Receptor sites are the location where the molecule of drug or medication binds and produces an effect causing the desired change. A patient's response to a medication is predicted by the proportion of the receptors that are bound or occupied by the drug [54].

There are limited numbers of receptor sites and there may be competition for these sites from both normal processes and other medications or drugs. Drugs that bind tightly with receptor sites are designated as having high intrinsic activity. Drug receptor sites are often conceptualized as being similar to a lock and key. Once the drug or medication is bound to the receptor site, a chemical messenger is triggered causing a cascade of biochemical events and processes that either enhance or inhibit the action of a cell [54].

The "ability to bind to a receptor is influenced by external factors, as well as by intracellular regulatory mechanisms. Baseline receptor density and the efficiency of stimulus-response mechanisms vary from tissue to tissue. Drugs, aging, genetic mutations, and disorders can increase (up-regulate) or decrease (down-regulate) the number and binding affinity of receptors[54]." Some agonists produce a greater response than their endogenous or naturally occurring counterparts do.

The concept of the drug – Receptor site relationship

A basic tenet of the science of pharmacology is that a relationship exists between the ideal effect or toxic effect of a medication and the level of concentration of the medication in the body. This is typically a function of the level of drug in the blood and forms the basis for therapeutic drug level monitoring. Serum drug level monitoring is critical for many medications because their narrow therapeutic window.

Nursing consideration: The NP must assess a particular drug's desired therapeutic concentration by considering both the unique physiological characteristics of a particular patient including pathologies the patient may be experiencing. This will allow the NP to discriminate between that particular patient and the average patient and will involve reviewing clinical practice guidelines, peer-reviewed literature, and details of clinical trials involving that particular medication.

Logically, it would appear that the larger the dose of drug given to a patient would result in a higher concentration of the drug at the receptor site. This only occurs up to a certain level, because once all of the possible receptor sites are either stimulated or blocked by a drug, then the total and maximum achievable response has been reached. This concept is also important to consider in situations of polypharmacy because multiple drugs may bind at the same receptor site.

In many cases, the bond between a medication and a drug receptor site is temporary, mitigated by the elimination of the medication from the site. This process is typically dependent on time and the health of the systems involved in drug excretion. This would be an example of a reversible action, the most typical physiologically occurring action. However, some drugs may permanently bind to a receptor site; this is much rarer.

The concept of affinity

Drugs have an affinity for their receptors, or chemical targets. Affinity is the property of the relationship between a drug and a receptor site to lock or bind together. Affinity is a measure of how well a drug can bind to its chemical target, a receptor site composed of protein. Some drugs have a higher affinity for their chemical targets. Drugs with a higher affinity will bind first, before any other drug molecule present. Some drugs have a higher affinity for their targets than physiological molecules. This can be very useful in drug action, especially where the physiological molecule is abundant and causing the problem or symptom the patient is experiencing.

The concept of drug selectivity

Selectivity is a quality of the drug receptor site that allows the site to determine and ultimately allow bonding with a chemical or a drug [54]. When a drug and a receptor have both high affinity and high selectivity, then the drug, even at a very low concentration, will bind to the specific receptor site and result in some receptor activity. Hence, drugs with both high affinity and specificity are excellent choices for treatment.

AGONISTS AND ANTAGONISTS

Drugs can be either agonists or antagonists at their target sites. This is a rather simple review of the concepts of agonism and antagonism as the action of a drug at its chemical target or receptor site.

Agonists

Agonists are drugs that bind to their targets and form a drug–receptor complex. Agonists activate the receptors to produce a response (known as full agonists) and have what is termed positive efficacy. Agonists are drugs that activate a particular cellular receptor site producing the same type of response as an endogenous substance. "An agonist is a drug that binds to a receptor and produces a functional response. Examples include morphine (μ-opioid receptor) and clonidine (α2-adrenoceptor)[55]."

Partial agonists

Drugs or medications that bind to a receptor but cause a diminished or less effective cellular response are partial agonists. The drugs that bind to their targets and activate them to produce a response which is less than that we would expect from a full agonist [55].

Antagonists

Antagonists are drugs that bind to their targets and form a drug–receptor complex, but without causing activation or response. They can block the receptor to its endogenous activator, thereby blocking normal function. They have zero efficacies. Antagonists are drugs or medications that bind to receptor sites preventing certain endogenous chemicals for binding and exerting action. For example, naloxone is an antagonists frequently used in opiate overdoses to competitively antagonize opioid receptors to reverse or reduce the adverse effects of the overdose [55].

The relationship between the drug dose and the response

When a medication is administered, absorption of the drug begins, creating a rise in the blood plasma level of the drug. No desirable or measurable effect occurs until there is an appropriate circulating concentration of the medication in the blood. At the minimally effective concentration, the drug will start to exert its action. If the absorption rate of the drug exceeds that of the normal rate of excretion, the therapeutic level is achieved. Alternate forms of administration can accelerate this process, such as administering the medication parenterally or sublingually. If the metabolism and elimination rates of the medication surpass the absorption rate, then the medication level concentration will diminish, thereby influencing the medication's efficacy and potentially becoming ineffective. Hence, the dosage level, the method of medication delivery, the frequency of medication administration, and the status of the excretory organs all play primary roles in maintaining therapeutic levels of a medication.

NPs must be cognizant of the dose and response ratio in order to ascertain how soon the medication will produce an effect (reach the minimum circulating concentration in the bloodstream), how long the drug will remain within the therapeutic window exerting the desired effect, and how long it will take for the drug to be metabolized and excreted, thereby dropping to a sub-therapeutic level.

If a rapid onset of action is necessary, then IV, IM, or sublingual administration may be necessary. For example, a patient having a panic attack may benefit from allowing lorazepam to dissolve under the tongue (sublingual administration) to allow for quicker resolution of the panic state can be achieved by swallowing the tablet. Of course, slower administration may be prudent if the therapeutic goal can be achieved without difficulty via the oral route.

PATHOGENS

Pathogenicity

Pathogenicity is the ability of an organism to cause illness in a living host (human, animal) [56]. Pathogens have the capability of causing disease either by invading tissues or by secreting toxins that damage tissue. Pathogenicity is measured by the ability of an organism to reproduce quickly or its ability to overwhelm the immune system. When an individual's immune system is compromised due to illness or immunosuppressive therapy, opportunistic pathogens might overcome the weakened immune system.

Virulence

Virulence is a quantitative measurement of the likelihood of a pathogen to cause disease. Virulence factors encompass the specific properties of a pathogen that enable it to invade a particular host and reproduce, thereby causing illness or disease. These factors include pathogenic toxins, particular cell surface properties, cell surface defenses including carbohydrates and/or proteins, and enzymatic properties of the pathogen. These factors are critically important to understanding the mechanism of action and efficacy of many anti-infective agents because it is through direct action on these virulence factors or processes that many anti-infectives exert their action [56].

A highly virulent organism or microbe is one that can cause significant disease even when the total microbial count is low. The virulence of an organism is mediated through two distinct processes – invasiveness and toxicity.

Nursing consideration: All nurses should be able to differentiate between an invading organism's pathogenicity and its virulence.

Invasiveness

"Invasiveness is the ability to invade tissues. It encompasses mechanisms for colonization (adherence and initial multiplication), production of extracellular substances which facilitate invasion (invasins) and ability to bypass or overcome host defense mechanisms[57]."

Toxicity

Some pathogens have the capacity to produce toxins, bacteria in particular are recognized to produce toxins that damage or kill human cells. Pathogens can produce both endotoxins and exotoxins. Endotoxins are generally located within the bacterial cell, and may be released by the activity of some antibiotics or by the cell's host defense mechanisms. Endotoxins generally affect the direct area surrounding the bacteria [58].

"Exotoxins are usually secreted by bacteria and act at a site removed from bacterial growth. However, in some cases, exotoxins are only released by lysis of the bacterial cell. Exotoxins are usually proteins, minimally polypeptides, that act enzymatically or through direct action with host cells and stimulate a variety of host responses. Most exotoxins act at tissue sites remote from the original point of bacterial invasion or growth. However, some bacterial exotoxins act at the site of pathogen colonization and may play a role in invasion" [58]. Exotoxins are usually associated with bacterial pathogens and their release may cause significant symptoms for a patient. Typically, a patient will present with generalized malaise, fever, chills, and other constitutional symptoms. Other pathogens including fungi and parasites may also release exotoxins causing debilitating illness [58].

Prior to initiating treatment for infection, the NP must first identify the offending pathogen (or at least make a reasonable guess based upon the clinical presentation of the patient). Secondly, the NP must know the susceptibility of the particular pathogen to particular drugs or medications. This requires an understanding of the morphology and pathogenic characteristics of the suspected offending pathogen. Thirdly, the NP must base the choice of drug or medication upon knowledge of and with full appreciation of the individual patient's specifics (core patient variables).

IDENTIFY THE PATHOGEN

Bacteria

Bacteria are typically identified by their shape, the ability of their cell wall to absorb stain, and by their ability to survive in oxygen depleted environments. The ability to absorb gram stain is typically the most efficacious. "A Gram stain preparation is perhaps the simplest, least expensive, and most useful of all the rapid methods of identification of bacterial (and some fungal) pathogens. This technique can be used to identify the presence and morphologic features of micro-organisms in body fluids that are normally sterile (cerebrospinal fluid, pleural fluid, synovial fluid, peritoneal fluid, urine). Preparations of sputum may also be helpful in revealing the nature of the infecting organism in patients with bacterial pneumonia[59]". Bacteria are classified as either gram positive or gram negative according to the ability of the bacterium to retain the violet color after staining. This distinction is useful when choose an antibiotic to treat a bacterial infection and antibiotics are typically grouped according to their effectiveness in combating different species of bacteria[59].

Viruses

Viruses are currently under intense research scrutiny as etiological agents in many infectious processes with significant morbidity and/or mortality outcomes. Identification of specific viruses is critical to developing appropriate interventions including vaccines and/or pharmacological interventions. This identification process can be laborious. What follows is a description of the typical process undertaken to identify a virus and its mutations. Cell cultures and electron microscopy are typically used to identify viruses.

Inoculation of patient specimens onto cultured cells or into laboratory animals enables biologic amplification of virus particles to levels where they can be detected by EM and identified to a virus family because, with a few exceptions, the morphologic features of all viruses within a given family are the same. Once recognized by EM, the findings can be confirmed by other techniques, including serologic testing, immunohistochemical (IHC) and indirect fluorescence antibody (IFA) assays, and molecular methods that can further characterize the virus to species and strain[61].

Fungi

Superficial fungal infections may be identified by the presenting symptoms or clinical presentation. Longer lasting or more extensive fungal infections may require identification via fungal cultures allowing for susceptibility testing. However, fungi take a long time to grow in culture, therefore biopsy, DNA, or RNA testing may be necessary [59].

The incidence of invasive mycoses is increasing, especially among patients who are immunocompromised or hospitalized with serious underlying diseases. Such infections may be broken into two broad categories: opportunistic and endemic. The most important agents of the opportunistic mycoses are Candida species, Cryptococcus neoformans, Pneumocystis jirovecii, and Aspergillus species. (although the list of potential pathogens is ever expanding); while the most commonly encountered endemic mycoses are due to Histoplasma capsulatum, Coccidioides immitis/posadasii, and Blastomyces dermatitidis [17].

Parasites

Infections caused by parasites affect may people living in the United States; such infections do not occur exclusively in underdeveloped countries. Parasites can be acquired from food, water, the soil, sexual contact, swimming water, etc. Although not as commonly seen in clinical practice as bacterial or viral infections, parasitic infections remain a significant cause of morbidity and mortality in the United States, particularly among certain populations such as patients with compromised immune systems. "Parasitic infections cause a tremendous burden of disease in both the tropics and subtropics as well as in more temperate climates. Of all parasitic diseases, malaria causes the most deaths globally. Malaria kills approximately 660,000 people each year, most of them young children in sub-Saharan Africa[63]."

Parasites are typically identified via microscopy with the application of stains. Specimens of body fluids, tissues, sputum, stool, etc. are collected and smears prepared for examination under fluorescence microscopy. Such evaluation allows for more accurate choices of treatments for parasites.

Prions

Testing for the presence of prions has historically been difficult, but recently the National Instititutes of Health announced the development of an antibody-based test to detect at least the causative agent of variant Creutzfeldt-Jacob disease (vCJD) in blood plasma [64]. Unfortunately, at this time there are no effective anti-infective treatments or medications for prion infection although much research is underway to develop vaccines and treatments for this devastating form of infection [64].

Regardless of the type of infective pathogen, all medications used to combat these infections fall under the umbrella category of anti-infective agents. Also included in this umbrella category are vaccines but information concerning these anti-infective agents will be covered elsewhere.

Anti-infective agents

Anti-infective agents function by targeting specific pathogens while avoiding human cellular structures. Selective toxicity is the ability of the antimicrobial to harm a pathogen (bacteria) without harming our own cells. Therefore, when discussing selective toxicity in terms of an antibiotic, health care workers are referring to the range between the dose necessary to inhibit or destroy the bacteria and the dose at which our own cells are harmed. Thus, an antibiotic that is far more toxic to the bacteria than our cells is said to have a greater selective toxicity [95].

The term anti-infective agents encompass multiple groups of drugs and medications. The major groups of anti-infective agents are below, followed by a common example:

- Penicillins natural and synthetic (penicillin G).
- Macrolide antibiotics (erythromycin).
- Fluoroquinolones (ciprofloxacin).
- Sulfonamides (sulfamethoxazole-trimethoprim).
- Antifungals (fluconazole).
- Antimalarial (chloroquine).
- Cephalosporins (cefazolin – first generation cephalosporin).
- Tetracyclines (tetracycline).
- Aminoglycosides (gentamycin).
- Anti-mycobacterial agents (dapsone).
- Antivirals (acyclovir).
- Antihelmintic agents (ivermectin).

Anti-infective agents may be classified according to several mechanisms including the organism/pathogen that is susceptible to the agent, the chemical composition and structure of the agent, and the mechanism of action of the agent. Antibiotics (both natural and synthetic) are the largest group of anti-infective agents and the first discovered. Penicillin was discovered in 1929 by Alexander Fleming. It proved to be a wonder drug saving millions of lives [65].

The specific mechanisms of action of the major anti-infectives will reviewed as each group is explored.

The history of antibiotics

Although these were not called antibiotics, various naturally occurring substances were used historically to treat infections. For example, molds and other plants were used in ancient Greece and India for wounds and infections. In Russia, the peasants often used warm soil to treat infections. In1640, an English researcher, John Parkington, noted that mold was useful for treating infections in his book on pharmacology. Numerous other cultures recognized the healing benefits of molds, herbs, and plants in ancient times [65].

The modern era of antibiotics began in 1928 when Sir Alexander Fleming discovered penicillin from the fungus Penicillium notatum thereby ushering desperately needed treatment of bacterial infections including syphilis, gangrene, and tuberculosis [65]. Unfortunately, this discovery came too late for the soldiers injured during World War I but was critical to the survival of the wounded during World War II [65].

"Antibiotics are agents that are 'selectively' toxic for bacteria (either killing them [bactericidal] or inhibiting their growth [bacteriostatic]) without harm to the patient. They can thus be ingested. By definition, these compounds must act on structures found in bacteria, but not in the host. Antibiotics work most efficiently in conjunction with an active immune system to kill infecting bacteria in the host[66]."

Access an infectious disease drug of choice tool here: *http://www.globalrph.com/bugs2.htm.*

Antibiotic resistance

In spite of almost 10 years of focusing on appropriate use of antibiotics, approximately 75 percent of antibiotic prescriptions written in pediatric practice are for otitis media, sinusitis, cough illness/ bronchitis, pharyngitis, and the common cold. Because the common cold, upper respiratory infections, and acute bronchitis are self-limiting illnesses usually caused by viruses, antibiotics have no role in management of uncomplicated cases[45].

Evidence-based practice alert! "According to the CDC, every year 2 million people in the United States become infected with antibiotic resistant bacteria and 23,000 people die each year as a direct result of these infections. Assisted living nurses and NPs caring for patients in these extended care facility are increasingly faced with residents who have infections with organisms such as Vancomycin-resistant Enterococcus, Methicillin-resistant Staphylococcus aureus, and Clostridium difficile[67]."

Currently, all antibiotic classes have resistant organisms, a consequence of indiscriminate prescribing historically. Unless new drug mechanisms of action, properties, or formulations are developed, NPs could find themselves limited in what to prescribe for certain types of infections. This resistance is not exclusive to bacteria; numerous other pathogens currently exhibit or in the future may exhibit resistance.

ANTIBIOTICS – PENICILLINS, CEPHALOSPORINS, CARBAPENEMS, MISCELLANEOUS ANTIBIOTICS

Antibiotics are among the most frequently prescribed drugs in primary care practice. An antibiotic from the penicillin family is usually the drug of choice for a susceptible organism because the low risk of toxicity in non-allergic patients. The most common infections treated with penicillins in ambulatory care are upper respiratory infections (URIs), otitis media, sinus infections, bronchitis, pneumonia, STDs, urinary tract infections, and wound infections. Other important uses of the penicillins are for the prophylactic treatment of endocarditis, for treatment of Helicobacter pylori in gastritis and peptic ulcer disease, and for Lyme disease.

WHEN TO PRESCRIBE AN ANTIBIOTIC AND WHEN NOT TO

Upper respiratory infections - Cough and acute bronchitis

Extensive guidelines regarding the management of bronchitis detail clearly not to use antibiotics for patients with acute bronchitis. Acute bronchitis, or inflammation and mucus production in the airways, is typically caused by viral infections, which do not respond to treatment with antibiotics. Patients presenting with acute bronchitis should be treated with antitussive agents and not antibiotics [96].

Chronic bronchitis

Distinguishing between acute bronchitis and an acute exacerbation of chronic bronchitis can guide practitioners. Chronic bronchitis is a condition typically associated with smoking and is a daily cough with sputum production occurring for at least 3 months at a time over a minimum of a 2-year period [97].

Patients with underlying chronic bronchitis may periodically become infected with a wide variety of distinct organisms including bacteria and fungi. The common organisms found in the sputum of patients with chronic bronchitis are most commonly viruses, as well as H. influenzae, S. pneumoniae, and M. pneumoniae. Gram staining may be inconclusive in these cases due to the colonization by the bacteria below the vocal cords therefore the use of antibiotics may be predicated upon the presence (or absence) of at least two of three symptoms. These include an increased sputum production, evidence of purulent sputum, and/or increased difficulty breathing (dyspnea) [68]. Additionally if the patient is displaying signs of a bacterial infection, such as increased purulence of sputum, a decision to prescribe an antibiotic may be indicated. Chest x-rays to discern if pneumonia is present are recommended. Antibiotics are recommended in patients with exacerbations of COPD or chronic bronchitis when they display three cardinal symptoms: increased dyspnea, increased sputum volume, and sputum purulence. The recommended length of therapy with antibiotics in these patients is generally between five to ten days. Antibiotic choices should be based on local bacterial resistance patterns [98].

Otitis media

Acute otitis media (AOM) is the most common presenting complaint that results in the prescribing of an antibiotic. Prior to initiating treatment for a middle ear infection, the NP must distinguish between AOM and otitis media with effusion (OME). AOM is diagnosed when the patient presents with fluid in the middle ear, an acute onset of symptoms, and signs of acute middle ear inflammation [69].

Contrast the above presentation of AOM with otitis media with effusion demonstrated by the presence of fluid in the middle ear without signs or symptoms of constitutional symptoms. OME may follow resolution of AOM or occur as a consequence of Eustachian tube dysfunction. Since OME does not represent an acute infectious process that could benefit from antibiotics, observation without use of antibiotics in a child with uncompleted AOM is a recommended. Appropriate treatment of OME will help minimize the unnecessary use of antibiotics and prevent antimicrobial resistance [69].

Viral AOM is very common. If bacterial infection is suspected, the most common bacterial organisms are S. pneumoniae, H. influenzae, and M. catarrhalis. Because the culturing of acute otitis media is difficult and invasive, it is usually treated based on clinical guidelines detailing the commonly infecting organisms [69].

If antibiotics are recommended, amoxicillin is the first-line drug of choice for AOM in the non-allergic patient, if the child has not received amoxicillin within the last 30 days. Patients who have received amoxicillin within the last 30 days or have concurrent purulent conjunctivitis may require treatment with amoxicillin/clavulanate[69].

If the patient fails to respond to amoxicillin within 48 to 72 hours, then reassessment of the diagnosis is indicated to exclude other causes of the illness and decide if the antibiotic choice should be changed. In general, if high-dose amoxicillin was

the initial choice, then amoxicillin/ clavulanate should be tried before moving to a different drug class. Almost 100 percent of M. catarrhalis strains and 18 to 42 percent of H. influenzae strains produce beta-lactamase, rendering them drug resistant. However, amoxicillin is still highly effective, safe, and inexpensive for AOM, compared with other antibiotics. The American Academy of Family Physicians (AAP) and American Academy Pediatrics (AAFP) guidelines recommend the length of treatment in children younger than age two years is 10 days. Children two to five years with mild to moderate AOM should be treated for seven days, and in children age 6 years and older with mild to moderate disease should be treated with a 5-to 7-day course of antibiotics. Persistent OME after therapy for AOM is expected and does not require treatment. These guidelines are the current standard of care[69].

Healthcare practitioners, infectious disease specialists, epidemiologists, and public health officials are expressing concern at the burgeoning problem of antimicrobial resistance; however, a parent with a sick child may lobby hard for antibiotic intervention. This dilemma is commonly faced in practice. Nurse practitioners must remain vigilant and prescribe antibiotic therapy only when appropriate, as recommended by current guidelines. The very real problem of antimicrobial resistance threatens the health of our patients, our neighbors, our co-workers, and our family members [70].

Urinary tract infections

Next to ear infections, urinary tract infections (UTIs) are responsible for thousands of office visits each year. Escherichia coli infection is responsible for most of the community-acquired UTIs. Treatment with nitrofurantoin is recommended due to low resistance rates and low risk of adverse effects. Trimethoprim/sulfamethoxazole can be used in areas where local resistance rates do not exceed 20 percent and can be used in patients who do not have sulfa drug allergies. Decisions regarding antibiotic agents should be individualized based on patients' allergies, tolerability, community resistance rates, cost, and availability [71].

Skin and tissue infections

Amoxicillin/clavulanate is recommended for treatment of infected animal bite wounds; amoxicillin/clavulanate can be used as prophylaxis of infection in animal bites in patients who are immunocompromised, asplenic, have advanced liver disease, have edema of the affected area, have moderate/severe injuries of the hands or face, or if the injury penetrates a joint [99].

Lyme disease

Lyme disease is caused by Borrelia burgdorferi and other Borrelia species, transmitted by tick bites. These ticks are endemic to various parts of the United States especially in the Northeast. Diagnosis is primarily based on clinical signs and symptoms although some serological testing is available. According to the Infectious Disease Society of America guidelines, amoxicillin 500mg three to four times daily for four to six weeks may be used upon presentation of an erythema migrans rash. Other agents, such as cefuroxime 500mg twice daily for four to six weeks, doxycycline 100mg twice daily for four to six weeks, or azithromycin 250 to 500mg daily for a minimum of 21 days can be used [72].

Penicillins – Mode of action – The cell wall

Penicillins are classified as beta-lactam drugs because their molecular structure includes a specific ring formation. Their chemistry, mode of action, and clinical effects are quite similar to other anti-infective agents with similar beta-lactam structures [100].

Bacteria have cell walls as a natural defense from potentially harmful substances. The key to the effectiveness of some antibiotics is the ability of the antibiotic to defeat this natural defense. Peptidoglycan is the primary component of the cell wall of bacteria. Regulated by the action of enzymes, carbohydrates and proteins are the building blocks that make up this natural defense for bacteria. Certain antibiotics have the ability to interfere with the construction of the cell wall. When this occurs, the cell wall can no longer be sustained or repaired resulting in cellular death. Penicillins, cephalosporins, carbapenems, and various other medications, including vancomycin, all act in this manner and are considered bactericidal. Because human cells lack a cell wall, there is virtually no action against host cells. Penicillins are bactericidal against sensitive organisms, meaning they are capable of killing bacteria [101].

Penicillins are the oldest group of antibiotics, and are most active against gram-positive bacteria. However, bacteria are able to mutate after repeated exposure to pencillins, and can produce and secret enzymes such as penicillinase, which breaks the beta-lactam ring of certain penicillins, rendering them ineffective. Penicillinase-resistant penicillins, such as nafcillin, may be necessary in these situations [100].

Use of penicillins

According to clinical practice guidelines, penicillin or amoxicillin are considered the drugs of choice for the treatment of Group A streptococcal pharyngitis followed by alternative first-generation cephalosporin medications, clindamycin, clarithromycin, or azithromycin [73]. Oral penicillin forms are generally well absorbed in the gastrointestinal (GI) tract, but some penicillins such as penicillin G are unstable in stomach acid secretions, thereby destroying much of the drug in the stomach. To produce therapeutic drug levels, penicillin G must be given parenterally. Another consideration is that kidney illness or insufficiency prolongs the half-life and can significantly increase the risk an adverse drug reaction secondary to drug toxicity [100].

Serious and occasionally fatal immediate hypersensitivity reactions do occur with the penicillins and anaphylactic shock may be a consequence of exposure to this group of medications. Anaphylactic reactions typically occur within 2 to 30 minutes after administration and signs and symptoms include nausea, vomiting, urticaria (hives), pruitus (itching), tachycardia, shortness of breath, diaphoresis, labored breathing, and potentially the loss of consciousness and ultimately collapse of the circulatory system. Treatment is the same as for any anaphylactic reaction and must be swift. Patients need to be counseled regarding risks if they have never received penicillin previously [100].

Other hypersensitivity reactions include skin rashes such as exfoliative dermatitis (red, scaly skin), and blood disorders, including anemias

and other abnormalities of the white blood cells. As with many antibiotics, common adverse reactions include GI symptoms, including nausea, vomiting, diarrhea, and epigastric distress. Use of broader-spectrum penicillins, or prolonged or repeated treatment with any broad-spectrum antibacterial agent (not exclusively penicillin), may result in changes to the normal bowel flora. This can lead to conditions sucha s Clostridium difficile colitis, presenting with symptoms of severe abdominal cramps and pain, watery and severe diarrhea that may be bloody, and fever. This pseudomembranous colitis or antibiotic-associated colitis is a serious consequence that may resolve with both supportive therapy and discontinuing the antibiotic [100].

The main drug interactions with penicillins is the potential for the reduced effectiveness of oral contraceptives so instruct your female patient to take extra precautions if becoming pregnant is undesirable to her [74].

Although interstitial nephritis was commonly seen older penicillin forms no longer in use, it can occur with any penicillin. High doses of procaine penicillin G have also been implicated in mental disturbances including dizziness, neuromuscular twitching, and auditory, visual, and taste hallucinations. Platelet disturbances may occur with parenteral dosages of various penicillins, and should be used with caution with patients with underlying clotting disorders [100].

Group 1 - Natural penicillins

Penicillin G is bacteriocidal for sensitive strains of bacteria, meaning penicillins can kill the bacteria as opposed to arresting the growth of the bacteria (bacteriostatic). The primary bacteriocidal action is inhibition of cell wall synthesis, primarily affecting gram-positive bacteria. For both penicillins and cephlosporins to demonstrate effective bacteriocidal properties, the bacteria must be actively growing thereby actively forming or synthesizing new cell walls [100].

Penicillins are divided into different groups or sub-classes depending on their unique characteristics [100]:

- Penicillinase sensitive compounds, also known as the natural penicillins.
- Penicillinase-resistant penicillins.
- Aminopenicillins.
- Carboxypenicillins.
- Ureidopenicillins and piperazine penicillin.

The natural penicillins are active against non-beta-lactamase producing gram-positive organisms, such as Streptococcus species, including S. pneumonia and group A streptococci, Enterococcus strains, and some non-penicillinase-producing Staphylococci. They also exhibit excellent activity against spirochetes, such as Treponema pallidum, the organism responsible for causing syphilis. Natural penicillins have limited use against gram-negative cocci such as Neisseria gonorrheae, and should not be used for treatment of gonorrhea due to increased risk of resistance [100].

The anti-staphylococcal, or penicillinase-resistant, penicillins, have a different spectrum of activity than the natural penicillins. This sub-group is effective against Staphylococcus aureus, although methicillin-resistant strains are not sensitive to penicillinase-resistant penicillins. This group of penicillins is less active against streptococcal infections than the natural penicillins [100].

The aminopenicillins have good efficacy against gram-positive organisms, such as Streptococcus species, Enterococcus species, and Listeria monocytogenes. They are also effective against gram-negative bacteria, including H. influenzae, E. coli, Proteus mirabilis, Salmonella species, and Shigella species, although some resistance is developing with ampicillin [100].

Evidence-based practice alert! A benefit to using penicillins is that they are relatively well-tolerated except in cases of hypersensitivity. Disadvantages are the risk of hypersensitivity and their relatively short half-life and short duration of action, requiring more frequent dosing [100].

Prototype: Penicillin G

Classification grouping: Antibacterial, cell wall inhibitor, natural substance.

Availability: Variety of compounds with slightly different pharmacokinetics.

Penicillin G – cell wall inhibitor	
Forms and indications for use	
Penicillin G Potassium/Sodium Treatment of anthrax; actinomycosis (abdominal, cervicofacial, or thoracic disease); botulism, gas gangrene, and tetanus; diphtheria; disseminated gonococcal infections (arthritis, endocarditis); empyema, endocarditis, meningitis, pericarditis, pneumonia, and septicemia caused by *streptococcus pyogenes*; group C, H, G, L, and M *streptococcus*; *streptococcus pneumoniae*; and non–penicillinase-producing strains of *staphylococcus aureus*; erysipelothrix endocarditis; fusospirochetosis (severe infections of the genital area, lower respiratory tract, and oropharynx [Vincent]); Haverhill or rat-bite fever; listeria infections, including endocarditis and meningitis; meningococcal meningitis and/or septicemia; *pasteurella* infections, including bacteremia and meningitis; and syphilis (congenital and neurosyphilis) [74].	
Penicillin G Procaine Treatment of moderately severe infections caused by penicillin G–sensitive micro-organisms that are sensitive to low and persistent serum levels achieved with this dose/form, including anthrax; diphtheria; erysipeloid; fusospirochetosis; group A streptococcal endocarditis; pneumococcal infections; rat-bite fever; skin and soft tissue infections; streptococcal infections without bacteremia; syphilis; yaws; bejel; and pinta [74].	
Penicillin G Benzathine Mild to moderate upper respiratory tract infections, venereal diseases (e.g., bejel, pinta, syphilis, yaws), and prophylaxis of rheumatic fever or chorea caused by penicillin G–sensitive micro-organisms that are susceptible to the low and very prolonged serum levels common to this dose form [74].	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness (such as *http://www.globalrph.com/penicillins.htm*) – dosages vary according to site of infection and type of organism. Penicillin (various formulations) dosing guidelines [74].	
Pharmacokinetics	
Route	IM or IV only for penicillin G forms. Oral for penicillin V.
Absorption	Peak concentrations are attained immediately after IV infusion is complete. Rapid absorption of aqueous penicillin G from IM and SC. Penicillin G benzathine is released slowly from IM injection sites.
Distribution	• Widely distributed but only low concentrations cross the blood–brain barrier in patients with non-inflammed meninges. • Crosses placenta. • Secreted in breast milk. • Binds to plasma proteins (60%).
Metabolism	Nonrenal clearance includes hepatic metabolism.
Primary Excretion	Kidney.
Adverse effects Penicillins are generally well tolerated; some urticaria or skin reactions may occur. Primary adverse effect is a severe hypersensitivity reaction resulting in anaphylaxis, typically minutes after administrations. Other adverse effects include nausea, vomiting, blood dyscrasias, and rare cardiac effects.	
Contraindications/precautions Penicillins are contraindicated in patients allergic to penicillins.	
Drug interactions Penicillins may decrease effectiveness of oral contraceptives. The bacteriostatic action of tetracyclines, macrolide antibiotics, and sulfonamides may inhibit bactericidal action of penicillin. Penicillins can increase the bleeding time and risk of bleeding with anticoagulants such as warfarin and heparin. Penicillin G may decrease the effectiveness of live vaccines.	
Pregnancy – Category B.	**Overdose** – Symptomatic management.
Special populations – There is decreased excretion in patients with hepatic or renal impairment.	

Summary of use of penicillin during lactation

Penicillin is acceptable to use during breastfeeding when the breastfeeding infant is not hypersensitive to penicillin [74].

Group 2 – Broad-spectrum penicillins (aminopenicillins)

Aminopenicillins are also broad-spectrum medications that are active against many of the same organisms as both the natural penicillins but have the advantage of increased efficacy against gram-negative bacteria. Therefore, aminopenicillins are extremely useful for treating gram-negative urinary and gastrointestinal (GI) pathogens, including Escherichia coli, Proteus mirabilis, Salmonella species, and Shigella species.

Aminopenicillins are also active against the many common gram-negative respiratory pathogens including haemophilus influenza. Some strains of the gram-negative organisms have developed resistance to aminopenicillins, hence the need for culture and sensitivity testing because of the ongoing development of more and more resistant strains [74].

Amoxicillin is a penicillin with sufficient ability to treat bacteria involved in otitis media, sinusitis, and community-acquired pneumonia [74]. It is the treatment of choice for children with otitis media [69].

Prototype: Ampicillin

Classification grouping: Antibacterial, cell wall inhibitor.

Availability: Capsule, oral suspension, powder for injection.

Aminopenicillins – cell wall inhibitor [102]	
Forms and indications for use	
Ampicillin Capsules: 250 and 500 mg. Powder oral suspension: 125 and 250 mg/5 mL. Powder for injection: 250 mg, 500 mg, 1 g, and 2 g. Infections with - E. coli, proteus mirabilis, neisseria gonorrhoeae, H. influenzae, salmonella, shigella, bordetella pertussis.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism.	
Pharmacokinetics	
Route	Oral, IM or IV.
Absorption	Well absorbed from GI tract when taken on an empty stomach; food affects absorption.
Distribution	• Widely distributed, crosses the blood–brain barrier only when meninges are inflammed. • Secreted in breast milk. • Binds to plasma proteins (20%).
Metabolism	Largely unmetabolized.
Primary excretion	Kidney.
Adverse effects Hypersensitivity, dizziness, fatigue, rash, diarrhea, blood dyscrasias, hypersensitivity.	
Contraindications/precautions Ampicillin is contraindicated in patients allergic to penicillins. Use with caution in renal disease.	
Drug interactions Ampicillin may decrease the effectiveness of oral contraceptives. Tetracyclines may inhibit the bactericidal effects of ampicillin. Food decreases absorption.	
Pregnancy – Category B.	**Overdose** – Symptomatic management.
Special populations – Ampicillin results in decreased excretion in patients with renal impairment.	

Group 3 – Cephalosporins

Cephalosporins are similar to penicillins in terms of mechanism of action, chemical structure, and toxicities. There are currently four distinct generations of cephalosporins with each generation having distinct therapeutic effect against either gram-positive or gram-negative bacteria. In general, as the designation increases from first to fourth generation, there is increased activity against gram-negative organisms and anaerobes, less activity against gram-positive organisms, and increased ability to withstand destruction [103].

Cephalosporins are bactericidal. They are most effective against rapidly growing organisms that are forming cell walls [104].

Cephalosporins that have oral formulations are well absorbed from the GI tract. Absorption may be delayed by food ingestion however; the ultimate amount of the drug that is absorbed is not affected. All cephalosporins are widely distributed to most body tissues and fluids; however, the ability to cross the blood–brain barrier differs by the generation of cephalosporin [103].

"The pharmacokinetic properties of the cephalosporins change during pregnancy, tending toward shorter half-lives, lower serum concentrations, and larger volumes distributed in the body and the increased clearance of the drug" [103]. In very young infants, these drugs may accumulate because of the underdevelopment of the kidneys resulting in extended half-lives. This will require modifications in dosage [103].

Like the penicillins, cephalosporins may produce allergic reactions in a small percentage of patients, therefore be aware that cross-sensitivities with any of the penicillins is a risk to be considered. Monitoring for therapeutic and adverse responses to antimicrobials requires clinical, microbiological, and laboratory data. Because the cephalosporins have a broad spectrum, signs and symptoms of pseudomembranous colitis associated with C. difficile, as well as other superinfections, must be recognized. Diarrhea is common with some cephalosporins and must be distinguished from pseudomembranous colitis [103].

Evidence-based practice alert! Obtain a stool sample to culture for C. difficile is indicated if the patient complains of more than three watery stools per day, or if there is blood in the patient's stool [103].

Although hemolytic anemia is rare with the cephalosporins, patients who develop signs of anemia within two to three weeks of cephalosporin initiation should have an assessment to determine if the cephalosporin is involved in the development of anemia. During extended or intense therapy, prudent practice dictates implementing periodic blood urea nitrogen (BUN) studies and creatinine evaluations to assess renal functioning. If renal impairment is suspected, then the dosage of the cephalosporin should be decreased to prevent further

renal impairment. Many older patients require dosage adjustment because of age-related changes in renal function [103].

There are approximately 20 different cephalosporins, classified into five generations of cephalosporins. The forth-generation group has only one drug, cefepime. Cefepime is effective in treating infections with gram positive cocci, as well as Pseudomonas aeruginosa, ESBL-producing K. pneumonia and E. coli, and beta-lactamase producing Enterobacteriaceae. The first fifth-generation drug, Ceftaroline, is effective against MRSA [104].

Patients who are receiving protracted courses of parenteral cephalosporins that affect clotting always require baseline and periodic assessment of prothrombin time. Administration of vitamin K may be indicated in patients who have prolonged prothrombin times. Patients taking these agents should also be observed for disulfiram-like (Antabuse) reactions, including abdominal cramping, facial flushing, headache, hypotension, palpitations, shortness of breath, diaphoresis, tachycardia, and or vomiting if exposed to ethyl alcohol [103].

Nursing consideration: Oral cephalosporins should be taken with food or milk, if they cause stomach irritation. Some cephalosporins must be taken 2 hours before or 1 hour after antacids that contain magnesium or aluminum, because these agents may impair absorption [103].

Other signs and symptoms of adverse effects that patients may experience when taking cephalosporins and should be advised to report include vaginal itching or discharge, sore mouth or throat, white patches on mucous membranes of mouth, easy bruising or bleeding, altered urine output, yellow skin or eyes, or unusual lethargy commencing after the drug is started. Development of skin rash, aching joints, hives, or respiratory problems may presage an allergic response and should also be reported. It is especially important to advise patients that cephalosporins cause false positives on urine testing for glucose when certain tests are used [103].

Evidence-based practice alert! Glucose test results should be confirmed by a second form of testing.

Class: First generation cephalosporins [103]

This group is most effective against gram-positive bacteria including staphylococci and streptococci. They do not cross the blood–brain barrier however. The primary method of elimination for this group is via the renal system.

Oral agents:
- Cephalexin (Keflex).
- Cephradine (Velosef).
- Cefadroxil (Duricef).
- Cefazolin (Ancef).

Organisms covered:
- Gram-positive cocci.
- Some gram-negative bacteria (Escherichia coli, klebsiella, proteus).

Class: Second generation cephalosporins [103]

This generation demonstrates a broader spectrum of bactericidal action against gram-negative bacteria, and may be less effective than first generation cephalosporins against gram-positive cocci [104]. They do not effectively cross the blood–brain barrier, so they are not typically used for infections of the central nervous system.

Second generation cephalosporins:
- Cefprozil (Cefzil).
- Cefuroxime (Ceftin, Zinacef).
- Cefaclor (Ceclor).
- Cefoxitin.
- Cefotetan.

Organisms covered:
- Gram-positive cocci.
- Certain gram-negative bacteria.

Class: Third generation cephalosporins [103,104]

This generation of cephalosporins demonstrates an even broader range of gram-negative bacteria. They are the treatments of choice for many infections, including central nervous system infections because of their ability to cross the blood–brain barrier. Specifically, they are active against klebsiella, E. coli, proteus, and H. influenzae.

Third generation cephalosporins:
- Cefixime (Suprax).
- Cefpodoxime (Vantin).
- Cefotaxime (Claforan).
- Ceftizoxime (Cefizox).
- Ceftriaxone (Rocephin).
- Ceftazidime (Fortaz).

Organisms covered:
- H. influenzae.
- E. coli.
- Klebsiella pneumoniae.
- Proteus mirabilis.
- Poor coverage against gram-positive cocci.
- No pseudomonas activity (except ceftazidime).

Prototype: Cefazolin

Classification grouping: Antibacterial, cell wall inhibitor. **Availability:** Capsule, oral suspension, powder for injection.

Cephalosporins – cell wall inhibitors	
Forms and indications for use [105]	
Cefazolin Powder for injection or IV administration. Infections with – gram-positive organisms primarily and some gram-negative organisms including S. aureus and Streptococci. Not effective against MRSA.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Cephalosporin dosing guidelines - *http://www.globalrph.com/cephalosporins.htm.*	
Pharmacokinetics	
Route	IM or IV.
Absorption	Well absorbed via IM route.
Distribution	• Bile concentrations can be up to five times higher than serum levels. • Crosses placenta.
Metabolism	Not metabolized.
Primary excretion	Kidney.
Duration of action	Half-life 1.8 to 2 hours.
Adverse effects Rash, nausea/vomiting/diarrhea, hypersensitivity, CNS hyperactivity, cholestasis, blood dyscrasias, increased BUN/creatinine.	
Contraindications/precautions Cephalosporin is contraindicated in patients hypersensitive to cephalosporins. Use with caution in renal disease.	
Drug interactions Nephrotoxic when concurrently used with aminoglycosides; may increase anticoagulant effect of warfarin.	
Pregnancy – Category B.	**Overdose** – Symptomatic management.
Special populations – Cephalosporin has decreased excretion in patients who have hepatic or renal impairment.	

Carbapenems

Carbapenems are bactericidal and demonstrate a very broad spectrum of antimicrobial activity. The drawback to this group is that they must be administered parenterally [106].

Prototype: Imipenem-cilastatin

Classification grouping: Antibacterial, cell wall inhibitor. **Availability:** Powder for injection.

Very broad spectrum imipenem-cilastatin – cell wall inhibitor	
Forms and indications for use [106,107]	
Imipenem-cilastatin Powder for injection or IV. Infections with – H. influenzae, anaerobes, most enterobacteriaceae, methicillin-sensitive staphylococci and streptococci.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism.	
Pharmacokinetics	
Route	IM or IV.
Absorption	Not absorbed PO.
Distribution	Protein bound: Approximately 20% for imipenem and 40% for cilastatin.
Metabolism	Imipenem is metabolized in the kidney when administered alone, cilastatin prevents renal metabolism when administered together.
Primary excretion	Kidney.
Duration of action	Half-life approximately 60 minutes.
Adverse effects Adverse effects of imipenem-cilastatin include nausea, vomiting, diarrhea, rash, pain or inflammation at injection site, tachycardia, convulsions, seizures, increased urine protein and creatinine, altered blood cell counts, electrolyte imbalance, and increased liver enzymes.	
Contraindications/precautions Imipenem-cilastatin is contraindicated in patients allergic to any component of imipenem/cilastatin. Use with caution in renal disease and in patients with brain lesions, head trauma, or history of seizures.	
Drug interactions Concurrent use with cyclosporine, or ganciclovir may increase risk of seizures.	
Pregnancy – Category C.	**Overdose** – Symptomatic management of ataxia and seizures.
Special populations – Imipenem-cilistatin has decreased excretion in patients with renal impairment; monitor elderly, neonates and young children for diarrhea and fluid/electrolyte imbalance.	

Miscellaneous cell wall inhibitors

This group has only one primary drug in its category of action. Vancomycin, which is not a penicillin, is currently the drug of choice for serious MRSA infection, except for vancomycin-resistant strains. Use of vancomycin has increased because of the development of organisms resistant to other drugs. Unfortunately, its widespread use is leading to the development of strains of vancomycin-resistant Enterococcus (VRE), greatly reducing treatment options for some infections, especially nosocomial infections in hospitals and long-term–care facilities [108].

Absorption of vancomycin from the GI tract is poor. Because of poor absorption, oral forms of vancomycin are unlikely to cause systemic adverse effects. Significant drug interactions with vancomycin include medications that also have ototoxic or nephrotoxic effects such as the aminoglycosides. Due to this risk of interactions, concomitant administration should be avoided whenever possible [108, 109].

Vancomycin is ototoxic, with increased risk in patients with renal dysfunction or underlying hearing loss. It should be used with extreme caution in these population. In addition, too rapid infusion of vancomycin risks the patient developing "Red Man syndrome", a histamine-mediated reaction causing flushing and itching of the face, neck, and shoulders. Vancomycin should be infused over a period of greater than 60 minutes to avoid this reaction [108, 109].

Prototype: Vancomycin

Classification grouping: Antibacterial, cell wall inhibitor.

Availability: Capsule, oral suspension, powder for injection.

Miscellaneous cell wall inhibitors	
Forms and indications for use [108,109]	
Vancomycin Capsules, injectable solution, powder for injection. Infections with – Most gram-positive bacteria including Streptococcus and Staphylococcus, as well as many strains of enterococci.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Link to a vancomycin calculator: *http://www.globalrph.com/vanco_single2.htm.* *http://clincalc.com/Vancomycin/.*	
Pharmacokinetics	
Route	Slow IV infusion, PO.
Absorption	Poorly absorbed PO.
Distribution	• Oral form does not typically enter systemic circulation. • IV for widely distributed to pleural, pericardial, ascitic and synovial fluids, urine, peritoneal dialysis fluid, and atrial appendage tissue. • Binds to plasma proteins (55%).
Metabolism	No apparent metabolism.
Primary excretion	Kidney.
Duration of action	Half-life 4–6 hours.
Adverse effects Adverse effects of vancomycin include flushing, hypotension, rash, nausea/vomiting/diarrhea, fever, chills, central nervous system effects (headache, fatigue, dizziness, vertigo). Vancomycin may be ototoxic with high serum concentrations resulting in tinnitus or hearing loss, as well as nephrotoxicity with elevated serum troughs, and anaphylaxis.	
Contraindications/precautions Vancomycin is contraindicated in any patient with previous hypersensitivity to this drug. Monitor carefully for hearing loss and use with caution in renal disease.	
Drug interactions Vancomycin is nephrotoxic when concurrently used with aminoglycosides, amphotericin B, or cisplatin. When vancomycin is used concurrently with methotrexate, there is an elevated risk of methotrexate toxicity.	
Pregnancy – Category C.	**Overdose** – Symptomatic management of renal impairment and hearing loss.
Special populations – Vancomycin has decreased excretion in patients with renal impairment. Monitor auditory function. Monitor urine output, monitor diarrhea in neonates, infants, young children due to risk of electrolyte imbalances.	

TETRACYCLINES, MACROLIDES, AMINOGLYCOSIDES (INHIBIT PROTEIN SYNTHESIS)

In order to survive and reproduce quickly, bacteria exhibit an accelerated metabolic rate, resulting in the synthesis of large amounts of protein material. Hence the effectiveness of this group of antibiotics. Tetracyclines, macrolides, aminoglycosides, and other miscellaneous drugs exert their bacteriocidal or bacteriostatic effect by interfering with the process of protein synthesis. Bacteria may become resistant to a variety of antibiotics including these that interfere with protein synthesis [103].

Clinical tips on interpreting culture and sensitivity reports: *http://clincalc.com/blog/?s=tetracycline.*

Group 1 – Tetracyclines

These earlier antibiotics were introduced in 1948, and used extensively for a variety of bacterial infections. Tetracyclines can cause phototoxicity, so sunlight and tanning lights should be avoided. Patients should be instructed to wear sunscreen, hats, and protective clothing if it is necessary for them to be exposed to the sun for even a few minutes. This includes sun exposure while driving as well [103].

Nursing consideration: Although uncommon, dizziness, lightheadedness, difficulties with balance may occur – more typically with the newer tetracyclines. The patient should stop taking tetracycline immediately if he or she develops headache or blurred vision to minimize the risk of permanent sequalae [103].

Some patients may experience liver toxicity manifested by nausea, vomiting, dark, concentrated urine, abdominal pain, or yellowing of the skin or eyes. Hepatotoxicity is less common with oral forms than IV forms, but it may be advisable to periodically assess liver function in patients on long term doxycycline or minocycline. Although the relationship between tetracyclines and decreased oral contraceptive efficacy is controversial, women of childbearing age should use a backup barrier method of contraception during tetracycline therapy and until the next menses. Tetracyclines may cause pigment changes of the teeth, which can be permanent [103].

This group of medications exerts bacteriostatic action with many gram-positive and gram-negative organisms, including Rikettsiae, Chlamydia, Mycoplasma, and Helicobacter pylori. Some tetracyclines, such as doxycycline, also exhibit activity against certain parasites, such as Plasmodium falciparum, the causative agent of malaria. The absorption of tetracyclines can be decreased by administration with food. Other precautions for this group of medications are the risk of colitis cause by Clostridium difficile, manifested by diarrhea as a result

of destruction of beneficial gastrointestinal flora in the presence of tetracycline medications [103,110,111].

There are a number of patients for whom the tetracyclines should be prescribed cautiously, including patients with renal impairment, patients with hepatic impairment, pregnant women, lactating women, and children. Young children may have tooth enamel defects as a consequence of use; tetracyclines should be avoided in children under eight years of age. Women of childbearing years should use alternative forms of birth control while taking tetracyclines. Extreme caution should be used in the presence of kidney dysfunction. Even usual doses of tetracycline may lead to excessive accumulation of the drugs and possible hepatotoxicity, so lower doses are required in renal patients under these circumstances. "There are serious concerns related to hepatotoxicity for IV forms of tetracycline. This is not a major concern with oral administration[103]."

The main drug–drug and drug–food interactions associated with tetracyclines are with antacids, iron salts, and dairy products. Concurrent administration can result in the formation of poorly soluble chelated compounds, decreasing antibiotic activity. Separation of these products from the administration of tetracyclines by at least 2 hours is recommended [103].

As with other antibiotics, the most common adverse reactions are associated with the gastrointestinal tract. Anorexia, nausea, vomiting, and diarrhea are caused by direct irritation of the intestinal lining. This can be addressed by taking the drug with food (but note potential food interactions), by reducing the dose, or by discontinuing the drug. Esophageal ulcers have occasionally occurred; taking tetracyclines with a full glass of water and remaining upright after administration can decrease the risk of this condition. Dermatological adverse reactions, including severe sunburns, have been noted [103].

Prototype: Tetracycline

Classification grouping: Antibacterial, bacterial protein synthesis inhibitor.

Availability: Capsule, topical.

Bacterial protein synthesis inhibitor	
Forms and indications for use [110,111]	
Tetracycline Capsules, oral suspension. Infections with – Susceptible strains of gram-positive and gram-negative bacteria, chlamydiae, rikettsiae, mycoplasma, and H. pylori. Adjunctive treatment for acne vulgaris. Bacteriostatic.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Tetracycline medications dosing guidelines - *http://www.globalrph.com/tetracyclines.htm.*	
Pharmacokinetics	
Route	Orally, topical.
Absorption	Adequately but incompletely absorbed from the GI tract, 60 to 80 percent absorbed after oral administration.
Distribution	• Widely distributed but only small amounts cross blood–brain barrier. • Crosses placenta. • Secreted in breast milk. • Binds to plasma proteins (65%).
Metabolism	Concentrated by the liver in the bile.
Primary excretion	Urine and feces.
Adverse effects Administration of tetracycline can result in bacterial or fungal superinfections. Other adverse reactions include nausea, vomiting, diarrhea, tooth discoloration, photosensitivity, anaphylaxis, blood dyscrasias, and rash.	
Contraindications/precautions Tetracycline is contraindicated in patients who have had an allergic response to any drug in this class. Tetracycline is not for use during pregnancy or in children less than eight years of age. Use with caution in patients with liver or kidney disease.	
Drug interactions Tetracycline may decrease the effectiveness of oral contraceptives. Calcium and iron supplements reduce tetracycline absorption. Dairy products reduce tetracycline absorption. Tetracycline may increase the anti-coagulant effect of anticoagulants.	
Pregnancy – Category D.	**Overdose** – Symptomatic management.
Special populations – Tetracycline results in decreased excretion in patients with hepatic or renal impairment; monitor urine output.	

Group 2 – Macrolides

The prototype drug in this group is erythromycin. Macrolides are active against some aerobic and anaerobic gram-positive organisms, including Corynebacterium. Atypical and intracellular organisms are also susceptible, including Mycoplasma, Legionella, Chlamydia and certain strains of Mycobacterium. The gram-negative spectrum of the oral macrolides includes Bordatella pertussis, T pallidum, and Campylobacter species. Macrolides are drugs of choice only for primarily the treatment of group A streptococcal and pneumococcal infections due to increased prevalence of resistance to penicillins, although some macrolide resistance is developing [112,113].

Macrolides are an excellent choice of medications for patients who are allergic to penicillin. Macrolides are primarily bacteriostatic [112].

Erythromycin is preferred in pregnancy, infants and children because of greater clinical experience [103].

Macrolides distribute readily to most body fluids. When the patient's meningeal tissues are inflamed, this class of antibiotic will enter the CSF [112].

As with the other antibiotics in this class, macrolides inhibit protein synthesis in the bacterium. Erythromycin destroys a similar range of micro-organisms as penicillin does and is can be used if a patient has a penicillin allergy or for a patient with whooping cough (Bordetella pertussis). Azithromycin is particularly useful in adults who have contracted community-acquired pneumonia. Macrolides are also useful in the treatment of community-acquired pneumonia (CAP) [103].

All macrolides can be given orally and they spread throughout most body fluids. Erythromycin is the prototypical drug in this group; however, azithromycin and clarithromycin have both become widely prescribed. Erythromycin inhibits an enzyme (CYP450 3A4) that is involved in the metabolism of numerous other drugs, resulting in inhibited metabolism of drugs metabolized by this enzyme. Hence, erythromycin has many drug interactions and must be used very cautiously in the presence of liver disease. Erythromycin may aggravate the weakness of patients who have myasthenia gravis and should be avoided [103,112].

The most common adverse reactions to erythromycin are dose-related gastrointestinal symptoms, including nausea, vomiting, abdominal pain, cramping, and diarrhea, as well as headache and the risk of pseudomembranous colitis [103,112,113].

Prototype: Erythromycin

Erythromycin is heavily metabolized by CYP450 3A4, which explains many of its drug interactions and its cautious use in the presence of hepatic impairment. When erythromycin is given concurrently with other medications metabolized by this enzymatic system, medications that include cyclosporine, valproic acid, and theophylline are excreted more slowly, and serum levels of the co-administered drug may increase, running the risk of toxic levels of exposure [103, 112, 113].

Erythromycin has been used extensively in infants and children; however, children who are being treated with Orap (pimozide) must avoid all exposures to erythromycin. Erythromycin is a very strong inhibitor of CYP450 enzymes, particularly CYP450 3A4. Drug–drug interactions with common drugs, including warfarin, theophylline, carbamazepine, selected benzodiazepines, and digoxin, occur. Combination of erythromycin with pimozide can result in serious dysrhythmias, because the inhibited metabolism of pimozide causes prolonged a QT complex interval of the cardiac cycle, potentially resulting in fatal cardiac dysrhythmias [113].

Other concerns about the use of erythromycin include the ability to antagonize the antibacterial effects of certain other antibacterial agents such as clindamycin, because both target the same area in the bacteria. This can result in erythromycin decreasing the effect of clindamycin; concurrent use of these two antibiotics is not recommended [113].

The most significant toxicity that may occur with erythromycin is via damage to the liver. Patients experiencing this dangerous drug toxicity may develop severe abdominal pain, enlargement of the liver, fever, and jaundice. Therapy with erythromycin should be discontinued immediately if these symptoms occur [113].

Classification grouping: Antibacterial, bacterial protein synthesis inhibitor.

Availability: Tablets, oral suspension, liquid, topical, IV.

<table>
<tr><th colspan="2">Bacterial protein synthesis inhibitor</th></tr>
<tr><td colspan="2">Forms and indications for use [112, 113]</td></tr>
<tr><td colspan="2">Erythromycin
Tablets, oral suspension, liquid, topical, injection.
Infections with –Effective against susceptible gram-positive and gram-negative bacteria including bordetella pertussis, leigonella pneumophila, M. pneumonia, and corynebacterium diptheriae.</td></tr>
<tr><td colspan="2">DOSAGES
Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Macrolides dosing guide - http://www.globalrph.com/macrolides.htm.</td></tr>
<tr><td colspan="2">Pharmacokinetics</td></tr>
<tr><td>Route</td><td>Orally, topical, IV.</td></tr>
<tr><td>Absorption</td><td>Orally, readily absorbed.</td></tr>
<tr><td>Distribution</td><td>• Widely distributed, but only small amounts cross blood–brain barrier.
• Secreted in breast milk.</td></tr>
<tr><td>Metabolism</td><td>Liver.</td></tr>
<tr><td>Primary excretion</td><td>Bile.</td></tr>
<tr><td>Duration of action</td><td>Half-life 1.5–2 hours.</td></tr>
<tr><td colspan="2">Adverse effects
Adverse effects of macrolides include nausea, vomiting, abdominal cramping, and possible anaphylaxis. Other adverse effects include hearing loss, tinnitis, and dizziness at high does.</td></tr>
<tr><td colspan="2">Contraindications/precautions
Macrolides are contraindicated in the presence of any allergic response any macrolide class drugs. Also contraindicated with coadministration of cisapride or pimozide, and fungal disease of the eye. Use with caution in patients with liver or kidney disease.</td></tr>
<tr><td colspan="2">Drug interactions
Macrolides may interfere with any drug metabolized by CYP450 3A enzymes. Grapefruit juice may increase bioavailability.</td></tr>
<tr><td>Pregnancy – Category B.</td><td>Overdose – Symptomatic management.</td></tr>
<tr><td colspan="2">Special populations –Macrolides decrease excretion in patients with hepatic or renal impairment monitor ethnic groups due to use of the P450 system. Monitor hearing.</td></tr>
</table>

Group 3 – Aminoglycosides

This group of antibiotics includes gentamycin, streptomycin, tobramycin, and neomycin and acts by inhibiting bacterial protein synthesis. Aminoglycosides are useful against most gram-negative aerobic and facultative anaerobic bacilli. However, these drugs are only bacteriocidal in a concentration-dependent manner. These medications are typically reserved to treat serious systemic infections caused by gram-negative organisms [114].

As with other groups, the resistance of micro-organisms to these drugs is increasing all the time. One of the most common drugs in this group is gentamicin. This is given by either the IV or IM route, as it is not absorbed by the gastrointestinal system. The drug has a fairly rapid half-life of 2 hours, necessitating the dose being given multiple times daily. The main problem with this drug is its serious toxic effects. It can have a devastating effect on the apparatus in the inner ear (ototoxicity). This means that the patient may suffer damage to either their hearing or their ability to balance. The second major side effect is damage to the kidney tubules (nephrotoxicity). This may be reversed if the drug is stopped. Due to these major problems, it is important that gentamicin be kept within a therapeutic range in the plasma through careful serum monitoring [114,115].

Prototype: Gentamicin

Classification grouping: Antibacterial, bacterial protein synthesis inhibitor.

Availability: Solution, topical.

<table>
<tr><th colspan="2">Bacterial protein synthesis inhibitor</th></tr>
<tr><td colspan="2">Forms and indications for use [114,115]</td></tr>
<tr><td colspan="2">Gentamicin
Solution for IM or IV, ophthalmic, otic, topicals.
Infections with – aerobic, gram-negative bacteria.</td></tr>
<tr><td colspan="2">BLACK BOX WARNING
Neurotoxicity/ototoxicity - “Increased risk with renal impairment, high dose, prolonged treatment; ototoxicity usually irreversible; other neurotoxic symptoms may include vertigo, numbness, tingling, muscle twitching, seizures; monitor renal function, peak/trough levels; audiograms in high risk patients; D/C treatment or decrease dosage if ototoxicity; avoid concurrent and/or sequential neurotoxic agents; avoid concurrent potent diuretics; other risk factors include advanced age or dehydration.

Nephrotoxicity - Increased risk with renal impairment, high dose, prolonged treatment; monitor renal function, peak/trough levels; D/C treatment or decrease dose if nephrotoxicity; avoid concurrent and/or sequential nephrotoxic agents; avoid concurrent potent diuretics; other risk factors include advanced age or dehydration.

Neuromuscular blockade - Neuromuscular blockade including respiratory paralysis possible with any route of administration; risk factors: concurrent anesthesia, neuromuscular blockers, or large citrate-anticoagulants blood transfusions[76].”</td></tr>
<tr><td colspan="2">DOSAGES
Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism.
Aminoglycoside dosage calculator - http://clincalc.com/Aminoglycoside/.
Aminoglycoside printable dosing nomograms - http://clincalc.com/Aminoglycoside/ExtendedIntervalNomograms.aspx.
Aminoglycoside dosing at a glance - http://www.globalrph.com/aminoglycoside_list.htm.</td></tr>
<tr><td colspan="2">Pharmacokinetics</td></tr>
<tr><td>Route</td><td>IM, IV, topical.</td></tr>
<tr><td>Absorption</td><td>Not absorbed orally.</td></tr>
<tr><td>Distribution</td><td>• Widely distributed but only small amounts cross blood–brain barrier.
• Concentrates in kidney and inner ear.
• Small amounts ecreted in breast milk.</td></tr>
<tr><td>Metabolism</td><td>Not metabolized.</td></tr>
<tr><td>Primary excretion</td><td>Kidney.</td></tr>
<tr><td>Duration of action</td><td>Half-life 2 hours.</td></tr>
<tr><td colspan="2">Adverse effects
Adverse effects include rash, nausea, vomiting, fatigue, blood dyscrasias, hypertension, hypotension, confusion, convulsions, dizziness, headache, alopecia, itching, joint pain, injection site pain/irritation, respiratory depression, allergic reactions. See section on BLACK BOX WARNING.</td></tr>
<tr><td colspan="2">Contraindications/precautions
Aminoglycosides are contraindicated in patients who have hypersensitivity to aminoglycosides. Avoid concurrent use with other neurotoxic or nephrotoxic drugs. Avoid use in patients with pre-existing kidney disease.</td></tr>
<tr><td colspan="2">Drug interactions
Increased risk of nephrotoxicity with other nephrotoxic drugs. Increased risk of neurotoxicity with other neurotoxic drugs. Increased risk of toxicity when administered with diuretics. Can increase the neuromuscular blocking effects of pancuronium, vecuronium, succinylcholine. NSAIDs can increase gentamicin levels, increasing risk of toxicity.</td></tr>
<tr><td>Pregnancy – Category D.</td><td>Overdose – Symptomatic management of serious kidney damage and ototoxicity.</td></tr>
<tr><td colspan="2">Special populations – In elderly patients, monitor drug levels and renal function frequently, due to ototoxic effects. Aminoglycosides may have decreased excretion in patients with hepatic or renal impairment; monitor renal function.</td></tr>
</table>

FLUOROQUINOLONES AND SULFONAMIDES

Fluoroquinolones and sulfonamides are increasingly important due to rapid resistance of bacteria to other treatment alternatives. This group is effective against both gram-positive and gram-negative bacteria. The therapeutic usefulness of this group of medications is increasing including in the potential for bioterrorism incidents as postexposure prophylaxis against the causative agent of anthrax [103].

Fluoroquinolones

The fluoroquinolones are powerful, synthetic, broad-spectrum antibiotics. They are a relatively newer class of antibiotics. The effect of food on absorption of fluoroquinolones is unknown, therefore the manufacturer of ciprofloxacin recommends taking it two hours after meals [103]. All drugs in this class are widely distributed throughout the body and demonstrate high levels in the prostate, lungs, and bile. These drugs are distributed widely to intracellular and extracellular fluids, and may be found in saliva, nasal and bronchial secretions, sputum, bile, lymph, and peritoneal fluid, making them particularly useful. They cross the blood–brain barrier poorly in the absence of inflammation; although, ciprofloxacin crosses this barrier in the presence of inflammation [103, 116].

Fluoroquinolones are excellent for effectiveness against organisms including E. coli, Enterobacter, Haemophilus species, M. catarrhalis, Legionella, Pseudomonas, and many others. Newer fluoroquinolones are effective against penicillin-resistant S. pneumoniae, whereas resistance has developed to the older fluoroquinolones. Older fluoroquinolones have little activity against anaerobic organisms, but are active against atypical organisms, including Chlamydia, Mycobacterium, and Mycoplasma species. Ciprofloxacin has full activity against P. aeruginosa [116].

The fluoroquinolones are divided into two groups; the older group is represented by ciprofloxacin and the newer group by levofloxacin. The newer group of fluoroquinolones is often referred to as the respiratory fluoroquinolones [103,116].

Fluoroquinolones are bactericidal and act by inhibiting bacterial DNA replication. In order for the bacteria to survive through replication, this information needs to be copied. To do this, enzymes are needed to uncoil parts of the super-coiled material and prepare it for replication, DNA gyrase and topoisomerase. Fluoroquinolones affects the ability of the bacteria to use topoisomerase [116].

Many scientists and clinicians are concerned that overuse of these agents has already eroded the utility of this group of drugs. Staphylococcus, Streptococcus, and Enterococcus species that were once susceptible to the fluoroquinolones have now developed resistance. To prevent increased development of resistance to this group of drugs, fluoroquinolones should not be used for infections for which other inexpensive, safe, and narrower-spectrum drugs are still effective. Rather, fluoroquinolones should be reserved for use when the alternative is costlier and more hazardous. All drugs in this class are well absorbed after oral administration [103, 116].

The most common antibiotic in this group is called ciprofloxacin, which is a broad spectrum antibiotic. Ciprofloxacin is useful as it is effective against micro-organisms that have become resistant to penicillins, cephalosporins, and aminoglycosides. This drug can be given orally and is well absorbed. Ciprofloxacin enters many tissues and particularly concentrates in the kidneys, prostate gland, and lungs, making it ideal for fighting infection in these areas of the body [103,116].

Renal impairment in a patient can result in increased half-lives, increasing the risk of side effects. This is especially of concern with older adults, who are likely to have some degree of reduced renal function. Virtually all of the fluoroquinolones require some degree of dosage adjustment for those patients with significant renal impairment [117].

As with tetracyclines, the rate of absorption of fluoroquinolones is diminished by metals (e.g., aluminum and magnesium); so, they should not be administered concurrently in a patient who is taking antacids that contain these elements [103,117].

If tenderness or inflammation occurs in any tendon, the patient should immediately discontinue the fluoroquinolone(s) medication(s) and notify the prescriber, rest whenever possible, and refrain from exercise of the affected joint. All of the fluoroquinolones have a black box warning regarding the risk of tendon rupture and tendonitis even after extensive use. The risk is increased in older patients; in patients taking corticosteroids; and patients with heart, kidney, or lung transplant. Seizures, increased intracranial pressure, and toxic psychoses have occurred with this class particularly in the elderly. Central nervous system excitement, including tremors, restlessness, sleeplessness, dizziness, lightheadedness, bad dreams, confusion, and hallucinations may occur. Diabetics should immediately report any signs or symptoms of hypoglycemia and should perform home blood glucose testing regularly. The drug should be discontinued at any signs of an allergic reaction, including hives, itching, yawning, or shortness of breath, because serious anaphylactic reactions have occurred during first exposure to a fluoroquinolones [103, 117].

Nursing consideration: All patients receiving treatment with fluoroquinolones should avoid direct sunlight, sun lamps, and tanning beds from the first dose until several days after therapy is completed. If sun exposure is unavoidable, counsel the patient about the proper use of sun blocking agents. Patients should withhold the drug and contact their healthcare provider about any blister, rash, or itching that occurs. Fluoroquinolones often cause dizziness or lightheadedness, so driving and hazardous activities should be avoided until a patient's reaction is known [103].

Prototype: Ciprofloxacin

Ciprofloxacin is the most effective of this class of agents against Pseudomonas aeruginosa, a gram-negative bacteria causing serious infections of the urinary tract system and other systems[116].

BP alert! Although an off-labeled use, ciprofloxacin as a single dose is recognized as an effective agent for eradicating the carriers of meningococcal species. Ciprofloxacin is also a first-line treatment of typhoid fever [103].

Diabetics should avoid fluoroquinolones if other equally effective antimicrobial drugs are available due to the risk of hypoglycemia. The patient with a prolonged QT complex interval or taking medications that increase the QT complex interval should be prescribed fluoroquinolones with caution, due to the risk of QT interval prolongation. Unless there are compelling reasons, fluoroquinolones should not be used by children and pregnant women. Most patients with impairments of the renal system should be prescribed lower dosages [103].

Other special populations may benefit from alternate antibacterial drug choices, including patients with severe cerebral arteriosclerosis or who are otherwise seizure prone (e.g., epilepsy, alcohol abuse, theophylline, or antipsychotic drug use). Patients taking theophylline and cyclosporine should have determinations of the plasma concentrations or blood levels of these agents, because they are extensively metabolized by CYP3A4, a hepatic drug-metabolizing enzyme that is moderately inhibited by ciprofloxacin [103].

Classification grouping: Antibacterial, bacterial DNA inhibitor.
Availability: Capsules, solution (IV, ophthalmic and otic).

Bacterial DNA inhibitor	
Forms and indications for use [116,117]	
Ciprofloxacin Capsules, IV solution, ophthalmic and otic solutions. Infections with –gram-negative bacteria including enterobacter, E. coli, haemophilus, moraxella catarrhalis, mycoplasma, legionella, pseudomonas aeruginosa, mycobacteria, and B anthracis spores.	
BLACK BOX WARNING **Tendinitis and tendon rupture** "Fluoroquinolones, including ciprofloxacin, are associated with an increased risk of tendinitis and tendon rupture in all ages. This risk is further increased in older patients usually over 60 years of age, in patients taking corticosteroid drugs, and in patients with kidney, heart, or lung transplants. **Muscle weakness avoid in myasthenia gravis** Fluoroquinolones, including ciprofloxacin, may exacerbate muscle weakness in persons with myasthenia gravis. Avoid Ciprofloxacin in patients with known history of myasthenia gravis[77]."	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Fluroquinolones dosing guidelines - *http://www.globalrph.com/fluoroquinolones.htm.*	
Pharmacokinetics	
Route	Oral, IV, ophthalmic and otic drops.
Absorption	70–80% absorbed.
Distribution	• Widely distributed but only small amounts cross blood–brain barrier. • Secreted in breast milk. • 20–40% protein bound.
Metabolism	Four metabolites, less active than the parent compound, have been identified that account for approximately 15 percent of the oral dose, three metabolites are associated with IV administration, accounting for 10 percent of the IV dose.
Primary excretion	Urine and feces.
Onset of action	Rapid.
Duration of action	4 hours (oral), 5 to 6 hours (IV).
Adverse effects Adverse effects include cardiovascular effects such as arrhythmia, QT prolongation, and tachycardia, rash, nausea, vomiting, diarrhea, dyspepsia, blood dyscrasias, increased liver enzymes, allergic reactions, phototoxicity, CNS symptoms of headache, insomnia, dizziness, tremor, mental status changes, seizures, and toxic psychosis, tendonitis or tendon rupture, and worsening of myasthenia gravis.	
Contraindications/precautions Fluoroquinolones are contraindicated in patients taking tizanidine and those who are hypersensitive to fluoroquinolones.	
Drug interactions Fluoroquinolones may increase the anticoagulant effect of warfarin. Ingestion of caffeine with ciprofloxacin can decrease caffeine clearance and lead to nervousness, anxiety, or tachycardia. Calcium-fortified products, iron, antacids, and mineral supplements may reduce the absorption of this antibiotic. Anti-arrhythmic agents should be avoided to reduce the risk of life-threatening arrhythmias. Blood levels of agents that are metabolized by CYP450 1A2 can increase when administered with ciprofloxacin, due to ciprofloxacin's inhibition of this enzyme, increasing the risk of toxicity of the co-administered agent.	
Pregnancy – Category C.	**Overdose** – Symptomatic management.
Special populations – Monitor for any tendon pain. Monitor renal and hepatic function with long term use.	

Sulfonamides

The sulfonamides were once major anti-infective medications, but the development of resistant strains of bacteria and the significant incidence of allergic reactions to sulfa drugs has resulted in this group of medications being reserved for treatment of urinary tract infections, alternative therapy options for drug-resistant organisms, and treatment of specific infections in immunocompromised hosts [103].

Nursing consideration: The goal of treatment of UTIs is the eradication of the organism, providing symptom relief (within approximately 48 hours of treatment), and preventing reoccurrence.

Infection can occur in any portion of the urinary tract, in children, adults, men, and women. However, women have a higher risk of UTIs because of anatomical differences. Infections that traverse from the lower urinary tract to the bladder or kidneys can be especially problematic. Bacteria ascending to the kidneys may cause pyelonephritis, a potentially dangerous condition. Patients with pyelonephritis often present with nausea, chills, severe flank tenderness, etc. Urinalysis typically will identify the pathogen or bacteria producing the infection. Sulfonamides and trimethoprim both have unique pharmacodynamic properties that are enhanced when combined [103].

UTIs are typically categorized as uncomplicated or complicated. Uncomplicated UTIs typically respond to either ciprofloxacin or trimethoprim-sulfamethoxazole. Complicated UTIs, however, often require more aggressive treatment and typically these complicated cases manifest in patients with other comorbidities. Sulfonamides are to be used cautiously for patients with even mild kidney dysfunction, and if used, the patient needs to be advised to increase fluid intake to prevent crystal or stone formation [103].

Sulfa drugs are effective against both gram-positive and gram-negative bacteria. The mode of action is by suppressing the synthesis of folic acid, necessary for bacterial growth. Bacteria make their own folic acid (unlike humans that require ingestion of foods or vitamins); therefore, interference with folic acid production is an effective mechanism to combat infectious pathogens.

This group of medications is bacteriostatic rather than bactericidal. Sulfonamides and trimethoprim both have distinctive synergistic effects when combined hence the prototype below [103].

Sulfonamides are effective against the susceptible organisms including E. coli, S. pyogenes, S. pneumoniae, H. influenzae, Nocardia, N gonorrhoeae, and some protozoa (Pneumocystis jiroveci and toxoplasmosis) [103].

Oral sulfonamides are absorbed readily from the gastrointestinal tract. They are distributed widely throughout the body, found in all body tissues, cross the blood–brain barrier and placenta, and enter breast milk. As with most antibiotics, common adverse reactions for sulfonamides are in the gastrointestinal tract, such as anorexia, nausea, vomiting, diarrhea, and abdominal pain. Advise patients of the risk of photosensitivity and precautions they should take [103].

"The increasing frequency of resistant organisms limits the use of these drugs in chronic and recurrent UTI [103]." Mutations cause organisms to develop resistance and cross-resistance between sulfonamides is common [103].

Trimethoprim (found in the combination therapy described below) is active against both gram-positive and gram-negative organisms. Gram-positive organisms include S. pneumoniae, and Staphylococci. The spectrum of gram-negative organisms includes Enterobacter, E. coli, K. pneumoniae, P. mirabilis, Salmonella, and Shigella. The protozoa P. carinii is also susceptible to this drug [103].

"Oral sulfonamides are absorbed readily from the gastrointestinal tract. They are distributed widely throughout the body and found in all body tissues. They readily enter the cerebrospinal fluid, pleura, the synovial fluids, and the eye. They cross the placenta, enter breast milk, and are bound to plasma proteins in varying degrees [103]". Trimethoprim is also well absorbed following oral administration. Distribution of trimethoprim into breast milk occurs with high concentrations. Although typically considered safe for infants over two months of age, premature infants and infants with hyperbilirubinemia or G6PD deficiency should not be breastfed while the mother is taking the drugs.

Trimethoprim concentrates in breast milk and, because it may interfere with folic acid metabolism, it should be used cautiously for nursing women. Trimethoprim is placed in Pregnancy Category C. "It crosses the placenta, producing similar levels in fetal and maternal plasma. Teratogenicity has occurred in animal studies. Because it may interfere with folic acid metabolism, trimethoprim should be used only when its benefits clearly outweigh fetal risks [103]."

Liver metabolism of trimethoprim is minimal with more than "80% of the drug excreted unchanged in the urine. Because it is so trimethoprim is so dependent on the kidney for excretion, elimination is delayed, and its half-life is increased in patients with renal impairment [103]", so it must be used with caution.

There are a number of patients in whom the sulfonamides and trimethoprim should be used with caution including patients with glucose-6-phosphate dehydrogenase (G6PD) deficiency, renal impairment, and folate deficiency. "Sulfonamides should be used with caution in patients who have blood dyscrasias and G6PD deficiency. Serious adverse reactions secondary to direct toxic effects on the bone marrow have sometimes resulted in death. They include agranulocytosis, aplastic anemia, and other blood dyscrasias. Acute hemolytic anemia resulting in increased destruction of red blood cells has resulted, usually with G6PD deficiency. Sore throat, fever, pallor, purpura, or jaundice may be early indications of these serious blood disorders. These problems occur only rarely with trimethoprim and only in conjunction with G6PD deficiency [103]."

"If a patient is on long-term therapy of trimethoprim or a sulfonamide, periodic assessment of the complete blood cell (CBC) count, hepatic function, and renal function should be conducted [103]." "There should also be periodic evaluation of pulmonary function for signs of fibrosis, physical examination for indications of peripheral neuropathy, and urine cultures because superinfections with Pseudomonas or Candida sometimes occur with chronic therapy [103]."

Any patient on these medications "who develops a cough, dyspnea, chest pain, or fever should receive a chest x-ray, sedimentation rate, and CBC to detect the signs of hypersensitivity and pulmonary fibrosis. Patients on long-term sulfonamide therapy should also have periodic urinalysis to check for crystalluria or urinary calculi formation. Patients with AIDS (acquired immune deficiency syndrome) are especially prone to adverse effects of sulfonamides [103]."

Prototype: Trimethoprim-Sulfamethoxazole (Bactrim)

Classification grouping: Antibacterial, folic acid inhibitor. **Availability:** Capsules, IV solution, oral solution.

Bacterial folic acid inhibitor	
Forms and indications for use [103,118,119]	
Trimethoprim-Sulfamethoxazole (Bactrim) Tablets, IV solution, oral suspension. Infections with – E. coli, S. pyogenes, S. pneumoniae, H. influenzae, nocardia, N gonorrhoeae, and some protozoa (Pneumocystis jiroveci and toxoplasmosis).	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism.	
Pharmacokinetics	
Route	Oral, IV.
Absorption	Readily absorbed.
Distribution	• Widely distributed and crosses blood–brain barrier. • Crosses the placenta. • Secreted in breast milk. • 70% protein bound.
Metabolism	Liver.
Primary excretion	Kidney.
Half life	8–10 hours (oral), 11-13 hours (IV).
Adverse effects Adverse effects include nausea, vomiting, rash, pruritus, peripheral neuropathy, pulmonary fibrosis, cough, hypoglycemia, hyperkalemia, hyponatremia, fever, anaphylaxis, epidermal necrolysis, blood dyscrasias, photosensitivity, increased BUN and serum creatinine, interstitial nephritis, and crystalluria.	
Contraindications/precautions Trimethoprim-sulfamethoxazole is contraindicated in patients who are hypersensitive to sulfites, sulfonamides, and thiazide diuretics. It is also contraindicated in patients with folate deficiencies, patients with severe renal impairment, severe liver impairment, and patients younger than two months of age.	
Drug interactions Trimethoprim-Sulfamethoxazole increases effect of oral anticoagulants. Avoid use with potassium-sparing diuretics such as spironolactone, ACE inhibitors, potassium supplements, and other medications that increase potassium, due to the risk of hyperkalemia. Trimethoprim-sulfamethoxazole can increase levels of digoxin, meglitinide, methotrexate, phenytoin, procainamide, dapsone, and pioglitazone. It can decrease the effects of cyclosporine, live vaccines, and tricyclic antidepressants. Phototoxicity can be augmented by tretinoin. Increased risk of hypoglycemia when combined with sulfonylureas.	
Pregnancy – Category C.	**Overdose** – Bone marrow depression may require concomitant use of leucovorin.
Special populations – Monitor patients for liver and renal laboratory function changes particularly in elderly patients. Do not breast-feed.	

ANTI-MYCOBACTERIAL AND ANTI-FUNGAL AGENTS

Anti-mycobacterial agents

Mycobacterial infections are difficult to cure because mycobacteria are relatively slow growing, therefore resistant to drugs that work on rapidly growing cells. The high concentration of lipids in the cell wall of mycobacteria are impermeable to many drugs; therefore many medications cannot penetrate them easily. Also this group of bacteria can become dormant and develop resistance easily [103].

A prime example is the mycobacterium responsible for tuberculosis infections. Throughout the centuries, tuberculosis or consumption has claimed untolled numbers of human lives. Because mycobacteria are so well protected by their fatty cell wall made up of many components including mycolic acid, treatment typically must occur for an extended period of time to allow the cell wall to be penetrated by a chemical agent. For tuberculosis, treatment typically occurs with a four drug regimen that is taken for the first two months, followed by three medications taken for four more months. Medications for tuberculosis are typically categorized as first-line and second-line drugs [120].

All of the anti-mycobacterial drugs have risks for hypersensitivity reactions, some of which may be severe. Peripheral neuropathy is the most common adverse reaction with isoniazid. The symptoms include symmetrical numbness and tingling in the extremities. Pyridoxine (Vitamin B6) prevents the development of peripheral neuropathy and is recommended for many patients taking isoniazid; some providers use pyridoxine for all patients taking this medication. Hepatotoxicity occurs in a significant percentage of patients taking isoniazid; therefore, careful monitoring of liver functions is required [121].

Group 1 – Anti-tuberculosis agent, anti-mycobacterial

Despite hopes that tuberculosis (TB) might be eradicated from the United States, in recent years, there has been an increase of TB in this country, and it is not uncommon to find patients with various stages of TB in your clinical practices. Patients initially acquire TB via the respiratory route [103].

EBP alert! This organism is especially dangerous because Mycobacterium tuberculosis may remain alive in respiratory droplets caused by sneezing, coughing, etc., for several hours, despite being outside of a human host [103].

"TB is usually caused by inhaling the Mycobacterium tuberculosis organism. This bacterium has a very tough envelope and can survive for long periods in dry conditions. This coating also protects the organism, making it resistant to destruction by the body's natural defenses. The bacterium can invade and survive within our phagocytic cells. The damage to the our tissues is due to the body's inflammatory response to the infection, rather that the result of any toxin released by the organism [95]."

Patients may present in a variety of stages of infection. The "initial infection of the lungs is called primary TB. The bacteria are engulfed by phagocytic cells in our lungs. These cells attempt to communicate with T lymphocytes, which attempt to resist the infection, but the increase in phagocytic cells at the site of infection is relatively ineffective. Instead, more and more of the phagocytic cells become infected by the bacteria and are carried into the lymphatic system where they eventually reach what is known as the hilar lymph nodes within the lungs. The body manages to wall off or encapsulate these infected phagocytes by creating pockets or tubercles. These are balls of infection with a necrotic (dead) center surrounded by infected phagocytic cells wrapped in a capsule of collagen (protein) fibers. These tubercles may then remain in the lungs but the patient suffers no further symptoms of the disease [95]." The tubercles are now however likely to trigger symptoms under certain conditions (often occurs when the patient discontinues treatment prematurely). If the individual's immune system becomes compromised, these tubercles becomes activated again from their state of dormancy. Reactivation of the disease may take place under a number of circumstances, for example poor nutrition, the age of the patient, and if the patient has a compromised immune system for the multiple reasons delineated earlier in this review [95].

This reactivation is secondary TB and it is at this point that "the lung tissue itself now becomes necrotic, creating large cavities. As with the tubercles, these cavities remain encapsulated by connective tissue and may lie dormant or become reactivated once again [95]."

"Isoniazid is the most active drug for the treatment of tuberculosis. It interferes with lipid and nucleic acid biosynthesis in growing organisms. It is also thought that isoniazid inhibits the synthesis of mycolic acids. These acids are important constituents [95]" for cell walls of mycobacteria but are not found in mammalian cells, which explains this high selectivity. This drug is bactericidal against susceptible mycobacteria [95].

Isoniazid readily diffuses into all body fluids including the cerebrospinal fluid, the pleural, and abdominal cavity fluids, the tissues, organs, as well as into saliva, sputum, and feces. It also crosses the placenta and enters breast milk [121].

The liver, in a process that is genetically controlled, primarily metabolizes isoniazid but there is great variability in metabolic rates among different populations. Due to genetic variability, individuals who are slow metabolizers will risk toxicity – this includes approximately 50% of all African Americans and Caucasians. Other populations including the additional 50% of African Americans, Caucasians, Alaskan natives, and Asians are rapid metabolizers of isoniazid. In patients who are rapid metabolizers of isoniazid, weekly dosing of the drug may result in sub-therapeutic levels and poor treatment response.

Isoniazid is excreted in the urine; 50 to 70 percent is excreted in 24 hours. Cautious use in renal impairment is recommended for isoniazid. Cautious use in the presence of hepatic impairment is also recommended for isoniazid [121].

EBP alert! Other concerns about special populations treated with isoniazid include the fact that patients who drink alcohol daily, use drugs of abuse, pregnant women or those immediately postpartum, patients with active chronic liver disease or significant renal impairment, and patients older than 35 years are at special risk for development of hepatitis while taking isoniazid [103].

Other considerations include knowing that hematologic alterations that may include a variety of anemias and thrombocytopenia have historically been recognized as a consequence of isoniazid treatment [103].

All of the anti-mycobacterial medications carry the risk of hypersensitivity in patients at varying dosages with peripheral neuropathy being the primary adverse reaction. Patients at greater risk to experience this adverse reaction include patients who are malnourished, pregnant, HIV positive, diabetics, or who have chronic liver disease, including alcoholics. This last population is of particular concern because of the higher incidence of tuberculosis among the homeless, substance abusing population [103,121].

Liver toxicity occurs in a significant number of patients taking isoniazid. The symptoms of liver toxicity are consistent with those associated with hepatitis illnesses and include abnormal LFTs, jaundice, and fatigue. Liver damage appears to be progressive, increasing with age. Concurrent use of ethyl alcohol and other liver toxic substances further increases the risk. Other adverse reactions associated with isoniazid include abnormal blood cell disorders, alterations in vitamin D metabolism and consequential hypocalcemia, and gynecomastia in male patients. This last adverse effect contributes to treatment inconsistencies and non-compliance among some patients [103,121].

Because of the relatively high proportion of adult patients with tuberculosis caused by organisms that are resistant to isoniazid, four drugs are necessary in the initial phase of therapy for the 6-month regimen to be maximally effective [120]. For the most up to date guidelines for multi-drug treatment of tuberculosis, please see the Centers for Disease Control and Prevention guidelines for treatment providers at *http://www.cdc.gov/tb/publications/guidelines/List_date.htm.*

Because of the long duration of necessary treatment and the complexity of the protocols in tuberculosis infections (both active and latent) patient teaching and ongoing support are necessary for treatment adherence. In particular, the use of multidrug therapy, which is critically important to diminish the risk of the development of resistance, can present very serious challenges in patient adherence to the protocols. Community support is available and a necessary component of the treatment regime beyond medication intervention [103].

Maintaining two- to four-drug protocol requires significant commitment on the part of the patient and any familial supports that may be available. Typically, outside, nonfamilial support is necessary, especially for populations who are considered high risk, including the homeless, impoverished, and immigrants. These populations typically have fewer contacts with health care providers resulting in lower rates of treatment compliance due to the length, expense, and complexities of treatment. A healthcare provider observing or giving the doses of the medication(s) has been demonstrated to be useful. However, this is practical in some weekly protocols, but impractical with daily dosing [103].

Other issues associated with treatment non-compliance with any of the chosen protocols are the adverse effects many patients experience. Gastrointestinal distress is quite common in the early stages of treatment; however, it is imperative that the patient continue the therapy. To support compliance, instruct patients to take all medications with food. Although this may delay absorption, the

effect of this delay does not ultimately affect the efficacy of the medication(s). Administration with food is preferable to dividing doses and changing the identified drug protocol. Other interventions may be taking the medications before sleep to diminish the patient's awareness of the gastrointestinal distress [122].

Prototype: Isoniazid

Classification grouping: Anti-tuberculosis agent, anti-mycobacterial.

Availability: Capsules.

Bacterial folic acid inhibitor	
Forms and indications for use [78,120,121]	
Isoniazid tablets Infections with – M. tuberculosis.	
BLACK BOX WARNING **Hepatotoxicity** "Severe hepatitis (including fatal) associated with INH treatment; most common in first three months but may occur at any time; monitor symptoms, interview patients every month; AST/ALT tests at baseline, then periodically if >35 years old; D/C treatment if LFTs >3-5x the upper limit of normal (ULN) or if signs/symptoms hepatic injury, use alternative TB treatment; if must restart wait until symptoms and LFTs resolve; restart at low dose, increase gradually, and immediately D/C if any s/symptoms recurrent hepatic injury; defer preventive treatment if acute hepatic disease; increased risk if daily alcohol use, chronic hepatic disease, and IV drug use; increase risk with age (highest risk 50-64 years old, risk decreased in patients >65 years old); possible increase risk in women, particularly black and Hispanic, and during post-partum period, consider more careful monitoring[78]."	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Anti-mycobacterial dosing guidelines - *http://www.globalrph.com/tuberculosis.htm*.	
Pharmacokinetics	
Route	PO, IM.
Absorption	Readily absorbed.
Distribution	• Diffuses readily into ascetic fluids, tissues, organs, saliva, sputum, and feces. • Crosses blood-brain barrier. • Crosses the placenta. • Secreted in breast milk.
Metabolism	Liver.
Primary excretion	50 to 70 percent excreted in urine in 24 hours.
Onset of action	Rapid.
Duration of action	Half-life 0.5 – 5 hours.
Adverse effects Rash, fever, paresthesia, convulsions, optic neuritis, dizziness, memory loss, psychosis, nausea, vomiting, epigastric distress, blood dyscrasias, hepatotoxicity, increased liver enzymes, bilirubinemia, jaundice, hepatitis, hyperglycemia, hypocalcemia, hypophosphatemia, gynecomastia, lupus-like syndrome, peripheral neuropathy. May cause vitamin B6 deficiency.	
Contraindications/precautions Previous allergy to this drug. Previous history of isoniazid-induced hepatic injury, drug fever, chills, or arthritis. Do not use in acute liver disease.	
Drug interactions Numerous drug-drug interactions. Aluminum containing supplements can decrease isoniazid absorption. When administered concurrently with disulfiram, gait disturbance, confusion, irritability, and aggressiveness may result. Ethyl alcohol should be avoided. Increases serum levels of carbamazepine potentially causing toxicity. May also increase phenytoin to toxic levels.	
Pregnancy – Category C.	**Overdose** – May be fatal. Symptomatic management and administering pyridoxine to correct metabolic acidosis.
Special populations – Monitor for liver and renal laboratory function changes particularly in the elderly. Genetic differences in metabolism so monitor ethnically diverse populations carefully. Do not breast-feed. Monitor AST levels due to risk of fatal hepatitis.	

Anti-fungal agents

Most fungi are completely resistant to typical antibiotics, therefore medications specifically targeting fungal infections have been developed to treat them. There are four main classes of anti-fungal drugs that have been developed. The first class, known as macrocyclic polyenes, includes amphotericin B, one of our prototypical drugs. The second main class, the azoles group, is comprised of two subgroups, the triazoles and imidazoles. The azoles include clotrimazole, miconazole, and fluconazole, another of our prototypical drugs. The third class is known as the allylamine antifungals, and includes terbinafine. The fourth main group consists of only one drug, flucytosine, reserved primarily for the management of invasive infections with cryptococcosis [103].

Nursing consideration: Candida opportunistic infections are especially problematic in immunocompromised patients.

Human cells and fungal cells share similar characteristics, so the development of medications that will target fungal cellular structures without harming human cells is a hallmark of drug development and treatment. The azoles have a broad spectrum of activity that includes

Candida species, Cryptococcus neoformans, and various mycoses including blastomycosis, coccidioidomycosis, and histoplasmosis. However, resistance to azoles occurs through a variety of processes and unfortunately, resistance is increasing as the azoles are used prophylactically rather than merely for active treatment against infection. Resistant strains of Candida are increasing especially among patients with AIDS [103].

All of the azoles as well as terbinafine have been associated with liver toxicity and cases of hepatitis that appear to resolve once drug treatment is discontinued. Patients with preexisting liver disorders however must be treated cautiously with routine laboratory studies to assess liver function. As noted below, the kidneys play a significant role in drug excretion therefore caution is also warranted in patients with preexisting kidney disease [103].

EBP alert! For patients with kidney impairment, dosage adjustment will need to be made with reductions of 50% of the typical dose necessary for patients with creatinine clearance less than 50mL/min. In addition, because of the necessary liver involvement to metabolize the azoles, patients with ethyl alcohol abuse or dependence (even if in full remission) must be treated cautiously [103].

Candida albicans, a member of the yeast family of fungi, is the fourth most common organism found in blood cultures in the United States. Luckily, several anti-fungal agents including clotrimazole, miconazole, and fluconazole are effective against vaginal candidiasis infections, some of which are available over the counter [103].

Fungal infections have increased secondary to immunosuppresive treatment for transplants, aggressive cancer chemotherapy, AIDS, and the use of broad-spectrum antibiotics [103].

Fungi are very complex organisms and typically require treatment based upon whether a superficial, subcutaneous, or systemic infection is present. Anti-fungal drugs typically act by targeting cholesterol ergosterol, a component of fungal cell walls [103].

Group 1 – Anti-fungal for systemic infections
Prototype: Amphotericin B deoxycholate

Classification grouping: Anti-fungal.

Availability: Powder for injection, topical.

Anti-fungal for systemic infection	
Forms and indications for use [79,103,123]	
Amphotericin B deoxycholate Power for injection. Infections with – Invasive fungal infections only.	
BLACK BOX WARNING **Invasive fungal infection -** "Use primarily for progressive potentially life-threatening fungal infections; avoid in noninvasive fungal disease including oral thrush, vaginal candidiasis, and esophageal candidiasis in patients with normal neutrophil counts. **Overdose prevention -** Use caution to prevent inadvertent overdose; verify product name and dosage if dose >1.5 mg/kg [79]."	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Anti-fungal Medication dosing guidelines - *http://www.globalrph.com/antifungal_home.htm.*	
Pharmacokinetics	
Route	IV.
Absorption	Maximum concentration 0.5 to 2mcg/mL.
Distribution	• Distributed to aqueous humor, synovium, inflamed pleura, and peritoneum. • 90% protein bound.
Metabolism	Not known.
Primary excretion	Kidney.
Duration of action	Plasma half-life approximately 24 hours, elimination half-life approximately 15 days.
Adverse effects Adverse effects include acute fever, chills, vomiting, anorexia, headache, ototoxicity, nephrotoxicity with electrolyte imbalances, dysrhythmias, cardiac arrest, occasionally hepatotoxic, possible anaphylaxis, blood dyscrasias, phlebitis, hypertension, tachycardia, chest pain, insomnia, anxiety, confusion, dizziness, tremor, rash, sweating, pharyngitis, tinnitus, nausea, diarrhea, abdominal pain, constipation, hematuria, kidney failure, anemia, bilirubinemia, increased liver enzymes, jaundice, allergic reaction, back pain, rigors, dyspnea, cough, hypoxia, epistaxis, pleural effusion, respiratory failure, chills/rigors, fever, organ failure, and infection.	
Contraindications/precautions: Hypersensitivity to the medication or components, use caution in patients with renal impairment or electrolyte disturbances.	
Drug interactions: Azole antifungals can cause antagonism, not recommended for coadministration. Increased risk of hypokalemia with corticosteroids. Increased risk of nephrotoxicity with cyclosporine, tactolimus, foscarnet, and other nephrotoxic agents. Increased risk of digitalis toxicity when administered with digoxin. Risk of acute pulmonary toxicity when administered with leukocyte transfusions. Amphotericin B increases risk of flucytosine toxicity when coadministered.	
Pregnancy – Category B.	**Overdose** – Cardiorespiratory arrest symptomatic treatment.
Special populations – Monitor patients for liver and renal laboratory function changes particularly in elderly patients. Monitor for hearing and balance changes, dizziness, or ringing in the ears. Do not breastfeed.	

Group 2 – Anti-fungal for systemic and superficial infections

Systemic mycoses are mostly opportunistic infections and their prevalence increased because "of increased use of immunosuppressive regimens in organ transplantation and in the treatment of malignancies, and the AIDS epidemic. However, most fungi are completely resistant to antibacterial drugs. Only few chemicals are known with activity against fungi and most of these are relatively toxic." One of the principal agents used for systemic mycoses are amphotericin B, a fungicidal antibiotic without antibacterial activity. It remains the most effective for severe systemic mycoses, and the prototypical drug fluconazole [124].

Fluconazole is cleared primarily by the kidneys therefore the half-life of the drug is impacted significantly in the presence of renal illness. Monitoring of kidney function is extremely important and plan on the need to adjust medication dosages in the presence of kidney disease with compromised kidney functioning [103].

Prototype: Fluconazole

Classification grouping: Anti-fungal.

Availability: Powder for injection, oral tablets, oral suspension.

Anti-fungal for systemic and superficial infection	
Forms and indications for use [103,125]	
Fluconazole Tablets, oral suspension, and IV solution. Infections with – Candida albicans.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism.	
Pharmacokinetics	
Route	IV, oral.
Absorption	Readily absorbed.
Distribution	• Widely distributed and crosses blood–brain barrier. • Secreted in breast milk. • 11 to 12% protein bound.
Metabolism	Liver.
Primary excretion	Kidney.
Duration of action	Half-life 20–50 hours.
Adverse effects Adverse effects include nausea, vomiting, and diarrhea, QT prolongation, headache, rash, blood dyscrasias, and hepatitis.	
Contraindications/precautions Contraindicated in patients who have hypersensitivity to this drug. Use with caution in patients with liver disease. Do not administer with cisapride.	
Drug interactions Patients can experience increased bleeding when administered concurrently with Coumadin. Increases levels of alfentanil, benzodiazepines, buspirone, corticosteroids, cyclosporine, losartan, nisoldipine, sulfonylureas, tacrolimus, theophylline, TCAs, vinca alkaloids, zidovudine, and zolpidem. Requires careful monitoring of phenytoin levels to prevent CNS toxicity. Cimetidine and rifampin can decrease fluconazole levels. Hydrochlorothiazide may increase fluconazole levels.	
Pregnancy – Category C.	**Overdose** –Causes hallucinations and paranoid behavior.
Special populations – Monitor patients for liver and renal laboratory function changes particularly in elderly patients. Monitor ethnically diverse populations due to metabolism through the P450 system.	

Group 3 – Anti-fungal for superficial infections

This group of infections (hair, scalp, nails, and mucous membranes) is typically not an emergency but can cause patients significant discomfort and distress. Included in this group of infections are Tinea corpora (ringworm), Tinea cruris (jock itch), Tinea pedis (athlete's foot), and Tinea unguium (nail plate fungus). This last fungal infection is very common in patients with diabetes due to circulatory system deficits. Infants and immunosuppressed individuals may manifest symptoms of oropharyngeal candidiasis (thrush). In addition, fungal infections of the nails are among the most difficult to treat because the nail plate prevents anti-fungal medications from penetrating to the site of infection. These medications are not effective typically for significant nail bed infections, which are best treated systemically with an antifungal agent.

Prototype: Nystatin

Classification grouping: Anti-fungal.

Availability: Powder for injection, topical.

Anti-fungal for superficial infection	
Forms and indications for use [103,126]	
Nystatin Cream, ointment, powder, tablets. Infections with – Candida albicans infections of the vagina, skin, and mouth.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism.	
Pharmacokinetics	
Route	Oral suspensions, troches, topical creams, vaginal tablets.
Absorption	Poorly absorbed.
Distribution	Not distributed.
Metabolism	Not metabolized.
Primary excretion	Unchanged in feces.
Duration of action	Half-life unknown.
Adverse effects Minor skin irritation, contact dermatitis, hypersensitivity.	
Contraindications/precautions Contraindicated in patients who have hypersensitivity to this drug. Safe for use in breastfeeding.	
Drug interactions None well documented.	
Pregnancy – Category C.	**Overdose** – Symptomatic treatment of nausea, vomiting, diarrhea.

PHARMACOLOGICAL MANAGEMENT OF PARASITIC INFECTIONS

Protozoa and parasitic worms are very widespread organisms that inhabit bodies of water, the soil, and numerous animal hosts. They are responsible for very significant morbidity and mortality worldwide. Further complicating treatment is the fact that these organisms may change form in the human body during their lifecycles and may migrate within the human body. This complicates the treatment of these infections significantly [131].

Group 1 – Anti-malarial

The organism that causes the most significant morbidity and mortality worldwide is Plasmodium, the parasite causing malaria. Plasmodium is carried by the female mosquito (vector) and endemic in many regions of the world. No age group is spared the devastating consequences of malarial infection [130].

Malaria may be caused by four distinct species of Plasmodium. When the mosquito bites a human host, the mosquito's saliva injects the parasite into the human body, where it must incubate for a period. Malaria may cause multiple organ system failures and be fatal. The goal of treatment for malaria is to interrupt the lifecycle of Plasmodium by interfering with its various phases with treatment initiated as soon as possible after the infection manifests [130].

The prototype drug in this category, chloroquine phosphate, has been used for malaria treatment and prevention of malaria for years. It is developing increasing resistance, but remains effective in Central America and the Middle East. Its use has been replaced by newer agents, such as atovaquone-proguanil, in areas with chloroquine-resistant malaria, but remains as a prototypic malaria medication [133].

Prototype: Chloroquine

Classification grouping: Anti-malarial. **Availability:** Tablet, IM solution.

Anti-malarial	
Forms and indications for use [128,129]	
Chloroquine phosphate tablets. Infections with – P. malariae, P. falciparum.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Anti-malarials / Anti-protozoals / Amebicide dosing guidelines - *http://www.globalrph.com/antimalarials.htm.*	
Pharmacokinetics	
Route	PO.
Absorption	Rapidly and almost completely absorbed.
Distribution	• Widely distributed, especially to liver, spleen, kidney, and lung, lesser extent to CNS. • Secreted in breast milk.
Metabolism	Liver.
Primary excretion	Kidney.
Duration of action	Half-life: 1 to 2 months.
Adverse effects Retinal damage, retinopathy, and macular degeneration associated with high doses. Other adverse effects include skin rash, auditory toxicity, neuropsychiatric disorders, blood dyscrasias, QT prolongation, hepatitis, seizures, nausea, vomiting, diarrhea, abdominal pain, headache, photosensitivity, tinnitus, muscle weakness, and extrapyramidal symptoms.	
Contraindications/precautions Patients with preexisting retinal field changes should not receive this drug. Baseline and periodic vision screening should occur. Patients with liver impairment or excessive ethyl alcohol use should be monitored carefully. Monitor for blood dyscrasias. Contraindicated for use with dronedarone, eliglustat, pimozide, and toremifene due to the risk of QT prolongation.	
Drug interactions Avoid concurrent use of antacids and laxatives containing aluminum as they can decrease GI absorption of chloroquine. May prolong the QT interval, so other medications that also prolong the QT interval can cause additive prolongation.	
Pregnancy – Category D.	**Overdose** – May be fatal, symptomatic treatment .
Special populations – Monitor for liver, retinal, and renal laboratory function changes particularly in the elderly. Urine may be rust colored.	

Group 2 – Treatment for non-malarial protozoan infections

Most of the world has adequate sanitation. However, some parts of the word, including some parts of the United States, are not completely free of unsanitary conditions. Giardia lamblia infection (giardiasis) is often transmitted by water contaminated with feces (drinking and recreational swimming bodies of water). Cryptosporidium parvum infection (cryptosporidiosis) has also been isolated from swimming waters, and can survive even in chlorinated water [132].

Other protozoan infections include toxoplasmosis and trichomoniasis, with the domestic cat in the primary host to the parasite causing toxoplasmosis, and transmission may occur to human owners via emptying a cat litter box. Pregnant women who contract toxoplasmosis have high rates of transmission to their fetuses that may result in stillbirth or spontaneous abortion. Trichomoniasis is a common STD that afflicts both men and women. Women typically exhibit characteristic symptoms while men are often asymptomatic resulting in re-infection of their partners [132].

Metronidazole is a drug that crosses classes being effective in both parasitic and bacterial infections. "Cautious use is recommended with metronidazole for patients with a history of blood dyscrasias. Seizures have occurred as an adverse reaction, and patients with a history of seizure disorder or neurological problems should use this drug with caution [103]."

"Patients with hookworm and whipworm infections may require iron replacement therapy. Eradication of pinworm infections usually requires simultaneous treatment of all household contacts; a vigorous hygiene program of cleaning bed linens, nightwear, and underwear; and good hand-washing habits. Contrary to popular belief, treatment of hookworm and pinworm infections does not require special diets or purging with laxatives before or after the antimicrobial drug [103]." Purging does not contribute to more rapid treatment success eradicating the organisms; patients should be instructed to avoid unnecessary interventions [103].

Prototype: Metronidazole

Metronidazole is a drug that crosses classes and therefore it is effective in both infections involving both parasites and bacteria. Metronidazole disrupts both nucleic acid and protein synthesis in organisms susceptible to its effects. With certain anaerobic bacteria, it is bactericidal. Metronidazole also possesses direct action on both trichomonas and amoeba infections, specifically against Trichomonas vaginalis and Entamoeba histobitica. Metronidazole is also active against H. pylori and anaerobic bacteria, including Bacteroides and Clostridium. Metronidazole has been effectively used in an off-label manner for infections involving G. lamblia and Gardnerella vaginalis [103].

Metronidazole has both anti-parasitic and anti-bacterial properties; therefore it is a reliable choice for common infections with protozoa including T. vaginalis, G. lamblia, and E. histoblica. Metronidazole is also used to treat less common parasites, including the protozoan *Balantidium coli, an organism that is ra*re in the United States, but can infect humans, especially world travelers. It is an intestinal protozoan parasite found in tainted food and water contaminated by fecal matter. *Balantidium coli* infection is generally asymptomatic, but patients with underlying co-morbidities may experience persistent diarrhea, abdominal pain, and sometimes a perforated colon. Metronidazole is also clinically appropriate in the treatment of Dracunculus medinensis, or guinea worm [103, 134].

Antibacterial uses of metronidazole include treatment of anaerobic bacterial infections, bacterial vaginosis and in the treatment of H. pylori in gastritis and peptic ulcer disease [103].

"Oral metronidazole is readily absorbed and widely distributed into most tissue and fluids, including the cerebrospinal fluid, breast milk, bone, liver abscesses, vaginal secretions, and seminal fluid.[103]" Metronidazole also crosses the placenta. Metabolism of metronidazole occurs primarily in the liver and the majority of its metabolites are excreted in urine [103].

Cautious use of metronidazole is recommended in patients with a history of blood disorders or with pre-existing seizure or other neurological disorders. Due to liver dysfunction, drug metabolism and drug clearance may be impacted, so caution is advised in the hepatically compromised patient [103].

Metronidazole is a category B drug during pregnancy, but as with most drugs, researchers and experts in the field recommend it not be used during the first trimester of pregnancy. Metronidazole has been used to treat trichomoniasis in the second and third trimesters of pregnancy safely and without consequence to the fetus. Despite more than 20 years of treatment with this medication and no reports of congenital abnormalities, premature births, intrauterine fetal deaths, or low birth weight neonates, caution should always guide treatment choices [103].

According to the FDA, a nursing mother who needs metronidazole should interrupt nursing for 24 hours and use a single-dose regimen. "Safety and efficacy of metronidazole in children have been established only for treatment of amebiasis; although, there are also drug dosages published for trichomoniasis and giardiasis [103]." Elimination of the drug appears to be inversely proportional to age (i.e., the younger the age of the child the more rapid the clearance of the drug) [103].

Anorexia, nausea, abdominal pain, dizziness, headache, and dry mouth commonly occur with metronidazole, along with abnormal taste sensations, including that of metal. Although annoying, these effects are mild and resolve relatively quickly. Occasionally a patient may experience nausea, abdominal pain, cramping, diarrhea, or rash. Taking metronidazole with meals or beverages may reduce the gastrointestinal distress. A very rare side effect may be seizures, but this is more likely to occur with individuals with an underlying seizure disorder [103].

Metronidazole works synergistically with warfarin, increasing the anticoagulant effect; practitioners should monitor patients' prothrombin times. Metronidazole creates a similar reaction to Antabuse when ethyl alcohol is ingested, so patients must avoid all ethyl alcohol during treatment and for at least 48 hours after treatment completion [103].

Trichomonas vaginal infections commonly occur shortly after the completion of a menstrual cycle and is characterized by a malodorous, frothy discharge and vaginal irritation. Although typically associated with sexual transmission, the organism responsible can live for weeks on moist or wet surfaces, including towels and toilet seats. Trichomonas vaginal infections can be treated with metronidazole in a one-time dose of 2 grams [103].

In the male patient, the infection may cause some discharge from the urethra but the infection is usually mild and often asymptomatic. Sexual partners should be counseled to use a condom during intercourse during treatment with metronidazole and the full course of treatment be completed to prevent re-infection. If the infection occurs during the first trimester of pregnancy, consider deferring treatment [103].

The life cycle of G. lamblia (Giardia) involves the cystic and larvae stages. The cyst form can live in cold water for months and subsequently ingested by humans, especially when drinking cold water from streams during outdoor activities. The larval stage that is actively growing lives in the small intestine can severely impair the mechanical process of digesting foods. Symptoms of Giardia infections range from completely asymptomatic to severe illness that is chronic in nature and accompanied by malnutrition secondary to the poor digestion of foods. Metronidazole is used in the United States to treat giardiasis, although it is not approved for this indication [103].

Classification grouping: Anti-infective, antiprotozoal.

Availability: Oral, IV, topical.

Non-malarial protozoan infection	
Forms and indications for use [103, 135]	
Metronidazole Tablet, suspension, solution. Infections with – Trichomoniasis vaginalis , entamoeba histolytica, giardia lamblia, cryptosporidium parvum, anaerobic bacteria and helicobacter pylori.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Metronidazole dosing guidelines - *http://www.globalrph.com/metronidazole_renal.htm.*	
Pharmacokinetics	
Route	Oral, IV, topical.
Absorption	Well absorbed.
Distribution	• Widely distributed and crosses blood–brain barrier. • Secreted in breast milk.
Metabolism	Liver.
Primary excretion	Primarily kidney and some feces.
Duration of action	Half-life 8 hours.
Adverse effects Adverse effects include anorexia, nausea, vomiting, diarrhea, abdominal pain, dizziness, headache, metallic taste, seizures, pruritis, rhinitis, vaginitis, vaginal discharge, Candidia infections, and flu like symptoms.	
Contraindications/precautions Hypersensitivity to the drug. Contraindicated in the first trimester of pregnancy in trichomoniasis patients.	
Drug interactions Consuming ethyl alcohol may precipitate a disulfiram-like syndrome. Treatment may increase lithium levels. Can increase the effect of warfarin. Cimetidine can prolong the half life of metronidazole.	
Pregnancy – Category B.	**Overdose** – Symptomatic treatment.
Special populations – Monitor patients for liver functions changes, particularly elderly patients. Urine may be rust colored. Do not breastfeed. In patients with bone marrow suppression, CBCs should be monitored for leucopenia. Discontinue treatment with any sign of central nervous system toxicity.	

ANTI-VIRAL TREATMENTS

Many human illnesses are caused by viruses, including pharyngitis, mononucleosis, hepatitis, gastroenteritis, influenza, herpes, and the common cold. Although simple in their structures, viruses are amazingly adaptive with diverse forms. Viruses are considered primitive structurally when compared to bacteria and fungi. They contain a genetic core of DNA or RNA that is surrounded by a protein coating that serves as a defensive structure [95].

Viruses are parasites located within cells that are dependent upon the cell's genetic material for reproduction. This is a cornerstone of anti-viral therapy, because effective treatment can include blockading entry of the virus into the cell or a medication entering the cell and actively interfering with viral multiplication. The associated risks include unintended harm to the cells as well as to the viral pathogen. Further complicating treatment with anti-viral therapy is that the virus reproduces quickly, often prior to a patient becoming symptomatic. Therefore, it is the nature of rapid viral replication and mutation that challenges treatment [95].

Influenza occurs globally with an annual attack rate estimated at 5 to 10 percent in adults and 20 to 30 percent in children. Illnesses can result in hospitalization and death mainly among high-risk groups (the very young, elderly or chronically ill). Worldwide, these annual epidemics result in about three to five million cases of severe illness, and about 250 000 to 500 000 deaths. In industrialized countries, most deaths associated with influenza occur among people age 65 years or older [80].

Worldwide, more than 530 million people are living with the herpes simplex virus type-2 (HSV2) and more than 290 million women have human papillomavirus (HPV) infection [81]. Humans are believed to be one of the only reservoirs for the herpes simplex virus (HSV) and it may lay dormant for many years. Infection with HSV is lifelong. HSV type 1 infections primarily occur in the mouth or lips.

HSV type 2 infections are primarily genital infections. Neonatal herpes infections are very dangerous with a significantly high mortality rate [136].

"130-150 million people globally have chronic hepatitis C infection. A significant number of those who are chronically infected will develop liver cirrhosis or liver cancer. Approximately 500 000 people die each year from hepatitis C-related liver diseases[82]." "An estimated 240 million people are chronically infected with hepatitis B (defined as hepatitis B surface antigen positive for at least 6 months). More than 780 000 people die every year due to complications of hepatitis B, including cirrhosis and liver cancer[83]." "Every year there are an estimated 20 million hepatitis E infections, over 3 million symptomatic cases of hepatitis E, and 56 600 hepatitis E-related deaths[84]." Contrast these data with the approximately 36.9 (34.3-41.1) million people living with HIV in 2014 [85] and it becomes clear the magnitude of illnesses of viral origins.

Unlike other anti-infective agents (e.g., bacteriocidal antibiotics) anti-viral medications do not kill the viruses that they target, but rather interfere with the virus' replication in the human host. The goal of anti-viral treatment is to initiate and maintain treatment to keep viral replication at bay. Both varicella and herpes can be effectively treated if medication intervention is initiated quickly. Patients need to seek treatment immediately if they develop symptoms of chickenpox [95,124].

Viruses are non-living infectious agents with simple structures capable of rapid mutation. They survive in living host cells. Viruses are numerous, mutate rapidly, and may coexist with their host without cause disease or illness. Viruses reproduce in several stages and anti-viral drugs target specific viral anatomic structures or particular parts of the replication/reproduction cycle [95,124].

Group 1 – Antiviral medication for herpes viruses

Pharmacotherapy for herpes simplex infections is aimed at limiting the duration of acute symptoms and lessening their intensity. An additional goal is to prevent recurrences of outbreaks. Acyclovir may trigger renal failure in patients due to crystal formation and precipitation of the drug in the kidneys. This reaction may occur more commonly in patients receiving parenteral doses of acyclovir; however, it may also occur in patients receiving oral forms of the medication, even in divided doses. To mitigate this, patients should drink sufficient fluids during the treatment period to remain well hydrated [103].

Nursing consideration: Teach patients the signs and symptoms of kidney problems, including abdominal pain, decreased frequency or volume when urinating, thirst, anorexia, nausea, and vomiting. Other reportable signs and symptoms include confusion, hallucinations, tremor, unsteady gait, and seizure activity [103].

Potential hematological adverse reactions can occur and present with symptoms including tiredness, fever, sore throat, chills, black, tarry stools, petichiae, and abnormal bruising or bleeding. Dry peeling or blistering skin associated with weakness of muscles, muscle cramps, rash, and itching may herald a serious adverse reaction [103].

Prototype: Acyclovir

Classification grouping: Antiviral for herpes viruses.

Availability: Tablet, IV solution, topical.

Antiviral for herpes viruses	
Forms and indications for use [103,137]	
Acyclovir Tablet, IV solution, topical. Infections with – HSV, cytomegalovirus (CMV), varicella-zoster virus (VZV), epstein-barr virus (EBV), herpes virus-type 6.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Anti-herpetic medications dosing guidelines - *http://www.globalrph.com/antibiotic/herpes.htm* .	
Pharmacokinetics	
Route	Oral, IV, topical.
Absorption	10–20% absorbed, minimal topical absorption.
Distribution	• Widely distributed, crosses blood–brain barrier. • Secreted in breast milk. • 9 to 33 percent protein bound.
Metabolism	Not metabolized.
Primary excretion	Kidney.
Duration of action	Half-life 2.5 to 3.3 hours.
Adverse effects Adverse effects include nausea, vomiting, diarrhea, anorexia, elevated hepatic enzymes, rash, itching, headache, confusion, blood dyscrasias, allergic reactions. IV route associated with nephrotoxicity and neurotoxicity.	
Contraindications/precautions Contraindicated in patients hypersensitive to acyclovir or valacyclovir. Use with caution in patients with kidney disease.	
Drug interactions Additive effect with other nephrotoxic drugs. Acyclovir can precipitate in bacteriostatic water.	
Pregnancy – Category B.	**Overdose** – Coma, seizures, renal failure. Hemodialysis may be initiated.
Special populations – Monitor patients for renal laboratory function changes, particularly elderly patients; also monitor patients for increased falling.	

Group 2 – Antiviral for influenza viruses

Influenza viruses are designated with the letters A, B, or C, with type A causing the most significant outbreaks historically. Type A influenza is responsible for multiple worldwide pandemics and deaths. Every year is a new flu season with new predictions of severity among different populations and age groups. The very young, the very old, and individuals with co-morbid illness are often the first victims to succumb to flu related mortality.

The best approach to annual influenza season is prevention in the form of vaccination. The challenge is the ability of the virus to mutate rapidly and the imperfect predictions of what particular strain will be problematic. This complicates vaccine development and hence the need for medications to treat active infections. There are very few antiviral medications to treat influenza and they should not be considered substitutes for vaccination; they may limit the severity of viral symptoms; but not necessarily prevent infection [103].

The Centers for Disease Control and Prevention (CDC) tracks influenza outbreaks worldwide to ascertain the specific strains of influenza infecting individuals worldwide and any mutations that occur. You may obtain weekly updates from the CDC as their scientists track specific strains and outbreaks in the United States. The CDC also provides treatment recommendations for the use of specific antiviral agents during flu season, including treatment updates when resistant strains emerge. Please visit the CDC's website for the latest information [138].

Prototype: Oseltamivir

Classification grouping: Antiviral influenza viruses, viral replication inhibitor.

Availability: Tablet, IV solution, topical.

Antiviral for influenza viruses	
Forms and indications for use [103,139]	
Oseltamivir Infections with – Influenza A and B.	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Anti-Influenza medication dosing guidelines - *http://www.globalrph.com/anti-influenza.htm.*	
Pharmacokinetics	
Route	Oral.
Absorption	Readily absorbed from GI tract.
Distribution	75% bioavailability, 42% protein bound.
Metabolism	Liver.
Primary excretion	Kidney.
Duration of action	Half-life (metabolite) 6 to 10 hours, parent drug 1 to 3 hours.
Adverse effects Adverse events include arrhythmia, agitation, confusion, hallucinations, nightmares, rash, conjunctivitis, nausea, vomiting, diarrhea, abdominal pain, allergic reactions.	
Contraindications/precautions Hypersensitivity to oseltamivir or inactive ingredients.	
Drug interactions Live vaccines should not be administered less than 2 weeks before or 48 hours after oseltamivir.	
Pregnancy – Category C.	**Overdose** – Nausea, vomiting.
Special populations – Remind patients that the use of oseltamivir is not a substitute for flu vaccination.	

Group 3 – Antiviral for hepatitis viruses

Viral hepatitis is a common infection. Hepatitis may be acute or chronic, with pronounced symptoms of fever, chills, or prolonged fatigue. Hepatitis A is spread through oral–fecal routes and may cause epidemics. In the United States, the spread of hepatitis A is often through contaminated food products. Currently, no anti-viral is specifically labeled for use with hepatitis A infection and treatment recommendations are to prevent infection through proper sanitation and hand washing [59].

Hepatitis B is primarily spread through contaminated blood and body fluids and through vertical transmission. The best treatment for hepatitis B infection is prevention through immunization. In its chronic form, hepatitis B pharmacotherapy may include antivirals, including lamivudine (prototype – see below) [59].

Hepatitis C is primarily transmitted through infected blood or body fluids. Sexual transmission can also occur. There is no vaccine for hepatitis C, because of its propensity to mutate rapidly. Treatment is typically with a combination of interferon and the antiviral ribavirin [59].

Prototype: Lamivudine

Classification grouping: Antiviral hepatitis viruses, especially HBV. **Availability:** Tablet.

Antiviral for hepatitis	
Forms and indications for use [59,86,140]	
Lamivudine Tablet. Infections with – HBV.	
BLACK BOX WARNING **Lactic acidosis/severe hepatomegaly with steatosis** "Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, associated with nucleoside analogue use alone or in combination; discontinue treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity. **Hepatitis B exacerbation** Severe acute HBV exacerbations in HBV or HBV/HIV co-infected patients upon lamivudine D/C. Monitor hepatic function closely for at least several months in HBV or HBV/HIV co-infected patients who D/C lamivudine. Initiate anti-HBV treatment, if needed. **Non-interchangeable forms** Lamivudine dosage forms used to treat HIV infection contain higher doses compared to lamivudine dosage forms used to treat chronic HBV infection. Ensure patients receive correct dosage form for indicated use. **HIV testing** Offer HIV counseling and testing before initiating lamivudine treatment for HBV and periodically during treatment; rapid emergence of HIV resistance may occur if unrecognized or untreated HIV infection due to subtherapeutic dose and inappropriate monotherapy with lamivudine treatment for HBV[86]."	
DOSAGES Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. Anti-hepatitis medications dosing guidelines - *http://www.globalrph.com/anti-hepatitis.htm*.	
Pharmacokinetics	
Route	Oral.
Absorption	86% bioavailable.
Distribution	• Secreted in breast milk. • Less than 36% bound to protein.
Metabolism	Metabolism is a minor route of elimination.
Primary excretion	Kidney, majority is excreted unchanged.
Duration of action	Half-life 5 to 7 hours.
Adverse effects Adverse effects include GI symptoms (e.g., nausea, vomiting, abdominal pain, decreased appetite and diarrhea), ear-nose-throat (ENT) infection, rash, pancreatitis, anemia, hepatomegaly, post treatment exacerbation of hepatitis B, and CNS symptoms including headache, fatigue, neuropathy, insomnia, dizziness, depression, neuropathy.	
Contraindications/precautions Contraindicated in patients with hypersensitivity to lamivudine or its components. Use cautiously in patients with kidney disease. Monitor hepatic enzymes and discontinue immediately if hepatotoxicity signs/symptoms are noted.	
Drug interactions Use cautiously in patients receiving medications that affect kidney or hepatic function. Methadone may delay absorption of lamivudine. Zalcitabine and lamivudine can inhibit phosphorylation of each other; combination of these two products is not recommended.	
Pregnancy – Category C.	**Overdose** – No antidote, treat symptomatically.
Special populations – Monitor patients for renal laboratory function changes, particularly elderly patients. Monitor children with history of pancreatitis. Monitor psychiatric patients carefully. Do not breastfeed.	

Group 4 – Antiviral for HIV – AIDS

Acquired immunodeficiency syndrome (AIDS) is caused by human immunodeficiency virus (HIV). This virus has two primary forms HIV-1 and HIV-2. Transmission occurs by being exposed to contaminated body fluids (blood, semen) and can be transmitted horizontally through direct contact or vertically in utero or through breastfeeding. Initially a deadly challenge when first appearing in the early 1980s, HIV infection has become a chronic illness in western industrialized countries. Albeit no cure exists, but individuals are now able to live relatively symptom free for years. However, challenges exist because of the ability of the virus to mutate, resulting in drug-resistant strains. Other non-industrialized countries, however, still bear a disproportionate number of cases that progress from HIV infection to full-blown AIDS. The goal when initiating treatment for HIV infection is early detection and intervention to reduce the total number of viruses that are replicating and to prevent vertical transmission from a woman to her fetus. The treatments for HIV infection are changing rapidly and the many combinations of therapies warrant an individual course. Therefore, one prototypical medication in the HIV treatment arsenal is described below to provide the reader with some information about this specialized class anti-virals that target RNA replication [103, 59].

Prototype: Zidovudine

Classification grouping: Antiretroviral, nucleoside reverse transcriptase inhibitor.

Availability: Tablet, IV solution.

Antiviral for HIV - AIDS

Forms and indications for use [59,103,141]

Zidovudine
Tablet, IV solution.
Infections with – HIV infection, postexposure prophylaxis in HIV-exposed healthcare workers, and to reduce transmission of HIV from an HIV-positive mother to her fetus.

BLACK BOX WARNING

Hematologic toxicity
"Zidovudine-associated neutropenia and severe anemia, especially in patients with advanced HIV.

Myopathy
Symptomatic myopathy associated with prolonged zidovudine use.

Lactic acidosis/severe hepatomegaly
Lactic acidosis and severe hepatomegaly with steatosis, including fatal cases, associated with nucleoside analogue use alone or in combination; suspend treatment if clinical or laboratory findings suggest lactic acidosis or hepatotoxicity[87]."

DOSAGES
Consult pocket or electronic reference for specific prescribing information by illness – dosages vary according to site of infection and type of organism. HIV solo or poly medication dosing guidelines - *http://www.globalrph.com/antivirals2.htm.*

Pharmacokinetics

Route	Oral or IV.
Absorption	Rapidly absorbed.
Distribution	• Widely distributed. • Secreted in breast milk. • Less than 38% protein bound.
Metabolism	Liver.
Primary excretion	Hepatic metabolism.
Duration of action	Half-life 0.5 to 3 hours.

Adverse effects
Adverse effects include GI symptoms (e.g., nausea, anorexia, and diarrhea), CNS symptoms (headache, malaise, asthenia, neuropathy, confusion, depression), rash, hearing loss, taste perversion, gynecomastia, increased liver enzymes, blood dyscrasias, cough, chills, fatigue, myalgia, and weakness.

Contraindications/precautions
Contraindicated in patients with severe allergic reactions to any component. Use may suppress bone marrow function. Use with caution in patients with preexisting anemia. Patients with impaired hepatic or renal function may require dosage reduction to prevent toxic accumulation.

Drug interactions
Use cautiously in patients receiving medications that affect kidney or hepatic function. Atovaquone, valproic acid, clarithromycin, probenecid, fluconazole, and methadone can increase serum levels and potential toxicity of zidovudine. Nelfinavir, clarithromycin, rifamycin, ribavirin, stavudine, and ritonavir can decrease zidovudine concentrations. Ganciclovir can cause life threatening hematologic toxicity when combined with zidovudine; concurrent use should be avoided. Doxorubicin can antagonize zidovudine, concurrent use should be avoided. Interferon can increase the risk of life threatening hematologic toxicities. Phenytoin levels can vary when administered with zidovudine.

Pregnancy – Category C.	**Overdose** – Treat symptomatically.

Special populations – Monitor patients for renal laboratory function changes, particularly in elderly patients. Monitor ethnically diverse populations carefully due to metabolism of this drug through the P450 system. Do not breastfeed.

Adverse drug reactions

Adverse drug reactions occur frequently and the main interventions to prevent these untoward events are maintaining prescriptive competency through education and research. Since many adverse drug reactions are dose-related, our success in preventing these reactions is contingent on our grasp of the principles of pharmacology that provide the scientific basis for dose selection.

This becomes critically important when we prescribe drugs that have a narrow therapeutic index. A drug interaction results when the effects of a drug are altered in some way by the presence of another drug, by food, or by environmental exposure. The risk of developing an adverse drug reaction (ADR) secondary to a drug–drug interaction increases significantly with the number of medications a patient is receiving.

A meta-analysis of adverse drug reactions in hospitalized patients [88] found serious adverse drugs reactions to be quite common. These authors further state:

> Perhaps, our most surprising result was the large number of fatal ADRs. We estimated that in 1994 in the United States 106 000 (95% CI, 76000–137000) hospital patients died from an ADR. Thus, we deduced that ADRs might rank from the fourth to sixth leading cause of death.
>
> Even if the lower confidence limit of 76 000 fatalities was used to be conservative, we estimated that ADRs could still constitute the sixth leading cause of death in the United States, after heart disease (743 460), cancer (529 904), stroke (150 108), pulmonary disease (101 077), and accidents (90 523); this would rank ADRs ahead of pneumonia (75 719) and diabetes (53 894). [88]

Perceptions about adverse drugs reactions vary among healthcare providers. For example, these authors noted:

> When the respondents were asked about the drugs causing ADRs, antibiotics and analgesics was the major group of drugs. Of these sulpha group of drugs, metronidazole, 3rd generation cephalosporins, NSAIDS like diclofenac, tramadol cause important ADRs. This is mainly because these are the most common therapeutic agents used in medical practice and the over usage and the unwanted usage of these drugs by the patients.
> The main manifestations produced by these drugs were skin rashes, epigastric pain, nausea, vomiting, diarrhea, followed by hypoglycemia, dizziness, drowsiness, seizure, tachycardia, tremors etc. These ADRs can be prevented by the restricted use and reduced dosage of the prescribed drugs. [89]

Medication prescriptive privileges for NPs are a significant responsibility requiring vigilance, continuing education, the use of evidence based guiding principles, and continuous quality improvement initiatives. Such activities can reduce the morbidity and mortality faced by patients and their family and concurrently reduces the professional liability faced by the nurse practitioners themselves.

According to CNA's Nurse Practitioner Claims Study (1998–2008), 17.7% of malpractice claims against nurse practitioners (NPs) involved medication. Among the most common errors were prescribing the wrong medication, prescribing the wrong dose, failing to properly discontinue a medication, and prescribing an incompatible, contraindicated, or interactive medication. [90]

Nurse pratitioners blend both nursing and medical knowledge and are required to have advanced understanding of pathophysiology, various disease processes, pharmacology and nursing science. These are the minimal requisite domains of knowledge to be a safe prescriber of medications and to make rational, informed decisions about medications for patient conditions.

Glossary of terms

- **Absorption**: The movement of a drug from its site of administration into the blood.
- **Additive effect**: Combining two drugs produces effect that is the sum of the individual drugs.
- **Aerosol**: Solid or liquid particles of drug suspended in a gas.
- **Affinity**: The strength of the bond between a particular drug or naturally occurring substance and a drug receptor site.
- **Agonist**: A drug (natural or synthetic) or naturally occurring body substance that will bind with a receptor site and produce a stimulating action.
- **Anaphylaxis**: Exaggerated hypersensitivity reaction to a previously encountered drug or foreign protein.
- **Antagonist**: A drug (natural or synthetic) or a naturally occurring body substance that will bind with a receptor site and block the action at that site.
- **Antagonistic action**: Combination of two drugs gives less than an additive effect (action).
- **Antidote**: Agent given to counteract an unwanted effect of a drug.
- **Bioavailability**: The degree of activity or amount of an administered drug or other substance that becomes available for activity in the target tissue.
- **Biotransformation**: Chemical alteration of a substance, especially of a drug, within the body, as by the action of enzymes.
- **Brand name**: Commercial name for a drug; trademark or trade name.
- **Chemical name**: Chemical formula for a drug.
- **Contraindications**: Inadvisable action, such as with medical treatment.
- **Cumulative effect**: When a drug is repeatedly administered and produces more pronounced outcomes when compared to the first dose.
- **Distribution**: The movement of absorbed drug in bodily fluids throughout body to target tissues.
- **Drug antagonism**: Combined effect of two drugs is less than sum of two drugs given separately.
- **Drug dependence**: Patient has a physiological withdrawal symptoms if the drug is stopped.
- **Drug-drug interaction**: Effects of drug are modified by another drug.
- **Efficacy**: The ability of a drug or naturally occurring substance to stimulate the receptor site to exert an action.
- **Elimination**: Removal of the drug from the body by organs of elimination.
- **Generic name**: Noncommercial name of a drug.
- **Half-life**: The duration of time that it takes for a half of a sample of particles, etc., to decay. We usually consider the half-life of a drug in relation to the amount of the drug in plasma.
- **Iatrogenic**: A condition caused by treatment (drug or procedures) administered by physicians or medical personnel.
- **Idiosyncrasy**: Abnormal or peculiar response to a drug.
- **Idiosyncratic reaction**: Unexpected effect produced in particularly sensitive patient, but not seen in most people.
- **Inhalation administration**: Administration of drugs in gaseous or vapor from or through the nose of mouth.
- **Metabolism**: The enzymatic alteration of drug structure to enhance excretion, inactivate a drug, increase the therapeutic action of a drug, activate a prodrug, increase, or decrease toxicity.

- **Parenteral administration**: Administration of a drug by injection into the skin, muscles, or veins (any route other than the digestive tract). Included are: subcutaneous, intradermal, intramuscular, intravenous, intrathecal, and intracavity injections.
- **Pathogenicity**: The potential capacity of certain species of microbes or viruses to cause a disease.
- **Potentiation**: Concurrent administration of drugs increases effect of another drug.
- **Receptor agonist**: Drug is a "perfect fit" on the receptor site.
- **Receptor antagonist**: Drug blocks or competes for the receptor site.
- **Resistance**: Lack of beneficial response.
- **Specificity**: The receptor site's ability to discern molecules similar structurally to the naturally occurring substance that will stimulate the drug receptor site.
- **Sublingual administration**: Drugs are given by placement under the tongue.
- **Synergism**: Combining two drugs produces an effect that is greater than the sum of the two drugs.
- **Tachyphylaxis**: Patient has quickly developing tolerance; initial response cannot be repeated; higher doses needed.
- **Teratogenesis**: The process by which congenital malformations are produced in an embryo or fetus.
- **Therapeutic window or index**: The range of medication in the blood stream known to produce desirable and non-toxic effects. These windows may be wide or very narrow.
- **Tolerance**: Drug produces decreased physiological response after repeated doses.
- **Transport**: Movement of a drug across a cell membrane into body cells.

Glossary of terms derived from multiple sources. Please see these additional reference materials available on the Internet:

- *http://medical-dictionary.thefreedictionary.com/.*
- *http://www.bumc.bu.edu/busm-pm/academics/resources/glossary/.*

REFERENCES

1. American Academy of Nurse Practitioners. (2015). NP Fact Sheet. Accessed November 11, 2015 at https://www.aanp.org/all-about-nps/np-fact-sheet.
2. American Association of Colleges of Nursing. (2011). The essentials of master's education in nursing. Accessed November 11, 2015 at http://www.aacn.nche.edu/education-resources/MastersEssentials11.pdf.
3. National Nursing Centers Consortium. NNCC State-by-State Guide to Laws Regarding Nurse Practitioner Prescriptive Authority and Physician Practice. (2014). Accessed November 11, 2015 at http://www.nncc.us/images_specific/pdf/2014StateGuideRegulationsGoverningNursePractitionerPractice.pdf.
4. Crigger, N., & Holcomb, L. (2008). Improving nurse practitioner practice through rational prescribing. Journal Nurse Practit, 4, 120-125. doi: Accessed November 11, 2015 at http://dx.doi.org/10.1016/j.nurpra.2007.12.004.
5. Goshen College (2015). Subject guides. Beyond googling: The invisible web. Accessed November 11, 2015 at: http://libraryguides.goshen.edu/content.php?pid=202832&sid=1694702.
6. Fears, J. (2004). The plague under marcus aurelius and the decline and fall of the Roman empire. Infect Dis Clin N Am, 18, 65-77.
7. Garrett, L. (1994). The coming plague. New York, NY: Penguin Books.
8. Centers for Disease Control and Prevention. (2012). Principles of Epidemiology in Public Health Practice, Third Edition. An Introduction to Applied Epidemiology and Biostatistics: Lesson 1: Introduction to Epidemiology Retrieved November 11, 2015, from http://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/index.html
9. Centers for Disease Control and Prevention. (2012). Principles of Epidemiology in Public Health Practice, Third Edition. An Introduction to Applied Epidemiology and Biostatistics: Lesson 1, Section 10: Chain of Infection. Retrieved November 11, 2015, from http://www.cdc.gov/ophss/csels/dsepd/ss1978/lesson1/section10.html
10. Weber, D. J., Rutala, W. A., Miller, M. B., Huslage, K., & Sickbert-Bennett, E. (2010). Role of hospital surfaces in the transmission of emerging health care-associated pathogens: Norovirus, Clostridium difficile, and acinetobacter species. Am J Infect Cont, 38, S25-S33.
11. Ford-Jones, E. L., & Kellner, J. D. (1995). "Cheap torches": An acronym for congenital and perinatal infections. Ped Infect Dis J, 14, 638-639.
12. Crosta, P. (2015). What is a virus? What is a viral infection? Retrieved November 11, 2015 from http://www.medicalnewstoday.com/articles/158179.php.
13. Bioinformatics, S. I. O. (nd). Viruses infecting humans. Retrieved November 11, 2015 from http://viralzone.expasy.org/all_by_species/656.html.
14. Mandal, A. (2013). Human diseases caused by viruses. Retrieved November 11, 2015 from http://www.news-medical.net/health/Human-Diseases-Caused-by-Viruses.aspx
15. National Institute of Allergy and Infectious Disease. (2009). Understanding microbes in sickness and in health. (NIH Publication No. 09-4914). Bethesda, MD: National Institute of Health. Retrieved November 12, 2015 from https://www.niaid.nih.gov/topics/microbes/Documents/microbesbook.pdf.
16. Nordqvist, C. (2013, May 23). What is fungus? What is fungi? Retrieved November 12, 2015, from http://www.medicalnewstoday.com/articles/158134.php
17. Pfaller, M. A., & Diekema, D. J. (2010). Epidemiology of invasive mycoses in north America. Critical Reviews in Microbiology, 36, 1-53. doi: doi:10.3109/10408410903241444. Accessed November 18, 2015 at http://www.tandfonline.com/doi/full/10.3109/10408410903241444.
18. Centers for Disease Control and Prevention. (2014). About Parasites. Retrieved November 12, 2015 from http://www.cdc.gov/parasites/about.html.
19. Goodsell, D. S. (2008). Prions. RCSB Protein Data Bank. doi: 10.2210/rcsb_pdb/mom_2008_5. Retrieved November 12, 2015 from http://www.rcsb.org/pdb/101/motm.do?momID=101.
20. Moreno, J. A., Halliday, M., Molloy, C., Radford, H., Verity, N., Axten, J. M., et al. (2013). Oral treatment targeting the unfolded protein response prevents neurodegeneration and clinical disease in prion-infected mice. Science Translational Medicine, 5, 206ra138. doi: 10.1126/scitranslmed.3006767. Retrieved November 12, 2015 from http://stm.sciencemag.org/content/5/206/206ra138.full.
21. American Association of Critical-Care Nurses. (2012). Scope and standards of practice for the acute care nurse practitioner Vol. 2013. L. Bell (Ed.). Retrieved November 12, 2015 from http://www.aacn.org/wd/practice/docs/acnp-scope-and-standards.pdf.
22. Hernandez, J., Goeckner, B., & Wanzer, L. (2011). Perioperative pharmacology: Pharmacotherapeutics, pharmacokinetics, and pharmacodynamics. AORN Journal, 93, 259-269. Retrieved November 12, 2015 from http://www.aornjournal.org/article/S0001-2092(10)01296-2/fulltext.
23. Tsai, H. H., Lin, H. H., Pickard, A. S., Tsai, H. Y., & Mahady, G. B. (2012). Evaluation of documented drug interactions and contraindications associated with herbs and dietary supplements - a systematic literature review. International Journal of Clinical Practice, 66, 1056-1078. Retrieved November 12, 2015 at http://onlinelibrary.wiley.com/doi/10.1111/j.1742-1241.2012.03008.x/full.
24. Niebyl, J. R., & Simpson, J. L. (2008). Global library of women's medicine. Retrieved November 12, 2015 from http://www.glowm.com/section_view/heading/Teratology%20and%20Drugs%20in%20Pregnancy/item/96#5091
25. Niebyl, J. R., & Simpson, J. L. (2008). Global library of women's medicine. Retrieved November 12, 2015 from http://www.glowm.com/section_view/heading/Teratology%20and%20Drugs%20in%20Pregnancy/item/96#intro
26. Sorensen, H. T., Skriver, M. V., Pedersen, L., Larsen, H., Ebbesen, F., & Schonheyder, H. C. (2003). Risk of infantile hypertrophic pyloric stenosis after maternal postnatal use of macrolides. Scandian Journal of Infectious Disease, 35, 104-106. doi: 10.1080/0036554021000027010. Accessed November 14, 2015 at http://www.tandfonline.com/doi/abs/10.1080/0036554021000027010.
27. Harmon, T., Burkhart, G., & Applebaum, H. (1992). Perforated pseudomembranous colitis in the breast-fed infant. Journal of Pediatric Surgery, 27, 744-746. Accessed November 14, 2015 at http://www.jpedsurg.org/article/S0022-3468(05)80106-X/abstract.
28. Blumberg, H. M., Burman, W. J., Chaisson, R. E., Daley, C. L., Etkind, S. C., Friedman, L. N., et al. (2003). American thoracic society/centers for disease control and prevention/Infectious Diseases Society of America: Treatment of tuberculosis. American Journal of Respiratory and Critical Care Medicine, 167, 603-662. doi: 10.1164/rccm.167.4.603
29. Ilett, K. F., & Kristensen, J. H. (2005). Drug use and breastfeeding. Expert Opinion on Drug Safety, 4, 745-768. doi: 10.1517/14740338.4.4.745
30. Moorhead, A. M., Amir, L. H., O'Brien, P. W., & Wong, S. (2011). A prospective study of fluconazole treatment for breast and nipple thrush. Breastfeeding Review, 19, 25-29. Accessed November 14, 2015 at http://search.informit.com.au/documentSummary;dn=880757213362081;res=IELHEA.
31. Hoppe, J. E., & Hahn, H. (1996). Randomized comparison of two nystatin oral gels with miconazole oral gel for treatment of oral thrush in infants. Antimycotics study group. Infection, 24, 136-139. Accessed November 14, 2015 at http://link.springer.com/article/10.1007%2FBF01713319#page-1.
32. Arguin, P. M., & Tan, K. R. (2013). Infections diseases related to travel. Malaria. Centers for disease control and prevention. CDC health information for international travel 2014. New York: Oxford University Press.
33. Noti, A., Grob, K., Biedermann, M., Deiss, U., & Bruschweiler, B. J. (2003). Exposure of babies to c15-c45 mineral paraffins from human milk and breast salves. Regulatory Toxicology and Pharmacology, 38, 317-325.
34. Workowski, K. A., & Berman, S. M. (2006). Sexually transmitted diseases treatment guidelines, 2006. MMWR: Recommendations and Reports, 55, 1-94.
35. Correa, N., Opler, L. A., Kay, S. R., & Birmaher, B. (1987). Amantadine in the treatment of neuroendocrine side effects of neuroleptics. Journal of Clinical Psychopharmacology, 7, 91-95. Accessed November 14, 2015 at http://www.researchgate.net/publication/20272497_Amantadine_in_the_Treatment_of_Neuroendocrine_Side_Effects_of_Neuroleptics.
36. de Vincenzi, I. (2011). Triple antiretroviral compared with zidovudine and single-dose nevirapine prophylaxis during pregnancy and breastfeeding for prevention of mother-to-child transmission of hiv-1 (kesho bora study): A randomised controlled trial. Lancet Infectious Diseases, 11, 171-180. doi: 10.1016/s1473-3099(10)70288-7. Accessed November 14, 2015 at http://www.thelancet.com/journals/laninf/article/PIIS1473-3099(10)70288-7/abstract.
37. Bae, W. H., Wester, C., Smeaton, L. M., Shapiro, R. L., Lockman, S., Onyait, K., et al. (2008). Hematologic and hepatic toxicities associated with antenatal and postnatal exposure to maternal highly active antiretroviral therapy among infants. AIDS, 22, 1633-1640. doi: 10.1097/QAD.0b013e328307a029 Accessed November 14, 2015 at http://journals.lww.com/aidsonline/pages/articleviewer.aspx?year=2008&issue=08200&article=00014&type=abstract.
38. Dryden-Peterson, S., Shapiro, R. L., Hughes, M. D., Powis, K., Ogwu, A., Moffat, C., et al. (2011). Increased risk of severe infant anemia after exposure to maternal haart, botswana. Journal of Acquired Immune Deficiency Syndromes, 56, 428-436. doi: 10.1097/QAI.0b013e31820bd2b6. Accessed November 14, 2015 at http://www.medscape.com/viewarticle/740712.
39. Gleckman, R. (1995). Antibiotic concerns in the elderly: A clinician's perspective. Infectious Disease Clinics of North America, 9, 575-590.
40. Millan, J., & Gleckman, R. (1997). Selecting the right antibiotics for elderly patients. Journal of Critical Illness, 12, 590-598.
41. Lin, R. Y. (1992). A perspective on penicillin allergy. Archives of Internal Medicine, 152, 930-937. Accessed November 14, 2015 at http://archinte.jamanetwork.com/article.aspx?articleid=616219.
42. Calandra, G., Lydick, E., Carrigan J., Weiss, L., & Guess, H. (1988). Factors predisposing to seizures in seriously ill infected patients receiving antibiotics: Experience with imipenem/cilastatin. American Journal of Medicine, 84, 911-918.
43. Krau, S. D. (2013). Cytochrome p450, part 1: What nurses really need to know. Nursing Clinics of North America, 48, 671-680. Accessed November 16, 2015 at http://www.sciencedirect.com/science/article/pii/S0029646513000893.
44. Lister Hill National Center for Biomedical Communications. (2013, 2013-12-03). What is pharmacogenomics? Retrieved November 16, 2015 from http://ghr.nlm.nih.gov/handbook/genomicresearch/pharmacogenomics
45. Centers for Disease Control and Prevention. (2013). Threat report 2013 | antimicrobial resistance | CDC. Accessed November 16, 2015 at http://www.cdc.gov/drugresistance/pdf/ar-threats-2013-508.pdf
46. Iverson Genetics. (2013). Dme genotype panel. from http://www.iversongenetics.com/dme-genotype.html
47. Gillette, J. R. (1973). Overview of drug-protein binding. Annals of the New York Academy of Sciences, 226, 6-17. doi: 10.1111/j.1749-6632.1973.tb20464.x
48. Schulte, U. (2008). Protein complexes – challenges and opportunities for drug discovery Retrieved November 19, 2013
49. Ciccone, C. D. (1995). Basic pharmacokinetics and the potential effect of physical therapy interventions on pharmacokinetic variables. Physical Therapy, 75, 343-351.
50. Dynamed. (2010, September 24). Short-acting antibiotics for 5 days might be less effective than longer course antibiotic treatments for children with aom. Retrieved 11/20/2013, 2013, from https://

dynamed.ebscohost.com/about/weekly-update/archived-updates/short-acting-antibiotics-5-days-might-be-less-effective-longer-
51. Hussar, D. A. (2013). Efficacy and safety: Concepts in pharmacotherapy: Merck manual professional. Merck Manual. Retrieved November 17, 2015, from http://www.merckmanuals.com/professional/clinical_pharmacology/concepts_in_pharmacotherapy/efficacy_and_safety.html?qt=clinical%20decision%20making&alt=sh
52. AIDS Info - National Institutes of Health. (2015). Education Materials - Therapeutic index. Accessed November 17, 2015 at https://aidsinfo.nih.gov/education-materials/glossary/865/therapeutic-index.
53. Waldman, S. A. (2002). Does potency predict clinical efficacy? Illustration through an antihistamine model. Annals of Allergy, Asthma & Immunology, 89, 7-11; quiz 11-12, 77. doi: 10.1016/s1081-1206(10)61904-7. Accessed November 17, 2015 at http://www.researchgate.net/publication/11239845_Does_potency_predict_clinical_efficacy_Illustration_through_an_antihistamine_model.
54. Moroney, A. C. (2013). Drug-receptor interactions: Pharmacodynamics: Merck manual professional. Retrieved November 17, 2015, from http://www.merckmanuals.com/professional/clinical_pharmacology/pharmacodynamics/drug%E2%80%93receptor_interactions.html
55. Lambert, D. (2004). Drugs and receptors. Continuing Education in Anaesthesia, Critical Care & Pain, 4, 181-184. doi: 10.1093/bjaceaccp/mkh049
56. State Key Laboratory for Molecular Virology and Genetic Engineering. (2015). Vfdb: Virulence factors database. Retrieved November 18, 2015, from http://www.mgc.ac.cn/VFs/
57. Todar, K. (2013). Mechanisms of bacterial pathogenicity. Retrieved November 18, 2015, from http://textbookofbacteriology.net/pathogenesis.html
58. Todar, K. (2013). Bacterial protein toxins. Retrieved November 18, 2015, from http://textbookofbacteriology.net/proteintoxins.html
59. Bennet J, Dolin R, Blaser M. (2015). Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases. Retrieved November 18, 2015, from https://books.google.com/books?id=BseNCgAAQBAJ&pg=PA2874&lpg=PA2874&dq=Principles+and+Practice+of+Infectious+Diseases++introduction+to+mycoses&source=bl&ots=0JJDu9aaS_&sig=OETAO5DYytb550ZNOgWHK9ZesHw&hl=en&sa=X&ved=0CF4Q6AEwCWoVChMIoN7J8ZybyQIVj6WICh19XgoQ#v=onepage&q=Principles%20and%20Practice%20of%20Infectious%20Diseases%20%20introduction%20to%20mycoses&f=false
60. Creighton University School of Medicine. (no date listed). Bacteria table. Accessed November 18, 2015 at https://medschool.creighton.edu/fileadmin/user/medicine/MMI/Files/Bacteria_Table.pdf.
61. Goldsmith, C. S., Ksiazek, T. G., Rollin, P. E., Comer, J. A., Nicholson, W. L., Peret, T. C., et al. (2013). Cell culture and electron microscopy for identifying viruses in diseases of unknown cause. Emerging Infectious Diseases, 19, 886-891. doi: 10.3201/eid1906.130173. Accessed November 18, 2015 at http://wwwnc.cdc.gov/eid/article/19/6/13-0173_article.
62. Lab Tests Online. (2013, 11/7/2012). Fungal tests: The test. from http://labtestsonline.org/understanding/analytes/fungal/tab/test
63. Centers for Disease Control and Prevention. (2014). CDC - Parasites - about parasites. Accessed November 18, 2015 at http://www.cdc.gov/parasites/about.html
64. National Institutes of Health. (2011). Media availability: Nih study describes fast, sensitive blood test for human prion disease. Accessed November 18, 2015 at http://www.niaid.nih.gov/news/newsreleases/archive/2011/Pages/prionBloodTest.aspx.
65. Dr. Hani. (2010). History of antibiotics. Retrieved November 18, 2015 from http://explorable.com/history-of-antibiotics
66. Fox, A. (2015). Antibiotics that affect the cell envelope. Retrieved November 18, 2015, from http://www.microbiologybook.org/fox/antibiotics1.htm
67. Allen, J. (2013). The threat of antibiotic resistance. Geriatric Nursing, 34, 519-520. doi: http://dx.doi.org/10.1016/j.gerinurse.2013.10.007
68. Irwin, R. S. (2006). Introduction to the diagnosis and management of cough: Accp evidence-based clinical practice guidelines. Chest, 129, 25S - 27S. Accessed November 18, 2015 at http://journal.publications.chestnet.org/article.aspx?articleID=1084233.
69. Lieberthal, A. S., Carroll, A. E., Chonmaitree, T., Ganiats, T. G., Hoberman, A., Jackson, M. A., et al. (2013). The diagnosis and management of acute otitis media. Pediatrics, 131, e964-999. doi: 10.1542/peds.2012-3488. Accessed November 18, 2015 at http://pediatrics.aappublications.org/content/early/2013/02/20/peds.2012-3488.
70. Centers for Disease Control and Prevention. (2015). Antibiotic Resistance Questions and Answers. Accessed November 18, 2015 at http://www.cdc.gov/getsmart/community/about/antibiotic-resistance-faqs.html.
71. Barber A et al. (2013). Urinary Tract Infections: Current and Emerging Management Strategies. Clinical Infectious Diseases. Accessed November 19, 2015 at http://cid.oxfordjournals.org/content/57/5/719.full.pdf+html.
72. Daniel J Cameron, Lorraine B Johnson & Elizabeth L Maloney (2014) Evidence assessments and guideline recommendations in Lyme disease: the clinical management of known tick bites, erythema migrans rashes and persistent disease, Expert Review of Anti-infective Therapy, 12:9, 1103-1135. Accessed November 18, 2015 at http://www.tandfonline.com/doi/l/10.1586/14787210.2014.940900#aHR0cDovL3d3dy50YW5kZm9ubGluZS5jb20vZG9pL3BkZi8xMC4xNTg2LzE0Nzg3MjEwLjIwMTQuOTQwOTAwQEBAMA==
73. Shulman, S. T., Bisno, A. L., Clegg, H. W., Gerber, M. A., Kaplan, E. L., Lee, G., et al. (2012). Clinical practice guideline for the diagnosis and management of group a streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. Clinical Infectious Disease, 55, 86-102. doi: 10.1093/cid/cis629. Accessed November 20, 2015 at http://cid.oxfordjournals.org/content/early/2012/09/06/cid.cis629.full.pdf+html.
74. Drugs.com. (2015). Complete penicillin g information from drugs.Com. Accessed November 20, 2015 at http://www.drugs.com/ppa/penicillin-g.html
75. Archer, G. L., & Polk, R. E. (Eds.). (1998). Treatment and prophylaxis of bacterial infections (14th ed.): McGraw-Hill, Inc (Health Professions Division).
76. Epocrates Online. (2013). Gentamicin black box warnings - epocrates online. Retrieved November 21, 2015, from https://online.epocrates.com/u/10b104/gentamicin/Black+Box+Warnings
77. Drugs.com. (2013). Ciprofloxacin official fda information, side effects and uses. Retrieved November 21, 2015, from http://www.drugs.com/pro/ciprofloxacin.html
78. Epocrates Online. (2013). Isoniazid entire monograph - epocrates online. Retrieved November 21, 2015, from https://online.epocrates.com/u/10a239/isoniazid
79. Epocrates Online. (2013). Amphotericin b deoxycholate black box warnings - epocrates online. Retrieved November 23, 2015 from https://online.epocrates.com/u/10b91/amphotericin+B+deoxycholate/Black+Box+Warnings
80. World Health Organization. (2014). Who | influenza (seasonal). WHO. Retrieved December 1, 2015, from http://www.who.int/mediacentre/factsheets/fs211/en/
81. World Health Organization. (2013). Who | sexually transmitted infections (stis). WHO. Retrieved December 1, 2015, from http://www.who.int/mediacentre/factsheets/fs110/en/
82. World Health Organization. (2015). Who | hepatitis c. WHO. Retrieved December 1, 2015, from http://www.who.int/mediacentre/factsheets/fs164/en/
83. World Health Organization. (2015). Who | hepatitis b. WHO. Retrieved December 1, 2015, from http://www.who.int/mediacentre/factsheets/fs204/en/
84. World Health Organization. (2015). Who | hepatitis e. WHO. Retrieved December 1, 2015, from http://www.who.int/mediacentre/factsheets/fs280/en/
85. World Health Organization. (2015). Who | hiv/aids. WHO. Retrieved December 1, 2015, from http://www.who.int/mediacentre/factsheets/fs360/en/
86. Epocrates, O. (2015). Lamivudine entire monograph - epocrates online. Retrieved December 1, 2015, from https://online.epocrates.com/u/10a703/lamivudine
87. Epocrates Online. (2015). Zidovudine entire monograph - epocrates online. Retrieved December 1, 2015, from https://online.epocrates.com/u/10a1182/zidovudine
88. Lazarou, J., Pomeranz, B. H., & Corey, P. N. (1998). Incidence of adverse drug reactions in hospitalized patients: A meta-analysis of prospective studies. JAMA, 279, 1200-1205. Accessed December 1, 2015 at http://jama.jamanetwork.com/article.aspx?articleid=187436.
89. Choudhary, A. K., Nivedhitha, S., Radhakrishna, L., Tirumalaikolundusubrimnian, P., & Manicvasagam, S. (2013). Perception of adverse drug reaction among doctors, nurses and pharmacists of a tertiary care rural teaching hospital. The Internet Journal of Pharmacology, 12. Accessed December 1, 2015 at http://ispub.com/IJPHARM/12/1/1566.
90. Buppert, C. (2011). 10 habits to adopt to avoid prescribing errors. Journal for Nurse Practitioners, 7, 600-601. Accessed December 1, 2015 at http://www.medscape.com/viewarticle/746952.
91. Christian, S., Dower, C., & O'Neil, E. (2007). Chart overview of nurse practitioner scopes of practice in the United States (pp. 8): Center for the Health Professions University of California, San Francisco. Accessed December 1, 2015 at http://www.health.state.mn.us/healthreform/workforce/npcomparison.pdf.
92. Pharmacist's Letter. (2010). Antibiotic and antifungal use during pregnancy and breastfeeding. Accessed November 14, 2015 at http://pharmacistsletter.therapeuticresearch.com/pl/ArticleDD.aspx?cs=&s=PL&pt=6&fpt=31&dd=250607&pb=PL&cat=4322#dd.
93. International Society of Ethnopharmacology. (2015). About Us. Accessed November 14, 2015 at http://www.ethnopharmacology.org/ISE_about_us.htm.
94. Rosenbaum, S. (2011). Basic Pharmacokinetics and Pharmacodynamics. Wiley (New Jersey). Accessed November 17, 2015 at http://www.amazon.com/Basic-Pharmacokinetics-Pharmacodynamics-Integrated-Simulations/dp/0470569069.
95. Barber P, Robertson D. (2012). Essentials of Pharmacology for Nurses. McGraw-Hill. Accessed November 18, 2015 at https://books.google.com/books?id=N2FFBgAAQBAJ&pg=PA55&lpg=PA55&dq=referring+to+the+range+between+the+dose+necessary+to+inhibit+or+destroy+the+bacteria+and+the+dose+at+which+our+own+cells+are+harmed&source=bl&ots=zM8VHma0Cf&sig=iiW3X5tyI3ezXy7HnzaRRCszb6g&hl=en&sa=X&ved=0CBwQ6AEwAGoVChMIutyRsaObyQIVSC2ICh1QuQlI.#v=onepage&q=referring%20to%20the%20range%20between%20the%20dose%20necessary%20to%20inhibit%20or%20destroy%20the%20bacteria%20and%20the%20dose%20at%20which%20our%20own%20cells%20are%20harmed&f=false.
96. Centers for Disease Control and Prevention. (2015). Bronchitis (Chest Cold).Accessed November 18, 2015 at http://www.cdc.gov/getsmart/community/for-patients/common-illnesses/bronchitis.html.
97. Fayyaz J. (2015). Bronchitis. Accessed November 18, 2015 at http://emedicine.medscape.com/article/297108-overview#showall.
98. Vestbo J, et al. (2013). Global Strategy for the Diagnosis, Management, and Prevention of Chronic Obstructive Pulmonary Disease. American Journal of Respiratory and Critical Care Medicine, Vol.187, No.4(2013), pp. 347-365. Accessed November 18, 2015 at http://www.atsjournals.org/doi/full/10.1164/rccm.201204-0596PP#.Vk0xiBCrRE4.
99. Stevens D et al. (2014). Practice Guidelines for the Diagnosis and Management of Skin and Soft Tissue Infections: 2014 Update by the Infectious Diseases Society of America. Clinical Infectious Diseases. Accessed November 18, 2015 at http://cid.oxfordjournals.org/content/early/2014/06/14/cid.ciu296.full.pdf+html.
100. Preston S, Drusano G. (No date given). Penicillins. Accessed November 18, 2015 at http://www.antimicrobe.org/d24.asp.
101. Lumibyte. (no date given). Antibiotic action and resistance: Inhibition of Cell Wall Synthesis. Accessed November 20, 2015 at http://lumibyte.eu/medical/antibiotic-action-inhibition-of-cell-wall-synthesis/.
102. Drugs.com. (2015). Ampicillin. Accessed November 20, 2015 at http://www.drugs.com/ppa/ampicillin.html.
103. Moser Woo T, Robinson M. (2015). Pharmacotherapeutics for Advanced Practice Nurse Prescribers, Fourth Edition. F. A. Davis Company. Accessed November 20, 2015 at https://books.google.com/books?id=2Q5hCgAAQBAJ&pg=PA708&lpg=PA708&dq=pharmacokinetic+cephalosporins+change+during+pregnancy,+tending+toward+shorter+half-lives,+lower+serum+concentrations,+and+larger+volumes+distributed+increased+clearance+of+the+drug&source=bl&ots=m3J7xaKeOE&sig=As6nMfmADXhiraRY-7c8DkxguRk&hl=en&sa=X&ved=0CBwQ6AEwAGoVChMI75mJtcibyQIVxS6ICh1CDAdv#v=onepage&q=pharmacokinetic%20cephalosporins%20change%20during%20pregnancy%2C%20tending%20toward%20shorter%20half-lives%2C%20lower%20serum%20concentrations%2C%20and%20larger%20volumes%20distributed%20increased%20clearance%20of%20the%20drug&f=false.
104. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Cephalosporins. Accessed November 20, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/cephalosporins.
105. Drugs.com. (2015). Cefazolin. Accessed November 20, 2015 at http://www.drugs.com/ppa/cefazolin.html.
106. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Carbapenems. Accessed November 21, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/carbapenems.
107. Drugs.com. (2015). Imipenem/cilastatin. Accessed November 21, 2015 at http://www.drugs.com/ppa/imipenem-cilastatin.html.
108. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Vancomycin. Accessed November 21, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/vancomycin.
109. Drugs.com. (2015). Vancomycin. Accessed November 21, 2015 at http://www.drugs.com/ppa/vancomycin.html.
110. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Tetracyclines. Accessed November 21, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/tetracyclines.
111. Drugs.com. (2015). Tetracycline. Accessed November 21, 2015 at http://www.drugs.com/ppa/tetracycline-hydrochloride.html.
112. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Macrolides. Accessed November 21, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/macrolides.
113. Drugs.com. (2015). Erythromycin. Accessed November 21, 2015 at http://www.drugs.com/ppa/erythromycin.html.
114. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Aminoglycosides. Accessed November 21, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/aminoglycosides.
115. Drugs.com. (2015). Gentamicin. Accessed November 21, 2015 at http://www.drugs.com/ppa/gentamicin.html.
116. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Fluoroquinolones. Accessed November 21, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/fluoroquinolones.
117. Drugs.com. (2015). Ciprofloxacin. Accessed November 21, 2015 at http://www.drugs.com/ppa/ciprofloxacin.html.
118. Schlecht H, Bruno C. (2015). Merck Manual, Professional Version: Trimethoprim and Sulfamethoxazole. Accessed November 22, 2015 at http://www.merckmanuals.com/professional/infectious-diseases/bacteria-and-antibacterial-drugs/trimethoprim-and-sulfamethoxazole.
119. Drugs.com. (2015). Trimethoprim and Sulfamethoxazole. Accessed November 22, 2015 at http://www.drugs.com/ppa/trimethoprim-sulfamethoxazole-co-trimoxazole.html.

120. Herchline T. (2015). Tuberculosis Medication. Medscape. Accessed November 22, 2015 at http://emedicine.medscape.com/article/230802-medication#showall.
121. Drugs.com. (2015). Isoniazid. Accessed November 21, 2015 http://www.drugs.com/ppa/isoniazid-isonicotinic-acid-hydrazide-inh.html.
122. Centers for Disease Control and Prevention. (2003). MMWR Morbidity and Mortality Weekly Report: Treatment of Tuberculosis.Vol 52 No RR-11. June 20, 2003. Accessed November 22, 2015 at http://www.cdc.gov/mmwr/pdf/rr/rr5211.pdf.
123. Drugs.com. (2015). Amphotericin B. Accessed November 24, 2015 at http://www.drugs.com/ppa/amphotericin-b.html.
124. van Boxtel C, Santoso B, Edwards IR. (2008). Drug Benefits and Risks – International Textbook of Clinical Pharmacology IOS Press. Accessed November 26, 2015 at https://books.google.com/books/about/Drug_Benefits_and_Risks.html?id=xQqVbRqA2N8C&printsec=frontcover&source=kp_read_button#v=onepage&q&f=false.
125. Drugs.com. (2015). Fluconazole. Accessed November 26, 2015 at http://www.drugs.com/ppa/fluconazole.html.
126. Drugs.com. (2015). Nystatin. Accessed November 27, 2015 at http://www.drugs.com/ppa/nystatin.html.
127. Epocrates. (2015). Nystatin topical entire monograph - epocrates online. Retrieved November 27, 2015, from https://online.epocrates.com/drugs/343010/nystatin-topical/monograph.
128. Drugs.com. (2015). Chloroquine. Accessed November 28, 2015 at http://www.drugs.com/ppa/chloroquine.html.
129. Epocrates. (2015). Chloroquine topical entire monograph - epocrates online. Retrieved November 28, 2015, from https://online.epocrates.com/drugs/172/chloroquine-phosphate.
130. Baron S. (1996). Medical Microbiology. 4th edition: Chapter 83: Malaria. Galveston (TX): University of Texas Medical Branch at Galveston. Accessed November 28, 2015 at http://www.ncbi.nlm.nih.gov/books/NBK8584/
131. Centers for Disease Control and Prevention. (2014). About Parasites. Accessed November 28, 2015 at http://www.cdc.gov/parasites/about.html.
132. Food and Drug Administration. (No date given). Bad Bug Book: Handbook of Foodborne Pathogenic Microorganisms and Natural Toxins. Accessed November 28, 2015 at http://www.fda.gov/downloads/Food/FoodborneIllnessContaminants/UCM297627.pdf.
133. Centers for Disease Control and Prevention. (2015). Treatment of Malaria: Guidelines For Clinicians (United States). Part 2: General Approach to Treatment and Treatment of Uncomplicated Malaria. Accessed November 28, 2015 at http://www.cdc.gov/malaria/diagnosis_treatment/clinicians2.html.
134. Centers for Disease Control and Prevention. (2013). Parasites – Balantidiasis (also known as Balantidium coli infection). Accessed November 30, 2015 at http://www.cdc.gov/parasites/balantidium/.
135. Drugs.com. (2015). Metronidazole. Accessed November 30, 2015 at http://www.drugs.com/ppa/metronidazole.html.
136. Health Assist. (2014). Herpes Simplex Virus: Transmission and Transmissibility. Accessed December 1, 2015 at http://www.healthassist.net/conditions/herpes.shtml.
137. Drugs.com. (2015). Acyclovir. Accessed December 1, 2015 at http://www.drugs.com/ppa/acyclovir.html.
138. Centers for Disease Control and Prevention. (2015). Weekly U.S. Influenza Surveillance Report. Accessed December 1, 2015 at http://www.cdc.gov/flu/weekly/.
139. Drugs.com. (2015). Oseltamivir. Accessed December 1, 2015 at http://www.drugs.com/ppa/oseltamivir-phosphate.html.
140. Drugs.com. (2015). Lamivudine. Accessed December 1, 2015 at http://www.drugs.com/ppa/lamivudine-3tc.html.
141. Drugs.com. (2015). Zidovudine. Accessed December 1, 2015 at http://www.drugs.com/ppa/zidovudine-azidothymidine-azt-compound-s.html.

BUGS AND DRUGS: PHARMACOLOGY OF INFECTIOUS DISEASE REVIEW

Final Examination Questions

Select the best answer for questions 1 through 10 and mark you answers on the Final Examination Answer Sheet found on page 141 or complete your test online at **nursing.elitecme.com**.

1. Criteria for choosing an effective drug for a disorder include:
   a. Asking the patient what drug they think would work best for them.
   b. Consulting nationally recognized guidelines for disease management.
   c. Prescribing medications that are available as samples before writing a prescription.
   d. Following U.S. Drug Enforcement Administration (DEA) guidelines for prescribing.

2. Nosocomial, or hospital-acquired, infections are a leading cause of morbidity and mortality in the United States. Which of the following is an all too commonly occurring nosocomial infection?
   a. Clostridium difficile.
   b. Herpes simplex.
   c. Toxoplasma gondii.
   d. Cryptococcus neoformans.

3. Parasites are primarily a disease of impoverished countries and rarely infect individuals in the United States; however infections do occur. One of the most common parasitic infections occurring in the United States is:
   a. Candida species.
   b. Malaria.
   c. Typhoid fever.
   d. Giardia species.

4. When determining drug treatment the NP prescriber should:
   a. Always use evidence-based guidelines.
   b. Individualize the drug choice for the specific patient.
   c. Rely on his or her experience when prescribing for complex patients.
   d. Use the newest drug on the market for the condition being treated.

5. The nurse practitioner chooses to give cephalexin every 8 hours based on knowledge of the drug's:
   a. Propensity to go to the target receptor.
   b. Biological half-life.
   c. Pharmacodynamics.
   d. Safety and side effects.

6. Factors that place a patient at risk of developing an antimicrobial resistant organism include:
   a. Age older than 50 years.
   b. School attendance.
   c. Travel within the United States.
   d. Indiscriminate prescribing historically.

7. Tommy is a 10 year old with sinusitis. Treatment for a child with sinusitis is:
   a. Amoxicillin.
   b. Azithromycin.
   c. Cephalexin.
   d. Levofloxacin.

8. The drug of choice for treatment of primary or secondary syphilis is:
   a. Ceftriaxone IM.
   b. Penicillin G Potassium/Sodium.
   c. Oral azithromycin.
   d. Oral ciprofloxacin.

9. Jonathan has been diagnosed with strep throat and needs a prescription for an antibiotic. He says the last time he had penicillin he developed a red, blotchy rash. The appropriate antibiotic to prescribe would be:
   a. Penicillin VK, since his rash does not sound like a serious rash.
   b. Amoxicillin.
   c. Cefadroxil (Duricef).
   d. Erythromycin.

10. Tricia is a 24-year-old female with a urinary tract infection. She is healthy, afebrile, and her only drug allergy is sulfa, which gives her a rash. An appropriate first-line antibiotic choice for her would be:
    a. Azithromycin.
    b. Trimethoprim/sulfamethoxazole.
    c. Ceftriaxone.
    d. Ciprofloxacin.

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Disorders of the Endocrine System: Anatomy, Physiology, and Current Treatment Initiatives

10 Contact Hours

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Faculty

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Content reviewer
June D. Thompson, DrPH, MSN, RN, FAEN

Audience

The target audience for this education program is nurses who want to improve their knowledge of the endocrine system, disorders affecting it, and current treatment initiatives.

Purpose statement

To improve the nurses knowledge of the endocrine system, disorders affecting it, and current treatment initiatives.

Learning objectives

- Describe the anatomy and physiology of the endocrine system.
- Identify diseases and disorders of the endocrine system.
- Explain the pathophysiology of diseases and disorders of the endocrine system.
- Identify the diagnostic process for diseases and disorders of the endocrine system.
- Describe treatment initiatives for diseases and disorders of the endocrine system.
- Discuss nursing interventions for patients dealing with diseases and disorders of the endocrine system.

How to receive credit

- Read the entire course, which requires a 10-hour commitment of time.
- Depending on your state requirements you will asked to complete either:
  - An attestation to affirm that you have completed the educational activity.
  - OR completed the test and submit (a passing score of 70 percent is required).

    Note: Test questions link content to learning objectives as a method to enhance individualized learning and material retention.
- Provide required personal information and payment information.
- Complete the MANDATORY Self-Assessment and Course Evaluation.
- Print the Certificate of Completion.

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Disclosures

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Introduction

The endocrine system is quite complex and works in conjunction with the nervous system to maintain the delicate balance that ensures homeostasis. It is imperative for nurses to understand how the endocrine system functions and how alterations in functioning can lead to a number of pathologies. This education program provides information on the anatomy and physiology of the endocrine system, disorders of the endocrine system, treatment options for endocrine pathologies, and nursing considerations related to care of patients suffering from such pathologies.

ANATOMY AND PHYSIOLOGY OF THE ENDOCRINE SYSTEM

Components of the endocrine system

The endocrine system, in conjunction with the nervous system, is responsible for regulating and integrating the metabolic activities of the body. It consists of **endocrine glands, hormones,** and **receptors** [1,2].

The **endocrine glands** secrete specific hormones produced by the body to regulate cell and organ activity [3]. The primary glands of the endocrine system are the [1]:

- Pituitary gland.
- Thyroid gland.
- Parathyroid gland.
- Adrenal glands.
- Pancreas.
- Thymus.
- Pineal gland.
- Gonads (ovaries and testes).

The **hormones** that are secreted by the glands of the endocrine system are chemical messengers that transfer information from one set of cells to another to coordinate bodily functions [3]. Hormones cause changes in the metabolic activities in specific cells while nerve impulses cause gland secretion and muscle contraction. Hormonal action is rather slow, but of prolonged duration. The action of nerve impulses, on the other hand, is rapid but of short duration [2].

Anatomy and physiology alert! There are two types of hormones. Group 1 hormones are those that bind to intracellular receptors and are lipophilic (have a strong affinity for lipids) such as the steroid hormones. Group II hormones are those that bind to cell surfaces and are hydrophilic (readily absorbing or dissolving in water) such as polypeptides, glycoproteins, and catecholamines [3].

Receptors, the third component of the endocrine system, are protein molecules. Receptors bind with other molecules (such as hormones) to cause specific physiologic changes in target cells [1].

Negative and positive feedback
The endocrine system depends on both negative and positive feedback for its regulation. Negative feedback takes place when the rate of production of a particular product decreases as the concentration of that product increases. Negative feedback manages the rate of production to avoid accumulation of a particular product. For example, as the amount of some hormones reach the desired level, the body stops or reduces the rate of their production to avoid excessive accumulation [1,3].

Positive feedback occurs when the rate of production of a particular product increases as the concentration of that product increases. Positive feedback is less common in the body than negative feedback. An example of positive feedback is the secretion of oxytocin that stimulates uterine muscle contraction during labor. As labor progresses, pressure on the cervix continues to stimulate oxytocin release, which continues to stimulate uterine muscle contraction [3].

Pituitary gland

The pituitary gland (also referred to as the hypophysis) is generally considered to be the most important gland of the endocrine system. It is responsible for the production of the hormones that control many functions of other endocrine glands [1,2]. Because of its importance, the pituitary gland is often called the master gland [1].

The pituitary gland is quite small, only about the size of a pea. It is located on the inferior side of the brain in the sella turcica of the sphenoid bone and is attached to the hypothalamus of the brain by the pituitary stalk [3].

The pituitary gland is divided into two primary regions: the **anterior lobe (adenohypophysis) and the posterior lobe (neurohypophysis)** [1,3].

The **anterior pituitary** is the larger of the two regions and produces six hormones that are regulated by the hypothalamus [1,2,3]:

- **Growth hormone (GH):** GH, also referred to as somatotropin, stimulates growth of bone and tissue. It accelerates the rate of body growth by stimulating the uptake of amino acid by the cells of the body, increasing tRNA synthesis, and promoting protein synthesis [3]. Deficiency of GH in children causes growth failure. In adults, GH deficiency leads to difficulty maintaining adequate amounts of body fat, muscle, and bone mass. This hormone is also linked to emotional well-being [2].
- **Thyroid-stimulating hormone (TSH):** TSH, or thyrotropin, stimulates the synthesis and release of thyroid hormones from the thyroid gland [1,3]. A lack of thyroid hormones because of a defect in the pituitary gland or in the thyroid itself is called hypothyroidism [2].
- **Adrenocorticotropic hormone (ACTH)**: ACTH stimulates the adrenal cortex to produce and secrete various steroid hormones [2,3].
- **Follicle-stimulating hormone (FSH):** FSH stimulates the ovaries in women and the testes in men. In women, this hormone stimulates the growth of ovarian follicles, and in men, it stimulates the spermatogenesis [1,3].
- **Luteinizing hormone (LH):** In females, LH stimulates maturation of ovarian follicles, ovulation, and stimulation of the corpus luteum to secrete estrogens and progesterone. In males, LH stimulates interstitial cells to secrete testosterone [3].
- **Prolactin (PRL):** PRL targets the mammary glands. This hormone promotes mammary gland development and stimulates milk production in females. PRL is regulated by the production of placental hormones during pregnancy and stimulation of the nipples during lactation [3].

The posterior pituitary accounts for about 25% of the gland and is responsible for the secretion of antidiuretic hormone (ADH) and oxytocin [1,2,3].

- **Antidiuretic hormone (ADH):** ADH controls water loss by the kidneys. It facilitates water reabsorption in the distal convoluted tubules and collecting ducts of the kidneys. Controlled by negative feedback, ADH release is stimulated by dehydration and increased plasma osmolarity [3].
- **Oxytocin:** Oxytocin targets the uterus and mammary glands, causing uterine contractions during childbirth and milk production for lactation. Secretion of this hormone is controlled by positive feedback [2,3].

Anatomy and physiology alert! The hormones of the posterior pituitary are produced by the hypothalamus and transported via nerves to the pituitary gland, where they are stored [1,2].

Nursing consideration: The pituitary gland is generally considered to be the body's "master gland." Since it produces hormones that control many of the functions of other endocrine glands it is essential that nurses are able to differentiate among the hormones it produces and their effects. Assessment of the endocrine system, in many ways, begins with assessment of pituitary functioning.

Thyroid gland

The thyroid gland is located in the neck immediately below the larynx and partially in front of the trachea. The two lateral lobes of the thyroid are found on either side of the trachea and are joined by a narrow bridge of tissue called the isthmus. This "joining" gives the gland its characteristic butterfly shape [1,2,3].

The thyroid hormones regulate the metabolism of the body and help maintain normal blood pressure, heart rate, digestion, muscle tone, and reproductive functions. The thyroid gland also contributes to bone growth and nervous system development in children [1,2].

The two thyroid lobes function as one unit to produce triiodothyronine (T3), thyroxine (T4), and calcitonin [2]. TSH, which is produced by the pituitary gland, triggers secretion of T3 and T4, which are collectively known as thyroid hormone [1,3].

Thyroid hormone is the major metabolic hormone of the body. It regulates metabolism by increasing the speed of cellular respiration. T3 and T4, referred to collectively as thyroid hormone [3]:

- Increase metabolic rate.
- Increase consumption of oxygen.
- Increase glucose absorption.
- Increase body temperature.
- Affect growth and development.
- Improve the effects of the sympathetic nervous system.

Calcitonin is responsible for maintaining the calcium level of the blood. It accomplishes this by slowing the release of calcium from bone. Calcitonin secretion is controlled by the concentration of calcium in the fluid surrounding thyroid cells [1].

Parathyroid glands

The parathyroid glands are the smallest endocrine glands and are embedded in the posterior surface of the thyroid glands [1,3]. These glands work together as one entity and produce parathyroid hormone (PTH) [1].

The primary function of PTH is to regulate calcium balance in the blood by adjusting the rate at which calcium and magnesium ions are lost in the urine. PTH release is stimulated by decreased levels of calcium in the blood [3]. PTH increases plasma calcium levels by [3]:

- Stimulating the formation and action of osteoclasts. Osteoclasts cause the breakdown of bone tissue, which releases calcium from the bones into the blood.
- Triggering kidney tubules to increase calcium reabsorption.
- Facilitating increased calcium absorption from the gastrointestinal (GI) tract.

Anatomy and physiology alert! PTH also increases the transport of phosphate ions from the blood to urine for excretion from the body [1].

Adrenal glands

The two adrenal glands each lie embedded in adipose tissue on the top of each kidney [1, 3]. They are triangular in shape and consist of two distinct structures: the outer adrenal cortex and the inner adrenal medullar. These structures function as separate endocrine glands [1,3]. The majority of the adrenal glands is made up of the adrenal cortex, which has three zones [1]:

- **Zona glomerulosa:** This is the outermost zone of the adrenal cortex. It produces mineralocorticoids (aldosterone and deoxycorticosterone), which help maintain fluid balance by increasing the reabsorption of sodium [1,3].
- **Zona fasciculata:** This middle zone is the largest of the three zones. It produces glucocorticoids including cortisol (hydrocortisone), cortisone, and corticosterone. These glucocorticoids help regulate metabolism and assist in the body's efforts to resist stress. This zone also produces small amounts of androgen and estrogen [1,3].
- **Zona reticularis:** This is the innermost zone. It produces some sex hormones [1].

The adrenal medulla is the inner layer of the adrenal gland and functions as part of the sympathetic nervous system. The adrenal medulla produces two catecholamines: epinephrine and norepinephrine [1, 3]. These hormones increase the release of ACTH and TSH [3].

The pancreas

The pancreas is a triangular shaped organ located in the abdomen along the curve of the duodenum. It extends from behind the stomach to the spleen [1,3].

The pancreas performs both endocrine and exocrine functions. Its endocrine function is to secrete hormones. Its exocrine function is to secrete digestive enzymes. The pancreas is composed primarily of acinar cells, which regulate pancreatic exocrine function [1,2,3].

The islet cells or islets of Langerhans are the pancreatic endocrine cells. They occur in clusters of cells scattered among acinar cells. The islets contain alpha, beta, and delta cells that produce the following hormones [1,3]:

- **Glucagon:** Glucagon is produced by the alpha cells. Glucagon is a hormone that stimulates glycogenolysis, which raises the blood glucose level by causing the breakdown of glycogen to glucose. Glucagon helps maintain blood glucose levels during fasting or starvation [1,3].
- **Insulin:** Insulin is secreted by beta cells that are innervated by adrenergic fibers. Insulin lowers the blood glucose level by stimulating movement of blood glucose across cells, converting glucose to glycogen [1,3].
- **Somatostatin:** Somatostatin is secreted by delta cells and inhibits the release of GH, corticotrophin, and certain other hormones [1].

Nursing consideration: Nurses are aware that diabetes mellitus is a significant problem in the United States. Therefore, knowledge of the pancreas and how it functions is critical to the nurse's ability to provide appropriate nursing care to those diagnosed with diabetes.

The thymus

The thymus is found below the sternum and contains lymphatic tissue. The thymus, which reaches its maximum size at puberty and then begins to atrophy, secretes the hormones thymosin and thymopoietin. These hormones promote peripheral lymphoid tissue growth [1,3].

Anatomy and physiology alert! The major role of the thymus seems to be related to the immune system since it produces T cells, which are critical to cell-mediated immunity [1].

The pineal gland

The pineal gland is located in the middle of the brain at the back of the third ventricle. It produces melatonin, which is believed to regulate circadian rhythms as part of the sleep-wake cycle, body temperature, cardiovascular function, and reproduction [1,2].

Gonads

The gonads are the primary source of sex hormones and include the ovaries in females and the testes in males [1,2].

- **Ovaries:** The ovaries are paired, oval-shaped glands located on either side of the uterus. The ovaries produce eggs (ova) and steroidal hormones estrogen and progesterone. These hormones promote development and maintenance of female sex characteristics, regulate the menstrual cycle, maintain the uterus for pregnancy, and in conjunction with other hormones, prepare the mammary glands for lactation [1,2].
- **Testes:** The testes are paired structures located in the scrotum in males. The testes produce spermatozoa and the male sex hormone testosterone, which stimulates and maintains male sex characteristics and incites the male sex drive [1,2].

HORMONAL RELEASE MECHANISMS

There are four main mechanisms that control the release of hormones [1,2]:

Pituitary: Target gland axis

The pituitary gland constantly monitors hormone levels. If levels decrease, the pituitary responds by increasing trophic hormones, which trigger their target glands to increase production of specific hormones. Trophic hormones include [1]:

- Corticotropin (regulates adrenocortical hormones).
- TSH (regulates T3 and T4).
- LH (regulates gonadal hormones).

If levels are increased, secretion of trophic hormones decreases [1].

Hypothalamic-pituitary-target gland axis

The hypothalamus produces trophic hormones that regulate anterior pituitary hormones. Thus, the hypothalamus controls anterior pituitary hormones, which regulate the hormones of their specific target glands [1].

Chemical regulation

Endocrine glands that are not controlled by the pituitary gland might be controlled by substances that stimulate gland secretions.

An example of chemical regulation is that of blood glucose levels, which regulate glucagon and insulin release [1].

Nervous system regulation

The central nervous system (CNS) assists in the hormonal regulation by [1]:

- The hypothalamus directly controls the secretion of ADH and oxytocin.
- Nervous system stimuli (such as pain, stress, and some drugs) affect ADH levels.
- The autonomic nervous system (ANS) controls catecholamine secretion by the adrenal medulla.
- Stress stimulates sympathetic stimulation, which, in turn, triggers the pituitary to release corticotrophin.

EBP alert! In order to accurately assess the endocrine system nurses must be aware of age-related changes in this system. Research shows that normal age-related changes in the endocrine system include decreased progesterone production, a 50% reduction in serum aldosterone levels, and a 25% decrease in cortisol secretion rate. Also, in stressful situations, an elderly person's blood glucose level is higher and remains elevated for a longer period of time than that of a younger adult's [1].

DISEASES AND DISORDERS OF THE ENDOCRINE SYSTEM

Arguably, with the exception of diabetes and malignancies of the thyroid, diseases and disorders of the endocrine system are not particularly well understood or even well known by many health care professionals (HCPs).

This education program provides information about the pathophysiology, diagnosis, treatment, and nursing considerations of nonmalignant diseases and disorders of the endocrine system.

Hypopituitarism

Hypopituitarism is a complicated clinical syndrome of deficiency in pituitary hormone production. This can occur when disorders affect the pituitary gland, hypothalamus, or surrounding structures [4].

Partial hypopituitarism and complete hypopituitarism (panhypopituitarism) occur in both adults and children. In children, these conditions may lead to dwarfism and delayed puberty. The prognosis may be good with prompt recognition, appropriate replacement therapy, and correction of underlying causes[1].

Hypopituitarism alert! Panhypopituitarism is characterized by involvement of all pituitary hormones. However, it is more likely that only one or more pituitary hormones are involved. This leads to only isolated or partial hypopituitarism [4].

Pathophysiology

Hypopituitarism can impair some or all production of the hormones produced or stored by the pituitary. Here is a review of the hormones associated with the pituitary [1,4].

- The anterior pituitary secretes TSH, FSH, LH, GH, ACTH, and prolactin.
- The posterior pituitary stores and secretes two hormones produced by the hypothalamus: vasopressin (ADH) and oxytocin.

The hormones of the pituitary target specific glands to stimulate hormones produced and secreted by those glands (e.g., TSH stimulates the thyroid to produce T3 and T4). Therefore, the function of the pituitary is assessed not by measuring pituitary hormones in isolation, but by the functioning of the target glands [4].

Etiology

The most common cause of primary hypopituitarism in adults is pituitary tumor or adenomas. Additional causes include traumatic brain injury, infection, irradiation, partial or total hypophysectomy during surgery, chemical agents, and, more rarely, granulomatous disease such as tuberculosis [5]. In children, congenital defects, trauma, or other underlying conditions may lead to the disease [4,5].

Secondary hypopituitarism is caused by a deficiency of releasing hormones produced by the hypothalamus as a result of trauma, infection, tumor, or an unknown cause. Sometimes hypopituitarism may have no identifiable etiology [4,5].

Clinical presentation

Primary hypopituitarism usually presents as a rather slow, predictable pattern of hormonal failures as the effects of anterior pituitary destruction become evident [4,5]. Clinical presentation depends on the severity of the disease and the number of hormones that are deficient. Clinical features usually begin with hypogonadism due to decreased FSH and LH levels [4,5]. In adults, this causes menstrual cessation in females and impotence in males [4,5]. Other effects include infertility and decreased libido [4].

Growth hormone (GH) deficiency usually follows next. In adults, this leads to [5]:

- Osteoporosis.
- Decreased lean-to-fat body mass index.
- Adverse lipid changes.
- Subtle emotional changes including dysphoria (feelings of unhappiness).
- Lethargy.

Eventually failure of thyrotropin leads to decreased TSH levels and hypothyroidism, and, finally, adrenocorticotropic (decreased corticotropin levels) failure leads to adrenal insufficiency [5].

Additional symptoms of hypopituitarism in adults include [4,5]:

- Diabetes insipidus.
- Hypothyroidism as evidenced by fatigue, lethargy, sensitivity to cold, and menstrual problems.

- Adrenocortical insufficiency as evidenced by hypoglycemia, anorexia, nausea, abdominal pain, and orthostatic hypotension.

Hypopituitarism alert! Acute cortisol insufficiency (adrenal crisis) is a life-threatening condition and requires immediate treatment [4].

Nursing consideration: Pathophysiology of the pituitary gland can cause life-threatening conditions. For example acute cortisol insufficiency (adrenal crisis) is a life-threatening condition. Therefore, it is essential that nurses recognize the signs and symptoms of pituitary pathology and take intervene promptly to ensure patients receive the necessary treatment.

In children, lack of GH causes short stature, delayed growth, delayed puberty, and, possibly, dwarfism [4,5]. Dwarfism is not often evident at birth but initial signs and symptoms appear in the first few months of life, and by 6 months, growth retardation is apparent [5].

Children with dwarfism may appear chubby because of fat deposits in the lower trunk. They experience a delay in secondary tooth eruption and growth generally continues at less than half the normal rate, which can linger into the patient's 20s or 30s. The average height of these individuals is 4 feet (122 cm), and body proportions are normal [5].

If hypopituitarism occurs prior to puberty, the development of secondary sex characteristics is prevented [4,5]. In males, these include [4,5]:

- Lack of facial and body hair.
- Undersized penis, testes, and prostate gland.
- Failure to initiate and maintain an erection.

In females, these include [4,5]:

- Lack of pubic hair.
- Lack of axillary hair.
- Failure to develop mature breasts.
- Primary amenorrhea.

Panhypopituitarism causes a significant number of both physiological and mental problems including [4,5]:

- Psychosis.
- Lethargy.
- Bradycardia.
- Orthostatic hypotension.
- Anorexia.
- Anemia.

Tumors of the pituitary can cause headache, vision problems (even blindness), and hemianopia. Hypopituitarism related to infection or surgery causes fever, vomiting, hypotension, and hypoglycemia [5].

Hypopituitarism alert! Clinical signs and symptoms of hypopituitarism do not usually become apparent until 75% of the gland is destroyed [5].

EBP alert! Unfortunately, research shows that clinical signs and symptoms of hypopituitarism do not generally become apparent until 75% of the gland is destroyed [5]. So nurses must be aware of any conditions that can lead to hypopituitarism and be alert to any indication that such pathology exists.

Diagnosis and epidemiology

Hypopituitarism is a rare disorder. According to the National Institutes of Health (NIH), it affects less than 200,000 persons in the United States and has an international incidence of 4.2 cases per 100,000 annually [4].

In any suspected case of hypopituitarism it is essential to rule out organic, non-endocrine causes of short stature, decreased/delayed growth, and other presenting clinical manifestations. Thyroid function must be carefully evaluated to determine if, for example, decreased levels of thyroid hormone is related to dysfunction of the thyroid, pituitary, or hypothalamus [5,6].

Computed tomography (CT) scans or **magnetic resonance imaging (MRI)** are useful in determining the presence of tumor or other abnormal masses in the pituitary gland or hypothalamus. **Radioimmunoassay** may show decreased blood levels of pituitary hormones [5].

Diagnosis is confirmed by measuring levels of GH in the blood following administration of regular insulin to induce hypoglycemia or levodopa to induce hypotension. Administration of these drugs should stimulate increased secretion of GH. If GH hormones remain low, despite attempting stimulation by regular insulin and/or levodopa administration, GH deficiency is confirmed [5].

Treatment and nursing considerations

Replacement of hormones secreted by the pituitary's target glands is essential. Complete loss of all anterior pituitary hormones is fatal without treatment [5]. Treatment also involves treatment of any underlying cause, such as surgical removal of tumors.

Hormone replacement therapy may include the following medications:

- **Corticosteroids:** Corticosteroids such as hydrocortisone or prednisone are used to replace adrenal hormones that are not being produced because of ACTH deficiency. Corticosteroids are administered orally [5,7].
- **Levothyroxine:** Levothyroxine (brand names Synthroid, Levoxyl) is administered to replace thyroid hormone caused by low or deficient TSH production [7].
- **Sex hormones:** For patients of child-bearing age, sex hormone administration may be beneficial. These may include testosterone in men and estrogen or a combination of estrogen and progesterone in women. Testosterone is administered via injection or through the skin with a patch or gel. Estrogen and progesterone can be administered via pills, gel, or patches [7]. Gonadotropins (LH and FSH) can be administered by injection to trigger ovulation in women and sperm production in men [7].
- **Growth hormone:** GH replacement is recommended for children as well as adults. GH or somatropin is administered as daily subcutaneous injections of one of several recombinant deoxyribonucleic acid GHs. Administration is accompanied by monitoring of serum IGF-1 levels. In children, administration can produce more normal height. In adults, administration of a growth hormone may have some benefit but will not make adults taller [5,7].

There are a number of nursing considerations related to treatment of hypopituitarism, including [4, 5, 6, 7]:

- Emphasize the need for life-long hormone replacement. Assess knowledge by having patients and families explain why hormone replacement is necessary, consequences of not taking replacements prescribed, and any possible adverse effects and what to do about them. Have patients/families demonstrate how to accurately take prescribed medications.
- Emphasize the importance of keeping HCPs informed of any and all medications the patient is taking in addition to hormone replacement therapy. Explain that this includes not only prescription medications but OTC (OTC) medications, herbal supplements, vitamins, minerals, weight loss products, and other

supplements. Any or all of these products can interact with each other and have the potential to cause adverse side effects.
- Until hormone replacement therapy is complete, monitor patients for signs of thyroid deficiency (lethargy, bradycardia, dry skin and hair, and constipation), adrenal deficiency (weakness, orthostatic hypotension, fatigue, weight loss, and hypoglycemia), and deficiency of gonadotropins (decreased libido, apathy, and lethargy).
- Since anorexia can be a significant problem, initiate a dietary consult to help patients and families develop a diet that patients find appealing. Patients should be monitored for changes in weight.
- Since orthostatic hypotension is a possibility, teach the patient to move slowly when changing positions, especially when going from lying to sitting and sitting to standing.
- Instruct patients to wear a medical identification bracelet.
- Refer the families of children with dwarfism to mental health resources for counseling. This disorder can cause significant stress for patients and families.

Nursing consideration: Patient/family education is essential for proper management of hypopituitarism. In particular, the need for life-long hormone replacement must be emphasized. Meticulous education regarding hormone replacement is critical!

HYPERPITUITARISM

Emily is a registered nurse who works on a busy medical-surgical unit. She attends graduate school two evenings a week. Thanks to her busy schedule she has lost touch with many of her neighbors. As she prepares to leave for school one early-summer evening, she notices her next-door neighbor watering his lawn. As she waves hello she notices that his movements seem slow and painful. Feeling concerned, Emily stops to chat. To her surprise she notices that his facial features seem quite different compared to the last time she saw him. His face seems "bigger" and he seems to be sweating excessively even though the evening is actually rather cool. He tells her that he thinks he must be getting arthritis since his "joints ache." His voice seems deeper and huskier than Emily recalls, and he mentions that he has made an appointment with "my eye doctor since I don't see as well as I used to and I am getting awful headaches." Emily is concerned. She is currently studying endocrine disorders and wonders if her neighbor is suffering from hyperpituitarism.

Hyperpituitarism, also known as acromegaly and gigantism, is a chronic, progressive disease characterized by hormonal dysfunction and disturbing skeletal overgrowth [5]. It occurs when the pituitary gland produces excessive amounts of GH [5,8].

It is important to differentiate between acromegaly and gigantism. The defining difference is the age of persons experiencing pituitary overproduction. Acromegaly affects adults. In adults, the bones increase in size including those of the hands, feet, and face. In children, excessive growth hormone leads to gigantism characterized by exaggerated bone growth and abnormal increases in height [5,8].

Acromegaly occurs after closure of the epiphyseal (rounded end of long bones). This leads to thickening of the bones, transverse bone growth, and visceromegaly (enlargement of the internal abdominal organs) [5].

Giantism starts before epiphyseal closure and causes proportional excessive growth of all body tissues. As the disease advances, loss of other trophic hormones (e.g., TSH, LH, FSH, and corticotropin) may cause malfunction of their target organs [5].

Patient prognosis depends on the underlying cause of the disease. However, hyperpituitarism usually reduces life expectancy unless it is diagnosed in a timely fashion and prompt treatment is initiated [5].

Incidence and etiology

Acromegaly is a rare disorder that affects males and females equally, usually between the ages of 30 and 50. About three to four people per every million are diagnosed annually [5].

Giantism can affect infants as well as children, but, fortunately, it is a very rare disorder with only 100 reported cases to date. Affected patients may reach as much as three times the normal height for their age. Adults may reach a height of more than 80 inches [5].

In adults, the most common cause of excessive GH production is a tumor. Most of these tumors are benign adenomas of the pituitary gland. The tumors themselves secrete excessive amounts of GH leading to clinical signs and symptoms. Neurological signs and symptoms such as headache and vision disturbances are the result of a tumor pressing on brain tissue [5,8].

Occasionally, non-pituitary tumors can cause hyperpituitarism. For example, tumors of the lungs adrenal glands, or pancreas may secrete GH. In some cases, tumors may produce growth hormone-releasing hormone (GH-RH). This hormone stimulates the pituitary to produce more GH [8].

Signs and symptoms

Acromegaly develops slowly with early signs not readily apparent. It may take years for signs and symptoms to become evident [5,8].

Acromegaly alert! Since the disease develops so slowly some people may notice physical changes in appearance only by comparing old and current photographs [8].

One of the most common initial signs of acromegaly is enlargement of the hands and feet. Patients may complain that their shoe size has steadily increased and that their rings no longer fit [8].

Symptoms can vary among patients but some general characteristics are evident. Excessive secretion of GH causes [5,8]:
- Overgrowth of cartilage and connective tissue, which results in a characteristic hulking appearance, enlarged nose, enlarged feet, thickened lips, tongue, fingers, and ears, changes in the shape of the face such as a protruding lower jaw and brow, and wider spacing between the teeth.
- Laryngeal hypertrophy and enlargement of the paranasal sinuses, which causes the voice to sound deep, husky, and hollow.
- Irritability, hospitality, and a variety of mental health disturbances may occur.

The effects of prolonged GH secretion eventually include bowlegs, barrel chest, arthritis, osteoporosis, kyphosis, hypertension, glucose intolerance, diabetes mellitus, and arteriosclerosis. Patients are at risk for the development of premature cardiovascular disease, colon polyps, and colon cancer [5].

Additional signs and symptoms include [5, 8]:
- Coarse, oily, thick skin.
- Excessive diaphoresis and body odor.

- Fatigue.
- Muscle weakness.
- Severe snoring because of upper airway obstruction.
- Impaired vision.
- Headaches.
- Pain and limited joint movement.
- Menstrual cycle irregularities.
- Erectile dysfunction.
- Enlarged liver, heart, kidneys, spleen, and other internal organs.

Diagnosis

Diagnosis is based on patient history, presenting signs and symptoms, and the results of various blood tests. Fasting blood samples for GH and insulin-like growth factor-1 (IGF-I) are obtained. Elevated levels of these hormones suggest acromegaly. However, the results from random samples are not conclusive [5,8].

The definitive test for verifying acromegaly is GH suppression test [8]. Baseline GH and glucose levels are obtained. A prescribed dose of glucose is then administered, after which GH and glucose levels are drawn at 10, 60, and 120 minutes after glucose ingestion [9]. Under normal conditions glucose suppresses GH secretion. So if a glucose infusion does not suppress GH levels to below accepted normal values, and these results are accompanied by characteristic clinical signs and symptoms, a diagnosis of acromegaly is likely [5,8].

Acromegaly alert! Patients should not be emotionally or physically stressed when obtaining blood samples for the GH suppression test since stress can elevate GH levels [9].

Nursing consideration: Nurses should teach patients and their families about the importance of obtaining blood samples when the patient is relatively calm since physical and/or emotional stress can elevate GH levels. Such education can help the accuracy of test results!

Various imaging tests may also be performed to diagnosis acromegaly. Skull x-rays, CT scans, MRI, and arteriography are may be used to determine the presence and extent of pituitary lesions. X-rays of the bones can show bone thickening and osteoporosis [5, 8].

Treatment and nursing considerations

Treatment focuses on reducing GH production and decreasing the adverse effects of excessive amounts of GH. Surgical removal or reduction of a tumor is essential when severe pathophysiology is present.

Surgical removal of pituitary tumors is complex and should be performed by surgeons who have experience in this procedure. Most of these types of tumors are removed via transsphenoidal surgery. During this procedure the surgeon removes the tumor via the nose and sphenoid sinus [5,8]. Tumor removal can normalize GH production, relieve pressure on surrounding tissues, and eliminate signs and symptoms. However, it may not be possible to remove the entire tumor depending on its size and location. In these cases, additional treatment may be necessary [5,8].

Nursing consideration: Vital signs and neurological status must be carefully monitored following surgery. Alterations in levels of consciousness, vision disturbances, unequal pupil size, vomiting, elevated blood pressure, or decreasing pulse rate, should be reported immediately. These signs may indicate increased intracranial pressure as a result of intracranial bleeding or cerebral edema [5].

If tumor cells remain following surgery radiation therapy may be prescribed to destroy any remaining cells and to gradually reduce GH levels. However, it may take some time, even years, for radiation to cause noticeable improvement in the signs and symptoms of acromegaly [8].

Radiation may be administered in one of two ways [5,8]:

- **Conventional radiation therapy:** Conventional radiation therapy is usually administered over a 4- to 6-week period. Note that the full effect of this type of radiation therapy may not be achieved for as long as 10 or more years post-treatment.
- **Stereotactic radiosurgery:** Stereotactic radiosurgery is also known as Gamma Knife radiosurgery. A high dose of radiation directed at the tumor cells is administered in a single dose while limiting radiation exposure to surrounding normal cells. This type of radiation therapy may bring GH levels to within normal limits within 3 to 5 years.

Acromegaly alert! Administration of stereotactic radiosurgery requires an extremely high level of technical skill and is available at only a few U.S. health care facilities. The type of radiation therapy used depends on the size and location of remaining tumor cells and the IGF-I levels [8].

Medications may also be prescribed to lower production or block the action of GH and include the following agents [8]:

- **Somatostatin analogues:** These drugs (e.g., octreotide and lanreotide) are synthetic forms of the hormone somatostatin. They act by interfering with excessive secretion of GH and promoting reduction in GH levels. Patients are initially injected subcutaneously three times a day with a short-acting form of octreotide to identify any resulting side effects and to evaluate its effectiveness. If the medication is tolerated, a long-acting form is administered intramuscularly once a month. Lanreotide is administered subcutaneously once a month.
- **Dopamine agonists:** Dopamine agonists such as cabergoline and bromocriptine are taken orally and act by reducing GH and IGF-I levels. These drugs may also decrease tumor size.

Dopamine agonist alert! Dopamine agonists trigger compulsive behaviors in some patients [8].

- **GH antagonists:** Pegvisomant, a GH antagonist, acts by blocking the effects of GH on the body. Patients (or family members) are taught to administer the medication via subcutaneous injection. This drug can help reduce/relieve symptoms and normalize IGF-I levels but does not lower GH levels or reduce the size of the tumor.

Treatment alert! If GH levels can be maintained at less than 1 ng/ml and IGF-I levels at normal range for age and gender, life expectancy is restored to that of age-matched controls [5].

Nursing considerations focus on monitoring appropriate blood levels, signs and symptoms, and patient/family education. Some of these considerations include [5, 6]:

- Teach patients and families how to administer medications. Stress the importance of adhering to any medication regimen as prescribed. Have patients/families demonstrate their knowledge of proper medication administration by demonstrating how to administer/take medications and describing the medications' actions, side effects, and how to deal with and when to report side effects. Warn patients and families not to stop taking medications without HCP approval.
- Stress how important it is for patients not to add or eliminate any medications without the approval of their HCPs. Emphasize that this includes not only prescription medications but vitamins, herbal preparations, minerals, OTC medications, and any other supplement such as weight loss products.
- Advise patients and families that patients should wear a medical alert bracelet at all times.
- Emphasize the importance of life-long follow-up examinations. Tumors may reoccur and life-long evaluation of hormone therapy is necessary.

Nursing consideration: Teaching patients and families how to take medications is often the responsibility of nurses. Nurses must be sure to assess the patients'/families' knowledge regarding the patient's medications. Be sure not to ask questions that can be answered simply with either a "yes" or a "no." For instance if the nurse asks, "Do you know what side effects your medicine might cause?" the patient/family may simply answer "yes" to avoid admitting they don't understand or to just satisfy the nurse. Instead say something like, "Explain what side effects your medicine might cause and what you should do if they happen."

Diabetes insipidus

Mark is a 35-year-old marketing executive. Since he sits at a desk for the majority of his working hours he enjoys biking and hiking during his leisure time. One afternoon he takes a nasty fall from his bicycle while cycling with his two young sons. He strikes his head on the sidewalk and sustains what his physician describes as a mild concussion. Several days later Mark experiences an abrupt onset of needing to void frequently. His urine is dilute, and he voids as much as 30 L/day. He experiences extreme thirst, and suffers from severe lack of sleep since he must get up to void several times a night. After several days he becomes weak and dizzy. Mark's wife insists on taking him to the emergency department where he is diagnosed as having diabetes insipidus.

Diabetes insipidus is a disorder of water metabolism as the result of a deficiency of antidiuretic hormone (ADH), also called vasopressin [5,11].

There are two primary forms of diabetes insipidus: central diabetes insipidus and nephrogenic diabetes insipidus [10].

- **Central diabetes insipidus:** Also called neurogenic, pituitary, or neurohypophyseal, central diabetes insipidus is marked by a decreased secretion of ADH.
- **Nephrogenic diabetes insipidus:** Nephrogenic diabetes insipidus is characterized by a decreased ability to concentrate urine because of resistance to the action of ADH in the kidneys.

Diabetes insipidus alert! Nephrogenic diabetes insipidus is a rare congenital disturbance of water metabolism due to renal tubular resistance to ADH (vasopressin)[5].

Incidence and etiology

Diabetes insipidus may begin in childhood or early adulthood and is more common in males than in females. The disease is characterized by excessive urination and excessive thirst accompanied by significant fluid intake [5,11]. Incidence is slightly higher today than in the past, but it is still a rare disorder affecting one in 25,000 people [5].

Central diabetes insipidus is the result of [5,11]:

- Intracranial neoplastic tumors.
- Metastatic lesions.
- Surgical removal of the pituitary or other neurosurgery.
- Skull fracture.
- Head trauma.

Nephrogenically, diabetes insipidus occurs due to [5,11]:

- Infection.
- Granulomatous disease.
- Vascular lesions.

In some cases, the exact cause of the disease may not be able to be identified [5].

Nephrogenic diabetes insipidus is the result of a defect in the areas of the kidneys that reabsorb water back into the bloodstream. It is less common central diabetes insipidus [5,11].

Nephrogenic diabetes insipidus may also be due to [5,10]:

- An inherited disorder wherein boys inherit the abnormal gene on the X chromosome from their mothers.
- Renal disease.
- Effects of drugs such as lithium.
- Hypercalcemia.
- Hypokalemia.
- Hyperglycemia.
- Certain drugs such as Amphotericin B, Cidofovir, and Didanosine.

Diabetes insipidus alert! Gestational diabetes insipidus occurs during pregnancy when an enzyme produced by the placenta destroys the mother's ADH [5].

Pathophysiology

Under normal conditions ADH is manufactured in the hypothalamus and stored in the posterior pituitary gland. When serum osmolality increases and circulating volume decreases, ADH is released into the general circulation. ADH increases water permeability of the distal and collecting tubules of the kidneys. This leads to reabsorption of water and decreased serum osmolality and increased circulating volume. These changes cause the release of ADH to stop [11].

In diabetes insipidus, interference with ADH synthesis, transport, or release causes decreased amounts of ADH to be released from the pituitary [5]. Thus, this lack of ADH causes [5,11]:

- Decreased renal tubular permeability to water.
- Decreased water reabsorption.
- Polyuria (excessive urinary output).
- Decreased urine osmolality.
- Decreased specific gravity.
- Increased serum osmolality.
- Increased thirst (polydipsia).

Diagnosis

Diagnosis is based on history, signs and symptoms, and various diagnostic tests.

Characteristic signs and symptoms of diabetes insipidus include [5,11]:

- Abrupt onset of extreme polyuria generally between 4 to 6 L/day. However, urinary output may be as high as 30 L/day.
- Extreme thirst.
- Nocturia.
- Extreme fatigue as the result of lost sleep due to nocturia.
- Dehydration.
- Poor skin turgor.
- Muscle weakness.
- Constipation.
- Dizziness.
- Hypotension.

Symptoms usually have an abrupt onset, starting within one to days after surgery, skull fracture, or stroke. As cerebral edema or increased intracranial pressure is relieved, symptoms stop as quickly as they began [5].

A number of complications are associated with prolonged polyuria. These include [5,11]:

- Hypovolemia.
- Hyperosmolality.
- Circulatory collapse.
- Loss of consciousness.
- CNS damage.
- Bladder distension.
- Enlarged calyces.
- Hydroureter (distention of the ureter).
- Hydronephrosis (collection of urine in the kidney).

Various diagnostic tests may help in the diagnosis of diabetes insipidus. Urinalysis reveals [5,11]:

- Almost colorless urine.
- Low urine osmolality (50 to 200 mOsm/kg of water, less than that of plasma).
- Low specific gravity (less than 1.005).

Additional diagnostic study results that suggest diabetes insipidus include [5,11]:

- Serum osmolality of 300 mOsm/kg.
- Serum sodium of 147 mEq/L.

Dehydration (or water deprivation) test is performed to differentiate ADH deficiency from other types of polyuria by comparing urine osmolality after dehydration and after ADH administration [5,11]. The dehydration test procedure involves [5,11]:

- Baseline vital signs, weight, and urine and plasma osmolalities are obtained.
- Patients are deprived of fluids. They must be monitored to be sure that they do not drink any fluids.
- Urine output, body weight, urine osmolality, urine specific gravity, and plasma osmolality are measured hourly.
- Vital signs are monitored for the duration of the test to detect orthostatic hypotension.
- Fluids are withheld until patients lose 3% of their body weight, which indicates severe dehydration.
- When urine osmolality fails to increase in three consecutive hourly measurements, patients are given 5 units of aqueous vasopressin (ADH) subcutaneously.
- Hourly measurements of urinary output and urine specific gravity continue.

Diabetes insipidus is diagnosed if "the increase in urine osmolality after ADH administration exceeds nine percent [11, pg 261]."

Patients with pituitary diabetes insipidus have decreased urinary output and increased urine specific gravity. Patients with nephrogenic diabetes have no response to the vasopressin administration [5,11].

Plasma or urinary evaluation of ADH may also be performed. Fluid restriction or the infusion of hypertonic saline infusion are conducted to establish if the origin of the diabetes insipidus is the result of damage to the posterior pituitary gland (neurogenic) or failure of the kidneys to respond to ADH (nephrogenic). In neurogenic diabetes insipidus ADH levels are decreased. In nephrogenic diabetes insipidus ADH levels are elevated [11].

Treatment and nursing considerations

Prognosis for patients with diabetes insipidus is generally good, depending on the underlying cause [5,10]. Mild cases of diabetes insipidus may require no treatment other than fluid replacement. Severe cases require that the underlying cause be identified and corrected or treated satisfactorily. Until this is accomplished, various types of vasopressin or of a vasopressin stimulant are administered to control fluid balance and to prevent dehydration [5,11].

There are several medications that can be used to treat diabetes insipidus, including:

- **Aqueous vasopressin** is used as part of the initial management of diabetes following head trauma or neurological procedure. The drug is administered subcutaneously or intramuscularly several times a day because it is only effective for 2 to 6 hours [5,11].
- **Desmopressin acetate (DDAVP)** is a synthetic, long-acting vasopressin analogue that is effective for 8 to 20 hours. It is administered via nasal spray and is absorbed through the mucous membranes. DDAVP can also be given subcutaneously, intravenously, or orally in tablet form administered at bedtime or in divided doses [5,11].
- **Lypressin** is a synthetic vasopressin replacement. It is administered as a short-acting nasal spray. However, there are several side effects associated with the drug that can be problematic. These include nasal congestion, nasal irritation, ulceration of nasal passages, substernal tightness of the chest, coughing, and dyspnea with large doses. Additionally, the drug has a variable absorption rate [11].

Treatment alert! If nephrogenic diabetes insipidus is caused by medication, discontinuing the medication allows the kidneys to recover [5].

The prognosis is good for patients who have uncomplicated diabetes insipidus as long as they receive adequate fluid replacement. But the presence of a serious underlying cause (such as cancer) can alter the prognosis depending on how successful treatment initiatives prove to be [5,11].

Nursing care emphasizes meticulous monitoring of intake and output, patient safety, and patient/family education. It is essential to facilitate fluid intake to prevent severe dehydration. Patients must be weighed daily and vital signs monitored carefully. Nurses must also be alert for the development of signs of hypovolemic shock such as cool, clammy skin, anxiety, confusion, rapid breathing, and generalized weakness [5,11].

Nursing consideration: Patient/family education is very important. Nurses must teach the following patient safety actions and education initiatives including [5].

- Instruct patients/families that patients may be weak and/or dizzy. They should be helped to ambulate as needed and cautioned to change positions slowly, especially when moving from lying to sitting or standing positions.
- Provide, and teach patients/families to provide, meticulous skin and mouth care since skin and mucous membranes may become dry and cracked.

- Explain that constipation is a possibility. Encourage the addition of more high-fiber foods to the patient's diet.
- Teach patients/families how to monitor patients' intake and output.
- Instruct patients/families to report weight gain since this may indicate the need for a decrease in medication dosage.
- Teach patients/families to report any return of polyuria. This may indicate that the dosage of medication is too low.
- Teach patients to wear a medical alert bracelet.
- Instruct patients to carry their medication with them at all times.
- Explain the importance of adhering to prescribed medication regimens. As previously mentioned, instruct patients never to stop taking medication unless told to do so by their HCPs. They also need to be instructed to apprise their HCPs of any medications they are taking including OTC medications, herbs, vitamins, minerals, and weight loss products.
- Ask patients/families to demonstrate their knowledge of their medications by having them explain how to take medications, side effects, and what to do if side effects occur. Patients/families should demonstrate how to safely administer their medications.

Childhood hypothyroidism

Jack and Maura are the proud parents of a baby girl, their first child. Maura gave birth yesterday afternoon and is preparing for discharge. Her obstetrician and the baby's pediatrician enter her room. They explain that as part of the routine newborn screening program, Maura's baby has been evaluated for congenital hypothyroidism. Results of the screening, unfortunately, show that the baby has congenital hypothyroidism.

Reduced thyroid hormone secretion during the development of the fetus or in early infancy causes congenital (CH) or neonatal hypothyroidism (also referred to as infantile cretinism). If the disease is not recognized or not adequately treated, infants develop persistent jaundice, hoarse crying, and respiratory problems. Older children experience dystrophy of bones and muscles, stunted growth, and mental deficiencies [5].

Nursing consideration: Since unrecognized or inadequately treated congenital hypothyroidism can have serious consequences nurses must be able to recognize the problem and be able to provide appropriate family education. Nurses must also be sure that newborns are appropriately screened.

Incidence and etiology

There are several types of hypothyroidism that affect children, including:

- **Congenital hypothyroidism (CH):** Occurs when the thyroid gland fails to develop or function normally before birth [12].
- **Acquired hypothyroidism-autoimmune hypothyroidism:** Occurs as the result of an autoimmune disorder called chronic lymphocytic thyroiditis (CLT). In CLT the child's immune system "attacks" the thyroid gland, causing damage and reduced functioning. Patients who have other types of autoimmune diseases (most often insulin-dependent diabetes) are at higher risk for developing CLT. It is estimated that 20% to 30% of people with diabetes will develop CLT. Thus, annual screening for CLT is often a routine part of diabetes care [12].
- **Acquired hypothyroidism-iatrogenic hypothyroidism:** Occurs in people who have had their thyroid glands surgically removed or medically destroyed [12].

CH is a common problem, occurring in about one in every 2,500 to 3,000 babies. Currently, all states in the United States test for CH as part of the routine newborn screening initiatives [12].

- Infantile cretinism (congenital or neonatal hypothyroidism) is three times more common in females than in males. Early diagnosis and treatment are essential for the best possible patient outcomes. If treatment begins before the age of 3 months the infant usually experiences normal growth and development. However, if treatment is not initiated within that timeframe and children remain untreated beyond the age of 2, irreversible mental retardation occurs. However, skeletal abnormalities are reversible with treatment [5].

  Infant cretinism is most often the result of defective embryonic development of the thyroid gland. The next most common cause of the disorder is related to an inherited enzymatic defect in the synthesis of thyroxine (T4). Less often, anti-thyroid drugs administered during pregnancy cause cretinism in infants. Cretinism in children over the age of 2 is usually due to chronic autoimmune thyroiditis [5].

Complications of untreated hypothyroidism in children are severe mental retardation and skeletal malformations including dwarfism and bone and muscle dystrophy [5].

Clinical presentation

At birth, the weight and length of the newborn with infantile cretinism appear normal. However, by the age of 3 to 6 months, the infant displays characteristic signs of hypothyroidism [5].

Hypothyroidism in children alert! Breast-fed infants with infantile cretinism experience a delayed onset of symptoms because breast milk contains small amounts of thyroid hormone [5].

Typical characteristics of hypothyroidism in children include the following signs [5,12]:
The infant:

- Sleeps excessively and is inactive.
- Seldom cries, but when he/she does, the cry is hoarse.
- Has a lowered metabolism and progressive mental impairment.
  - Exhibits abnormally deep tendon reflexes and hypotonic abdominal muscles.
  - Has a puffy and swollen face and droopy eyelids.
  - Has a short forehead, puffy, wide-set eyes, a broad, upturned nose, and a vacant, dull facial expression.
  - Has a protruding abdomen.
  - Has feeding problems.
  - Displays slow, awkward movements.
  - Has cold, coarse, dry, and thickened skin.
  - Has dry brittle hair.
  - Has a slow pulse rate and below normal body temperature.
  - Becomes jaundiced because his/her immature liver cannot metabolism bilirubin.
  - Has a large, protruding tongue that obstructs respirations, forcing him/her to breathe through the mouth.

Hypothyroidism in children alert! Appropriate treatment for the child who acquires hypothyroidism after the age of 2 can prevent mental retardation. But growth retardation causes short stature, delayed epiphyseal maturation, and a head that looks unusually large because of the stunted growth of arms and legs [5].

Diagnosis

Diagnosis is based on the results of thyroid function screening, which measures thyroid hormone and serum TSH levels. Hypothyroidism is diagnosed when TSH levels are above normal and thyroid hormone levels are below normal [12].

Thyroid scans and radioactive iodine uptake tests results show decreased uptake levels and the absence of thyroid tissue in children. Characteristic electrocardiogram changes are bradycardia and flat or inverted T waves in infants who have not received treatment. X-rays show an absence of the femoral or tibial epiphyseal line and significantly delayed skeletal development [5].

Treatment and nursing considerations

Hypothyroidism in children (as well as adults) is generally treated with thyroid hormone replacements. Replacement therapy for children who are less than age one involves administration of oral levothyroxine. Initial doses are of moderate strength and are gradually increased to levels appropriate for life-long maintenance [5,12].

Hypothyroidism treatment alert! A too rapid increase in the dosage of thyroid hormone can trigger thyrotoxicity. Signs and symptoms of thyrotoxicity include tachycardia, vomiting, hypotension, tremor, weakness, shortness of breath, cough, swollen extremities, and coma. Thyrotoxicity can reach crisis levels (thyrotoxic crisis or thyroid storm) and is fatal without treatment that includes anti-thyroid medications, correction of electrolyte imbalance, and treatment of any cardiac arrhythmias [5,11].

Nursing consideration: Nurses must be aware that doses of thyroid replacement therapy are higher in children compared to adults because children metabolize thyroid hormone much more quickly [5].

Parents of children with hypothyroidism need support and encouragement as they learn to deal with their child's need for life-long treatment and monitoring. Early detection and treatment are essential if mental retardation is to be avoided.

Hypothyroidism alert! When working with parents of newborns be alert to any comments they may make about how "quiet" and "good" their babies are. Parents may mistake lack of activity, sleeping for long periods of time, and lack of crying as signs of a "good" baby, when these behaviors may actually indicate hypothyroidism [5].

Teach parents to monitor their child's pulse rate and to report tachycardia immediately. Be sure to explain that the normal infant heart rate is about 120 beats per minute. Explain that positioning the baby on his/her side will help prevent airway obstruction, especially if the child's tongue is unusually large. Tell the parents to keep the infant warm and to take steps to keep his/her skin moist [5].

Explain that the child will need to adhere to a long-long treatment plan with thyroid supplements. Stress the need for strict adherence to the prescribed medication regimen. Have the parents demonstrate their knowledge of administering medication by observing them give the child his/her medication. Assess their knowledge of medication overdose by having them list the signs of overdose such as tachycardia, sweating, fever, irritability, and insomnia. Emphasize that compliance with treatment is absolutely essential to prevent mental impairment, or if impairment has already occurred, to prevent further impairment [5,12].

Parents whose children are mentally impaired need support and understanding. Refer them to community resources and support groups. They need to be helped to focus on the child's strengths and to participate in education programs that will help their children reach maximum potential [5].

Finally, when working with pregnant women, explain how important it is for them to have a diet that includes iodine-rich foods as part of efforts to reduce the risk of infantile cretinism [5]. Efforts to help the fetus grow and develop normally prior to birth can significantly reduce the risk for many disorders and diseases that affect newborns, infants, and children.

Adult hypothyroidism

Lauren is an RN who is pursuing a doctorate in nursing practice. As part of her work in endocrinology she has been asked to write a hypothetical clinical study of an adult with hypothyroidism. She would like to find something "different" to focus on as part of her research. Lauren decides to develop a case study based on the clinical presentation of an adult who has hypothyroidism caused by chronic autoimmune thyroiditis or Hashimoto's disease. Hashimoto's disease is not frequently discussed even though it is a common thyroid gland disorder and should provide Lauren the challenge she is looking for.

Many endocrine orders are not especially prevalent (compared to other diseases and disorders) and may go unrecognized because of HCPs' lack of knowledge or exposure to such disorders. Even diseases of the thyroid, that are, arguably, more easily recognized and prevalent, can go undetected for lengthy periods of time causing delays in treatment that can not only be frustrating for the patient, but, at times, dangerous as well.

Incidence and etiology

Hypothyroidism is more common in females than in males and in people with Down syndrome, and frequency increases with age. There has been a significant increase in incidence in the United States among persons aged 40 to 50 [5,11].

There are two classifications of hypothyroidism: primary and secondary. Primary hypothyroidism is due to a disorder of the thyroid gland itself. Secondary hypothyroidism is the result of a failure to stimulate normal thyroid function [11].

EBP alert! There are a number of causes of hypothyroidism. Research has been able to identify the frequency of each cause. It is important that nurses know the various causes of the disease and the frequency of each.

The most common cause of hypothyroidism is the primary form and is usually caused by, in order of frequency [6]:

- **Autoimmune disease:** Autoimmune disease hypothyroidism is also referred to as chronic thyroiditis or Hashimoto's disease. It occurs at any age but is most often found in middle-aged women and in persons who have a family history of thyroid disease. Autoimmune hypothyroidism is caused by a reaction of the immune system against the body's thyroid gland and affects between 0.1% and 5% of all adults in Western countries. In rare cases this disease is related to other endocrine disorders caused by the immune system such as adrenal insufficiency and type 1 diabetes. Hashimoto's disease begins and progresses slowly, taking months or even years for a diagnosis to be made [13].

- **Use of radioactive iodine:** The use of radioactive iodine to treat thyroid cancer, for example, may destroy healthy thyroid cells as well as malignant cells. This can lead to hypothyroidism [5,6].
- **Thyroidectomy:** Thyroidectomy involves the surgical removal of part or all of the thyroid gland. It is performed as a treatment for thyroid cancer or goiter [5,6].
- **Diet that is deficient in iodine:** The thyroid uses iodine to produce thyroid hormone. A diet that is deficient in iodine may interfere with the thyroid's ability to produce adequate amounts of thyroid hormone [5,6,11].
- **Subacute thyroiditis:** Subacute thyroiditis is a self-limiting, painful inflammation of the thyroid gland. It is most often associated with viral infections [6].
- **Lithium therapy:** Lithium may decrease thyroid hormone levels [5,14].
- **Overtreatment with anti-thyroid drugs:** Too large a dose of anti-thyroid drugs (used to treat hyperthyroidism) can lead to hypothyroidism [5,6].

Secondary hypothyroidism occurs as a result of insufficient secretion of TSH caused by disease or trauma of the pituitary gland [6].

Pathophysiology

When the thyroid gland fails to produce adequate amounts of thyroid hormone, or when the thyroid is not adequately stimulated to produce thyroid hormone, there is a general reduction in the rate of all physical and mental processes. Cellular enzyme systems and oxidation are depressed. Cellular metabolic activity decreases, which reduces oxygen consumption. Thus, there is less oxidation of nutrients for energy and less body heat [6].

Hypothyroidism alert! Even though hypothyroidism is not an uncommon disorder, it can go unrecognized for long periods of time. This is because initial signs and symptoms can be vague and nonspecific, making recognition and diagnosis a challenge [5,6].

Complications

There are a number of potential complications of hypothyroidism. These include [5,6]:

- Benign intracranial hypertension.
- Bleeding tendencies.
- Cardiovascular disease such as arteriosclerosis, impaired peripheral circulation, ischemic heart disease, heart failure, and cardiomegaly (enlarged heart).
- Carpal tunnel syndrome.
- Deafness.
- Fertility problems.
- GI problems such as achlorhydria (absence of hydrochloric acid), pernicious anemia, megacolon (abnormal dilation of the colon), and intestinal obstruction.
- Iron deficiency anemia.
- Psychiatric disturbances.

The most serious and dramatic complication of hypothyroidism is myxedema coma, which commonly causes death. Myxedema coma usually progresses slowly. However, stressors such as infection, trauma, exposure to cold, or myocardial infarction can intensify hypothyroidism, causing myxedema coma to develop abruptly [5,6].

The respirations of patients in myxedema coma are quite depressed, leading to an increase in the partial pressure of carbon dioxide in arterial blood. Cardiac output is decreased, and cerebral hypoxia occurs and progresses. Heart rate slows, and blood pressure drops. The patient becomes hypothermic and stuporous [6].

Myxedema coma alert! Myxedema coma is a medical emergency and requires life-saving actions. Patients are admitted to the intensive care unit. Most experts recommend the intravenous administration of thyroid hormones. Electrolyte and volume disturbances must also be corrected [5,6].

Clinical presentation and diagnosis

The early clinical manifestations of hypothyroidism are vague and nonspecific. These include fatigue, lethargy, unexplained weight gain, menstrual changes, forgetfulness, reduced attention span, constipation, and sensitivity to cold, especially of the hands and feet [5,6].

As the disease progresses, signs and symptoms more characteristic of hypothyroidism become evident. These include [5,6,11]:

- Anorexia.
- Decreased libido.
- Drooping upper eyelids.
- Dry, flaky, thick skin.
- Hoarseness.
- Menorrhagia (painful menstruation).
- Muscle cramps.
- Paresthesia (numbness or tingling of extremities).
- Puffy face.
- Puffiness under the eyes.
- Stiff joints.
- Thick, brittle nails.
- Thinning, dry hair.

Additional signs, symptoms, and complications related to specific body systems eventually develop [5,6,11].

- **Cardiovascular system:** Elevated cholesterol, arteriosclerotic and ischemic heart disease, heart failure, cardiomegaly, poor peripheral circulation, and pericardial and pleural effusions.
- **CNS**: Ataxia, intention tremors, carpal tunnel syndrome, gradually progressing mental impairment, and psychiatric disturbances.
- **GI system:** Achlorhydria (absence of hydrochloric acid), pernicious anemia, adynamic (weak) colon, megacolon, and obstruction of the intestine.
- **Hematologic system:** Anemia, iron deficiency anemia, and bleeding tendencies.
- **Reproductive system:** Impaired fertility.
- **Senses:** Deafness and nystagmus (rapid, involuntary movement of the eyes).

Severe hypothyroidism is referred to as myxedema. Its characteristic traits include thickened facial features, rough, hard, dough-like, cool skin, bradycardia, weak pulse, muscle weakness, delayed reflexes, and sacral and/or peripheral edema. Hyponatremia may also be present, and the thyroid tissue may not be readily palpable [5,11].

Untreated, myxedema may gradually progress to myxedema coma (see Complications) [5,11].

Nursing consideration: Because initial symptoms are vague it is important that nurses and other HCPs be alert to the possibility of hypothyroidism.

In addition to clinical manifestations, several tests are used to confirm the diagnosis of hypothyroidism.

In primary hypothyroidism (hypothyroidism is due to a disorder of the thyroid gland itself), TSH levels are elevated. In secondary hypothyroidism (hypothyroidism is due to failure to stimulate normal thyroid function as a result of hypothalamic or pituitary insufficiency), TSH levels are decreased [5,6]. Radioimmunoassay shows low T3 and T4 levels [5,6]. Serum cholesterol, alkaline, phosphatase, and triglyceride levels are elevated. Normocytic normochromic anemia may be evident [5]. Electrocardiogram (ECG) shows sinus bradycardia, low voltage of QRS complexes, and flat or inverted T waves [6].

Treatment and nursing considerations

Treatment for mild cases of hypothyroidism involves gradual thyroid replacement with levothyroxine (Levoxyl, Synthroid), a synthetic form of the T4 thyroid hormone. This medication is a stable for of the thyroid hormone and is given orally once a day [5,14,15]. Occasionally, liothyronine is given for inadequate T3 levels [5].

Other thyroid hormone replacements are available, but as of this writing are not often recommended for replacement therapy. These medications include desiccated thyroid hormone, T3 (triiodothyronine), and various combinations of thyroid hormones T3 and T4 [15].

For severe cases of hypothyroidism such as myxedema coma it is essential to provide more aggressive quick-acting treatment including [6]:

- Administration of T3 since it acts more quickly than T4. In unconscious patients it is administered via nasogastric tube.
- Administration of sodium levothyroxine (Synthroid) parenterally for the restoration of T4 levels. Parenteral administration continues until the patient regains consciousness.
- Administration of oral thyroid hormone after the patient regains consciousness and is able to swallow oral preparations.
- Initiate steroid therapy if the rapid administration of thyroid hormone triggers adrenal insufficiency.

Nursing consideration: It is imperative to monitor vital signs carefully when levothyroxine is administered. Rapid correction of hypothyroidism can trigger cardiac problems. Elderly patients are at particular risk for hypertension and heart failure. Chest pain and/or tachycardia should be reported immediately. Teach patients and families to report any signs of cardiovascular disease such as chest pain and rapid heart rate as well [5].

Nurses must be alert to signs and symptoms of hyperthyroidism after thyroid hormone replacement begins. There is always a danger of over-correction leading to abnormally high thyroid hormone levels. Teach patients and families about these signs and symptoms (restlessness, sweating, and unexplained excessive weight loss) and to report their occurrence to their HCPs immediately [5,6].

Treatment alert! Warn patients and families that thyroid hormone replacement therapy may increase the effects of digoxin and anticoagulants. Teach them to monitor the patient's pulse and to monitor for signs of bleeding such as bleeding gums and blood in stools [6].

Encourage patients to wear medical alert bracelets at all times. Warn patients and families to take thyroid replacement therapy exactly as prescribed and to never discontinue taking their medication unless told to do so by the prescribing physicians. Emphasize that they must tell any physician or HCP (such as dentists or nurse practitioners) who prescribes medications for them about their hypothyroidism [5,6].

As always, teach patients and families not to take any additional medications or supplements without the approval of the physician who is supervising their hormone replacement therapy. This includes OTC medications, herbal preparations, vitamins, minerals, weight loss products, or any other supplements [5,6].

Treatment alert! Explain to patients and families that patients will need to take life-long hormone replacement therapy. Warn them that replacement therapy must not be discontinued even when they begin to feel better and signs and symptoms begin to subside and resolve [5,6].

Teach patients and families to make sure that patients take good care of their skin, which is generally dry and flaky. Emphasize that special attention should be paid to boney prominences [5].

Make sure that patients and families are aware of the signs and symptoms of worsening hypothyroidism, myxedema, and myxedema coma and to seek immediate medical help if they occur [5,6]. Caution patients and families to report any infection or occurrence of other diseases and disorders since these problems can affect hypothyroidism and mediation effectiveness [5,6].

Patients may be concerned about weight gain and begin to diet or to use weight loss products without health care supervision. Warn patients that it is essential to have an adequate nutritional intake. Work with patients and families to plan a well-balanced, low calorie diet to help with appropriate weight loss. Remind them that excessive rapid weight loss may be a sign of hyperthyroidism and to report such an occurrence [5,6].

Constipation is common among patients suffering from hypothyroidism. To reduce and/or prevent constipation encourage adequate fluid intake and a diet high in fiber. Stool softeners may be prescribed, as well as cathartics, as needed [5,6].

Help patients and families access community resources available for support and education. Include reliable, accurate Internet sites as part of this education. Caution patients and families not to believe everything they may read on the Internet as it relates to hypothyroidism. Help patients and families to critique Internet sites for reliability and validity.

Hyperthyroidism

Janice is a 32-year-old fashion consultant. She majored in fashion design with a minor in marketing in college. Janice's husband, Dennis, is a business major, and it has been their dream to start their own business, establishing an exclusive upscale fashion boutique. Dennis' parents are prominent members of the community and have agreed to invest in this business venture with the condition that his mother also works in the boutique "to keep an eye on things." Initially things go well, but as time goes on Janice feels increasingly stressed. Her mother-in-law is constantly criticizing Janice's decisions and tells her that "my friends will never come here unless you make this a really exclusive establishment." Dennis is sympathetic but tells Janice that they must be patient until they earn enough money to buy his parents out of their share of the business. Janice begins to loss a considerable amount of weight despite having an increased appetite. She complains of feeling "jittery" and that her "heart pounds every time I have to go to work." Janice also develops an extreme intolerance to heat. She and Dennis attribute these symptoms to stress. One cold winter afternoon, after listening to another round of her mother-in-law's criticism, Janice states that she simply can't stand how hot it is in the boutique. She goes outside and, despite the cold and significant snowfall, stands on the sidewalk in her sleeveless dress in an attempt to become more comfortable. Dennis, summoned from the office by his mother, finds Janice and insists that he take her to see their family physician at once. After listening to Janice's recent history and conducting a few diagnostic tests, the physician diagnoses Janice with Graves' disease, a form of hyperthyroidism.

Hyperthyroidism (also referred to as thyrotoxicosis or Graves' disease) is a metabolic imbalance characterized by excessive amounts of thyroid hormone in the bloodstream [5,6]. Fortunately, with treatment, most patients lead normal lives [5].

Incidence, etiology, and pathophysiology

Hyperthyroidism is more common in women than in men and affects about 2% of the female population [6].

A number of factors can increase the risk for development of hyperthyroidism. These include [5,11,16]:

- **Family history:** It is believed that genetic factors can make people more vulnerable to the disease. There is a marked increased incidence of the disease in monozygotic twins.
- **Gender:** The disease is more prevalent among women.
- **Age:** Most patients are over the age of 40. Only 5% of patients with hyperthyroidism are younger than 15 years of age. The incidence of Graves' disease, however, is highest between the ages of 30 and 40.
- **Coexistence of other autoimmune disorders:** People with other autoimmune disorders such as type 1 diabetes or rheumatoid arthritis are at increased risk for the development of hyperthyroidism.
- **Smoking:** Cigarette smoking can increase risk for hyperthyroidism.
- **Pregnancy:** Women who are pregnant or who have recently given birth are at increased risk, especially if they also have genetic predisposition to the disease.
- **Stress:** Both physical and emotional stress can trigger the onset of hyperthyroidism.
- **Excessive dietary intake of iodine:** Excessive dietary intake of iodine can trigger hyperthyroidism onset.

The most common type of hyperthyroidism is Graves' disease, which is characterized by diffuse hyperfunction of the thyroid gland, increased thyroxine (T4) production, enlargement of the thyroid gland, and multiple system changes [5,6]. Graves' disease is associated with ophthalmopathy, when the tissues and muscles behind the eyes become swollen causing the eyeballs to protrude. Graves' disease may subside spontaneously [6]. Its exact cause is unknown but it occasionally coexists with abnormal iodine metabolism and other types of endocrine disorders [5].

The second most common type of hyperthyroidism is toxic adenoma, which is a small, benign nodule in the thyroid gland that secretes thyroid hormone. Its incidence is highest in the elderly, but its etiology is unknown. Toxic adenoma's clinical manifestations are similar to those of Graves' disease in many respects, but it does not cause ophthalmopathy [5,11]. Nor does it cause pretibial myxedema (localized skin lesions) or acropachy (soft tissue swelling with underlying bone changes at the site of new bone formation), which are also associated with Graves' disease [5,11].

Remaining types of hyperthyroidism include [5,11]

Thyrotoxicosis factitia is a form of hyperthyroidism that is due to chronic ingestion of thyroid hormone. The hormone is ingested by patients with thyroid carcinoma in an attempt to suppress TSH or by patients who are abusing thyroid hormone in an attempt to lose weight.

Functioning metastatic thyroid carcinoma is a rare disease. It causes the thyroid gland to produce excessive amounts of thyroid hormone.

A TSH-secreting pituitary tumor also causes excessive production of thyroid hormone.

Subacute thyroiditis is a granulomatous inflammation of the thyroid that is triggered by a virus. It causes transient hyperthyroidism, fever, pain, pharyngitis, and thyroid gland tenderness.

Silent thyroiditis is a transient form of hyperthyroidism that is self-limiting.

Hyperthyroidism alert! Clinical hyperthyroidism can be triggered by excessive dietary intake of iodine or by stress in patients who have latent hyperthyroidism [5].

In Graves' disease, an autoimmune reaction causes thyroid-stimulating antibodies to bind to and stimulate the TSH receptors of the thyroid gland. The cause of this autoimmune response is unknown. Disease development is associated with genetic factors, other autoimmune disorders, and the production of auto-antibodies formed because of a fault in suppressor T-lymphocyte function [11].

Complications

There are a number of complications associated with hyperthyroidism. These include [5]:

- Corneal ulcers.
- Decreased libido.
- Fertility problems.
- Gynecomastia.
- Hyperpigmentation.
- Muscle atrophy.
- Muscle weakness.
- Myasthenia gravis.
- Osteoporosis.
- Paralysis.

Cardiovascular complications such as arrhythmias, cardiac insufficiency, and cardiac decompression may occur. Cardiovascular complications are most common in elderly patients [5].

Nursing consideration: Thyroid storm is the most serious complication of hyperthyroidism. Also referred to as thyrotoxic crisis, thyroid storm usually occurs in patients with preexisting, though often undiagnosed, thyrotoxicosis. Untreated, it is usually fatal [5,11].

When excessive amounts of T3 and T4 are produced systemic adrenergic activity increases, which leads to overproduction of epinephrine. Excessive amounts of epinephrine cause significant hypermetabolism that, in turn, leads to rapid cardiac, GI, and sympathetic nervous system decompensation. Hypertension, tachycardia, vomiting, extreme irritability, and temperature up to 106 °F can occur. Thyroid storm can progress to delirium, coma, and death. The onset of thyroid storm is abrupt and triggered by stressors such as trauma, surgery, infection, or serious events such as stroke, myocardial infarction, preeclampsia, or pulmonary embolism [11].

Clinical presentation

The characteristic signs and symptoms of hyperthyroidism are [5,6,11]:

- Enlarged thyroid gland (also referred to as goiter).
- Exophthalmos (abnormally protruding eyes and a characteristic staring gaze).
- Heat intolerance.
- Nervousness.
- Inability to sit still.
- Weight loss even though appetite is increased.

- Diaphoresis.
- Diarrhea.
- Tremors.
- Palpitations.

Hyperthyroidism alert! Although exophthalmos is considered by many HCPs to be the most characteristic sign of hyperthyroidism, it is actually absent in many patients with the disease [5].

Hyperthyroidism alert! Most of the signs and symptoms of hyperthyroidism are due to an increased metabolic rate, excessive heat production, increased cardiovascular and neuromuscular activity, and sympathetic nervous system hyperactivity [6].

Hyperthyroidism affects every system of the body. Therefore, a multitude of signs and symptoms may be apparent. The following is a review of additional signs and symptoms according to body systems.

- **Cardiovascular system:** Cardiovascular system effects are seen most often in elderly patients. Cardiac effects include arrhythmias (usually atrial fibrillation), tachycardia with a full, bounding pulse, cardiac insufficiency, visible point of maximal impulse, cardiac decompensation, and resistance to the prescribed therapeutic dose of digoxin in patients who are taking the drug [5,6,11].
- **CNS:** CNS signs and symptoms are most commonly seen in younger patients. For example, patients may complain of having difficulty concentrating. This is because an increased production of T4 accelerates cerebral functioning. An increase in basal metabolic rate can lead to anxiety, nervousness, mood swings, and emotional instability. Some patients may even develop overt psychosis. Increased activity in the area of the spinal cord that controls muscle tone can lead to tremors, shaky handwriting, and clumsiness [5,11].
- **GI system:** Anorexia may develop. Patients may complain of nausea and vomiting because of increased GI motility and peristalsis. Patients may notice an increase in the number of stools, soft stools, and/or diarrhea. The liver may become enlarged.
- **Integumentary system:** Skin is warm, smooth, moist, thick, flushed, and has a velvet-like texture. There is evidence of hyperpigmentation and loss of skin color in blotches (vitiligo). Plaque-like or nodular skin lesions may be noted. The hair is fine and soft and begins to gray prematurely. Hair loss is evident in both men and women. Nails are fragile and there is separation of the distal portion of the nail from the nail bed [11].
- **Musculoskeletal system:** There is muscle weakness accompanied by muscle atrophy. Osteoporosis and acropachy are also possibilities [11].
- **Reproductive system:** Women may experience menstrual abnormalities such as oligomenorrhea (abnormally light or infrequent menstrual periods) and amenorrhea (absence of menstruation), impaired fertility, decreased libido, and a higher incidence of spontaneous abortions. Men may develop gynecomastia (abnormal development of mammary glands) due to an increase in estrogen levels. They may also experience a decrease in libido [5,11].
- **Senses:** Patients blink infrequently as a result of exophthalmos. This leads to dry eyes, reddened conjunctiva and cornea, and corneal ulcers. Patients have difficulty looking upward and strabismus (the eyes do not "line up" at the same time and therefore cannot look at the same object at the same time) [5,11].

Diagnosis

Diagnosis is made based on the presenting clinical picture, a thorough history and physical examination, and evaluation of blood hormone levels [5,6].

Diagnostic alert! Although many of the signs and symptoms of hyperthyroidism are deemed to be "characteristic" of the disease, it is important for nurses and other HCPs to be alert to their development. Early recognition and prompt treatment are important.

In hyperthyroidism palpation of the thyroid gland may reveal that the gland is asymmetrical and lobular. It may actually be enlarged to as much as 3 to 4 times its normal size. Enlargement of the liver may also be noted [5,11].

A full, bounding pulse may be palpated along with a heart rate indicative of tachycardia [11].

Evaluation of reflexes may show hyperreflexia [11].

When auscultating the heart, the examiner may detect a rapidly accelerating heart beat that may be confirmed on ECG as paroxysmal supraventricular tachycardia or atrial fibrillation. Other findings may include [11]:

- Systolic murmur.
- Wide pulse pressure.
- Audible bruit over the thyroid gland (may indicate toxicity).

EBP alert! Research shows that that cardiovascular signs and complications are especially likely in elderly patients. Monitor elderly patients for such signs and complications very carefully [5,11].

The following tests are used to confirm a diagnosis of hyperthyroidism [5,6,11]:

- Radioimmunoassay shows elevated serum T4 and T3.
- TSH levels are decreased.
- Thyroid scan shows an increased uptake of radioactive iodine.

Diagnostic alert! Thyroid scan is contraindicated if the patient is pregnant [5].

- Ultrasound confirms the presence of subclinical ophthalmopathy.
- In Graves' disease the thyroid stimulating immunoglobulin is positive.

Treatment and nursing considerations

Treatment initiatives depend on any underlying causes, the size of the goiter, patient age, severity of the disease, and any complications that are present [6].

Anti-thyroid medications

Anti-thyroid medications are used for children, young adults, pregnant women, and for those patients who are unable to tolerate or who refuse other types of treatment [5,6,11,16]. Examples of such medications include propylthiouracil (PTU) and methimazoke (Tapazole). They act by depressing the synthesis of thyroid hormone by inhibiting thyroid peroxidase. PTU is given in daily divided doses. Tapazole is given in a single daily dose [6].

Anti-thyroid medications may also be used before or after radioiodine therapy as a supplemental treatment [16]. Side effects of both PTU and Tapazole include rash, joint pain, liver failure, or a decreased white blood cell (WBC) count. Use of Tapazole is associated with a slight risk of birth defects, thus PTU is the preferred drug for use in pregnant women [16].

Treatment continues until the patient becomes clinically euthyroid (having normal thyroid function). This can take from 3 months to 2 years. If normal thyroid function cannot be maintained without therapy, radiation or surgical intervention is recommended [6]. Medications are discontinued gradually to prevent exacerbation [6].

Beta blockers

Beta blockers do not prevent or inhibit thyroid hormone production. However, they do limit the effects of excessive amounts of thyroid hormone on the body. Beta blockers can provide fairly quick relief of some signs and symptoms such as arrhythmias, tremors, anxiety, irritability, diaphoresis, diarrhea, muscle weakness, and heat intolerance [6,16].

Radioactive iodine therapy

Radioactive iodine (radioiodine) acts by limiting secretion of thyroid hormone by destroying thyroid tissue. Given by mouth, dosage of the drug is controlled so that hypothyroidism does not occur. As the thyroid gland shrinks, signs and symptoms decrease gradually over a period of several weeks to several months. Radioactive therapy may increase Graves' ophthalmopathy. This is usually temporary and mild. However, if the patient is already affected with moderate to severe eye problems, this type of therapy may be contraindicated [6,16].

Radioactive iodine therapy alert! The primary advantage of radioactive iodine therapy is that it can result in a lasting remission of hyperthyroidism. However, use of radioactive iodine therapy can cause the patient to become permanently hypothyroid [6].

While patients are receiving iodine therapy they must be observed for signs and symptoms of iodine toxicity such as swelling of the buccal mucosa, excessive salivation, skin eruptions, and/or coryza (inflammation of the nasal mucous membranes). If side effects occur the use of iodides is discontinued [6].

Surgery

If other therapeutic interventions are not effective surgery (subtotal thyroidectomy) may be necessary. Surgery is also used for patients who have large goiters. Most of the thyroid gland is removed, necessitating life-long thyroid hormone replacement. Risks associated with subtotal thyroidectomy include damage to vocal cords and the parathyroid glands [16].

Treatment of Graves' ophthalmopathy

Mild cases of Graves' ophthalmopathy are managed by using OTC artificial tears during the day and lubricating gels at night [16]. For severe cases the following interventions may be prescribed [16].

- **Administration of corticosteroids:** Corticosteroids such as prednisone are given to reduce swelling behind the eyes.
- **Eye muscle surgery:** Inflammation may shorten the muscles of the eyes, making them too short for the eyes to properly align. During surgery, the surgeon cuts the eye muscles and reattaches them further back in the eye to facilitate alignment. More than one surgical procedure may be needed.
- **Orbital decompression surgery:** The surgeon removes the bone between the eye socket and the sinuses. This allows the eyes to move back to their normal position. This procedure is indicated if vision loss is possible due to pressure on the optic nerve.
- **Orbital radiotherapy**: Targeted x-rays, administered over a period of several days, are used to destroy some of the tissue behind the patients' eyes. This procedure was once quite common. Recent studies, however, suggest that this procedure provides no benefit for patients with mild to moderately severe Graves' ophthalmopathy.
- **Prisms**: Prisms in eyeglasses are used to correct double vision because of Graves' disease. Prisms work for some, but not all, patients affected with double vision.

Emergency treatment of thyroid storm

Thyroid storm is a medical emergency requiring prompt treatment. Treatment initiatives include [5,6]:

- Prevention of new thyroid hormone synthesis with thioamides such as PTU.
- Prevention of thyroid hormone release using iodine (Lugol's solution).
- Inhibition or control of the side effects of thyroid hormones with corticosteroids and beta blockers such as Inderal.
- Initiatives targeted at the systemic effects of thyroid hormones include the use of a cooling blanket and acetaminophen (Tylenol) for excessive body heat, administration of intravenous fluids and electrolytes to correct dehydration and electrolyte imbalance, and treatment of the trigger event (e.g., heart attack and other physical and emotional stressors).

Nursing actions focus on actions that help patients and families deal with the effects of the disease, compliance with treatment, and knowledge acquisition to help them lead normal lives.

Environmental considerations

The following interventions are appropriate for both home and hospital environments [5,6]:

- Provide a calm quiet environment to combat anxiety and promote rest.
- Teach patients and families relaxation techniques such as meditation and deep breathing exercises.
- Refer patients and families to community resources for counseling to help deal with emotional stressors.
- Promote sleep and relaxation as much as possible.

Nutritional needs

Nutritional needs focus on fluid and electrolyte replacement and promotion of a healthy diet [5,6]. Nurses should:

- Monitor intake and output and weight.
- Provide examples of a healthy, yet high calorie diet since weight loss is usually an issue.
- Monitor intravenous infusions and the patency of the intravenous site.
- Monitor lab results pertaining not only to hormone levels but electrolyte levels as well.

Skin care

Maintaining skin integrity is a priority. Nurses should take, and teach patients and families to take, the following steps to maintain skin integrity [5,6]:

- Monitor skin turgor.
- Monitor for diaphoresis and body odor due to excessive sweating.
- Encourage the patient to bathe frequently with cool water and to change clothing and bed linens when they become damp.
- Avoid soaps that are drying to the skin such as perfumed soaps and shower gels.
- Apply lotion and lubricants to skin, especially boney prominences.
- Monitor skin for reddened or open areas. Teach patients to use a long-handled mirror to check areas of the skin on the back, the buttocks, and behind the legs.

Adherence to medication regimen

- Caution patients to wear a medical identification bracelet.
- Explain how to take medications. Have patients and families verbalize knowledge of their medication regimens by asking them to state what medication(s) they must take, dose, route, time, action, side effects and what to do if adverse effects occur. Be especially careful to explain signs of hypothyroidism, which may indicate that the doses of their anti-thyroid medications are too high.
- As always warn patients not to discontinue medications unless told to do so by their HCPs and to tell their HCPs providers about any medications they are taking including prescription, OTC, herbs, vitamins, minerals, and weight loss products.

Most patients affected by hyperthyroidism can lead normal lives. However, they need ongoing, life-long monitoring and adherence to any treatment regimens prescribed. They also need support and contact information for persons and resources that can help them deal with the disease and its effects.

Thyroiditis

Margaret gave birth to her first child 3 months ago. She has become anxious and irritable and complains of fatigue and, a "racing" heart. Margaret has begun to lose weight even though her appetite is good and she is eating more than she usually does. Her mother and friends laugh at Margaret's concerns and regale her with stories about how tired and nervous they were after the birth of their first children. "Wait until you have three like me, then you can complain!" one friend tells her. Margaret becomes more and more distraught until one day, she breaks down in tears while attempting to place the baby in his car seat for a visit to his pediatrician. Margaret's next door neighbor, a retired RN, notices her distress and comes to help. Margaret tells her neighbor about her symptoms and says, "Everyone tells me I'm just over-reacting to being a new mother but I think something is really wrong!" The neighbor volunteers to babysit the next day so that Margaret can visit her family physician. When she returns, Margaret thanks her neighbor profusely. "The doctor says I have an inflamed thyroid gland. She says it doesn't happen often after giving birth, but that it's happened to me. Wait until I tell my mother and friends! This will shut them up!"

Thyroiditis is inflammation of the thyroid gland. It is most prevalent in people between the ages of 30 and 50, and is more common in women than in men. The highest incidence is in the Appalachian region of the United States [5].

Types of thyroiditis

There are several forms of thyroiditis, which usually have three phases: overactive thyroid (hyperthyroidism), underactive thyroid (hypothyroidism), and return to normal [17].

However, not all forms allow for the return of normal thyroid functioning. Some patients need life-long follow-up and thyroid hormone replacement [5,19].

Postpartum thyroiditis

Postpartum thyroiditis is an uncommon disorder characterized by inflammation of the thyroid gland within the first year following childbirth [18]. Its exact etiology is unknown, but it is associated with an immune system reaction/underlying autoimmune thyroid condition [18,19].

Women at increased risk for postpartum thyroiditis are those who have [18]:

- An autoimmune disorder such as type 1 diabetes.
- A history of previous thyroid problems.
- A history of postpartum thyroiditis.
- A family history of thyroid problems.
- High concentrations of anti-thyroid antibodies.

Most women who develop postpartum thyroiditis experience a return to normal thyroid function within 12 to 18 months of symptom onset. However, some women experience lingering signs and symptoms and can develop permanent complications [18,19].

There are generally two phases of postpartum thyroiditis. The first phase usually occurs within 1 to 4 months after giving birth and lasts for 1 to 3 months [18]. Signs and symptoms of the first phase are caused by inflammation and release of thyroid hormone and include [18]:

- Anxiety.
- Fatigue.
- Increased sensitivity to heat and heat intolerance.
- Irritability.
- Insomnia.
- Palpitations.
- Rapid heartbeat.
- Tremors.

Later in the disease process, thyroid cells become impaired and signs and symptoms of hypothyroidism might become evident such as [18]:

- Aches and pains.
- Constipation.
- Dry skin.
- Fatigue and lack of energy.
- Increased sensitivity to cold and cold intolerance.
- Trouble concentrating.

Postpartum thyroiditis alert! Some women with the disease develop symptoms only of hyperthyroidism or only of hypothyroidism, but not both [18].

Treatment varies depending on signs, symptoms, and thyroid hormone levels [5,18]. Most women do not need treatment, but are simply monitored for severity of signs and symptoms and thyroid hormone levels, which are usually assessed every 4 to 8 weeks [18].

For severe signs and symptoms of hyperthyroidism, women may be prescribed beta blockers to inhibit the effects of the excessive amounts of thyroid hormone on the body. These drugs are not usually prescribed for women who are breastfeeding; however, propranolol might be recommended because it is not as concentrated in breast milk as other beta blockers [18].

For those women who experience severe signs and symptoms of hypothyroidism, thyroid replacement therapy might be prescribed for 6 to 12 months. After medication is discontinued, women are monitored at 2, 3, and 6 months for recurrence of hypothyroidism. If lab results are normal, hormone levels are then checked on an annual basis [18].

Nursing consideration: Nurses are in a unique position to facilitate proper health care for new mothers. Teach them (and their families and friends) not to attribute unusual signs and symptoms as simply stress related to caring for a newborn. As described in the hypothetical scenario at the beginning of this section, sometimes new mothers' health concerns are dismissed as trivial combined with an attitude that "all new mothers are tired and anxious." Help women monitor their health and recognize the occurrence of signs and symptoms that need medical evaluation.

Hashimoto's thyroiditis

Hashimoto's thyroiditis is a chronic progressive disease of the thyroid gland. It is an autoimmune disorder characterized by thyroid infiltration of lymphocytes. This causes progressive destruction of the parenchyma and hypothyroidism if left untreated. As the immune system "attacks" thyroid gland it gradually swells, and damage is sustained [6,19].

Hashimoto's thyroiditis is generally thought to be the most common cause of adult hypothyroidism. Its exact etiology is unknown, but it is believed to be genetically transmitted and perhaps related to Graves' disease. Ninety-five percent of Hashimoto's thyroiditis cases occur in women in their 40s or 50s, and incidence of the disease is increasing [6].

Clinically, the disease progresses very slowly, taking months or even years to be identified [19]. Clinical manifestations of Hashimoto's thyroiditis include [6,19]:

- Slow development of a firm, enlarged thyroid gland.
- Low basal metabolic rate.
- No gross nodules of the thyroid gland.
- T3 and T4 may be normal initially, but levels fall below normal as the disease progresses and thyroid tissue is destroyed.
- Anti-thyroglobulin antibodies and anti-microsomal antibodies are nearly always present.
- Symptoms of an underactive thyroid gland appear such as fatigue, weight gain, constipation, dry skin, and depression.

Hashimoto's thyroiditis cannot be cured, and low levels of thyroid hormone are usually permanent. Thus, life-long treatment with thyroid hormone replacement is usually necessary [19]. Insufficient or delayed treatment may result in a significantly sized goiter (thyroid gland enlargement). If the goiter compresses the trachea or causes other complications, surgical resection may be needed [6,19].

For detailed nursing considerations see the section on hypothyroidism.

Subacute thyroiditis

Subacute thyroiditis is a self-limiting, painful inflammation of the thyroid gland that usually occurs following a viral infection [5,6]. The disease is associated with a three-phase clinical course of hyperthyroidism, hypothyroidism, and return to normal thyroid gland functioning. It is estimated that sub acute thyroiditis may be responsible for 15% to 20% of patients presenting with hyperthyroidism and 10% of patients presenting with hypothyroidism [20].

There are three forms of subacute thyroiditis [20]:

- **Subacute granulomatous thyroiditis:** Also known as subacute painful or deQuervain thyroiditis.
- **Lymphocytic thyroiditis:** Also known as subacute painless thyroiditis.
- **Subacute postpartum thyroiditis:** See section on postpartum thyroiditis.

Subacute thyroiditis predominantly affects younger women. Its clinical course is characterized by four stages [20]:

- **Stage 1:** High thyroid levels occur when thyroid follicles are destroyed and thyroid hormones are released into the bloodstream. This hyperthyroidism stage lasts for between 4 and 10 weeks.
- **Stage 2:** The disease goes into remission and thyroid hormone levels return to normal.
- **Stage 3:** At this stage, the thyroid is depleted of colloid and cannot produce adequate amounts of thyroid hormone, which leads to hypothyroidism. This stage may last up to 2 months. The hypothyroidism is usually mild and no thyroid hormone therapy is required unless the patient presents with significant signs and symptoms of hypothyroidism.
- **Stage 4:** The disease resolves itself and normal thyroid functioning is restored as thyroid follicles regenerate. Ninety percent to 95% of patients experience a return to normal thyroid function.

Subacute thyroiditis alert! About 10% of patients experience permanent hypothyroidism, necessitating long-term or life-long thyroid hormone replacement [6].

General signs and symptoms of sub acute thyroiditis include [6]:

- Pain, swelling, and tenderness of the thyroid gland that lasts for several weeks or months and then disappears.
- Fever, sore throat, referred ear pain.
- Fever, malaise, and chills.

Depending on the stage of the disease, patients may present with symptoms of hyper- or hypothyroidism. Hyperthyroidism symptoms include anxiety, nervousness, irritability, insomnia, weight loss, and heat intolerance. Hypothyroidism symptoms include lethargy, cold intolerance, weight gain, and constipation [5,6].

Treatment of this usually self-limiting disease is supportive. Analgesics to reduce pain, a restful environment, and emotional support to help relieve anxiety generally facilitate recovery [6].

Riedel thyroiditis

Riedel thyroiditis (also known as Riedel's thyroiditis) is a rare, chronic inflammatory disease of the thyroid gland. The disease is characterized by a "dense fibrosis that replaces normal thyroid parenchyma [21]." The fibrotic process extends to nearby structures of the neck and reaches beyond the thyroid capsule. Function of the thyroid depends on the amount of normal thyroid tissue that has been replaced with fibrotic tissue. Although most patients retain normal thyroid functioning, about 30% of them become hypothyroid [21].

Riedel thyroiditis alert! *Some experts believe that Riedel thyroiditis is not a disorder of the thyroid gland, but rather is a symptom of the systemic disorder multifocal fibrosclerosis. It is estimated that about 33% of Riedel thyroiditis cases are linked to findings of multifocal fibrosclerosis when diagnosed [21].*

Riedel thyroiditis is usually self-limiting, and patients have a favorable prognosis. However, there are some potential complications of the disease including airway obstruction, dysphagia (difficult, painful swallowing), dysphonia (hoarseness), hypothyroidism, hypoparathyroidism, and stridor because of compression of the trachea by the thyroid gland [21].

Miscellaneous types of thyroiditis

There are several other types of thyroiditis. These include [19]:

- **Acute or infectious thyroiditis:** This type of thyroiditis is usually due to a bacterial infection. Symptoms include sore throat, feeling generally sick, enlargement of the thyroid gland, and, occasionally, symptoms of hyperthyroidism or hypothyroidism. Symptoms usually resolve as the infection is treated with appropriate antibiotics.
- **Drug-induced thyroiditis:** Drug-induced thyroiditis is triggered by various drugs such as interferon (antiviral or immune response modifier), amiodarone (antiarrhythmic), and some anticancer drugs (e.g., sunitinib). Symptoms of hyperthyroidism or hypothyroidism may occur, but these usually resolve when drugs causing them are discontinued.
- **Painless thyroiditis:** The signs and symptoms of painless thyroiditis are similar to those of postpartum thyroiditis. However, painless thyroiditis can occur in both men and women and is not associated with childbirth. Painless thyroiditis usually causes a stage of high thyroid hormone levels, followed by a phase of low thyroid hormone levels, and, ultimately, a return to normal in about 12 to 18 months.
- **Radiation induced thyroiditis:** Radiation induced thyroiditis is triggered when radiation iodine treatment is used to treat overactive thyroid glands or for certain cancers. Resulting damage to the thyroid can cause symptoms of high or low levels of thyroid hormone. Hypothyroidism after treatment with radioactive iodine is usually permanent, and life-long thyroid hormone replacement therapy is needed.

Nontoxic goiter

Melanie is a 58-year-old partner in a prestigious law firm. After menopause, Melanie gained a bit of weight and has been rigidly dieting and vigorously exercising to maintain a trim figure. She has begun to notice some difficulty swallowing and a slight swelling in the front of her neck. Melanie dismisses these symptoms as annoying and continues with her busy lifestyle. During her annual physical exam her nurse practitioner notices the swelling and recommends some diagnostic laboratory tests. After reviewing the results of the tests and physical exam findings, Melanie is diagnosed with a "simple" goiter.

Goiter is an abnormal enlargement of the thyroid gland. A simple, or nontoxic goiter is enlargement of the thyroid gland that is not due to inflammation or cancer and is not due to abnormal thyroid function [5,22].

Nontoxic goiter is most common in females, particularly during adolescence, pregnancy, and menopause. During these periods of a female's life, the demand for thyroid hormone increases [11].

Goiter alert! Toxic goiter, as compared to nontoxic goiter, stems from long-standing nontoxic goiter and is found in elderly people. Toxic goiter manifests itself as an enlarged thyroid gland that develops small rounded masses and secretes excessive amounts of thyroid hormone [11].

Pathophysiology

Nontoxic goiter occurs when the thyroid gland is unable to secrete sufficient thyroid hormone to meet the needs of the body. In an attempt to compensate for this insufficiency, the thyroid gland enlarges. Enlargement usually overcomes mild to moderate hormonal deficiencies [11].

Steps involved in the production of a nontoxic goiter are [5,11]:

- Impaired thyroid hormone synthesis and depletion of glandular organic iodine increase the thyroid glands response to normal levels of TSH.
- Increased response to normal TSH levels is accompanied by increases in thyroid gland mass and cellular activity, which compensate for mild deficiencies in the synthesis of thyroid hormone. Thus, metabolic function is normal even in the presence of a goiter.
- If an underlying disorder does exist or develop, and is severe, both a goiter and hypothyroidism may develop.

Depending on the size of the goiter, dysphagia and even respiratory distress may develop [5].

Types of nontoxic goiter

Nontoxic goiter is categorized as either endemic or sporadic.

Endemic goiter affects more than 10% of a population [22]. Its development is usually due to a diet that is inadequate in iodine, which, in turn, leads to inadequate synthesis of thyroid hormone. In Japan, however, goiter due to excessive intake of seaweed-containing iodine has been identified [11].

In the United States, some geographic locations have actually been dubbed "goiter belts" since they have a high incidence of endemic

goiter due to a lack of iodine in soil and water. These areas include the Midwest, Northwest, and Great Lakes region [11]. However, the introduction of iodized salt in the United States has drastically reduced the incidence of the disorder [5].

Sporadic goiter is the most common cause of goiter in the United States [22]. Sporadic goiter is usually the result of ingestion of large amounts of goitrogenic foods or drugs. Goitrogenic foods and drugs are those that contain substances that decrease the production of T4. Examples of such foods are cabbage, soybeans, peanuts, peaches, peas, strawberries, spinach, and radishes. Examples of drugs that decrease T4 production are propylthiouracil, iodides, lithium, cobalt, and aminosalicylic acid [11].

Experts believe that genetic defects may be responsible for inadequate T4 synthesis or damaged metabolism of iodine. However, because many families live in close geographic proximity inherited factors may contribute to the incidence of both endemic and sporadic goiters [5].

Diagnosis of nontoxic goiter

Diagnosis is based on patient history and physical exam. It is important to rule out other disorders that can cause goiter and have similar effects but can range from mild to serious and even life-threatening such as thyroid carcinoma, Graves' disease, and various types of thyroiditis [5].

Diagnostic alert! HCPs must always be alert to the influence of medications and diet on health. As in the cause of nontoxic goiter, foods and medications can be a major influence on its development [5,11].

Since nontoxic goiter does not adversely alter the patient's metabolic state, clinical manifestations of the disease develop solely due to thyroid gland enlargement [5]. Symptoms of nontoxic goiter include [5,11]:

- Dysphagia.
- Respiratory distress.
- Stridor.

There is swelling and neck distention and, if the goiter is large enough, obstruction of venous return that causes venous engorgement. Rarely, large goiters may prompt the development of collateral venous circulation in the chest. Venous obstruction may make the patient dizzy or trigger syncope when the arms are raised above the head [5,11].

Diagnostic tests show [5,11]:

- Normal or elevated levels of TSH.
- Normal levels of thyroid hormones.

Diagnostic alert! Abnormalities in T3, T4, and TSH rule out a diagnosis of nontoxic goiter [11].

- Thyroid antibody titers are generally normal. Increases in thyroid antibody titers suggest chronic thyroiditis.
- Radioactive iodine uptake is usually normal. However, results may increase if the patient has an iodine deficiency or a biosynthetic defect.
- Urinalysis results may show low urinary excretion of iodine.

Ultrasound of the thyroid or radioisotope scanning may be used to identify malignancies or nodules that need to be biopsied [5,11].

Treatment and nursing considerations

Treatment focuses on reduction of thyroid hyperplasia. The treatment of choice for nontoxic goiter is thyroid hormone replacement therapy with levothyroxine dessicated thyroid or liothyronine. Such treatment inhibits secretion of TSH and allows the thyroid gland to rest [5,11].

Small doses of iodine in the form of Lugol's solution or potassium solution are given to patients whose goiter is caused by iodine deficiency [5,11].

Patients must be cautioned to take medication exactly as prescribed. Patients' and families' knowledge of how to administer medication, dose, route, action, and side effects must be assessed. Patients must inform their HCPs of any and all medications they are taking in conjunction with drugs used to treat goiter including prescription, OTC, herbs, vitamins, minerals, and any other supplements [5,14].

Other treatment initiatives include [5,11]:

- **Diet:** Patients who have sporadic goiters must be taught to avoid goitrogenic foods and medications. Patients who are taking such medications should be cautioned not to discontinue such drugs without approval of the prescribing physician or nurse practitioner. Patients must inform these providers about goiter development and what medications have been prescribed to treat the goiter. Patients with endemic goiters should be instructed to use iodized salt to include necessary amounts of iodine in their diet.
- **Radiation:** Radioiodine ablation therapy to the thyroid gland is administered to destroy cells that concentrate iodine for the production of thyroid hormone.
- **Surgery:** Patients who have large goiters that do not respond to other treatment measures may need surgery. Partial removal of the thyroid gland (subtotal thyroidectomy) may relieve pressure on adjacent structures.

Patients with large goiters may experience embarrassment because of their appearance and fear permanent disfigurement. Nurses and other HCPs should provide emotional support and the importance of adhering to prescribed treatment initiatives.

Hypoparathyroidism

Jane has recently undergone a thyroidectomy as part of the treatment for thyroid cancer. Following surgery Jane develops tremors triggered by voluntary movement, paresthesia, headaches, and severe anxiety. Diagnostic evaluation shows electrolyte imbalances indicative of hypoparathyroidism. It seems that during surgery to remove the thyroid gland, parathyroid tissue had also been removed.

Hypoparathyroidism is an uncommon condition caused by a deficiency of PTH. Since PTH is essential to the regulation and maintenance of calcium and phosphorus, hypoparathyroidism is characterized by hypocalcemia and neuromuscular hyper-excitability [6,23].

Etiology and pathophysiology

Hypoparathyroidism can be acute or chronic, and is categorized as idiopathic or acquired [5,23].

The most common cause of hypoparathyroidism is due to accidental removal or destruction of parathyroid tissue or circulation to such tissue during thyroidectomy or radical neck dissection [5,6].

EBP alert! Research shows that hypoparathyroidism is most often due to the accidental removal or destruction of parathyroid tissue or circulation to such tissue. Therefore, nurses caring for patients who have undergone thyroid surgery or radical neck dissection must be vigilant in monitoring for signs and symptoms of hypoparathyroidism.

Rarely, acquired hypoparathyroidism is caused by massive thyroid irradiation, ischemic infarction of the parathyroid glands during surgery, or from tuberculosis, neoplasms, trauma, sarcoidosis, or hemochromatosis [5].

Acquired hypoparathyroidism may be reversible if the cause is hypomagnesemia (causing impairment of hormone synthesis), suppression of normal gland functioning because of hypercalcemia, or from delayed maturation of parathyroid functioning [5].

Idiopathic hypoparathyroidism may be linked to autoimmune disease or the congenital absence of the parathyroid glands [5,23].

Research shows the following statistics as they relate to hypoparathyroidism [5]:

- The incidence is 4 out of 100,000 people.
- Incidence of idiopathic and reversible forms is highest in children.
- Incidence of the irreversible acquired form is highest in older patients who have undergone surgery for hyperthyroidism or other pathology of the head and neck.

Hypoparathyroidism can cause a myriad of effects that lead to severe hypocalcemia and hyperphosphatemia. Recall that PTH is not regulated by either the pituitary or hypothalamus. This hormone maintains blood calcium levels by increasing bone resorption and GI absorption of calcium. PTH maintains an inverse relationship between serum calcium and phosphate levels [5].

Insufficient PTH secretion leads to decreased resorption of calcium from the renal tubules, decreased absorption of calcium in the GI tract, and decreased resorption of calcium from bone. Serum calcium falls to below normal levels triggering signs and symptoms of hypocalcemia such as neuromuscular irritability, increased deep tendon reflexes, and tremors [6].

Since calcium and phosphate have an inverse relationship serum phosphate levels increase, and excretion of phosphate by the kidneys decreases [5,6].

A number of complications are associated with hypoparathyroidism. These include [5]:

- Arrhythmias.
- Cataracts.
- Delayed mental development in children.
- Loss of consciousness.
- Osteoporosis.
- Tetany.

Several of these preceding complications are irreversible. Irreversible complications include [23]:

- Mental retardation in children.
- Stunted growth.
- Cataracts.
- Deposits of calcium in the brain that causes problems with equilibrium and seizures.

Signs and symptoms

Mild hypothyroidism may be asymptomatic. However, the disorder usually produces hypocalcemia and elevated phosphate levels that affect the central nervous system in particular and other body systems as well [5].

Characteristic signs of hypoparathyroidism as manifested by hypocalcemia are [5,6]:

- **Tetany:** Manifested by muscle hypertonia and tremors and spasmodic or uncoordinated movements triggered by attempts at voluntary movements.
- **Chvostek's Sign:** Hyperirritability of the facial nerve manifested by a spasm of facial muscles, which occurs when muscles or branches of the facial nerve are tapped.
- **Trousseau's Sign:** Carpopedal spasm (spasmodic contractions of the muscles of the hands and feet) triggered within three minutes after a blood pressure cuff is applied to the arm and inflated to 20 mmHg above patient's systolic pressure.
- **Laryngeal spasm**.

Additional clinical manifestations of hypoparathyroidism include [5,6,23]:

- Abdominal pain.
- Anxiety.
- Arrhythmias.
- Brittle nails.
- Cataracts.
- Depression.
- Dry, coarse skin.
- Dry, dull hair.
- Fatigue.
- Headaches.
- Memory problems.
- Mood swings.
- Muscles aches and cramps.
- Painful menstruation.
- Paresthesia (tingling or burning sensations in fingers, toes, and lips).
- Patchy loss of hair.
- Renal colic is there is a history of calculi.
- Weakness of tooth enamel causing decay and tooth loss.
- Weakness.

Hypoparathyroidism alert! CNS signs and symptoms are exaggerated during pregnancy, infection, thyroid hormone withdrawal, before menstruation, hyperventilation, and right before menstruation [5].

Diagnosis

Diagnosis is made on the basis of the patient's history and physical, presenting signs and symptoms, and the results of specific diagnostic tests. These tests include [5,6]:

- **Serum phosphorous level:** Elevated.
- **Serum calcium level:** Hypocalcemia indicated by a serum calcium level of 7.5 mg/100 ml or less.
- **Serum magnesium level:** Decreased.
- **Electrocardiogram (ECG):** As a result of hypocalcemia ECG shows prolonged QT and ST intervals.
- **Bone density:** If hypoparathyroidism is chronic bone density may be increased.

Diagnostic alert! Monitor patient for signs of heart block and decreased cardiac output due to prolongation of QT and ST intervals. Also monitor patients for signs of digoxin toxicity such as arrhythmias, nausea, fatigue, and vision changes since the reversal of hypocalcemia may quickly lead to digoxin toxicity [5,6].

Treatment and nursing considerations

Early detection and treatment are essential if complications such as cataracts and brain calcifications are to be prevented [5].

Treatment alert! Cimetidine (Tagamet) interferes with normal parathyroid function, especially if renal failure is also a problem. Any interference with parathyroid function increases the risk of hypocalcemia [6].

Calcium absorption requires the presence of vitamin D. Therefore, treatment of hypoparathyroidism must include vitamin D along with the administration of supplemental calcium [5].

Intravenous calcium administration is needed in the presence of acute life-threatening tetany. The most effective calcium solution is ionized calcium chloride (10%). All intravenous calcium preparations are given slowly since it is a highly irritating solution that stings and causes thrombosis. The patient experiences burning flushing feelings of the skin and tongue. However, the intravenous calcium solution also seems to rapidly relieve feelings of anxiety [6].

Additional treatment measures include [5,6,23]:

- Vitamin D to promote calcium absorption. If patients are unable to tolerate the pure forms of vitamin D alternatives such as dihydrotachysterol (if liver and kidney functions are adequate) or calcitriol (if liver and kidney functions are compromised).
- Thiazide diuretic therapy. Thiazide diuretics can increase blood calcium levels. If patients do not respond to calcium administration thiazide diuretics may be added to the treatment regimen. Be sure that loop diuretics are not prescribed since these can actually decrease calcium levels.
- Correction of preexisting hypomagnesemia.
- Provision of a high-calcium, low-phosphorus diet.
- Sedatives and anticonvulsants may be administered to control spasms and tremors until calcium levels return to normal.

Treatment alert! Chronic tetany requires life-long treatment with oral calcium and vitamin D supplements unless it is of a reversible form [5].

Nursing consideration: Nurses must provide very careful patient education regarding the importance of adhering to medication regimens. In cases where life-long treatment is necessary nurses must also be sure to provide emotional support and carefully monitor patients for adherence to their medication schedules.

Patients with a history of tetany who are awaiting a diagnosis of hypoparathyroidism need to have a patent intravenous line. Intravenous calcium preparations, a tracheotomy tray, and endotracheal tube should be kept at the bedside of hospitalized patients so that swift intervention is possible in the event of laryngospasm [5]. Be alert for the onset of minor muscle twitching, which may signal the onset of tetany [5].

Parents should be taught how to plan a diet that is rich in calcium and low in phosphorus. High calcium foods include dairy products, green leafy vegetables, broccoli, kale, and fortified orange juice and breakfast cereals. Phosphorus-rich foods to avoid include carbonated soft drinks, meats, and eggs [23].

Additional patient education measures to be implemented include [5,6,23]:

- Always provide written as well as verbal instructions. Make sure that information is written in terms that the patients and families can understand and in a language with which they are comfortable.
- Teach patients and families to stay alert for development of even minor muscle twitching and laryngospasm. These can signal tetany onset and HCPs should be notified immediately.
- Teach patients and families signs and symptoms of hypercalcemia and hypocalcemia and what to do if they occur. Assess their knowledge by having them describe these signs and symptoms.

Patient education alert! When providing patient/family education never simply hand out written instructions or assess knowledge by asking, "Do you understand how to take your medication?" or "Do you know what the symptoms of low calcium are?" These kinds of questions require only a "yes" or "no" answer. Many patients and families will simply answer "yes" rather than admit they don't understanding something. Assess knowledge by having them describe or list things such as signs and symptoms or side effects of medication. Have them demonstrate how to take medication to assess accuracy and knowledge.

- Teach safe and accurate medication administration. Have patients and families demonstrate correct medication administration and actually describe how and when to take it as well as any possible side effects. Do not forget to teach patients and families what to do if side effects occur. Stress the importance of having them keep their primary HCP informed of all medications (including OTC drugs and supplements such as herbs and vitamins).
- Warn patients not to substitute OTC preparations for their prescribed medication without approval of their HCPs. Some patients may try to do this in an attempt to save money because of the cost of prescription drugs. If this is an issue, refer patients and families to appropriate financial resources. Since calcium and vitamin D may be prescribed, patients may assume that less expensive OTC preparations will "work" just as well as prescription medications. Teach patients that OTC preparations may not have the same ingredients and/or the same strength as those in prescription medications, and, therefore, will not have the desired therapeutic effect.
- Caution patients and families to have their serum calcium level checked according to HCP orders (usually at least 3 times a year).
- Advise patients to wear medical alert bracelets.
- Provide information about skin care. Patients may have dry, scaly skin. Advise them not to use drying or irritating soaps or shower gels, especially those that are heavily perfumed. Encourage the use of therapeutic creams or lotions to moisten skin.
- Encourage patients to take good care of their nails, which may become brittle and dry. Instruct patients to keep their nails clean and well-trimmed to keep them from splitting.

Hyperparathyroidism

Grace is a 52-year-old women's college basketball coach at a prestigious university. She leads a busy life and travels frequently. She has been suffering from low back pain for many months, which she attributes to the strain of travel and physical activity related to her coaching responsibilities. Lately she has begun to notice some weakness in her legs accompanied by significant loss of appetite and nausea. She is losing sleep because of the onset of polyuria, which necessitates many trips to the bathroom at night. Because of her hectic travel schedule she has not made time to have these symptoms evaluated by a physician. Finally, at the conclusion of another successful basketball season, Grace consults her family physician about her ongoing symptoms. Her physician performs a thorough physical examination including evaluation of electrolyte levels, which show elevated blood calcium levels. Further diagnostic work-up shows a high concentration of serum PTH. Grace's physician diagnoses hyperparathyroidism.

Incidence

Hyperparathyroidism is the unregulated, hypersecretion of PTH [6,24]. The disease can occur at any age but is most common among women older than 50 years of age [6]. Hyperparathyroidism is a common disorder, although its prevalence is slowly decreasing [24]. It affects one in 1,000 people and is two to three times more common in females than in males [5].

Etiology and pathophysiology

There are two types of hyperparathyroidism: primary and secondary.

- **Primary hyperparathyroidism:** In primary hyperparathyroidism, one or more of the parathyroid glands enlarge, increasing PTH secretion, and promoting the elevation of serum calcium levels. The most common cause of primary hyperparathyroidism (in about 80% of cases) is single parathyroid adenoma (benign tumor of epithelial tissue). Parathyroid hyperplasia (enlargement of the parathyroid glands) is responsible for about 20% of cases. Note that parathyroid malignancy accounts for less than 1% of all cases of hyperparathyroidism [5,6,24].
- **Secondary hyperparathyroidism**: Secondary hyperparathyroidism is the overproduction of PTH due to a chronic abnormal stimulus. This is usually due to chronic renal failure. Other causes include vitamin D deficiency or osteomalacia (softening of bone) [5,6,24].

Chronic overproduction of PTH causes in increased levels of serum calcium [6]. The normal negative feedback mechanism does not function, and chronic excessive resorption of calcium from bone due to excessive parathyroid hormone can lead to osteopenia (loss of some bone density). Other symptoms of hyperparathyroidism are due to hypercalcemia specifically but are not specific to hyperparathyroidism [24].

In secondary hyperparathyroidism overproduction of PTH in patients with renal failure add to the pathophysiology of bone disease found in patients on dialysis [24]. The abnormality that causes hyperparathyroidism causes hypocalcemia rather than the hypercalcemia caused by primary hyperparathyroidism [5].

Hyperthyroidism alert! Tertiary hyperparathyroidism refers to excessive secretion of PTH following secondary hyperparathyroidism of long duration and resulting in hypercalcemia. Some experts use the term tertiary hyperparathyroidism to refer to secondary hyperparathyroidism that lingers after successful renal transplantation [24].

Possible complications stemming from hyperparathyroidism include [5]:

- Cardiac arrhythmias.
- Heart failure.
- Hypertension.
- Hypoparathyroidism after surgery.
- Osteoporosis.
- Peptic ulcers.
- Renal calculi.
- Renal failure.

Signs and symptoms

Clinical manifestations of primary hyperparathyroidism are due to hypercalcemia and are evident is several body systems, including [5]:

- **Cardiac system**: Arrhythmias, hypertension, and cardiac standstill (cessation of cardiac output) [6].
- **CNS**: Hyperparathyroidism causes depression of neuromuscular function as evidenced by emotional instability, alterations in levels of consciousness, general fatigue, personality changes, depression, stupor, and, possibly coma [5,6].
- **GI system**: Pancreatitis, ongoing, severe epigastric pain that radiates to the back, peptic ulcers, abdominal pain, anorexia, nausea, and vomiting [5].
- **Musculoskeletal system**: Significant muscle weakness and atrophy, especially in the legs. Chronic low back pain and bones that easily fracture because of bone degeneration, bone pain, chondrocalcinosis, and occasional severe osteopena [5].
- **Renal system**: Elevated calcium levels cause nephrocalcinosis, possible recurring nephrolithiasis that may lead to renal insufficiency. Various renal signs and symptoms such as polyuria, are among the most common effects of hyperthyroidism [5].
- **Miscellaneous effects**: Skin necrosis, cataracts, anemia, and subcutaneous calcification [5].

Secondary hyperparathyroidism decreased serum calcium levels cause symptoms of hypocalcemia with skeletal deformities accompanied by signs and symptoms of the underlying disease [5]. Secondary hyperparathyroidism may be prevented by ensuring a diet that contains adequate amounts of calcium or by taking calcium and vitamin D supplements [5].

Diagnosis

Diagnosis is based on history, clinical manifestations, identification of underlying disorders, and the results of diagnostic tests.

Primary hyperparathyroidism diagnosis

The following findings are indicative of primary hyperparathyroidism [5,6]:

- Radioimmunoassay shows high serum PTH accompanied by hypercalcemia. The hypercalcemia must be noted on at least two separate tests to validate consistency of results.
- Elevated chloride and alkaline phosphate levels and a decreased serum phosphorus level.
- Elevated uric acid and creatinine levels.
- Increased basal acid secretion.
- Skeletal changes are revealed on x-ray.

Early diagnosis of hyperparathyroidism can be difficult and complications may be evident before diagnosis is confirmed. CT scan can identify parathyroid tumors more quickly than traditional X-rays. Sestamibi scan can help to assess tumor location [6].

Secondary hypoparathyroidism diagnosis

Laboratory findings in the presence of secondary hypoparathyroidism show [5]:

- Normal or slightly decreased serum calcium levels.
- Significantly elevated phosphorus levels.

Diagnostic work-up is performed to identify the underlying cause of the disease [5].

Treatment and nursing considerations

Treatment of primary hyperparathyroidism may include surgical removal of abnormal parathyroid tissue and initial management of hypercalcemia [5,6].

Treatment of hypercalcemia includes [6]:

- Administration of intravenous normal saline solution and diuretics such as Lasix and Edecrin to increase urinary excretion of calcium for those patients who are not in renal failure.
- Administration of agents to inhibit bone resorption of calcium. These include Aredia, Cibacalcin, or Didronel.
- Administration of oral phosphate as an anti-hypercalcemia agent.
- Restriction of dietary calcium and discontinuation of drugs that might facilitate hypercalcemia such as thiazides, and vitamin D.
- Dialysis for patients in renal failure or for those whose hypercalcemia does not respond to other treatments.
- Reduced dosage of digoxin since hypercalcemic patients are more vulnerable to the toxic effects of this drug.
- Monitoring of calcium (daily), blood urea nitrogen (BUN), potassium, and magnesium levels.

Surgical removal of parathyroid tissue may relieve bone pain within 3 days of the surgery. Unfortunately, renal damage may be irreversible [5].

Surgical alert! All but half of one remaining parathyroid gland is needed to maintain normal PTH levels [5].

Nursing consideration: Following surgery nursing interventions include [5,6]:

- Monitor intake and output.
- Provide adequate fluid and electrolyte replacement.
- Strain all urine for renal calculi.
- Limit dietary intake of calcium.
- Monitor for urinary tract infections, hematuria, and renal colic.
- Take safety precautions to prevent pathologic fractures, to which the patient is prone.
- Monitor for signs of tetany.
- Monitor fluid and electrolyte levels.

Pathology of hyperparathyroidism involves significant effects of hypercalcemia. Now, postoperatively, the patient must be monitored for hypocalcemia. Such signs and symptoms include [6]:

- Paresthesia.
- Positive Chvostek's sign: Tapping the check over the facial nerve causes a twitch of the lip or facial muscles.
- Positive Trousseau's sign: Carpopedal spasm induced by applying a blood pressure cuff and occluding circulation in the arm.
- Take safety precautions if the patient is prone to seizures.

Treatment of secondary hyperparathyroidism focuses on correction and treatment of the underlying cause. Remember that secondary hyperparathyroidism causes hypocalcemia as opposed to primary hypothyroidism, which causes hypercalcemia. Generalized treatment initiatives include [5]:

- Vitamin D therapy.
- Administration of oral calcium preparation in the presence of renal disease.
- Administration of a new classification of drugs (calcimimetics) approved for the treatment of secondary hyperparathyroidism. These drugs act by stopping the secretion of PTH.

Patients with chronic secondary hyperparathyroidism may find that the parathyroid glands do not revert to normal function even after calcium levels have been returned to normal [5].

Adrenal insufficiency

Jackie is 55-year-old account executive with a major industrial company in a small urban area. She complains of not being able to get over the "flu" that she has had for nearly a month. She feels week, tired, has lost weight, and has periods of nausea, vomiting, and diarrhea. Her colleagues tease her that she has not been taking sick time from work but has actually been vacationing at the beach. They make these comments because Jackie appears to be deeply suntanned, especially in the creases of her hands, elbows, and knees. She also notices that several scars over her knees appear to be darker. Jackie discusses her symptoms with the company's nurse. The nurse is disturbed, believing that these symptoms may indicate an endocrine disorder. After consulting several reference books the nurse wonders if Jackie may be suffering from Addison's disease.

Adrenal insufficiency, also known as Addison's disease and adrenal hypofunction, is the result of hypofunction of the adrenal glands [5,25]. The disease occurs in two forms: primary and secondary [25].

- Primary adrenal insufficiency: The primary form (commonly referred to as Addison's disease) originates within the adrenal glands and is characterized by a decrease in mineralocorticoid, glucocorticoids, and androgen secretion [11,25].
- Secondary adrenal insufficiency: The secondary form of the disease occurs secondary to a disorder (e.g., pituitary tumor) outside the adrenal glands. In this form, aldosterone secretion may not be affected [5,11]. Secondary adrenal insufficiency is more common than Addison's disease [25].

Incidence

Adrenal hypofunction affects males and females in equal numbers and can occur at any age [5,11]. Hypofunction of the adrenal glands affects one in 16,000 neonates congenitally. In adults, 8 in 100,000 people are affected [5].

Etiology

Primary adrenal hypofunction is defined as occurring when more than 90% of both adrenal glands are destroyed [5,25]. The majority of cases (up to 80% of Addison's disease cases) are caused by an autoimmune process in which circulating antibodies specifically "attack" adrenal tissue [5,25]. Autoimmune Addison's disease occurs primarily in middle-aged females and gradually destroys the adrenal cortex, the outer layer of the adrenal glands [25].

In primary adrenal hypofunction, the adrenal glands may be the only glands affected. However, other endocrine glands may be affected as well, something that is referred to as polyendocrine deficiency syndrome [25].

Polyendocrine deficiency syndrome appears in two forms: type 1 and type 2 [25]. Type 1 is inherited and occurs in children who, in addition to adrenal insufficiency, may also have [25]:

- Underactive parathyroid glands.
- Slowed sexual development.
- Pernicious anemia.
- Chronic fungal infections.
- Chronic hepatitis.

Type 2 polyendocrine deficiency syndrome, sometimes referred to as Schmidt's syndrome, is also inherited but usually affects young adults and includes [25]:

- Underactive thyroid gland.
- Slowed sexual development.
- Diabetes.
- Vitiligo (loss of pigment on areas of the skin).

Other causes of primary adrenal hypofunction include [5,25]:

- **Tuberculosis:** Tuberculosis can destroy the adrenal glands. It was once the chief cause of primary adrenal insufficiency, but now accounts for only 10% to 15% of Addison's diseases in developed countries. However, current research shows an increase in primary adrenal hypofunction due to tuberculosis of the adrenal glands and cytomegalovirus infection. Cytomegalovirus primarily affects people who have weakened immune systems.
- Malignancy of the adrenal glands.
- Surgical removal of the adrenal glands.
- Hemorrhage into the adrenal glands.
- Genetic defects.
- Medication induced adrenal hypofunction from such agents as antifungal medications and the anesthetic etomidate.

The occurrence of secondary adrenal hypofunction may be traced to a temporary form of the disorder that occurs when long-term corticosteroid is discontinued. Such long-term therapy causes the adrenal glands to produce less of their hormones. Once the prescription corticosteroids are discontinued the adrenal glands may not resume production of their own hormones in a timely fashion. This can lead to secondary adrenal hypofunction [5,25].

Secondary adrenal hypofunction alert! Prescription corticosteroids should always be discontinued gradually over a period of time ranging from weeks to months to reduce the chances of adrenal insufficiency [25].

- Surgical removal of pituitary tumors.
- Infections of the pituitary.
- Reduction of blood flow to the pituitary.
- Pituitary radiation for treatment of pituitary tumors or tumors of adjacent structures.
- Surgical removal of portions of the hypothalamus.
- Surgical removal of the pituitary gland.

Adrenal crisis

Adrenal insufficiency can sometimes lead to adrenal crisis, a critical deficiency of mineralocorticoids and glucocorticoids. Adrenal crisis is the most serious complication related to adrenal hypofunction. It can develop gradually or abruptly [5,11,25].

Adrenal crisis is most likely to develop in people who [5,11]:

- Fail to respond to hormone replacement therapy.
- Abruptly stop hormone or prescribed steroid therapy.
- Experience trauma, surgery, or other types of physiologic stress that exhaust the body's provisions of glucocorticoids in someone who has adrenal hypofunction.
- Undergo bilateral adrenalectomy.
- Develop adrenal gland thrombosis following a severe infection (referred to as Waterhouse-Friderichsen syndrome).

During adrenal crisis, there is a swift decline in the steroid hormones cortisol and aldosterone. This decline impacts the liver, stomach, and kidneys [11]. Adrenal crisis produces [5,25]:

- Significant weakness and fatigue.
- Abrupt severe pain in the lower back, abdomen, or legs.
- Severe nausea and vomiting.
- Dehydration.
- Hypotension.
- Loss of consciousness.

Occasionally, adrenal crisis can cause patients to develop a high fever followed by hypothermia. Untreated adrenal crisis can lead to vascular collapse, renal shutdown, coma, and death [5].

Adrenal crisis requires immediate, life-saving interventions. An intravenous bolus of hydrocortisone must be administered followed by fluid resuscitation. Later doses of hydrocortisone are given intramuscularly or are diluted with dextrose in saline solutions and given intravenously until the patient stabilizes [5,25].

With swift, appropriate treatment, adrenal crisis usually resolves quickly. Patients may need maintenance doses of hydrocortisone to maintain stability [5].

Nursing consideration: Persons at risk for adrenal crisis should wear a medical alert bracelet and carry a corticosteroid injection with them at all times and be taught how to inject themselves. Nurses should teach the patients' and their families and friends how to administer the injection as well in case the patient loses consciousness and is unable to inject him/herself [25].

Pathophysiology of adrenal insufficiency

The adrenal glands, located just above the kidneys, produce cortisol and aldosterone. These hormones help regulate blood pressure, metabolism, and the way the body responds to stress. Adrenal hormones also help to produce androgens and estrogens [25].

The adrenal hormone cortisol, a glucocorticoid, affects almost every tissue and organ in the body. Cortisol helps maintain blood pressure, slow the immune system's inflammatory response, and regulate metabolism[11,25].

In the event of adrenal insufficiency, decreased levels of cortisol can have the following effects on specific organs [11,25]:

- **Liver**: Reduced hepatic glucose output leading to hypoglycemia which can progress to dangerous levels.
- **Stomach**: Reduced levels of digestive enzymes leading to nausea, vomiting, cramps, and diarrhea.

Decreased levels of aldosterone can have the following effects [11,25]:

- **Kidneys**: Sodium and water loss accompanied by potassium retention. Electrolyte imbalances can lead to hypoglycemia and adverse cardiac effects.
- **Heart**: Arrhythmias, decreased output, hypotension.

Untreated the effects of adrenal hypofunction can progress to adrenal crisis causing shock, coma, and death [11].

Signs and symptoms

The most common signs and symptoms of adrenal hypofunction include [5,25]:

- Abdominal pain.
- Anorexia.
- Craving salty foods.
- Depression.
- Decreased libido in women.
- Diarrhea.
- Diaphoresis.
- Fatigue (chronic or long-lasting).
- Headache.
- Hypoglycemia.
- Hypotension (especially orthostatic hypotension).
- Irritability.
- Menstrual abnormalities.
- Nausea.
- Vomiting.
- Weakness.
- Weight loss.

Addison's disease usually causes a characteristic, conspicuous bronze coloration of the skin. Patients appear to be deeply suntanned especially in the creases of the hands, over the metacarpophalangeal joints, elbows, and knees. Scars may darken, areas of vitiligo appear, and increased pigmentation of the mucous membranes, particularly of the gingival mucosa [5].

Adrenal hypofunction alert! Abnormalities in skin and mucous membrane coloration are due to decreased secretion of cortisol, which makes the pituitary gland secrete excessive amounts of corticotropin and melanocyte-stimulating hormone [5].

As the disease progresses, additional cardiovascular effects may become evident such as decreased cardiac output, decrease in heart size, and a weak, irregular pulse [5,11]. Other clinical manifestations include [5,11,25]:

- Decreased ability to tolerate even the smallest amount of stress.
- Poor coordination.
- Hypoglycemia.
- Retardation of pubic and axillary hair growth.
- Amenorrhea.

Secondary adrenal hypofunction produces similar clinical manifestations to those of primary adrenal hypofunction but without hyperpigmentation because corticotropin and melanocyte stimulating hormone levels are low. Aldosterone secretions may continue to be fairly normal in the secondary type so electrolyte levels may also be normal and hypotension may not occur [5,11].

Diagnosis

After a thorough history and physical and evaluation of signs and symptoms various lab studies are used to confirm a diagnosis of adrenal hypofunction and to categorize the disease as primary or secondary [5,11].

Analysis of plasma and urine shows decreased levels of corticosteroid concentrations. A high level of corticotropin suggests primary adrenal hypofunction. A low level of corticotropin suggests secondary adrenal hypofunction [5,11].

A rapid corticotropin test (ACTH stimulation test) is used to evaluate plasma cortisol response to corticotropin. First, plasma cortisol samples are obtained. Then an intravenous infusion of cosyntropin is administered. Plasma samples are obtained at 30 and 60 minutes after cosyntropin infusion. If plasma cortisol levels do not increase, adrenal insufficiency is suspected [11].

In patients who have characteristic signs and symptoms of Addison's disease the following laboratory tests indicate acute or crisis level adrenal hypofunction [5,11]:

- Increased potassium serum calcium, and blood urea nitrogen levels (BUN).
- Decreased serum sodium levels.
- Elevated hematocrit, lymphocyte, and eosinophils counts.
- X-rays show decreased heart size and adrenal calcification.
- Decreased plasma cortisol levels in plasma. Levels are less than 10 mcg/dL in the morning. Levels are lower at night.

Adrenal hypofunction diagnostic alert! Note that testing cortisol levels takes considerable amounts of time. Therefore, adrenal crisis treatment should not be delayed while waiting for the results of this particular test [11].

After a diagnosis of Addison's disease is made, the following tests may help HCPs determine if the disease is related to tuberculosis or to antibodies associated with autoimmune Addison's disease [25]:

- **Abdominal ultrasound:** Performed to identify adrenal gland abnormalities such as an increase or decrease in size, nodules, or the presence of calcium deposits that may suggest bleeding.
- **Tuberculin skin test:** A positive test suggests adrenal insufficiency related to tuberculosis.
- **Antibody blood test:** The presence of antibodies associated with autoimmune Addison's disease helps to confirm diagnosis.

After a diagnosis of secondary adrenal insufficiency is made, the following tests may be performed to assess pituitary gland functioning [25]:

- **CT scan:** A CT scan can show the size and shape of the pituitary gland and abnormalities such as nodules or tumors.
- **MRI:** An MRI provides three dimensional images of the hypothalamus and the pituitary gland to detect abnormalities in size and the presence of tumors, nodules, or other abnormalities.
- **Hormonal blood tests:** Hormonal blood tests are used to evaluate pituitary functioning.

Treatment and nursing considerations

All patients affected by primary or secondary adrenal hypofunction need life-long corticosteroid replacement therapy. Cortisone or hydrocortisone is administered because these agents have a mineralocorticoid effect [5,11].

To minimize or prevent dehydration and hypotension, a synthetic drug that acts as a mineralocorticoid (oral fludrocortisones) may be given. Testosterone injections may be given to women who experience a decrease in libido and muscle weakness. However, testosterone injection may cause masculinizing effects [11].

Special nursing considerations include [5,25]:

- Monitor for signs of adrenal crisis. Teach patients and families how to recognize adrenal crisis and to seek immediate emergency medical attention if it occurs.
- Explain that corticosteroid therapy must be taken for the rest of the patients' lives. Teach patients how to take their medication and have them demonstrate knowledge of these medications by demonstrating how to take them and being able to state the name of the drug(s), route, dose, action, and side effects. As always,

keep HCPs aware of any medications and supplements they are taking.
- Advise patients to wear medical alert bracelets that contain the name of the drugs they are taking and the doses of these drugs.
- Teach patients (and their families) who are diabetic that steroid replacement therapy may require insulin dosage adjustments and to monitor their blood glucose levels with particular care. Tell them to consult with the HCP who helps manage their diabetes that they are on life-long corticosteroid therapy so that he/she can adjust treatment plans accordingly.
- Advise patients to take steroid therapy in the morning since administration in the late afternoon or evening may stimulate the CNS and cause insomnia.
- Advise patients to use caution in their daily activities because steroid therapy can make it easier for some patients to bruise.
- Advise patients who are anorectic to try eating 6 small meals a day instead of 3 large ones. Explain that a late-morning snack may help prevent hypoglycemia.
- Advise patients and families that the dose of corticosteroid therapy may need to be increased during times of stress such as physical illness or emotional trauma.
- Advise patients and families that infection, trauma, injury, or profuse diaphoresis may trigger an adrenal crisis.
- Teach patients that they should keep an emergency kit containing hydrocortisone in a prefilled syringe for use in times of stress or adrenal crisis. Have patients and families demonstrate their ability to give themselves hydrocortisone injections.

Hyperaldosteronism

Emma is a 40-year-old chemistry professor at a private university. She has a family history of diabetes mellitus and has recently been diagnosed with the disease. Her family physician, however, is concerned that there is something "more" than diabetes causing additional signs and symptoms such as muscle weakness, increased neuromuscular irritability, and irregular heart rate. Lab studies show low levels of potassium, which could account for the preceding "additional" symptoms. Emma does not take diuretics nor has she had any recent illness that would contribute to GI losses such as vomiting or diarrhea. Searching for a cause of the hypokalemia (abnormally low potassium), the physician does a more detailed diagnostic work-up. After extensive diagnostic testing, Emma is found to have a benign aldosterone-producing adrenal adenoma, which is triggering hypersecretion of aldosterone.

Hyperaldosteronism, also referred to as Conn's syndrome or aldosteronism, is the hypersecretion of the mineralocorticoid aldosterone by the adrenal cortex. Such extreme secretion causes excessive reabsorption of sodium and water, and excessive renal excretion of potassium [5].

Etiology and incidence

Benign aldosterone-producing adrenal adenoma is the cause of hyperaldosteronism in 70% of patients. The cause is unknown in 15% to 30% of patients. Rare causes of hyperaldosteronism are bilateral adrenocortical hyperplasia (affecting children) and cancer. Incidence is 3 times greater in females compared to males and occurs most often in persons between the ages of 30 and 50 [5].

Pathophysiology

Hyperaldosteronism may be classified as primary or secondary. Primary hyperaldosteronism refers to a chronic excess of aldosterone that is independent of the renin-angiotensin system. This disorder actually causes a suppression of plasma renin activity [5,26].

Primary hyperaldosteronism primarily affects adults. Incidence peaks in the fourth to sixth decades of life. About 60% of cases of primary hyperaldosteronism are due to an idiopathic hyperaldosteronism (IHA). An estimated 40% of cases are due to an aldosterone-producing adenoma (APA). Only about 1% of cases are classified as inherited and are most likely to occur during childhood [26].

In primary hyperaldosteronism, excess aldosterone facilitates sodium reabsorption by the kidneys, which leads to mild hypernatremia, hypokalemia, and increased extracellular fluid (ECF) volume. Intravascular fluid volume also increases and causes volume-dependent hypertension and increased cardiac output [5].

Hyperaldosteronism alert! Eating large amounts of English black licorice or licorice-like substances can cause a syndrome that mimics primary hyperaldosteronism. This is because glycyrrhizic acid, a substance found in licorice, has a mineralocorticoid action [5].

Nursing consideration: Nurses should caution patients about eating excessive amounts of licorice or licorice substances since excessive intake can cause a primary hyperaldosteronism-like syndrome.

Secondary hyperaldosteronism describes a diverse group of disorders due to an extra-adrenal abnormality that triggers the adrenal gland to increase production of aldosterone. It occurs in two forms: one that is associated with hypertension and one that is not [5,26].

The form associated with hypertension is caused by conditions that elevate blood pressure through increased renin production such as pregnancy and taking hormonal contraceptives. The form of secondary hyperaldosteronism that is not associated with hypertension may be due to conditions such as nephritic syndrome, hepatic cirrhosis with ascites, and heart failure, all of which commonly cause edema [5].

The following complications are associated with hyperaldosteronism [5]:
- Arrhythmias.
- Heart failure.
- Ischemic heart disease.
- Left ventricular hypertrophy.
- Neuromuscular irritability.
- Paresthesia.
- Seizures.
- Tetany.

Diagnosis

Diagnosis depends on history and physical, signs and symptoms, and specific diagnostic tests.

Most of the presenting clinical manifestations of hyperaldosteronism are due to hypokalemia. Signs and symptoms related to decreased potassium include [5,26]:
- Fatigue.
- Headaches.
- Intermittent, flaccid paralysis.
- Muscle weakness.
- Paresthesia.

Metabolic alkalosis may also occur, leading to hypocalcemia. If hypocalcemia occurs, the patient may also exhibit tetany [5].

Diabetes mellitus is frequently found in conjunction with hyperaldosteronism because hypokalemia, which causes the majority of clinical effects of hyperaldosteronism, can interfere with proper secretion of insulin. Hypertension, vision problems, polyuria, and polydipsia may also occur [5].

Diagnostic alert! Ongoing low levels of serum potassium in patients who do not have edema, are not taking diuretics, have not had GI tract losses due to vomiting or diarrhea, and who have a normal sodium intake strongly suggest hyperaldosteronism [5].

In hyperaldosteronism, serum bicarbonate levels are often elevated accompanied by alkalosis. Other tests show significantly increased urinary aldosterone levels, increased plasma aldosterone levels, and in secondary hyperaldosteronism, increased levels of plasma renin [5].

Typically the plasma aldosterone concentration (PAC) to plasma renin activity (PRA) ratio test is used as a screening tool for hyperaldosteronism. This test measures the plasma PAC to PRA ratio. A high ratio of PAC to PRA suggests primary hyperaldosteronism, but additional testing is usually performed to confirm diagnosis [27].

Tests used to confirm primary hyperaldosteronism include [27]:

- Captopril suppression test: Patients are given a single dose of the antihypertensive drug captopril after which plasma aldosterone and renin are measured. In patients with primary hyperaldosteronism blood levels of aldosterone remain high and renin levels are low.
- 24-hour urinary excretion of aldosterone test: Patients ingest a high-sodium diet for 5 days after which the amount of aldosterone in the urine is measured. In patients with primary hyperaldosteronism, aldosteronism will not be suppressed by the salt load, and the level of aldosterone in the urine will be high [27].
- Saline suppression test: Patients are given intravenous salt solutions after which blood levels of aldosterone and renin are measured. In patients with primary hyperaldosteronism the level of aldosterone in the blood is still high, and the level of renin is low even after this salt loading [27].

A suppression test is also helpful in differentiating between primary and secondary hyperaldosteronism. Patients receive oral desoxycorticosterone for 3 days while plasma aldosterone levels and urinary metabolites are continuously measured. In secondary hyperaldosteronism, levels decrease but levels remain the same in primary hyperaldosteronism [5].

Treatment and nursing considerations

Treatment measures for unilateral hyperaldosteronism (only one adrenal gland is affected) include surgical adrenalectomy of the affected gland, administration of a potassium sparing diuretic, and restriction of sodium [5]. In the presence of bilateral adrenal hyperplasia, administration of spironolactone (the drug of choice) is recommended for the management of primary hyperaldosteronism [5,14]. Eplerenone, an aldosterone-blocking antihypertensive, may also be prescribed as well as steroid hormone replacement therapy [5,14]. Treatment of secondary hyperaldosteronism focuses on correction of the underlying cause and management of the clinical manifestations of the hyperaldosteronism [5,26].

Special nursing considerations include [5]:

- Monitoring for signs of tetany and hypokalemia such as cardiac arrhythmias, weakness, and paresthesia. Teach patients to recognize these signs and to report them to their HCPs promptly.
- Monitoring for signs of rising serum potassium levels and signs of adrenal hypofunction (especially hypertension) after adrenalectomy.
- Collaborating with the dietician, patients, and families, to develop a low sodium, high potassium diet.
- Teach patients who are taking the potassium-sparing diuretic spironolactone to be alert to the development of signs of hyperkalemia. Patients should be informed that long-term use of this drug may lead to impotence and gynecomastia.
- Advise patients who are taking steroid hormone replacement therapy to wear a medical identification bracelet.

Cushing's syndrome

Brenda is a 30-year-old financial counselor. She suffers from rheumatoid arthritis and has taken prednisone for a significant period of time in an attempt to control the increasingly severe effects of the disease. Lately, Brenda has begun to notice some troubling new symptoms. She complains about gaining weight, and that this excess weight is especially noticeable over the trunk of her body and on her face, which she says has gotten "round." She feels weak, and minor cuts and scratches "take forever" to heal. Brenda also notices an increase in facial hair over her lip and chin. Brenda attributes these signs and symptoms to the effects of rheumatoid arthritis, which she says has "ruined" her life. Brenda is in no hurry to report these new problems, believing that nothing can be done to resolve them. "I'll just wait until my next regular doctor's appointment next month." When Brenda next sees her physician these new signs and symptoms have gotten worse, and she has begun to experience upper gastric pain, menstrual irregularities, and emotional liability. Her physician is alarmed by Brenda's appearance and the new signs and symptoms that have arisen. Based on Brenda's history and presenting clinical picture the physician initiates a diagnostic work-up to confirm her suspicion that Brenda has Cushing's syndrome.

Cushing's syndrome is a hormonal disorder caused by prolonged exposure of the body's tissues to excessive levels of adrenocortical hormones, especially cortisol, related corticosteroids, and, to a lesser extent, androgens and aldosterone [5,28].

Cushing's syndrome produces a characteristic clinical picture that includes fat deposits of the face, neck, and trunk and purple striae on the skin. Prognosis depends on the underlying cause of the syndrome. Prognosis is poor in persons who do not receive treatment and in people with untreatable ectopic corticotropin producing cancer [5].

Cushing's syndrome alert! If excess of glucocorticoids is due to a pituitary dependent condition, it is called Cushing's disease [11].

Review of the role of cortisol

The hypothalamus sends corticotropin-releasing hormone (CRH) to the pituitary gland. CRH triggers the pituitary to secrete adrenocorticotropin hormone (ACTH), which stimulates the adrenal glands to release adrenocortical hormones such as cortisol and, to a lesser extent, androgens and aldosterone [5,28].

Cortisol is essential to many critical body functions. Cortisol [28]:

- Helps maintain blood pressure and cardiovascular function.
- Reduces the inflammatory response of the immune system.
- Balances the effects of insulin.
- Regulates the metabolism of proteins, carbohydrates, and fats.
- Helps the body respond to stress.

Cushing's syndrome alert! Since cortisol helps the body respond to stress, pregnant women in the last 3 months of pregnancy and highly trained athletes have high levels of this hormone [28].

EBP alert! Since research shows that cortisol levels help in the stress response, nurses must know (and anticipate) that such levels are elevated during the last three months of pregnancy and in highly trained athletes. Knowing this can help you explain results to patients and families and avoid unnecessary diagnostic testing if elevated levels in these patients are thought to be abnormal.

Under normal conditions, when the amount of cortisol in the bloodstream is adequate, the hypothalamus releases less CRH, which decreases pituitary secretion of ACTH. However, if the adrenal glands, pituitary, or hypothalamus are damaged or diseased, proper regulation of cortisol levels can become skewed [28].

Incidence and etiology

Cushing's syndrome is 10 times more common in women than in men and is most often diagnosed in persons between the ages of 25 and 40. It affects 13 out of every one million people [5,6].

Cushing's syndrome can be categorized as three types [11]:

- **Primary:** Primary Cushing's syndrome is due to disease of the adrenal cortex.
- **Secondary:** Secondary Cushing's syndrome is caused by hyperfunction of cells that secrete corticotropin in the anterior pituitary gland.
- **Tertiary:** Tertiary Cushing's syndrome is due to dysfunction or injury of the hypothalamus.

The majority of cases of Cushing's syndrome (70%) are caused by excess production of corticotropin. This leads to hyperplasia (excessive cell proliferation) of the adrenal cortex [5,11]. Causes of corticotropin overproduction include [5,11,28]:

- Pituitary hypersecretion (Cushing's disease) usually due to pituitary adenomas.
- A corticotropin-producing tumor located in another organ especially a cancerous tumor of the pancreas or bronchus. This is sometimes referred to as ectopic ACTH syndrome.
- Administration of synthetic glucocorticoids including glucocorticoid steroid hormones such as prednisone, which may be taken for asthma, rheumatoid arthritis, and other inflammatory diseases.

The remaining 30% of patients are affected by Cushing's syndrome that is caused by cortisol-secreting adrenal tumors that are usually benign. However, in infants, the usual cause is adrenal cancer [5,11].

Etiology alert! Rarely, Cushing's syndrome may be due to an inherited tendency to develop tumors of one or more of the endocrine glands [28].

Complications

There are a number of complications associated with Cushing's syndrome. These complications are related to pathological effects of the disorder [5,6,11]:

- Lipidosis, a disorder of fat metabolism, may occur.
- Increased gastric secretion, pepsin production, and decreased amounts of gastric mucous can lead to the development of peptic ulcers.
- Increased hepatic gluconeogenesis and insulin resistance may lead to impaired glucose tolerance.
- Increased calcium resorption from bone can cause osteoporosis and pathological fractures.
- Decreased lymphocyte production, hyperglycemia, and inhibited antibody formation can lead to frequent infections and/or slow healing of wounds.
- Sodium and water retention contribute to the development of hypertension, which is quite common in persons with Cushing's syndrome. Ischemic heart disease and heart failure may develop.
- Increased adrenal androgen production can cause menstrual problems and disturbances in sexual function.
- A decreased ability to cope with physical or psychological stress can lead to mental health disturbances that can range in severity from mood swings to psychosis.

Signs and symptoms

Cushing's syndrome can have adverse effects on multiple body systems. Effects are directly related to the adrenocortical hormone involved [5].

Differentiation between Cushing's syndrome and cushingoid syndrome! Differentiating between Cushing's syndrome and cushingoid syndrome can be challenging. Chronic depression, alcoholism, and long-term treatment with corticosteroids can combine to produce cushingoid syndrome, an adverse consequence characterized by fat deposits between the shoulders and around the waist and many systemic abnormalities. Cushing's syndrome has similar signs, but can be differentiated from cushingoid syndrome by the additional presence of hypertension, renal problems, hyperglycemia, muscle weakness, tissue wasting, and frequently changing emotional states (emotional lability) [5].

Signs and symptoms of Cushing's syndrome can be grouped according the body system affected.

- **Cardiovascular system:** Sodium and water retention leads to hypertension, left ventricular hypertrophy, expanded blood volume, edema, weight gain, fatigue, capillary weakness stemming from protein loss, bleeding, petechiae, and ecchymosis [5,6].
- **Endocrine and metabolic systems:** Diabetes mellitus, decreased glucose tolerance, fasting hyperglycemia, and glycosuria [5].
- **Gastrointestinal system:** Increased gastric secretion, pepsin production, and decreased gastric mucous can cause peptic ulcer [5,11].
- **Immune system:** Excessive levels of adrenocortical hormones can cause decreased lymphocyte production and suppressed antibody formation. This increases the likelihood of infection, slows the wound healing process, and decreases the body's ability to withstand stress [5,6].

Cushing's syndrome alert! Immune system suppression can mask infection, even severe infections [5]. It is important for HCPs to recognize, and to teach patients and families to recognize, even the slightest signs of infection.

- **Integumentary system:** Characteristic fat pads form above the clavicles, over the upper back (buffalo hump) on the face (moon face), and around the trunk. Arms and legs are slender because of muscle wasting. Acne and hirsutism (male patterned hair growth)

are evident in females. Purplish striae are evident on the skin. The skin is thin and fragile, and scalp hair thins [5,6,11].

- **Musculoskeletal system**: Muscle weakness because of low potassium levels is evident. Loss of muscle mass may occur. Decreased bone mineral often leads to pathologic fractures and, in children, skeletal growth retardation [5,6,11].
- **Renal/urologic system**: Sodium and fluid retention occurs. There is increased excretion of potassium, inhibited antidiuretic hormone secretion, and formation of ureteral calculi [5].
- **Reproductive system**: Increased androgen leads to hypertrophy of the clitoris and amenorrhea or oligomenorrhea in women. Sexual dysfunction and loss of libido may also occur [5,6].

Diagnosis

Diagnosis depends on the patient's clinical presentation and the results of various diagnostic tests. The first step in the diagnostic process is the review of signs and symptoms, especially notable being the characteristic moon face, buffalo hump, muscle weakness, and purple striae [5]. A clinical picture that suggests Cushing's syndrome requires determination of plasma steroid levels. Plasma cortisol levels should be obtained in the morning since levels are higher in the morning and decrease gradually throughout the day. In the presence of Cushing's syndrome cortisol levels do not fluctuate. They remain consistently elevated throughout the day. Analysis of a 24-hour urinary cortisol collection provides evidence of consistently elevated cortisol levels [5,11].

If morning plasma cortisol levels are elevated, and 24-hour urinary cortisol collection show consistent elevation, Cushing's syndrome is considered to be likely and should be confirmed by additional testing [5,11]. Test results indicative of Cushing's syndrome include [6,11]:

- Significantly elevated plasma cortisol levels.
- Increased blood glucose levels.
- Glucose intolerance.
- Reduced eosinophils.
- Hypokalemia.
- Elevated urinary 17-hydroxycorticoids and 17-ketogenic steroids.
- In the presence of an adrenal tumor, ACTH plasma levels are elevated. ACTH levels that are higher in the petrosal sinuses than in a vein in the forearm suggest the presence of a pituitary adenoma.
- Elevated salivary cortisol levels are considered significant.
- Elevated WBC count.
- CT scan, MRI, and/or ultrasound are used to detect the presence and location of a tumor in the pituitary or adrenal glands.

High dose dexamethasone suppression test is used to determine if Cushing's syndrome is due to pituitary dysfunction. If dexamethasone suppresses plasma cortisol levels, the test is considered positive. Failure to suppress plasma cortisol levels indicates the presence of an adrenal tumor or non-endocrine, corticotropin-secreting tumor. HCPs should be aware that this test can produce false positive results [4,11].

Treatment

The goals of Cushing's syndrome treatment are to [5,11]:

- Restore hormonal balance.
- Reverse Cushing's syndrome.

Treatment strategies may include surgery, radiation therapy, or drug therapy. Specific treatment depends on the underlying cause of the disease [6,11].

Surgical intervention

Surgery is performed to remove adrenal or pituitary (hypophysectomy) tumors. Pituitary tumors may be removed via the transsphenoidal approach, during which the pituitary is removed through the nasal cavity, sphenoid sinus, and into the sella turcica [6]. Transsphenoidal hypophysectomy is extremely delicate surgery, and patients are usually referred to medical facilities that specialize in this type of surgery. The success rate when performed by a surgeon experienced in this procedure is more than 80%. If the surgery is not successful, or provides only a temporary cure, it can be repeated, often with good outcomes [28].

If a tumor has grown beyond the sella turcica a transfrontal craniotomy may need to be performed. If there is hyperplasia of both adrenal glands, bilateral adrenalectomy may be needed [6].

Nursing consideration: Before surgery, the patient must undergo treatment to control edema, diabetes, hypertension, and other cardiovascular effects caused by Cushing's syndrome. Patients must be especially careful to avoid infection prior to and after surgery [5,11].

Immediately prior to surgery, the administration of glucocorticoids can help prevent acute adrenal hypofunction during the surgery itself. During and after surgery, cortisol therapy should be administered to help the patient deal with the physiologic stress caused by the removal of the pituitary or adrenal gland(s) [5, 11].

In the event that normal cortisol production resumes, steroid therapy may be gradually tapered and ultimately discontinued, usually within a period of 12 to 18 months [5,6,11]. However, if both adrenal glands have been removed (bilateral adrenalectomy), or if the entire pituitary has been removed (total hypophysectomy), life-long steroid replacement therapy is necessary [5,11].

Radiation therapy

If surgical approaches fail, or if a patient is not a candidate for surgery, radiation therapy is a possible alternative treatment. Radiation treatment to the pituitary gland is generally administered over a 6-week period. Improvement is noted in 40% to 50% of adults and up to 85% of children [28].

Another option is stereotactic radiosurgery or gamma knife radiation. This allows for the delivery of radiation in a single high-dose treatment [28].

Radiation alert! It may take months or even years for patients to feel better after receiving radiation treatment alone. Radiation in conjunction with cortisol-inhibiting drugs can help speed up the recovery process [28].

Medications

Patients with non-endocrine corticotropin-producing tumors require excision of the tumor followed by drug therapy. Drug therapy is also administered if the patient cannot undergo surgery. Medications prescribed include [5,6,11]:

- **Mitotate:** Mitotate (Lysodren) is toxic to the adrenal cortex. Its administration is referred to as medical adrenalectomy. Side effects of this drug include nausea, vomiting, diarrhea, somnolence, and depression.
- **Meryrapone:** Meryrapone (Metopirone) is given to control hypersecretion of steroids in those who fail to respond to mitotane.
- **Aminoglutethimide:** Aminoglutethimide (Cytadren) blocks cholesterol conversion to pregnenolone. This blocks cortisol production. Side effects include GI disturbances such as nausea, vomiting, and diarrhea, somnolence, and skin rashes.
- A combination of **aminoglutethimide, cyproheptadine, and ketoconazole** may be prescribed in an effort to decrease levels of cortisol.
- **Aminoglutethimide** may be given alone or along with metyrapone as part of the treatment for metastatic adrenal cancer.

Nursing considerations: Nursing considerations of particular interest include [5,6]:

- Monitor patients carefully for signs of infection. Patients with Cushing's syndrome are especially prone to infection.
- Facilitate physical and emotional rest. Cushing's syndrome can trigger periods of emotional lability. Adequate rest is essential to help relieve some of this instability.
- Monitor weight, intake and output, electrolyte levels, hormone levels, and glucose levels.

After bilateral adrenalectomy and/or pituitary surgery it is important that nurses [5,6]:

- Caution the patient to wear a medical identification bracelet.
- Instruct patients to inform their HCPs immediately if they develop infections, physical illness, and/or significant emotional stress, which may trigger the need for increased dosage of hormone therapy.

Teach patients to take replacement steroid therapy with food or with antacids to reduce gastric irritation. It is often recommended that two-thirds of the dosage be taken in the morning and one-third in the early afternoon. This should mimic natural rates of adrenal secretion.

Adrenogenital syndrome

Donna is nearly 14 years old and has not yet begun to menstruate. She is starting to develop a faint mustache, which has made her the target of ridicule by her peers. Concerned, Donna's mother, Shirley, decides to take her to be evaluated by a gynecologist. Physical examination shows excessive growth of axillary hair, failure to menstruate, and an enlarged clitoris. The physician orders a battery of diagnostic tests including serum electrolyte, aldosterone, renin, and cortisol levels.

Test results in conjunction with history and physical findings indicate adrenogenital syndrome.

Adrenogenital syndrome, perhaps more commonly known as congenital adrenal hyperplasia, is a syndrome caused by disorders of adrenocortical steroid biosynthesis. Most cases of the syndrome are due to the failure of the adrenal glands to produce enough cortisol [5,29].

Incidence

- If adrenogenital syndrome is inherited, it is referred to as **congenital adrenal hyperplasia (CAH)**. The syndrome may also be caused by an adrenal tumor (adrenal virilism) [5,29].

Adrenogenital syndrome alert! A salt-losing form of CAH in neonates may cause a fatal adrenal crisis [5].

Some experts describe CAH as having two major types [29]:

- Classic CAH is the more severe form of the disease. It is usually diagnosed in infancy or early childhood.
- Non-classic CAH is the less severe form, which is usually recognized in late childhood or early adulthood.

CAH is "the most prevalent adrenal disorder in infants and children" with simple virilizing CAH and salt-losing CAH being the most common forms [5]. Acquired adrenal virilism is a rare form of the disorder, affecting twice as many females as males [5]. About one in 10,000 to 18,000 infants are born with CAH [5,30].

Pathophysiology

CAH is an inherited autosomal recessive trait. It is usually due to insufficient production of cortisol. Production of mineralocorticoids such as aldosterone and androgens such as testosterone may also be affected [29].

Various compensatory mechanisms are enacted to combat inadequate production of cortisol. For example:

- **Simple virilizing CAH:** There is a deficiency of 21-hydroxylase, which leads to cortisol deficiency. This deficiency triggers an increase in corticotropin secretion as a compensatory mechanism. The corticotropin increase causes the production of large amounts of cortisol precursors and androgens that do not need 21-hydroxylase for synthesis. Excess androgens cause male characteristics to appear early in males or inappropriately in females [5,30].
- **Salt-losing CAH:** In this form of CAH, 21-hydroxylase is almost completely absent. This leads to an increase in corticotropin secretion, which leads to excessive production of cortisol precursors including those that are salt-wasting. At the same time cortisol and aldosterone levels that are dependent on 21-hydroxylase fall sharply. This abrupt decrease combined with excess amounts of salt-wasting compounds can trigger an acute adrenal crisis. Adrenal androgen production increases, and masculinization occurs [5].

Complications

A number of complications are associated with CAH including [5]:

- Adrenal tumor.
- Altered growth patterns and abnormalities in external genitalia and sexual maturity.
- Cardiovascular collapse and cardiac arrest in neonates.
- Hyperkalemia.
- Hypertension.
- Infertility.

Acquired adrenal virilism

Although the focus of this education program is CAH, it is important to also describe acquired adrenal virilism and its effects. Acquired adrenal virilism occurs in the presence of adrenal tumors, malignancies, or adenomas. This disorder is rare, can occur at any age, and is twice as common in females as in males [5].

Symptoms vary with age and include [5]:

- Prepubescent females: Pubic hair, enlarged clitoris, delayed development of breasts, and delayed or absent menses.
- Females, especially those who are middle-aged: Appearance of dark hair on face, legs, arms, chest and back, oily skin, menstrual irregularities, development of masculine muscle mass, breast and uterine atrophy, and pubic hair that extends toward the navel.

- Prepubescent males: Significant enlargement of genitalia with penis and prostate development equal to that of an adult male, failure of testicular maturation, and hirsutism.
- Males: There are no obvious signs in males. The identification of a tumor is usually accidental.

The following diagnostic results indicate acquired adrenal virilism [5]:
- Elevated urinary total 17-ketosteroids.
- Significantly elevated dehydroepiandrosterone levels.
- Normal serum electrolyte levels.
- Kidney x-rays may show kidney displacement caused by a tumor.

Treatment involves surgical excision of the tumor and/or radiation and chemotherapy as needed. Prognosis is very good for patients who have slow-growing and non-recurring tumors [5].

Signs and symptoms of CAH

Signs and symptoms of CAH depend on the severity of the disease and the age of the patient [30].

Female with simple virilizing CAH:
Females have ambiguous genitalia such as an enlarged clitoris with a urethral opening at the base. There may be some labioscrotal fusion but the genital tract and gonads are normal [5].

As she ages and reaches puberty she develops [5,29,30]:
- Facial hair.
- Deep voice.
- Acne.
- Early appearance of pubic and axillary hair.
- Failure to menstruate.

Male with simple virilizing CAH:
The neonate male does not have obvious abnormalities. But at puberty he has accentuated masculine characteristics including a deep voice and an enlarged penis with frequent erections [5].

CAH alert! Both males and females may be taller than other children their age because they experience rapid bone and muscle growth. However, excessive androgen levels cause early epiphyseal closure, which leads to short adult height [5].

Females and males with salt-losing CAH
The salt-losing form of CAH is more severe than the simple form and causes more complete virilization in females. Male external genitalia (but without testes) develop [5,29,30].

Males with salt-losing CAH have no abnormalities in external genitalia. Thus, diagnosis immediately after birth is difficult and usually delayed until severe signs and symptoms develop.

In severe cases, signs of salt-losing CAH infants may develop as soon as 2 to 3 weeks after birth in both males and females. These signs include vomiting, diarrhea, dehydration, low potassium and sodium levels, and abnormal heart rhythms [29,30]. Infants are apathetic and fail to eat. These signs indicate the onset of adrenal crisis, which, unless treated promptly, may lead to cardiovascular collapse and cardiac arrest [5].

Diagnosis

Physical examination shows ambiguous genitalia in females or, in severe forms of the disease, females may have overt male external genitalia. Precocious puberty (onset of puberty before the age of 9) in both females and males is also indicative of CAH [5].

Laboratory findings that help confirm the diagnosis of CAH include [5, 30]:
- Elevated plasma 17-ketosteroids that can be suppressed by giving oral dexamethasone.
- Elevated urinary levels of hormone metabolites.
- Elevated plasma 17-hydroxprogesterone level.
- Normal or decreased urinary levels of 17-hydroxycorticosteroids.

Diagnosis alert! Adrenal crisis or evidence of adrenal hypofunction in the first week of life suggests salt-losing CAH [5].

Treatment

Treatment focuses on return of hormone levels to normal or to near normal [5,30]. This involves administering a large, intramuscular dose of cortisone or hydrocortisone. Dosage is adjusted according to urinary 17-ketosteroid levels. Infants receive hormonal therapy intramuscularly until they reach the age of 18 months after which they can be given the hormones orally [5].

Patients with ambiguous external genitalia undergo sex chromatin and karyotype studies to determine their genetic sex. Females who have male external genitalia undergo reconstructive surgery between the ages of 1 and 3 years following evaluation of the impact of cortisone therapy [5].

Instruct patients' parents that the child should wear a medical identification bracelet explaining that they are on long-term steroid therapy. Counseling and emotional support should be provided as parents deal with the psychological impact of CAH [5,30].

Hermaphroditism

Hermaphroditism is a condition appropriately mentioned as part of a discussion of CAH. Hermaphroditism is a rare condition in which children have both ovarian and testicular tissues.

External genitalia are usually ambiguous, but may also be completely male or female, which effectively "hides" hermaphroditism until puberty. The child with hermaphroditism almost always has a uterus and ambiguous gonads. Fertility, however, is rare [5].

Lab studies similar to those of CAH are performed to rule out congenital adrenal hyperplasia [5].

Sexual assignment is based on the anatomy of the external genitalia. Reconstructive surgery, during which inappropriate reproductive organs are removed, is performed as early as possible to prevent the development of incongruous secondary sex characteristics at puberty. Hormonal replacement may be needed [5].

Parents need emotional support and counseling as they deal with their choice of sexual assignment of their children [5].

Pheochromocytoma

Pheochromocytoma is a rare, catecholamine-secreting tumor associated with hyperfunction of the adrenal medulla leading to an excessive secretion of epinephrine and norepinephrine. It may trigger life-threatening hypertension as well as an increase in metabolism and hyperglycemia [5,6,31].

Although this disease is potentially fatal, prognosis is good with appropriate treatment. Kidney damage associated with the disease, however, is irreversible [5].

Incidence and etiology

Pheochromocytoma affects all races and both men and women. It can occur at any age, but is most common between the ages of 30 and 60 and rare in people over the age of 65 [5,6].

The majority of pheochromocytoma tumors are benign, but 10% are malignant with associated metastasis [6]. Ninety-five percent of pheochromocytomas are located in the abdomen, and may occur as the result of an inherited autosomal dominant trait [5].

Complications

Complications associated with pheochromocytoma include [5, 6]:

- Heart failure.
- Irreversible damage to the kidneys.
- Retinopathy.
- Stroke.

Signs and symptoms

Pheochromocytoma causes episodes typically characterized by [31]:

- Headaches.
- Palpitations.
- Diaphoresis.
- Severe, possibly life-threatening, hypertension.

Occurrence of these episodes can vary from once every two months to as often as 25 times a day, and they may last from seconds to hours. As time goes by, these episodes usually occur more often and become more severe as the tumor grows in size [5,31]. Episodes can occur spontaneously or follow specific triggering events such as exercise, smoking, urination, or a change in environmental or body temperature [5].

Additional clinical manifestations that may also be part of pheochromocytoma episodes include [5,31]:

- Abdominal pain.
- Anxiety.
- Constipation.
- Fever.
- Flank pain.
- Pallor.
- Paresthesia.
- Sense of impending doom.
- Tachycardia.
- Tremors.
- Warmth or flushing.
- Weight gain or weight loss.

Nursing consideration: Pheochromocytoma is often diagnosed during pregnancy when the expanding uterus puts pressure on the tumor, thus, triggering more frequent attacks. These attacks can lead to stroke, cardiac arrhythmias, acute pulmonary edema, or hypoxia, any of which can be fatal to mother and/or fetus. The risk of spontaneous abortion is significant, but most infant deaths take place during labor or immediately after birth [5].

Diagnosis

The most common indicator for pheochromocytoma is continuous hypertension and a history of episodes characteristic of the disease [5,31]. The tumor itself is rarely palpable, and findings from diagnostic laboratory tests are necessary to confirm diagnosis [5,31].

The following tests are used to diagnosis pheochromocytoma [5,6,31]:

- Urine plasma catecholamine levels: A baseline specimen is obtained and another obtained during an episode of hypertension. Levels are elevated during a hypertensive episode.
- Total plasma catecholamines: Levels are 10 to 50 times above normal.
- Clonidine suppression test: In normal patients, results show decreased plasma catecholamine levels. However, in those persons with pheochromocytoma, levels remain unchanged.
- CT scans or MRIs: Imaging tests are used to identify tumor location.

Analysis of a 24-hour urine specimen is used to confirm a diagnosis of pheochromocytoma [5]. "Increased urinary excretion of total free catecholamines and their metabolites, VMA and metanephrine, as measured by analysis of 24-hour urine specimen, confirms pheochromocytoma [5]."

Nursing consideration: To makes sure that urine catecholamine measurements are reliable, nurses must teach patients to avoid foods high in vanillin for 2 days before urine collection of VMA. Examples of such foods include coffee, nuts, chocolate, and bananas [5].

Treatment

The treatment of choice for pheochromocytoma is surgical resection of the tumor, which usually cures the hypertension [31]. It is important that specific preoperative measures be taken beginning 1 to 2 weeks prior to surgery to control blood pressure and prevent intraoperative hypertensive crisis [5,31].

Measures to achieve preoperative medial stabilization include [31]:

- Administration of an alpha-adrenergic blocker or metyrosine.
- Volume expansion with isotonic sodium chloride solution.
- Facilitation of liberal salt intake.
- Administration of a beta blocker only after sufficient alpha blockade to "avoid precipitating a hypertensive crisis from unopposed alpha stimulation [31]."
- Administration of the last doses of oral alpha and beta blockers on the morning of surgery.

Postoperatively, the following measures are taken [5]:

- Administration of intravenous fluids.
- Administration of plasma volume expanders.
- Administration of vasopressors.

Persistent hypertension is possible in the period immediately following surgery as are acute episodes of headaches, palpitations, anxiety, and diaphoresis. Management of hypertensive crisis or acute episodes includes administration of push or drip intravenous phentolamine or nitroprusside to control and normalize blood pressure [5].

For persons who are not able to withstand surgery, alpha-adrenergic blockers and beta-adrenergic blockers are administered to help control the effects of catecholamine and to prevent acute episodes [5].

Treatment alert! Rarely, pheochromocytoma is malignant. If this is the case, surgery to excise the tumor is followed by radiation and/or chemotherapy as needed [5,31].

Additional postoperative nursing considerations include [5,31]:

- Monitor blood pressure meticulously. If hypertensive crisis occurs, blood pressure and heart rate should be monitored every 2 to 5 minutes until the patient stabilizes.
- Monitor glucose levels.
- Provide a quiet, calm environment since anxiety, noise, and excitement can trigger a hypertensive episode.
- Keep the room cool since postoperative adrenal gland secretions cause profuse diaphoresis. Change clothing and bed linens frequently.

Treatment alert! Blood pressure may also drop drastically in the postoperative period, especially during the first 24 to 48 hours after surgery. Monitor for signs of severe hypotension [5].

If the occurrence of pheochromocytoma is due to a suspected autosomal dominant transmission, family members should also be tested for this problem [5].

Multiple endocrine neoplasia

Multiple endocrine neoplasia (MEN) is an inherited disorder in which 2 or more of the endocrine glands develop hyperplasia, an adenoma, or a malignancy. These pathologies can occur at the same time or consecutively [5].

There are 2 types of MEN that are well recorded [5]:

- **MEN I**, also called Werner's syndrome, occurs because of a defect in a gene that carries the code for the protein menin [32]. This defect leads to hyperplasia and tumors of the pituitary and parathyroid glands, islet cells of the pancreas, and, rarely, the thyroid and adrenal glands [5].
- **MEN II**, also called Sipple's syndrome, is a rare familial malignancy caused by genetic mutation [33]. It usually involves medullary cancer of the thyroid and hyperplasia and tumor growth of the adrenal medulla and parathyroid glands [5,33].

MEN I is the more common form [5].

Incidence and etiology

MEN is usually due to autosomal dominant inheritance. It affects twice as many females as males and can occur at any time from adolescence through old age. However, it is rare in children [5].

Signs and symptoms

Clinical manifestations of MEN depend on the glands involved. The most common signs and symptoms of MEN I are those of hyperparathyroidism, including hypercalcemia, followed by ulcer development because of increased production of gastrin from non-beta islet cell tumors of the pancreas (Zollinger-Ellison syndrome). Hypoglycemia may occur as a result of pancreatic beta cell tumors that lead to increased production of insulin [5].

Here is a list of possible signs and symptoms related to MEN I [5,32]:

- Abdominal pain.
- Amenorrhea.
- Anxiety.
- Black, tarry stools.
- Confusion.
- Decreased appetite.
- Decreased libido.
- Epigastric pain relieved by eating or taking antacids.
- Fatigue.
- Feeling bloated after eating.
- Headache.
- Loss of facial hair in men.
- Mental changes.
- Muscle pain.
- Nausea and vomiting.
- Sensitivity to cold.
- Unintentional weight loss.
- Vision disturbances.
- Weakness.

MEN II signs and symptoms are related to the gland(s) affected by the malignancy. For example, an affected thyroid gland causes an enlarged thyroid mass, elevated calcitonin, and sometimes, evidence of Cushing's syndrome. Adrenal medulla tumors cause headache tachycardia-related arrhythmias, and elevated blood pressure. If the parathyroid glands are affected, signs and symptoms are caused by the development of renal calculi [5].

Diagnosis

Clinical manifestations will indicate the type of diagnostic tests needed. Signs and symptoms that suggest particular gland involvement indicate the type of testing to be done. For example, upper gastric pain and ulcers due to Zollinger-Ellison syndrome indicate the need for pancreatic evaluation. In fact, 50% of patients with Zollinger-Ellison syndrome are ultimately diagnosed with MEN [5].

CT scans, MRIs, and x-rays may be used to identify tumor location [5,32]. Examples of additional tests, based on the presenting clinical picture include [32]:

- Fasting blood sugar.
- Cortisol levels.
- Serum electrolyte levels.
- Serum levels of various hormones depending on specific signs and symptoms.
- Tumor biopsies.

Since MEN is predominantly a hereditary disorder family members may undergo genetic testing [5,32].

Treatment

Treatment focuses on tumor removal and therapy to control any residual symptoms [5]. Treatment of malignant tumors may include, in addition to surgical removal, radiation therapy and chemotherapy depending on the size of the tumor, the surgeon's ability to remove all of the tumor, and if there is evidence of metastasis [5,32,33].

Side effects of particular tumors such as hypertension with adrenal medullary tumor or treatment of peptic ulceration with MEN I must be dealt with in conjunction with tumor removal. If significant amount of specific glandular tissue is removed, hormonal replacement therapy is necessary [5].

Diabetes mellitus

Diabetes mellitus (DM) is a chronic disease of glucose intolerance. It is caused by a complete or relative deficiency of insulin or by a resistance to insulin characterized by disturbances in protein, fat, and carbohydrate metabolism [5,6].

In the United States, DM is [5,11]:

- The fifth leading cause of death.
- A contributing factor in approximately 50% of heart attacks.
- A contributing factor in about 75% of strokes.
- A contributing factor in renal failure.
- A contributing factor in peripheral vascular disease.
- The leading cause of new blindness.

Types of diabetes, incidence, and etiology

DM affects approximately 6.3% of the U.S. population or 18.2 million people. About 5.2 million people are not even aware that they have the disease, and incidence increases with age [11].

There are three types of DM.

- **Type 1:** Type 1 diabetes occurs when the beta cells in the pancreas are destroyed or suppressed. Formerly referred to as juvenile diabetes or insulin-dependent diabetes, type 1 diabetes is subdivided into idiopathic and immune-mediated types. In idiopathic diabetes there is permanent deficiency of insulin and no evidence of autoimmunity. In immune-mediated diabetes the body produces an autoimmune attack on pancreatic beta cells, and the pancreas becomes inflamed. By the time signs and symptoms appear, 80% of the beta cells are destroyed. Some experts, however, believe that beta cells are not destroyed but disabled and may later be reactivated [5,6,11].
- **Type 2:** Type 2 diabetes, formerly referred to as adult-onset diabetes or non-insulin dependent diabetes, may be attributed to insulin resistance in target tissues, abnormal insulin secretion, or overproduction of glucose (inappropriate hepatic gluconeogenesis) [6,11].

Type 2 diabetes alert! Type 2 diabetes may also develop as a consequence of obesity. In fact, most patients with type 2 diabetes are obese [5].

- **Secondary diabetes:** Secondary diabetes is so-called because this type occurs "secondarily" to another condition or event. The factors that trigger secondary diabetes include [11]:
  - Physical or emotional stress that can cause prolonged elevation of cortisol, epinephrine, glucagon, and GH. Such elevations increase blood glucose levels and demands on the pancreas.
  - Pregnancy, which causes weight gain, high levels of estrogen, and high levels of placental hormones [11]. This type of diabetes is referred to as gestational diabetes mellitus (GDM). Glucose levels usually return to normal after the women gives birth. However, women who have had GDM have a 40% to 60% chance of developing type 2 diabetes within 5 to 10 years [5].
  - Use of specific medications such as adrenal corticosteroids, hormonal contraceptives, and other drugs that oppose the desired effects of insulin [11].

Risk factors for type 2 diabetes

Risk factors for type 2 diabetes include [5,6]:

- Black, Hispanic, Pacific Islander, Asian-American, or Native Americans.
- Family history of diabetes.
- High density lipoprotein cholesterol of less than 35 mg/dl or triglyceride of greater than 250 mg/dl.
- History of GDM.
- Hypertension.
- Obesity.
- Older than 45 years of age.
- Sedentary lifestyle.
- Significantly impaired glucose tolerance.

Complications

Patients with DM have a risk of numerous complications that can affect every system of the body. Possible complications include [5,6,11]:

- Cardiovascular disease.
- Gastroparesis (delayed gastric emptying and feelings of fullness after eating).
- Impaired ability to fight infection.
- Nephropathy.
- Nocturnal diarrhea.
- Orthostatic hypotension.
- Peripheral and autonomic neuropathy.
- Peripheral vascular disease.
- Retinopathy.
- Skin disease (diabetic dermopathy).
- Urinary tract infections (UTIs).
- Vaginitis.

EBP alert! Research now shows that glucose readings do not need to be as elevated as once believed for complications to occur. This means that exact glucose control is more important than ever [11].

Acute complications of hyperglycemic crisis

Acute complications of hyperglycemic crisis may occur with diabetes. Failure to treat these complications appropriately can lead to coma or even death. These two complications are diabetic ketoacidosis (DKA) and hyperosmolar hyperglycemic nonketotic syndrome (HHNS) [11].

DKA is seen most often in patients who have type 1 diabetes. It may actually be the first sign of the disease. HHNS is seen most often in patients who have type 2 diabetes, but it can occur in any patient whose insulin tolerance is stressed or who has undergone procedures

such as peritoneal dialysis, Hemodialysis, tube feedings, or total parenteral nutrition [11].

These complications occur when inadequate levels of insulin cause interferes with the body cells' ability to take in glucose and convert it to energy. Thus, glucose accumulates in the blood, and the cells lack the energy needed to function. This triggers the liver to convert glycogen to glucose and still more glucose is released into the blood. But no matter how much glucose is manufactured and released into the bloodstream, the cells are not able to utilize it because of insulin deficiency [5,11,6].

Blood glucose levels become grossly elevated, serum osmolarity increases, and high amounts of glucose are present in the urine (glycosuria). This triggers osmotic diuresis and massive fluid loss, which, in turn, causes electrolyte loss. Water loss is greater than glucose and electrolyte loss and dehydration continues along with a decreased glomerlular filtration rate and an eventual reduction of the amount of glucose excreted in the urine. As glucose excretion decreases, blood glucose levels continue to increase. This cycle continues, and if not stopped, leads to shock, coma, and death [11].

DM alert! DKA also leads to the conversion of fats into glycerol and fatty acids, which cannot be quickly metabolized and accumulate in the liver. There they are converted into ketones. Ketones accumulate in the blood and urine, causing acidosis [11].

DKA and HHNS are medical emergencies and require immediate treatment to correct fluid loss, electrolyte imbalances, and acid-base imbalances. Insulin is administered to correct hyperglycemia [5,6,11].

Signs and symptoms

DM may develop gradually or abruptly [5,11]. The most common symptom is generalized fatigue. Hyperglycemia "pulls" fluid from the tissues of the body, which causes characteristic symptoms (in both type 1 or type 2 diabetes) of polyuria (excessive urination), excessive thirst (polydipsia), and excessive eating (polyphagia) [5,6,11].

Other signs and symptoms include [5,6,11]:

- Dehydration.
- Dry, itchy skin.
- Frequent infections of the skin.
- Poor skin turgor.
- Unexplained weight loss.
- Vision changes.
- Weakness.

Type 1 diabetes usually causes a rapid development of symptoms including effects of muscle wasting and loss of subcutaneous fat [11].

Persons affected by type 2 diabetes generally have a symptom onset that is vague and gradual [5,11].

Diagnosis

According to American Diabetes Association (ADA) guidelines, DM can be diagnosed if patients manifest any of the following [5]:

- Symptoms of DM plus a random, nonfasting blood glucose level equal to or greater than 200 mg/dl.
- Fasting blood glucose equal to or greater than 126 mg/dl.
- Oral glucose tolerance test (2-hour sample) results equal to or greater than 200 mg/dl.

Diagnostic alert! Questionable results require that diagnosis be confirmed by repeat testing on a different day [5].

The ADA recommends the following testing guidelines [5]:

- Test people aged 45 and older who have no symptoms every 3 years.
- People with characteristic signs and symptoms should be tested immediately.
- High risk groups should be tested frequently.

An ophthalmologic exam may reveal diabetic retinopathy. Acetone is present in urine, and blood tests for glycosylated hemoglobin show recent glucose cortisol [5].

Blood glucose levels are classified by the ADA as [5]:

- Normal: <100 mg/dl.
- Prediabetes: 100 to 125 mg/dl.
- Diabetes: >126 mg/dl.

Treatment and nursing considerations

Treatment goals are to optimize blood glucose levels and decrease complications [11].

Medications

Many types of drugs are used to treat DM. Treatment of type 1 DM includes insulin replacement. Current forms of insulin replacement therapy include single-dose, mixed-dose, split-mixed dose, and multiple-dose regimens, which may be administered via an insulin pump. Insulin may be rapid, intermediate, or long-acting or a combination of rapid- and intermediate-acting [5,11].

Persons with type 2 DM may require oral antidiabetic medications that stimulate insulin production, increase cellular sensitivity to insulin, and suppress hepatic gluconeogenesis [5].

A variety of drugs have proven helpful in treating DM such as [5,14]:

- Sulfonylureas, which stimulate pancreatic insulin release.
- Meglitinides, which cause immediate, brief release of insulin and are given before meals.
- Biguanides, which decrease hepatic glucose production.
- Alpha-glucosidase inhibitors, which slow glucose breakdown and decrease postprandial glucose peaks.
- Thiazolidinediones, which enhance the action of insulin.
- Synthetic analogue of human amylin, which helps control glucose and is used with insulin.

Diet

Patients require in-depth dietary instruction. Each patient's diet is planned specifically for him/her and should take into consideration dietary preferences to facilitate compliance. Patients with type 2 diabetes often need to lose weight. If this is the case, weight loss strategies should be incorporated into the diet plan [5,6].

Exercise

Exercise is encouraged as part of a healthy lifestyle and is especially helpful in the management of type 2 diabetes. Exercise facilitates weight loss, improves glucose tolerance, and increases insulin sensitivity [11].

Additional nursing considerations

In addition to diet, exercise, and medication administration, nurses must teach patients how to monitor their blood glucose levels and to care for equipment used for such monitoring. Blood pressure control and smoking cessation reduces complication onset and progression [5,6,11].

Patients must be taught to take meticulous care of their skin and seeking prompt treatment for infection. Special attention should be paid to care of the feet. Teach patients to wash feet daily and dry them carefully, especially between the toes. Inspect the feet for corns, calluses, redness, bruising, and any breaks in the skin. Abnormalities should be reported to the physician promptly. Advise patients never to walk barefoot and to wear non-constricting shoes [5].

Stress the need to report and numbness or pain in the hands and feet and any changes in voiding patterns (e.g., incontinence), which may indicate diabetic neuropathy. All blisters, cuts, and scrapes should be carefully treated. Teach patients signs and symptoms of UTIs and to report these signs and symptoms to their HCPs promptly [5,11].

Explain the importance of keeping all scheduled medical appointments and encourage annual eye examinations. Caution patients to contact their HCPs in the event of illness, injury, and/or infection since they may necessitate a medication dose adjustment [5].

Teach patients and families the signs of acute complications of diabetic therapy, particularly the signs and symptoms of hypoglycemia. Signs and symptoms of hypoglycemia include anxiety, mental changes, dizziness, weakness, pallor, tachycardia, diaphoresis, seizures, confusion, and loss of consciousness that may progress to coma. Teach patients and families that if these signs and symptoms occur, patients should immediately be given carbohydrates such as glucose tablets, honey, or fruit juice. If patients are unconscious, they should be given glucagon or dextrose IV [5,6,11].

Patients and families must also be taught to recognize ketoacidosis. Signs and symptoms of ketoacidosis include acetone breath (fruity-smelling breath), weak, rapid pulse, polyuria, thirst, deep, rapid respirations (Kussmaul's respirations), changes in level of consciousness, and stupor. Prompt treatment with IV fluids, insulin, and, often, potassium replacement is necessary [5].

Elder considerations

Several important issues involve elderly patients. These include [5,6,11]:

- Cells become more resistant to insulin with aging. This decreases the older adult's ability to metabolize glucose. Additionally, insulin release from the pancreas is delayed, and sudden concentrations of glucose occur. Such concentrations cause more prolonged hyperglycemia in elders.
- The thirst mechanism is less efficient in the elderly than in younger adults and children. Thus older adults may not experience the polydipsia that is characteristic of DM in younger adults.
- Healing is often slower in elders than in younger patients. DM compounds this delay in healing.

CASE STUDY SCENARIOS AND STUDY QUESTIONS

The endocrine system and its pathologies are complex topics. Compounding the complexity is the fact that many endocrine disorders are uncommon, and many HCPs have not had experience in working with patients who are dealing with endocrine pathologies. Recognition and treatment initiation, as well as providing appropriate nursing interventions, depend on a thorough knowledge of the glands of the endocrine system, hormonal production and actions, and clinical manifestations of pathologies. Education offerings must provide opportunities for review. Therefore, the following case study scenarios and study questions have been developed to reinforce the learner's ability to recognize the various endocrine disorders and their management.

The endocrine and nervous systems work together to regulate and integrate metabolic activities of the body. Differentiate the ways endocrine hormones and nerve impulses regulate such activities.

The hormones that are secreted by the glands of the endocrine system are chemical messengers that transfer information from one set of cells to another to coordinate bodily functions [3]. Hormones cause changes in the metabolic activities in specific cells while nerve impulses cause gland secretion and muscle contraction. Hormonal action is rather slow, but of prolonged duration. The action of nerve impulses, on the other hand, is rapid but of short duration [2].

Andrea is preparing an oral presentation on the pituitary gland as part of her graduate work in nursing. When discussing this gland she must differentiate between the anterior and posterior regions of the pituitary. How can she do this?

Recall that the pituitary is the "master gland." It is divided into two regions: the anterior lobe or adenohypophysis and the posterior lobe or neurohypophysis [1,2,3]. The larger anterior lobe produces 6 hormones that are regulated by the hypothalamus: growth hormone (GH), thyroid stimulating hormone (TSH), adrenocorticotropic hormone (ACTH), follicle-stimulating hormone (FSH), luteinizing hormone (LH), and prolactin (PRL) [1,2,3]. The posterior pituitary is responsible for the secretion of antidiuretic hormone (ADH) and oxytocin [2,3].

Another important differentiation between the actions of the anterior and posterior pituitary is that the anterior pituitary actually produces 6 hormones. Production is regulated by the hypothalamus, which responds to negative and positive feedback mechanisms. The posterior pituitary stores ADH and oxytocin, which are actually produced by the hypothalamus [1,2,3].

Andrea (and other HCPs) must be aware of the pituitary's role in endocrine functioning. They must know what hormones are secreted by the pituitary and how these hormones act on various body systems.

Jennifer is a professor of nursing. She is developing an exam that deals with endocrine function. Several of the questions are designed to assess students' knowledge of what glands produce specific hormones. Here are some samples of questions that Jennifer has written.

Which gland is responsible for manufacturing a hormone that is the major metabolic hormone of the body? What is the hormone called?
The correct answer would be the thyroid gland, which produces thyroid hormone, the major metabolite hormone of the body. Thyroid hormone increases metabolic rate, oxygen consumption, glucose absorption, and body temperature. It also affects growth and development and improves the effects of the sympathetic nervous system [3].

What pancreatic cells produce glucagon? What pancreatic cells produce insulin?
The alpha cells produce glucagon, which raises the blood glucose level by causing the breakdown of glycogen to glucose. The beta cells secrete insulin, which lowers blood glucose levels by facilitating movement of blood glucose across cells, converting glucose to glycogen [1,3].

Researchers are investigating the role of which gland in regulation of the sleep-wake cycle?
The pineal gland, which is located in the middle of the brain, produces melatonin, which is believed to regulate circadian rhythms as part of the sleep-wake cycle [1,2].

What are the primary sources of sex hormones?
The gonads are the primary source of sex hormones. In female, the ovaries produce eggs and the steroidal hormones estrogen and progesterone. In male, the testes, located in the scrotum, produce spermatozoa and the male sex hormone testosterone [1,2].

Give an example of a hormone that is controlled by positive feedback. What is the function of this hormone?
Oxytocin is controlled by positive feedback. It targets the uterus and mammary glands, causing uterine contractions during childbirth and milk production for lactation. Oxytocin is produced by the hypothalamus and transported via nerves to the pituitary gland, where it is stored and then secreted when needed [1,2,3].

What pituitary hormone is secreted in response to a state of dehydration?
ADH (antidiuretic hormone) release is stimulated by dehydration and increased plasma osmolarity. ADH controls water loss by the kidneys. It facilitates water reabsorption in the distal convoluted tubules and collecting ducts of the kidneys. Controlled by negative feedback, ADH release is stimulated by dehydration and increased plasma osmolarity [3].

What is the major role of the thymus?
The major role of the thymus seems to be related to the immune system since it produces T cells, which are critical to cell-mediated immunity [1].

The endocrine system depends on both negative and positive feedback. Differentiate between negative and positive feedback.
The endocrine system depends on both negative and positive feedback for its regulation. **Negative feedback** takes place when the rate of production of a particular product decreases as the concentration of that product increases. Negative feedback manages the rate of production to avoid accumulation of a particular product. For example, as the amount of some hormones reach the desired level, the body stops or reduces the rate of their production to avoid excessive accumulation [1,3].

Positive feedback occurs when the rate of production of a particular product increases as the concentration of that product increases. Positive feedback is less common in the body than negative feedback. An example of positive feedback is the secretion of oxytocin that stimulates uterine muscle contraction during labor. As labor progresses, pressure on the cervix continues to stimulate oxytocin release, which continues to stimulate uterine muscle contraction [3].

Hypopituitarism is a rare disorder that usually presents as a rather slow, predictable pattern of hormonal failures. What are the clinical manifestations of this disease? Why do they occur?
The pituitary gland secretes TSH, FSH, LH, GH, ACTH, prolactin, ADH, and oxytocin [1,4]. Clinical manifestations depend on the severity of the disease and on the number of hormones that are deficient. Presenting signs and symptoms usually begin with hypogonadism because of decreased FSH and LH levels. In adults, this causes females to stop menstruating, and decreases libido in males. Signs and symptoms of GH deficiency usually follow including osteoporosis, lethargy, subtle emotional changes, adverse lipid changes, and decreased lean-to-fat body mass [4,5].

In children, lack of GH leads to short stature, delayed growth, delayed puberty, and, possibly dwarfism. If hypopituitarism occurs before puberty, the development of secondary sex characteristics is prevented. In males, this means lack of facial and body hair, undersized penis, testes, and prostate gland, and failure to initiate and maintain an erection. In females, there is a lack of pubic and axillary hair, failure to develop mature breasts, and primary amenorrhea [4,5].

It is important to note that clinical signs and symptoms of hypopituitarism do not usually become apparent until 75% of the gland is destroyed [5].

Hypopituitarism that involves all of the pituitary hormones is called _____.
Panhypopituitarism. It is characterized by involvement of all pituitary hormones. However, it is more likely that only one or more pituitary hormones are involved. This leads to only isolated or partial hypopituitarism [4].

Clinical signs and symptoms of hypopituitarism do not usually become apparent until 75% of the gland is destroyed [5].

What causes dwarfism in children? What signs and symptoms first indicate dwarfism and when do they appear?
In children, lack of GH causes short stature, delayed growth, delayed puberty, and, possibly, dwarfism [4,5]. Dwarfism is not often evident at birth but initial signs and symptoms appear in the first few months of life, and by six months growth retardation is apparent [5].

Danielle has been diagnosed with acromegaly. What endocrine gland disorder causes this disorder? What clinical manifestations are associated with this disease? How is it treated?
Acromegaly is formally known as hyperpituitarism and is a chronic, progressive disease characterized by hormonal dysfunction and disturbing skeletal overgrowth. Hyperpituitarism also causes giantism. The difference between acromegaly and gigantism is the age of the person affected. Acromegaly affects adults and has a slow, gradual progression. Overgrowth of cartilage and connective tissue, a big nose, enlarged hands and feet, thickened lips, tongue, gingers, and ear, and changes in the shape of the face are characteristic features. The voice deepens, the skin becomes coarse, oily, and thick, and there is extreme diaphoresis. A variety of mood changes and mental health disturbances may occur. Acromegaly affects males and females equally, usually between the ages of 30 and 50 [5,8].

Gigantism can affect infants and children and is a very rare disorder, affecting only 100 persons to date. Affected children may reach as much as three times the normal height for their age [5].

The most common cause of excessive GH production is a tumor, usually a benign adenoma of the pituitary gland. Treatment involves surgical removal of the tumor and reducing GH production. Removal of a pituitary is complex and should be performed only by surgeons who are experienced in this type of surgery. If the entire tumor cannot be removed via surgery, radiation may be needed to destroy remaining tumor cells and reduce GH levels. Various medications may be prescribed to lower production or block the action of GH.

Since acromegaly progresses so slowly, what is one way that patients and families actually notice changes in the patient's physical appearance?
Since the disease develops so slowly some people may notice physical changes in appearance only by comparing old and current photographs [8].

Several endocrine disorders interfere with normal levels of GH. Therefore, it is important to remember what important point when obtaining blood samples for GH suppression test?
Patients should not be emotionally or physically stressed when obtaining blood samples for the GH suppression test since stress can elevate GH levels [9].

What is stereotactic radiosurgery? Why is it performed? Who should perform it?
Stereotactic radiosurgery is also known as Gamma Knife radiosurgery. It is performed in order to direct radiation at tumor cells. For example, in cases of acromegaly when it is necessary to destroy pituitary tumor cells and to gradually reduce GH levels, stereotactic radiosurgery may be used. A high dose of radiation directed at the tumor cells is administered in a single dose while limiting radiation exposure to surrounding normal cells. This type of radiation therapy may bring GH levels to within normal limits within three to five years. Administration of stereotactic radiosurgery requires an extremely high level of technical skill and is available at only a few United States health care facilities.

Mark is a healthy 30-year-old sales manager at a luxury car dealership. While accompanying a potential buyer on a test-drive, a motorcycle runs a red light and crashes into Mark's car. The airbag deploys and strikes Mark's head with considerable force. Mark is evaluated at the hospital and diagnosed with a mild concussion. Three days later Mark returns to work feeling fine and resumes his busy schedule. However, later in the afternoon, Mark complains of feeling dizzy and weak. He is extremely thirsty and begins to void large quantities of urine. Mark leaves work early, telling his boss that he is too tired even to drive himself home. His wife arrives to take him home. Alarmed she insists that he see their family physician. Upon arrival at the doctor's office Mark heads straight for the nearest bathroom, overwhelmed by an urgent need to void. His doctor arranges for Mark to be transported to the hospital for further evaluation. Mark is found to have a subdural hematoma that is increasing intracranial pressure.

In addition to the subdural hematoma, what is causing some of Mark's symptoms? Why have they occurred? What treatment is needed?
Mark is exhibiting signs of diabetes insipidus, a water metabolism disorder due to a deficiency of antidiuretic hormone (AHD). There are several types of diabetes insipidus. Central diabetes insipidus is the result of intracranial neoplastic tumors, metastatic lesions, surgical removal of the pituitary, skull fracture, or, as in Mark's case, head trauma. The cerebral hematoma is causing intracranial pressure. Once that pressure is relieved, Mark's symptoms will most likely stop as quickly as they began [5,11].

Prognosis is good since relieving the intracranial pressure is the focus of treatment for Mark. He will also need fluid replacement and supportive measures to control fluid balance until the intracranial pressure is relieved.

When and why does gestational diabetes insipidus occur?
Gestational diabetes insipidus occurs during pregnancy when an enzyme produced by the placenta destroys the mother's ADH [5].

Hilary and Nathan have two children. Steven, an active three year old who is "into everything" is a "real handful" his parents say. Even as a baby, Steven was "a challenge." He awoke frequently during the night and seldom seemed to need to nap. As a toddler Steven constantly "explores" and seldom sits still. His favorite word, of course, is "no." Hilary gave birth to a baby girl three months ago. Her ecstatic parents tell everyone what a "good" baby little Angela is. She seldom cries, sleeps through the night and naps during the day, and, as her parents describe her, is very "calm." Nathan's mother is concerned, however. "This baby is way too "good," she thinks. The baby has a puffy face and droopy eyelids. Her parents attribute this to "baby fat" and "sleepiness." Nathan's mother believes that something is really wrong.

Is Nathan's mother right or wrong? Is little Angela simply a "good" baby or is there something more ominous going on?
Little Angela is displaying behaviors that are characteristic of hypothyroidism in children. This is a common disorder that affects one in every 2,500 to 3,000 babies [12]. Timing of recognition and treatment is critical. If treatment begins before the age of three months the infant usually experiences normal growth and development. However, if the baby remains untreated beyond the age of two, irreversible mental retardation occurs. Skeletal abnormalities, however, are reversible with treatment [5].

Infant hypothyroidism (cretinism) is usually due to defective embryonic development of the thyroid gland. The next most common cause is related to an inherited enzymatic defect in the synthesis of thyroxine [5].

What aspects of Angel's clinical manifestations indicate childhood hypothyroidism? What additional signs and symptoms would you anticipate finding on physical examination?

Angela is inactive, seldom cries, and sleeps excessively. Her face is puffy and her eyelids droop. Additional signs and symptoms of childhood hypothyroidism include [5,12]:

- Hoarse cry.
- Abnormally deep tendon reflexes and hypotonic abdominal muscles.
- Short forehead, puffy, wide-set eyes, broad, upturned nose, and a vacant, dull facial expression.
- Protruding abdomen.
- Feeding problems.
- Cold, coarse, thick, and dry skin.
- Dry, brittle hair.
- Slow pulse.
- Below normal body temperature.
- Jaundice.
- Large, protruding tongue.

Angela will require life-long thyroid hormone replacements. Doses in children are higher than in adults because children metabolize thyroid hormone much more rapidly. Initial doses are of moderate strength, but are gradually increased to attain levels adequate for life-long maintenance [5].

A word of caution about thyroid hormone replacements! Too rapid increase in dosage can lead to thyrotoxicity. Signs and symptoms include tachycardia, vomiting, hypotension, tremor, weakness, shortness of breath, cough, swollen extremities, and coma. Immediate emergency treatment is needed [5,11].

Parents should be taught to differentiate between signs and symptoms of a "good" baby and pathology.

Differentiate among the various types of hypothyroidism that affect children.

- Congenital hypothyroidism (CH): Occurs when the thyroid gland fails to develop or function normally before birth [12].
- Acquired hypothyroidism-autoimmune hypothyroidism: Occurs as the result of an autoimmune disorder called chronic lymphocytic thyroiditis (CLT). In CLT the child's immune system "attacks" the thyroid gland, causing damage and reduced functioning. Patients who have other types of autoimmune diseases (most often insulin-dependent diabetes) are at higher risk for developing CLT. It is estimated that 20% to 30% of diabetics will develop CLT. Thus, annual screening for CLT is often a routine part of diabetic care [12].
- Acquired hypothyroidism-iatrogenic hypothyroidism: Occurs in people who have had their thyroid glands surgically removed or medically destroyed [12].

Louise is preparing for oral comprehensive exams as part of her doctor of nursing science degree. One of the areas of focus is endocrinology. Her study group members are taking turns asking each other to present information as part of their preparation for these exams. Louise is asked:

What is myxedema coma? What causes it? How is it treated? How should Louise respond?
Myxedema coma is the most serious and dramatic complication of hypothyroidism. It often leads to death. This complication usually has a slow progression. However, stressors such as infection, trauma, exposure to cold, or heart attack can intensify hypothyroidism, causing

myxedema coma to develop abruptly [5,6]. Since initial signs and symptoms of hypothyroidism can be vague and nonspecific patients may go undiagnosed for long periods of time. This can increase the possibility that a gradual development of myxedema coma may be the dramatic event that triggers diagnosis.

Signs and symptoms of myxedema coma are significantly depressed respirations, decreased cardiac output, and progressively worsening cerebral hypoxia. Heart rate slows, and blood pressure drops. Patients become hypothermic and stuporous [6].

Treatment involves I.V. administration of thyroid hormones and correction of electrolyte and volume imbalances [5,6]. In order to save the patient's life, treatment must be swift, and the patient's condition monitored in the hospital setting. It is therefore imperative that HCPs be taught to recognize myxedema coma and to initiate immediate treatment.

The day arrives for Louise to take her oral comprehensive examination. The examiners ask Louise to:

- *Define and describe the clinical manifestations of Graves' disease.*
- *Identify risk factors that increase the risk for its development.*
- *What treatment initiatives are appropriate for Graves' disease?*

How do you think Louise should respond to these questions?

Graves' disease, or hyperthyroidism, is a metabolic imbalance characterized by excessive amounts of thyroid hormone in the bloodstream [5,6]. Risk factors for its development include [5,11,16]:

- Family history of the disease.
- Being female.
- Being over the age of 40. Only 5% of patients with hyperthyroidism are younger than 15 years of age. However in Graves's disease specifically, incidence is highest between the ages of 30 and 40.
- Coexistence of other autoimmune disorders.
- Smoking.
- Pregnancy.
- Stress.
- Excessive dietary intake of iodine.

Characteristic signs and symptoms of hyperthyroidism include [5,6,11]:

- Enlarged thyroid gland (also referred to as goiter).
- Exophthalmos (abnormally protruding eyes and a characteristic staring gaze).
- Heat intolerance.
- Nervousness.
- Inability to sit still.
- Weight loss even though appetite is increased.
- Diaphoresis.
- Diarrhea.
- Tremors.
- Palpitations.

Hyperthyroidism affects every system of the body. Additional signs and symptoms as they relate to body systems include [5,6,11]:

- **Cardiovascular system:** Arrhythmias, tachycardia, full bounding pulse, cardiac insufficiency, and resistance to the prescribed therapeutic dose of digoxin. Cardiovascular effects are seen most often in elderly patients.
- **CNS:** These effects are most often seen in younger patients. They include trouble concentrating, nervousness, anxiety, mood swings, emotional instability that may progress to psychosis, tremors, and clumsiness.
- **Gastrointestinal system:** Anorexia, nausea, vomiting, diarrhea, and enlarged liver.
- **Integumentary system:** Warm, smooth, moist, thick, flushed skin. Loss of skin color in blotches. Fine and soft hair that begins to gray prematurely. Hair loss in men and women. Fragile nails.
- **Musculoskeletal system:** Muscle weakness and atrophy.
- **Reproductive system:** Menstrual abnormalities, impaired fertility, decreased libido, and higher incidence of spontaneous abortions in women. Gynecomastia and decreased libido may be found in men.
- **Senses:** Exophthalmos causes patients to blink less frequently. This leads to dry eyes, reddened conjunctiva and cornea, and corneal ulcers. Patients also have trouble looking upward and strabismus [5,11].

Treatment depends on any underlying causes, the presence and size of goiter, the age of the patient, disease severity, and any current complications [6].

General treatment initiatives include [5,6,11,16]:

- Anti-thyroid medications. Medication administration continues until normal thyroid levels are reached. This can take from three months to two years. If normal levels cannot be reached, radiation or surgical intervention is recommended. Medications must be discontinued gradually to prevent exacerbation.
- Beta blockers, although they do not prevent or inhibit thyroid hormone production, do limit the effects of excessive amounts of thyroid hormone on the body.
- Radioactive iodine therapy limits secretion of thyroid tissue by destroying tissue. It can cause a permanent remission of hyperthyroidism, but may also cause the patient to become permanently hypothyroid.
- Surgery to remove part of the thyroid gland is performed to reduce secretions. If most of the thyroid gland is removed life-long thyroid hormone replacement therapy is necessary.
- Ophthalmopathy is managed by OTC artificial tears during the day and lubricating gels at night.

What is thyroid storm? What are its clinical manifestations?

Thyroid storm is the most serious complication of hyperthyroidism. Also referred to as thyrotoxic crisis, thyroid storm usually occurs in patients with preexisting, though often undiagnosed, thyrotoxicosis. Untreated, it is usually fatal [5,11]. When excessive amounts of T3 and T4 are produced systemic adrenergic activity increases, which leads to overproduction of epinephrine. Excessive amounts of epinephrine cause significant hypermetabolism that, in turn, leads to rapid cardiac, gastrointestinal, and sympathetic nervous system decompensation. Hypertension, tachycardia, vomiting, extreme irritability, and temperature up to 106 °F can occur. Thyroid storm can progress to delirium, coma, and death. The onset of thyroid storm is abrupt and triggered by stressors such as trauma, surgery, infection, or serious events such as stroke, myocardial infarction, preeclampsia, or pulmonary embolism [11].

Differentiate among the various types of thyroiditis.

Thyroiditis is defined as inflammation of the thyroid gland. It is most prevalent in people between the ages of 30 and 50 and is more common in women than in men [5]. The disease usually occurs in three phases: overactive thyroid, underactive thyroid, and return to normal [17]. For patients who do not experience a return to normal thyroid functioning, life-long follow-up and thyroid hormone replacement [5,19].

There are five types of thyroiditis:

- **Postpartum thyroiditis:** This is an uncommon disorder characterized by inflammation of the thyroid gland within the first year following childbirth. It is associated with an immune system reaction/underlying autoimmune thyroid condition [18,19]. Some women may experience signs and symptoms only of hyperthyroidism or only of hypothyroidism, but not both [18]. Most women who develop postpartum thyroiditis experience a return to normal thyroid function within 12 to 18 months [18].
- **Hashimoto's thyroiditis:** Hashimoto's thyroiditis is a chronic progressive disease of the thyroid gland. It is an autoimmune disorder characterized by thyroid infiltration of lymphocytes. As the immune system "attacks" its own thyroid, the gland gradually swells, and damage is sustained [6,19]. Thyroid hormone levels are abnormally low. This type of thyroiditis cannot be cured, and

low thyroid hormone levels are usually permanent. Thus, life-long thyroid hormone replacement is usually necessary [19].

- **Subacute thyroiditis:** Subacute thyroiditis is a self-limiting, painful inflammation of the thyroid gland that usually occurs following a viral infection [5,6]. Ninety to 95% of patients experience a return to normal thyroid function. The remaining 10% experience permanent hypothyroidism and require life-long thyroid hormone replacement [6].
- **Riedel thyroiditis:** Riedel thyroiditis is a rare, chronic inflammatory disease of the thyroid gland. The thyroid undergoes dense fibrosis that replaces normal thyroid parenchyma. Most patients retain normal thyroid functioning, but about 30% become hypothyroid [21].
- **Miscellaneous types:** These include acute or infectious thyroiditis due to a bacterial infection; drug induced thyroiditis caused by various drugs (e.g. amiodarone); painless thyroiditis, which produces signs and symptoms similar to postpartum thyroiditis but is not associated with childbirth; and radiation induced thyroiditis that is triggered when radiation iodine treatment is used to treat overactive thyroid glands or for certain cancers [19].

Carla is an RN who works in a busy pediatric private office practice in the Great Lakes region. Mrs. Reynolds brings her three year old daughter in for a wellness checkup. Carla notices that Mrs. Reynolds has a slight swelling in the front of her neck and slight neck distention. Mrs. Reynolds seems to be breathing rather heavily even though she is sitting down. Carla offers her a cup of water, which Mrs. Reynolds refuses saying, "I must be getting a sore throat. I seem to be having trouble swallowing lately." Although Carla's clinical experience as a HCP has been primarily in pediatrics she begins to wonder if Carla has a thyroid problem. Carla encourages Mrs. Reynolds to see a physician. Mrs. Reynolds does so and later calls Carla to thank her. It turns out that Mrs. Reynolds does have a thyroid problem, but has normal levels of thyroid hormones.

What type of thyroid problem does Mrs. Reynolds have?
Mrs. Reynolds has been diagnosed as having a nontoxic goiter. It occurs when the thyroid gland is unable to secrete sufficient thyroid hormone to meet the needs of the body. The thyroid gland enlarges as a compensatory mechanism, which usually overcomes mild to moderate hormonal deficiencies. Hence, thyroid hormone levels are normal [5,11,22].

Treatment focuses on reduction of thyroid hyperplasia. The treatment of choice is thyroid hormone replacement therapy with levothyroxine dessicated thyroid or liothyronine, which inhibits secretion of TSH and allows the thyroid gland to rest [5,11].

Small doses of iodine in the form of Lugol's solution or potassium solutions are given to patients whose goiter is caused by iodine deficiency [5,11].

Other treatment initiatives include [5,11]:

- **Diet:** Avoid foods such as cabbage, soybeans, peanuts, peaches, peas, spinach, strawberries, and radishes, which decease the production of T4 [11,22].
- **Radiation:** Radiation ablation therapy may be used to destroy cells that concentrate iodine for thyroid hormone production.
- **Surgery**: Large goiters that do not respond to other treatments may require partial removal of the thyroid gland.

Accidental removal of parathyroid tissue during thyroidectomy may cause symptoms related to what electrolyte imbalance?
Hypoparathyroidism is an uncommon condition caused by a deficiency of parathyroid hormone (PTH). Since PTH is essential to the regulation and maintenance of calcium and phosphorus, hypoparathyroidism is characterized by hypocalcemia and neuromuscular hyper-excitability [6, 23].

Characteristic signs of hypoparathyroidism include [5,6]:

- **Tetany:** Manifested by muscle hypertonia and tremors and spasmodic or uncoordinated movements triggered by attempts at voluntary movements.
- **Chvostek's Sign:** Hyperirritability of the facial nerve manifested by a spasm of facial muscles, which occurs when muscles or branches of the facial nerve are tapped.
- **Trousseau's Sign:** Carpopedal spasm (spasmodic contractions of the muscles of the hands and feet) triggered within three minutes after a blood pressure cuff is applied to the arm and inflated to 20 mm Hg above patient's systolic pressure.
- **Laryngeal spasm.**

Central nervous signs and symptoms of hypoparathyroidism are exaggerated during what conditions?
Central nervous system signs and symptoms are exaggerated during pregnancy, infection, thyroid hormone withdrawal, before menstruation, hyperventilation, and right before menstruation [5].

What drug interferes with normal parathyroid function especially if renal failure is also a problem?
Cimetidine (Tagamet) interferes with normal parathyroid function. Remember that any interference with parathyroid function increases the risk of hypocalcemia.

In the event of acute, life-threatening tetany, what treatment measures must be initiated immediately?
Intravenous calcium administration is needed in the presence of acute life-threatening tetany. The most effective calcium solution is ionized calcium chloride (10%). All intravenous calcium preparations are given slowly since it is a highly irritating solution that stings and causes thrombosis. The patient experiences burning flushing feelings of the skin and tongue. However, the intravenous calcium solution also seems to rapidly relieve feelings of anxiety [6].

Hyperparathyroidism is a fairly common disorder, affecting one in 1,000 people and is two to three times more common in females than in males [5]. It is defined as the unregulated, hypersecretion of parathyroid hormone (PTH) [6,24].

Differentiate between the two types of hyperparathyroidism.

Explain the pathophysiology of hyperparathyroidism.

Describe treatment initiatives for hyperparathyroidism.
There are two types of hyperparathyroidism: primary and secondary.

- Primary hyperparathyroidism: In primary hyperparathyroidism one or more of the parathyroid glands enlarge, increasing PTH secretion and causing elevated serum calcium levels. The most common cause of primary hyperparathyroidism is a single parathyroid adenoma, a benign tumor. Parathyroid hyperplasia is responsible for the remainder of cases [5,6,24].
- Secondary hyperparathyroidism: Secondary hyperparathyroidism is due to a chronic abnormal stimulus, usually chronic renal failure, vitamin D deficiency, or osteomalacia [5,6,24].

Chronic overproduction of PTH causes increased serum calcium levels. Normal negative feedback mechanisms do not function, and chronic excessive resorption of calcium can lead to osteopenia (loss of some bone density). In secondary hyperparathyroidism overproduction of parathyroid hormone in patients with renal failure add to the pathophysiology of bone disease found in patients on dialysis [24].

Clinical signs and symptoms of primary hyperparathyroidism are due to hypercalcemia and include arrhythmias, hypertension, emotional instability, fatigue, personality changes, severe epigastric pain, peptic ulcers, chronic low back pain, muscle weakness and atrophy, polyuria, cataracts, anemia, and calcifications [5,6].

Secondary hyperparathyroidism causes signs and symptoms of hypocalcemia as well as the underlying disorder. Secondary hyperparathyroidism may be prevented by ensuring a diet that contains

adequate amounts of calcium or by taking calcium and vitamin D supplements [5].

Treatment of hypercalcemia includes [6]:

- Administration of intravenous normal saline solution and diuretics such as Lasix and Edecrin to increase urinary excretion of calcium for those patients who are not in renal failure.
- Administration of agents to inhibit bone resorption of calcium. These include Aredia, Cibacalcin, or Didronel.
- Administration of oral phosphate as an anti-hypercalcemia agent.
- Restriction of dietary calcium and discontinuation of drugs that might facilitate hypercalcemia such as thiazides, and vitamin D.
- Dialysis for patients in renal failure or for those whose hypercalcemia does not respond to other treatments.
- Reduced dosage of digoxin since hypercalcemic patients are more vulnerable to the toxic effects of this drug.
- Monitoring of calcium (daily), blood urea nitrogen (BUN), potassium, and magnesium levels.

Surgical removal of parathyroid tissue may relieve bone pain within three days of the surgery. Unfortunately, renal damage may be irreversible [5].

Treatment of secondary hyperparathyroidism focuses on correction and treatment of the underlying cause. Remember that secondary hyperparathyroidism causes hypocalcemia as opposed to primary hypothyroidism, which causes hypercalcemia. Generalized treatment initiatives include [5]:

- Vitamin D therapy.
- Administration of oral calcium preparation in the presence of renal disease.
- Administration of a new classification of drugs (the calcimimetics) approved for the treatment of secondary hyperparathyroidism. These drugs act by stopping the secretion of PTH.

Patients with chronic secondary hyperparathyroidism may find that the parathyroid glands do not revert to normal function even after calcium levels have been returned to normal [5].

Andrea is a nurse practitioner. One of her patients has just been diagnosed with Addison's disease. The patient, who is also a nurse, is distraught, and has many questions about the disease. Andrea needs to do a great deal of patient education. She begins by explaining what Addison's disease is, what causes it, prognosis, and treatment options.

What do you think Andrea will tell her patient?
Addison's disease is also known as adrenal hypofunction or adrenal insufficiency. It occurs in two forms: primary and secondary. Primary adrenal insufficiency is the form commonly referred to as Addison's disease. It originates within the adrenal glands and is characterized by a decrease in mineralocorticoid, glucocorticoids, and androgen secretion [11,25].

Secondary adrenal insufficiency occurs secondary to a disorder outside of the adrenal glands such as a pituitary tumor [5,11].

Adrenal hypofunction affects about eight in 100,000 people [5].

Up to 80% of cases of Addison's disease cases are caused by an autoimmune process in which circulating antibodies specifically "attack" adrenal tissue. This disease is found primarily in middle-aged females and gradually destroys the adrenal cortex [25].

All patients affected by Addison's disease, in fact all patients affected by either primary or secondary adrenal hypofunction, need life-long corticosteroid replacement therapy in the form of cortisone or hydrocortisone [5,11].

Andrea should tell her patient that she must take corticosteroid replacement therapy for the rest of her life. The patient should be instructed to wear a medical alert bracelet as well. She should also tell her patient [5,25]:

- To keep her HCP informed of any medications she takes including prescription, OTC, herbal preparations, vitamins, minerals, and other supplements.
- To take steroid therapy in the morning since taking steroids in the late afternoon or evening may stimulate the central nervous system and cause insomnia.
- Caution her that steroid therapy can make it easier to bruise.

Additional nursing concerns include advising patients who are diabetic that steroid replacement therapy may require insulin dose adjustments [5,25].

Patients must also be warned about the possibility of adrenal crisis.

Adrenal crisis is a critical deficiency of mineralocorticoids and glucocorticoids. It is the most serious complication of adrenal hypofunction and can develop gradually or abruptly. It is most likely to occur in patients who fail to respond to hormone replacement therapy, who abruptly stop hormone therapy, who experience physiologic stress, who undergo bilateral adrenalectomy, or who develop an adrenal gland thrombosis [5,11,25].

Signs and symptoms of adrenal crisis include [5,25]:

- Significant weakness and fatigue.
- Abrupt severe pain in the lower back, abdomen, or legs.
- Severe nausea and vomiting.
- Dehydration.
- Hypotension.
- Loss of consciousness.

Untreated adrenal crisis can lead to vascular collapse, renal shutdown, coma, and death. Patients need to receive an emergency bolus of hydrocortisone followed by fluid resuscitation. Patients should carry an emergency kit with a corticosteroid injection with them at all times. They and their families and friends should be taught how to administer the injection [25].

Mark has a real weakness for black licorice, and eats large quantities of it. Eating large amounts of black licorice can cause signs and symptoms that mimic what disease? Why does this occur?
Eating large amounts of English black licorice or licorice-like substances can cause a syndrome that mimics primary hyperaldosteronism. This is because glycyrrhizic acid, a substance found in licorice, has a mineralocorticoid action [5].

Why is diabetes mellitus often found in conjunction with hyperaldosteronism?
Diabetes mellitus is frequently found in conjunction with hyperaldosteronism because hypokalemia, which causes the majority of clinical effects of hyperaldosteronism, can interfere with proper secretion of insulin.

What electrolyte imbalance is strongly linked to a diagnosis of hyperaldosteronism?
Ongoing low levels of serum potassium in patients who do not have edema, are not taking diuretics, have not had GI tract losses due to vomiting or diarrhea, and who have a normal sodium intake strongly suggest hyperaldosteronism [5].

What saline suppression test results would you expect to find in patients who have hyperaldosteronism?
Patients are given intravenous salt solutions after which blood levels of aldosterone and renin are measured. In patients with primary hyperaldosteronism the level of aldosterone in the blood is still high, and the level of renin is low even after this salt loading [27].

In cases of primary hyperaldosteronism, what results would you expect the 24-hour urinary excretion of aldosterone test to show?
Patients ingest a high-sodium diet for five days after which the amount of aldosterone in the urine is measured. In patients with primary hyperaldosteronism, aldosteronism will not be suppressed by the salt load, and the level of aldosterone in the urine will be high [27].

Cushing's syndrome is a hormonal disorder caused by prolonged exposure of the body's tissues to excessive levels of adrenocortical hormones, especially cortisol, related corticosteroids, and, to a lesser extent, androgens and aldosterone [5, 28].

Differentiate between Cushing's syndrome and Cushing's disease.
If excess of glucocorticoids is due to a pituitary dependent condition, it is called Cushing's disease [11].

What groups of people may have high levels of cortisol not related to pathological processes?
Since cortisol helps the body to respond to stress, pregnant women in the last three months of pregnancy and highly trained athletes have high levels of this hormone [28].

Differentiate among the three types of Cushing's syndrome.
Cushing's syndrome can be categorized as three types [11]:

- **Primary:** Primary Cushing's syndrome is due to disease of the adrenal cortex.
- **Secondary:** Secondary Cushing's syndrome is caused by hyperfunction of cells that secrete corticotropin in the anterior pituitary gland.
- **Tertiary:** Tertiary Cushing's syndrome is due to dysfunction or injury of the hypothalamus.

Differentiate between Cushing's syndrome and cushingoid syndrome.
Differentiating between Cushing's syndrome and cushingoid syndrome can be challenging. Chronic depression, alcoholism, and long-term treatment with corticosteroids can combine to produce cushingoid syndrome, an adverse consequence characterized by fat deposits between the shoulders and around the waist and many systemic abnormalities. Cushing's syndrome has similar signs, but can be differentiated from cushingoid syndrome by the additional presence of hypertension, renal problems, hyperglycemia, muscle weakness, tissue wasting, and frequently changing emotional states(emotional lability) [5].

Complete this sentence. In Cushing's syndrome immune system suppression can mask_____.
Immune system suppression can mask infection, even severe infections [5]. It is important for HCP to recognize, and to teach patients and families to recognize, even the slightest signs of infection.

Describe how radiation therapy is used to treat Cushing's syndrome.
If surgical approaches fail, or if a patient is not a candidate for surgery, radiation therapy is a possible alternative treatment. Radiation treatment to the pituitary gland is generally administered over a six-week period. Improvement is noted in 40% to 50% of adults and up to 85% of children [28].

It may take months or even years for patients to feel better after receiving radiation treatment alone. Radiation in conjunction with cortisol-inhibiting drugs can help speed up the recovery process [28].

In Cushing's syndrome, patients with non-endocrine corticotropin-producing tumors require excision of the tumor followed by drug therapy. Drug therapy is also administered in the event that patient cannot undergo surgery. One of the drugs used is Lysodren.

How does Lysodren work?
Mitotate (Lysodren) is toxic to the adrenal cortex. Its administration is referred to as medical adrenalectomy. Side effects of this drug include nausea, vomiting, diarrhea, somnolence, and depression.

Adrenogenital syndrome, perhaps more commonly known as congenital adrenal hyperplasia, is a syndrome caused by disorders of adrenocortical steroid biosynthesis. Most cases of the syndrome are due to the failure of the adrenal glands to produce enough cortisol [5,29]. Inherited adrenogenital syndrome is referred to as congenital adrenal hyperplasia (CAH).

Which is the more severe form of CAH? What are its clinical manifestations?
The salt-losing form of CAH is more severe than the simple form and causes more complete virilization in females. Male external genitalia (but without testes) develop [5,29,30].

Males with salt-losing CAH have no abnormalities in external genitalia. Thus, diagnosis immediately after birth is difficult and usually delayed until severe signs and symptoms develop.

In severe cases signs of salt-losing CAH infants may develop as soon as two to three weeks after birth in both males and females. These signs include vomiting, diarrhea, dehydration, low potassium and sodium levels, and abnormal heart rhythms [29, 30]. Infants are apathetic and fail to eat. These signs indicate the onset of adrenal crisis, which, unless treated promptly, may lead to cardiovascular collapse and cardiac arrest [5].

What does adrenal crisis or evidence of adrenal hypofunction in the first week of life suggest?
Adrenal crisis or evidence of adrenal hypofunction in the first week of life suggests salt-losing CAH [5].

Define hermaphroditism.
Hermaphroditism is a condition appropriately mentioned as part of a discussion of CAH. Hermaphroditism is a rare condition in which children have both ovarian and testicular tissues. External genitalia are usually ambiguous, but may also be completely male or female, which effectively "hides" hermaphroditism until puberty. The child with hermaphroditism almost always has a uterus and ambiguous gonads. Fertility, however, is rare [5].

How is sexual assignment made in hermaphroditism?
Sexual assignment is based on the anatomy of the external genitalia. Reconstructive surgery, during which inappropriate reproductive organs are removed, is performed as early as possible to prevent the development of incongruous secondary sex characteristics at puberty. Hormonal replacement may be needed [5].

Complete this sentence: Research indicates that about _____of patients newly diagnosed with hypertension have _____.
Research indicates that about 0.5% of patients newly diagnosed with hypertension have pheochromocytoma [5].

Pheochromocytoma causes episodes that are generally characterized by what four factors?
Pheochromocytoma causes episodes typically characterized by [31]:

- Headaches.
- Palpitations.
- Diaphoresis.
- Severe, possibly life-threatening, hypertension.

Urine collection of VMA (vanillylmadelic acid) is part of the diagnostic process for pheochromocytoma.

What dietary instructions should the nurse provide prior to this test?
Instruct patients to avoid food that are high in vanillin (such as coffee, nuts, chocolate, and bananas) for two days prior to collection of urine [5].

Treatment of choice for pheochromocytoma is surgical resection of the tumor, which usually cures the associated hypertension. It is important that specific measures be taken prior to surgery to control blood pressure and prevent intraoperative crisis.

What measures should be taken preoperatively?
Preoperative measures include [31]:

- Administration of an alpha-adrenergic blocker or metyrosine.
- Volume expansion with isotonic sodium chloride solution.
- Facilitation of liberal salt intake.
- Administration of a beta blocker only after sufficient alpha blockade to "avoid precipitating a hypertensive crisis from unopposed alpha stimulation [31, pg. 2].
- Administration of the last doses of oral alpha and beta blockers on the morning of surgery.

Frank is a registered nurse who is certified in critical care. His 45-year-old sister-in-law telephones him one evening in great distress. She has just been diagnosed with multiple endocrine neoplasia and has an appointment with an endocrinologist to discuss treatment options next week. She asks Frank to accompany her. She also tells Frank that "I have the kind that isn't cancer." Frank agrees to go with her, but realizes that he must do some research on the disorder in order to be helpful. He is not familiar with multiple endocrine neoplasia and wonders what his sister-in-law meant by "the kind that isn't cancer."What is some information that would be helpful for Frank to know?

There are two types of multiple endocrine neoplasia (MEN) that are well recorded. These are [5]:

- **MEN I:** MEN I, also called Werner's syndrome, occurs because of a defect in a gene that carries the code for the protein menin [32]. This defect leads to hyperplasia and tumors of the pituitary and parathyroid glands, islet cells of the pancreas, and, rarely, the thyroid and adrenal glands. It is the more common form of MEN [5].
- **MEN II:** MEN II, also called Sipple's syndrome, is a rare familial malignancy caused by genetic mutation [33]. It usually involves medullary cancer of the thyroid and hyperplasia and tumor growth of the adrenal medulla and parathyroid glands [5,33].

Autosomal dominant inheritance is the usual cause of MEN. It affects twice as many females as males, can occur at any age from adolescence through old age, but is rare in children [5].

Clinical manifestations of MEN depend on the glands that are affected. Frank needs to find out what signs and symptoms have affected his sister-in-law and if her physician has talked about specific gland involvement.

Treatment focuses on tumor removal and therapy to control any residual symptoms. Frank will need to discuss specific gland involvement, tumor size and location, postoperative therapy, and recommendations for surgeons who have experience in the type of surgery that will be needed.

Differentiate among the different types of diabetes.

There are three types of DM.

- **Type 1:** Type 1 diabetes occurs when the beta cells in the pancreas are destroyed or suppressed. Formerly referred to as juvenile diabetes or insulin dependent diabetes, type 1 diabetes is subdivided into idiopathic and immune-mediated types. In idiopathic diabetes there is permanent deficiency of insulin and no evidence of autoimmunity. In immune-mediated diabetes the body produces an autoimmune attack on pancreatic beta cells, and the pancreas becomes inflamed. By the time signs and symptoms appear, 80% of the beat cells are destroyed. Some experts, however, believe that beta cells are not destroyed but disabled and may later be reactivated [5,6,11].
- **Type 2:** Type 2 diabetes, formerly referred to as adult-onset diabetes or non-insulin dependent diabetes, may be attributed to insulin resistance in target tissues, abnormal insulin secretion, or overproduction of glucose (inappropriate hepatic gluconeogenesis) [6,11].
- **Secondary diabetes:** Secondary diabetes is so-called because this type occurs "secondarily" to another condition or event. The factors that trigger secondary diabetes include [11]:
    - Physical or emotional stress that can cause prolonged elevation of cortisol, epinephrine, glucagon, and GH. Such elevations increase blood glucose levels and demands on the pancreas.
    - Pregnancy, which causes weight gain, high levels of estrogen, and high levels of placental hormones [11]. This type of diabetes is referred to as gestational diabetes mellitus (GDM). Glucose levels usually return to normal after the women gives birth. However, women who have had GDM have a 40% to 60% chance of developing type 2 diabetes within five to 10 years [5].
    - Use of specific medications such as adrenal corticosteroids, hormonal contraceptives, and other drugs that oppose the desired effects of insulin [11].

Identify the diagnostic criteria for DM according to the American Diabetes Association (ADA) Guidelines.

DM can be diagnosed if patients manifest any of the following [5]:

- Symptoms of DM plus a random, nonfasting blood glucose level equal to or greater than 200 mg/dl.
- Fasting blood glucose equal to or greater than 126 mg/dl.
- Oral glucose tolerance test (2-our sample) results equal to or greater than 200 mg/dl.

How are blood glucose levels classified according to the American Diabetes Association?

- Normal: <100 mg/dl.
- Prediabetes: 100 to 125mg/dl.
- Diabetes :>126 mg/dl.

What are the ADA recommended testing guidelines for DM?

The ADA recommends the following testing guidelines [5]:

- Test people age 45 and older who have no symptoms every three years.
- People with characteristic signs and symptoms should be tested immediately.
- High risk groups should be tested "frequently."

There are several important issues regarding DM and elderly patients. What are they?

Issues particular to elderly patients include [5,6,11]:

- Cells become more resistant to insulin with aging. This decreases the older adult's ability to metabolize glucose. Additionally, insulin release from the pancreas is delayed, and sudden concentrations of glucose occur. Such concentrations cause more prolonged hyperglycemia in elders.
- The thirst mechanism is less efficient in the elderly than in younger adults and children. Thus older adults may not experience the polydipsia that is characteristic of DM in younger adults.
- Healing is often slower in elders than in younger patients. DM compounds this delay in healing.

Stacey is a busy high-school junior. She is a star on the girls' basketball team. She is also a diabetic. Stacey injected herself with her usual dose of insulin this morning. However, it is an especially stressful Friday for Stacey. Tonight is an important game. If her team wins this game they will progress to the district semi-finals. Stacey can barely eat her lunch and does not eat her usually snack prior to the game. "I'm just too nervous to eat." Early in the game Stacey begins to feel anxious, weak, and dizzy. Her heart is pounding. She attributes this to anxiety until her coach calls for a time out and asks her if she ate lunch and her snack prior to game-time? Stacey admits that she did not eat much today? "Did you take your insulin today?" The coach suspects that Stacey might be developing a problem.

What would you suspect that Stacey is developing?

Stacey is most likely hypoglycemic as a result of taking her insulin without proper nutritional intake. Signs and symptoms of hypoglycemia include anxiety, mental changes, dizziness, weakness, pallor, tachycardia, diaphoresis, seizures, confusion, and loss of consciousness that may progress to coma. Stacey should immediately be given carbohydrates such as glucose tablets, honey, or fruit juice. If patients are unconscious, they should be given glucagon or dextrose I.V. [5,6,11]. Fortunately Stacey's coach recognizes the signs and symptoms of hypoglycemia. Persons close to Stacey (and all persons who have DM) should be taught to recognize these signs and symptoms and what to do if they occur.

Jeremy is a college sophomore who has had DM for several years. He hates injecting himself with insulin and often delays giving himself these injections. One Monday morning, after a late night of partying, Jeremy sleeps very late. His roommate awakens him excitedly. "What is wrong with you? We have a huge chemistry exam in 20 minutes!" Jeremy bolts out of bed, dresses quickly, and rushes to class. On the way he grabs a snack from the student union. He does not remember to take his insulin.

Midway through the exam Jeremy begins to feel weak and is unable to concentrate. His heart is racing and he feels extremely thirsty.

What is happening to Jeremy?

Jeremy is experiencing ketoacidosis. Signs and symptoms of ketoacidosis include acetone breath (fruity-smelling breath), weak, rapid pulse, polyuria, thirst, deep, rapid respirations (Kussmaul's respirations), changes in level of consciousness, and stupor. Prompt treatment with I.V. fluids, insulin, and, often, potassium replacement is necessary [5].

Jeremy's friends should be taught to recognize signs of ketoacidosis and hypoglycemia. If Jeremy is unable to make rational decisions his friends may need to be able to not only recognize when he is in trouble but what to do if trouble occurs. Hypoglycemia is often quickly corrected, if recognized promptly, with simple measures such as providing glucose tablets, honey, or fruit juice. Ketoacidosis may be more problematic if not treated promptly.

Implications for nursing continuing education

Seldom does a day go by without media-grabbing headlines pertaining to health care. Whether it be about treatment breakthroughs, new means of prevention, or implications for safe and appropriate care, such news usually has significant implications for nurses.

Those implications, in part, require that nurses acquire new knowledge and/or psychomotor skills. In other words, the necessity for new knowledge acquisition is a almost a daily task. To add to the plethora of new knowledge requirements is the need to become familiar with diseases and disorders that are not particularly common.

Since many endocrine diseases and disorders are uncommon, and some are quite rare, how can nurses be expected to recognize the sometimes subtle signs and symptoms of what could be serious pathologies?

Nursing professional development specialists are generally responsible for planning, developing, implementing, and evaluating the continuing education endeavors of the nursing department. It is a challenge just to keep up with accrediting organization mandates and education offerings that help nurses to provide care to nurses in various health care specialties. Issues surrounding the recognition of these diseases and provision of nursing care to persons affected by these and other pathologies increase the need for nursing continuing education. How can administrators and managers facilitate continuing education efforts?

There is a need for creativity. Education is not solely delivered in a classroom setting. Various means of distance education can be used to offer brief "spurts" of education. E-mail, texts, and alerts can be sent to nurses' iPhones, computers, and other devices. A disease that is uncommon can be highlighted on a weekly basis and important highlights pertaining to signs and symptoms, pathophysiology, risk factors, and treatment can be provided.

Of course, nurses themselves are primarily responsible for their own education. They cannot rely exclusively on their employing organizations to provide all of the continuing education that is so critical to their professional endeavors. Nurses should suggest education topics for development by nursing professional development and for department-based and unit-based education.

Here are some sources for nurses who are interesting in expanding their knowledge of endocrine disorders and other topics pertinent to the practice of nursing.

- **Professional associations:** Nurses should join and become active in professional organizations including those pertaining to their particular nursing specialty. These organizations often provide continuing education using various modalities.
- **Professional journals:** Most journals are offered in hard copy and via electronic media. Keeping abreast of new developments in health care in general and nursing in particular can be facilitated by reading reliable professional nursing journals.
- **Companies that specialize in continuing education for HCPs:** These companies offer continuing education on a wide variety of topics. Many companies offer a variety of ways to obtain continuing education including in-person seminars, hard copy catalogues, and online programming. These companies can usually be relied upon to offer education offerings that provide contact hours for licensure renewal.
- **Professional books:** Many nurses opt to purchase professional references that can be downloaded onto their various electronic devices, thus making resources readily accessible.
- **Professional libraries:** Most health care facilities have their own resource centers. Nurses should be encouraged to find out about the resources within their own organizations.
- **Organizational committees and task forces:** In this age of shared governance staff nurses are assuming more and more responsibility for managing their own practice. Part of this responsibility often includes serving on various committees and task forces. Meetings of these groups often provide opportunities for continuing education.
- **Colleagues:** Nurses need to be able to rely on each other for support and as education resources. An atmosphere of open communication should be part of every health care organization. This atmosphere should encourage nurses to not only share their knowledge with each other but to be able to ask questions without fear of embarrassment.
- **Internet resources:** Internet resources such as the Joint Commission, the Centers for Disease Control (CDC), and other organizations that are known to be reliable sources of accurate information also used for education. Many such organizations have downloadable apps that can be accessed quickly for frequent, even daily updates on issues of importance to nurses and other HCPs. These apps can also be used to search for information specific to particular signs and symptoms and diseases and disorders.

Summary

The endocrine system is quite complex and works in conjunction with the nervous system to maintain the delicate balance that ensures homeostasis. Even slight variations in its functioning can cause significant body disturbances.

Several endocrine diseases and disorders are fairly common, such as thyroid disorder and diabetes mellitus. However, still more of them are uncommon and even rare, making recognition a challenge. To compound the complexity of caring for patients affected by endocrine pathologies, many of these diseases and disorders have insidious onsets, and initial signs and symptoms can be vague and mimic a variety of problems.

It is essential that nurses pursue continuing education from a variety of sources to acquire knowledge about the endocrine system and nursing considerations when caring for patients with diseases and disorders of this body system.

In addition to pursuing their own educational opportunities nurses must enhance their skills as patient/family educators. Many endocrine diseases require life-long follow-up including hormonal replacement. The abilities of patients and families to adhere to life-long treatment regimens depend, in large part, on the ability of nurses to effectively teach them how to do so. Nurses must assess patient/family knowledge acquisition objectively by having them demonstrate necessary psychomotor skills and verbally explain other important points such as a description of signs and symptoms, how to deal with complications, and medication side effects.

To conclude, pathologies of the endocrine system can prove to be challenging to nurses and other HCPs. They are complex, often uncommon diseases and disorders. Nurses may be among the first HCPs to recognize their existence. They may also be among the first to facilitate proper evaluation and treatment of these conditions.

References

1. Comerford, K. C. (Ed.). Anatomy & physiology made incredibly easy. Philadelphia: Wolters Kluwer Health/Lippincott Williams Wilkins.
2. Emedicinehealth. (2014). Anatomy of the endocrine system. Retrieved May 5, 2014 from http://www.emedicinehealth.com/anatomy_of_the_endocrine_system/article_em.htm.
3. Van De Graaff, K., & Rhees, R. W. (2011). Schaum's easy outlines: Human anatomy and physiology (2nd. Ed.). New York: McGraw-Hill.
4. Corenblum, B. (2013). Hypopituitarism (Panhypopituitarism). Retrieved may 24, 2014 from http://emedicine.medscape.com/article/122287-overview.
5. Durkin, M. T. (2013). Professional guide to diseases (10th ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.
6. Nettina, S. M. (2010). Lippincott manual of nursing practice (9th ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.
7. Mayo Clinic. (2013). Hypopituitarism. Retrieved May 26, 2014 from http://www.mayoclinic.org/diseases-conditions/hypopituitarism/basics/treatment/con-20019292?p=1.
8. Mayo Clinic. (2013). Acromegaly. Retrieved May 26, 2014 from http://www.mayoclinic.org/diseases-conditions/acromegaly/basics/definition/con-20019216.
9. Pagana, K. D., & Pagana, T. J. (2014). Mosby's manual of diagnostic and laboratory tests (5th ed.). St. Louis: Elsevier Mosby.
10. Khardori, R. (2014). Diabetes insipidus. Retrieved May 28, 2014 from http://emedicine.medscape.com/article/117648-overview.
11. Eckman, M., & Share, D. (Eds.). (2013). Pathophysiology made incredibly easy (5th ed.). Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.
12. Children's Hospital of Philadelphia. (no date given). Hypothyroidism in children. Retrieved May 28, 2014 from http://www.chop.edu/service/pediatric-thyroid-center/pediatric-thyroid-disorders/hypothyroidism.html#hypothyroidism-treatment.
13. Medline Plus. (2014). Chronic thyroiditis (Hashimoto's disease). Retrieved May 30, 2014 from http://www.nlm.nih.gov/medlineplus/ency/article/000371.htm.
14. Comerford, K. C. (2014). Nursing 2014 drug handbook. Philadelphia: Wolters Kluwer Health/Lippincott Williams & Wilkins.
15. emedicinehealth. (2014). Hypothyroidism medications. Retrieved May 30, 2014 from http://www.emedicinehealth.com/hypothyroidism/page6_em.htm#hypothyroidism_medications.
16. Mayo Clinic. (2011). Graves' disease. Retrieved June 2, 2014 from http://www.mayoclinic.org/diseases-conditions/graves-disease/basics/risk-factors/con-20025811?p=1.
17. University of Maryland Medical Center. (2013). Thyroiditis. Retrieved June 1, 2014 from https://umm.edu/health/medical/altmed/condition/thyroiditis.
18. Mayo Clinic. (2013). Postpartum thyroiditis. Retrieved June 1, 2014 fromhttp://www.mayoclinic.org/diseases-conditions/postpartum- thyroiditis/basics/definition/con-20035474?p=1.
19. NHS. (2012). Thyroiditis. Retrieved June 1, 2014 from http://www.nhs.uk/conditions/thyroiditis/Pages/Introduction.aspx.
20. Lee, S. L. (2012). Subacute thyroiditis. Retrieved June 1, 2014 from http://emedicine.medscape.com/article/125648-overview.
21. Guerin, C. K. (2014). Riedel thyroiditis. Retrieved June 2, 2014 from http://emedicine.medscape.com/article/125243-overview. 21].
22. Lee, S. L. (2013). Nontoxic goiter. Retrieved June 4, 2014 from http://emedicine.medscape.com/article/120392-overview
23. Mayo Clinic. (2014). Hypoparathyroidism. Retrieved June 5, 2014 from http://www.mayoclinic.org/diseases-conditions/hypoparathyroidism/basics/definition/con-20030780?p=1.
24. Kim, L. (2014). Hyperparathyroidism. Retrieved June 5, 2014 from http://emedicine.medscape.com/article/127351-overview.
25. NIH. (2014). Adrenal insufficiency and Addison's disease. Retrieved June 5, 2014 from http://endocrine.niddk.nih.gov/pubs/addison/addisons_508.pdf.
26. Chrousos, G. P. (2012). Hyperaldosteronism. Retrieved June 8, 2014 from http://emedicine.medscape.com/article/920713-overview.
27. The American Association of Endocrine Surgeons. (no date given). Primary hyperaldosteronism: Diagnosis. Retrieved June 11, 2014 from http://endocrinediseases.org/adrenal/hyperaldosteronism_diagnosis.shtml.
28. National Endocrine and Metabolic Diseases Information Service. (2012). Cushing's Syndrome. Retrieved June 8, 2014 from http://endocrine.niddk.nih.gov/pubs/cushings/cushings.aspx.
29. Mayo Clinic. (2014). Congenital adrenal hyperplasia. Retrieved June 10, 2014 from http://www.mayoclinic.org/diseases-conditions/congenital-adrenal-hyperplasia/basics/definition/con-20030910?p=1.
30. MedlinePlus. (2012). Congenital adrenal hyperplasia. Retrieved June 10, 2014 from http://www.nlm.nih.gov/medlineplus/ency/article/000411.htm.
31. Blake, M. A. (2014). Pheochromocytoma. Retrieved June 8, 2041 from http://emedicine.medscape.com/article/124059-overview.
32. MedlinePlus. (2012). Multiple endocrine neoplasia (MEN) I. Retrieved June 8, 2014 from http://www.nlm.nih.gov/medlineplus/ency/article/000398.htm. Type 1
33. Medscape. (2014). Type 2 multiple endocrine neoplasia. Retrieved June 8, 2014 from http://emedicine.medscape.com/article/123447-overview.

DISORDERS OF THE ENDOCRINE SYSTEM: ANATOMY, PHYSIOLOGY, AND CURRENT TREATMENT INITIATIVES

Final Examination Questions

Choose the best answer for questions 11 through 20 and mark your answers on the Final Examination Sheet found on Page 141 or take your test online at **nursing.elitecme.com.**

11. Insulin is secreted by the alpha cells of the pancreas and is responsible for elevating blood glucose levels during fasting or starvation.
    a. True.
    b. False.

12. A blood glucose level of 100 to 125 mg/dl is classified as prediabetes.
    a. True.
    b. False.

13. Characteristic signs and symptoms of diabetes insipidus include polyuria, extreme thirst, nocturia, poor skin turgor, and dehydration.
    a. True.
    b. False.

14. Assessing GH levels is important in hyperpituitarism. It is important to remember that patients should not be emotionally or physically stressed when obtaining blood samples for the GH suppression test since stress can elevate GH levels.
    a. True.
    b. False.

15. Ketoacidosis requires prompt treatment including administration of glucose tablets, honey, or fruit juice.
    a. True.
    b. False.

16. The most common cause of multiple endocrine neoplasia (MEN) is familial malignancy.
    a. True.
    b. False

17. Clinical hyperthyroidism can be triggered by excessive dietary intake of iodine or by stress in patients who have latent hyperthyroidism.
    a. True.
    b. False.

18. Adrenal insufficiency is also referred to as Cushing's syndrome.
    a. True.
    b. False.

19. Hermaphroditism is a rare condition in which children have both ovarian and testicular tissues.
    a. True.
    b. False.

20. The endocrine glands secrete specific hormones produced by the body to regulate cell and organ activity.
    a. True.
    b. False.

ANCCKS10ESE17

Heroin Use in America: Identification, Treatment, and Prevention

4 Contact Hours

Original Release Date: 2/1/2016 **Expiration Date: 2/1/2019**

Faculty

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Deborah Converse graduated with a degree in Psychology from Stetson University in Deland, Florida and received an MA in Education for Emotionally Disabled Students from the University of Central Florida. She was awarded National Board Certification in 2000 as an Exceptional Needs Specialist, Birth -21+ endorsement.

In addition to teaching, Deborah has written programs, developed curriculum and conducted in-service training for school districts to promote the inclusion of special needs students in all educational and employment programs.

Content reviewer
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Audience

The target audience for this course includes all health care professionals responsible for the assessment and care of teens and adults who are at risk for heroin use.

Purpose statement

The purpose of this course is to familiarize professionals with basic information concerning heroin addiction, which has reached epidemic proportions in the United States and around the globe. This includes facts about heroin and addiction, effects on the brain, progression of the disease, psychological and physical effects of short-term and chronic use, screening, treatment, and prevention. The course covers background information and statistics on the escalation of heroin addiction in the United States from 1850 to 2014 including causative factors. The review includes evidence-based treatment and prevention programs, as well as the current trends in progress to advance prevention and treatment of the disease.

Learning objectives

Upon completion of this course, the nurse will be able to:

- Discuss the composition and properties of three types of heroin.
- Compare and contrast the effects of heroin on the brain based on the mode of transmission. Define terms relevant to heroin use.
- Describe today's heroin epidemic.
- Describe the etiology of heroin addiction.
- Describe the signs and symptoms of heroin use.
- Explain the differences between the psychological and physical effects of short-term and chronic heroin use.
- Discuss immediate and long-term treatment methods including three evidence-based therapies to treat heroin use.
- Highlight special nursing considerations when caring for patients who are or who are at risk for becoming addicted to heroin.

How to receive credit

- Read the entire course, which requires a 4-hour commitment of time.
- Depending on your state requirements you will asked to complete either:
  - An attestation to affirm that you have completed the educational activity.
  - OR completed the test and submit (a passing score of 70 percent is required).

    Note: Test questions link content to learning objectives as a method to enhance individualized learning and material retention.
- Provide required personal information and payment information.
- Complete the MANDATORY Self-Assessment, and course evaluation.
- Print the Certificate of Completion.

Accreditations and approvals

Elite is accredited as a provider of continuing education by the American Nurses Credentialing Center's Commission on Accreditation.

Individual state nursing approvals

In addition to states that accept ANCC, Elite is an approved provider of continuing education in nursing by: Alabama, Provider #ABNP1418 (valid through April 30, 2021); California Board of Registered Nursing, Provider #CEP15022; District of Columbia Board of Nursing, Provider # 50-4007; Florida Board of Nursing, Provider #50-4007; Georgia Board of Nursing, Provider #50-4007; and Kentucky Board of Nursing, Provider #7-0076 (valid through December 31, 2019).

Activity director

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Disclosures

Resolution of Conflict of Interest
In accordance with the ANCC Standards for Commercial Support for continuing education, Elite implemented mechanisms prior to the planning and implementation of the continuing education activity, to identify and resolve conflicts of interest for all individuals in a position to control content of the course activity.

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Introduction

The purpose of this course is to familiarize professionals with basic information concerning heroin addiction, which has reached epidemic proportions in the United States and around the globe. This includes facts about heroin and addiction, effects on the brain, progression of the disease, psychological and physical effects of short-term and chronic use, screening, treatment, and prevention. The course covers background information and statistics on the escalation of heroin addiction in the United States from 1850 to 2014 including causative factors. The review includes evidence-based treatment and prevention programs, as well as the current trends in progress to advance prevention and treatment of the disease.

Background

Addiction to opiates, in the form of opium, became a significant problem in the United States during the 1850s. Morphine was introduced as a replacement because it was thought to be weaker and non-addictive. Soon, morphine addiction became an even larger problem, and the solution was the introduction of heroin. Heroin, also thought to be non-addictive, was developed in 1898 by the Bayer pharmaceutical company in Germany as a treatment for tuberculosis and to address morphine addiction [1]. The addiction cycle continued because heroin turned out to be even more addictive than morphine. Continuing the cycle, methadone was introduced to address heroin addiction. Methadone was also developed in Germany in 1937 as an anesthesia for surgery and was exported to the United States in 1947 under the name "Dolophine" [1]. Methadone was later used to treat heroin addiction but brought with it a new set of problems if not managed properly. Heroin rapidly became a significant health problem in the United States, and over the next 150 years, the death rate due to heroin addiction has soared to 20 times higher than the drug-free population.

EBP alert! Research shows that opiates have increasing addictive properties as "new" drugs are introduced in attempts to decrease the problem of addiction. Nurses must be aware of the addictive properties of such drugs and work to not only educate the public but their healthcare colleagues as well[1].

What is heroin and how does addiction happen?

Heroin is part of the class of drugs called opioids. The name relates to the heroin molecule that binds to the opioid receptors in the body. The term "opiates" refers to natural, or semi-natural opioids, and heroin has the chemical name diacetylmorphine. Heroin is derived from morphine which occurs naturally in the latex sap of the seed pod of opium poppy plants, which grow in Mexico, Columbia, Turkey, Asia, Afghanistan, and parts of Europe [2].

Heroin and morphine bind to the opioid receptors in the brain and body but heroin binds more effectively, enhancing pain relief and euphoria in the addict. Heroin and morphine, along with codeine, hydrocodone, oxycodone, and oxymorphone are similar in structure because they all bind to the opioid receptor. Many substances can be used to cut heroin, including sugar, caffeine, flour, baby powder, starch, powdered milk, quinine, strychnine, other poisons and drugs which increase the likelihood of death. Strychnine (rat poison), is deadly and if ingested, the person will show behavioral effects similar to other drug-induced behaviors, but marked physical symptoms include muscle tightness, pain, spasms in the muscles and jaw, rigidity of the arms and legs, and arching of the neck and back [2].

Nursing consideration: Nurses MUST know the substances that are used to cut heroin and the effects these substances have on persons who use the drug [2].

Heroin may be adulterated with compounds that are added to cheaply enhance the euphoric effects. Examples of adulterants are acetaminophen, opiate painkillers, or anesthesia-like xylocaine. Users think that their numbness and "high" is coming from high quality heroin, when in fact, it is due to the combination of an adulterant. Sometimes adulterants produce the opposite effects to heroin, such as cocaine or other stimulants, and this combination can cause lethal effects on the central nervous system. Other adulterants, such as fentanyl, can be lethal because it is 200 times more potent than heroin. In March 2014, 22 people in Pennsylvania died due to overdose, in

which stamp-sized bags of heroin were mixed with prescription fentanyl [7]. Fentanyl is a synthetic opioid that binds to the opioid receptors in the brain, and when combined with heroin, produces a deadly high [3]. The danger is that users will take the same dose of heroin as usual, but the effects may be enough to stop their breathing or heart due to central nervous system depression. Other dangerous adulterants, such as levamisole accelerate the heart rate and destroy the immune system, which leads to life-threatening infections throughout the body [3].

EBP alert! Research shows that the "high" some users experience actually come from compounds added to heroin. Persons who use or are considering using heroin need to know the dangers associated with heroin and compounds used to cheaply enhance euphoric effects [3].

Composition and properties of three types of heroin

Not only do the addicts buying heroin on the street not know what substances are used to cut the drug, they also do not know the potency of the drug. The purity or the heroin can increase the chance of overdose and death. Street heroin is sold in different forms including:

- Black tar.
- Brown powder.
- White powder heroin.

The purest form is a white powder that may be rose or gray depending on which diluting substances are used to "cut" the heroin to increase the bulk, weight, and profit. Black tar heroin is identified as a ball or chunk of hard, sticky, black or brown material, which is the cheapest and easiest form to make because it is incompletely processed from opium [1]. The next level of processing uses lactose as a diluting agent, which produces brown powder heroin. Some darker colored heroin contains dirt, ground-up brown paper, and black shoe polish as fillers. Contaminants and bacteria in black tar heroin have been known to carry allergens, botulism spores, and necrotizing bacteria causing poisoning, tissue damage, toxic shock, and death [2]. Death may also occur because these contaminants may not dissolve, thus blocking arteries and veins, which cut off blood and oxygen supply causing a deadly aneurism, stroke, or heart attack. Decreased blood flow due to contaminants may also lead to damage, infection, and ultimately failure of vital organs, as well as convulsions and death.

Effects of heroin on the brain

Street heroin can range from highly potent to forms that are mostly fillers, adulterants, and garden-variety contaminants, but all forms of heroin are dangerous, especially when injected. During the process of manufacturing heroin, a number of chemicals may be left behind, including calcium oxide, ammonia, chloroform, hydrochloric acid, and acetic anhydride, which are all lethal ingredients [2]. White powder heroin is a salt form known as diacetylmorphine hydrochloride, and even though white heroin is the purest form, it will still contain lethal contaminants. The purer the heroin, the whiter and shiner it appears, while the more heavily cut heroin will appear duller in color [2].

When injected, heroin enters blood stream and the effects are felt within seconds, as opposed to snorting or smoking the drug, in which it may take the user ten to fifteen minutes to feel the effects. Immediately following the heroin injection, users often describe feeling a strong euphoric "rush" or a sensation of exhilaration, euphoria, extroversion, enhanced sensations, increased social and communication skills, heightened sexual performance, and a general feeling of well-being [1]. Less pleasant are the dry mouth; warm, flushed skin; heavy arms and legs; and confused mental state. After the euphoria, users experience feeling alternately drowsy and awake, often described as being "on the nod [2]." When the drug is smoked or snorted the initial powerful rush of euphoria may absent but the later effects will be the same. Users often start by smoking or snorting heroin but progress to injecting to get the enhanced rush. When heroin enters the body and crosses the blood-brain barrier, it is changed to morphine and binds to opioid receptors that are located throughout the brain and body [3]. Opioid receptors transmit nerve signals in the brain centers involved in signaling pain/pleasure perception, motivation, and reward. Heroin initially increases pleasurable feelings, decreases pain, and motivates the user to seek the "reward" of another heroin high. Opioid receptors located in the brain stem control nervous system function that signal critical processes such as blood pressure and respiration [8]. Heroin overdose often involves a suppression of breathing, due to the effects of heroin that cancel the signal for the body to breathe, often with deadly results.

Nursing consideration: It is essential that nurses know how heroin is distributed, its various forms, and its common street names such as H, horse, harry, boy, scag, shit, smak, stuff, white junk, and white stuff [2,3,37].

Tolerance and dependence

Over time with chronic heroin use, the structure and function of the brain changes. These changes cause individuals to develop tolerance to the drug, requiring increasingly larger amounts to reach a high. The next progressive stage is physical heroin dependence and individuals need to use the drug to avoid withdrawal symptoms known as drug sickness. Psychological dependence follows in which users believe they cannot live without heroin and drug-seeking behaviors motivate their every action.

Withdrawal

Severe withdrawal symptoms occur if individuals try to taper or stop their heroin use. In a few hours after the last heroin dose, the person will begin to feel withdrawal symptoms which may include vomiting, anxiety, insomnia, diarrhea, chills, muscle spasms, panic, hyper movements, and severe drug cravings [8]. It is very difficult and medically dangerous for the individual to go through withdrawal without medical assistance, and individuals will likely relapse to avoid the sickness of withdrawal.

Nursing consideration: Persons attempting to withdraw from heroin use should be provided with medical and nursing care delivered by professionals experienced in helping such patients [8,37].

Definitions

The following definitions are included in the National Institute for Drug Addiction (NIDA) publication on the Science of Drug Abuse and Addiction [3].

Addiction: A chronic, relapsing disease, characterized by compulsive drug seeking and use accompanied by neurochemical and molecular changes in the brain. (See below.)

Agonist: A chemical compound that mimics the action of a natural neurotransmitter and binds to the same receptor on nerve cells to produce a biological response.

Antagonist: A drug that binds to the same nerve cell receptor as the natural neurotransmitter but does not activate the receptor, instead blocking the effects of another drug.

Attention-deficit hyperactivity disorder (ADHD): A disorder that typically presents in early childhood, characterized by inattention, hyperactivity, and impulsivity.

Anxiety disorders: Varied disorders that involve excessive or inappropriate feelings of anxiety or worry. Examples are panic disorder, post-traumatic stress disorder (PTSD), social phobia, and others.

Buprenorphine: A partial opioid agonist for the treatment of opioid addiction that relieves drug cravings without producing the "high" or dangerous side effects of other opioids.

Bipolar disorder: A mood disorder characterized by alternating episodes of depression and mania or hypomania.

Co-morbidity: The occurrence of two disorders or illnesses in the same person, either at the same time (co-occurring co-morbid conditions) or with a time difference between the initial occurrence of one and the initial occurrence of the other (sequentially co-morbid conditions).

Conduct disorder: A repetitive and persistent pattern of behavior in children or adolescents in which the basic rights of others or major age-appropriate societal norms or rules are violated.

Craving: A powerful, often uncontrollable desire for drugs.

Depression: A disorder marked by sadness, inactivity, difficulty with thinking and concentration, significant increase or decrease in appetite and time spent sleeping, feelings of dejection and hopelessness, and, sometimes, suicidal thoughts or an attempt to commit suicide.

Detoxification: A process of allowing the body to rid itself of a drug while managing the symptoms of withdrawal; often the first step in a drug treatment program.

Dopamine: A brain chemical classified as a neurotransmitter, found in regions of the brain that regulate movement, emotion, motivation, and pleasure.

Dual diagnosis/mentally ill chemical abuser (MICA): Other terms used to describe the co-morbidity of a drug use disorder and another mental illness.

Major depressive disorder: A mood disorder having a clinical course of one or more serious depression episodes that last two or more weeks. Episodes are characterized by a loss of interest or pleasure in almost all activities; disturbances in appetite, sleep, or psychomotor functioning; a decrease in energy; difficulties in thinking or making decisions; loss of self-esteem or feelings of guilt; and suicidal thoughts or attempts.

Mania: A mood disorder characterized by abnormally and persistently elevated, expansive, or irritable mood; mental and physical hyperactivity; and/or disorganization of behavior.

Mental disorder: A mental condition marked primarily by sufficient disorganization of personality, mind, and emotions to seriously impair the normal psychological or behavioral functioning of the individual. Addiction is a mental disorder.

Methadone: A long-acting opioid agonist medication shown to be effective in treating heroin addiction.

Naloxone: An opioid receptor antagonist that rapidly binds to opioid receptors, blocking heroin from activating them. An appropriate dose of naloxone acts in less than two minutes and completely eliminates all signs of opioid intoxication to reverse an opioid overdose.

Naltrexone: An opioid antagonist medication that can only be used after a patient has completed detoxification. Naltrexone is not addictive or sedating and does not result in physical dependence; however, poor patient compliance limits effectiveness. A new, long-acting form of naltrexone called Vivitrol® is now available that is injected once per month, eliminating the need for daily dosing, improving patient compliance.

Neonatal abstinence syndrome (NAS): NAS occurs when heroin from the mother passes through the placenta into the baby's bloodstream during pregnancy, allowing the baby to become addicted along with the mother. NAS requires hospitalization and treatment with medication (often a morphine taper) to relieve symptoms until the baby adjusts to becoming opioid-free.

Neurotransmitter: A chemical produced by neurons to carry messages from one nerve cell to another.

Opioid: A natural or synthetic psychoactive chemical that binds to opioid receptors in the brain and body. Natural opioids include morphine and heroin (derived from the opium poppy) as well as opioids produced by the human body (e.g., endorphins); semi-synthetic or synthetic opioids include analgesics such as oxycodone, hydrocodone, and fentanyl.

Opioid use disorder: A problematic pattern of opioid drug use, leading to clinically significant impairment or distress that includes cognitive, behavioral, and physiological symptoms as defined by the new Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-V) criteria. Diagnosis of an opioid use disorder can be mild, moderate, or severe depending on the number of symptoms a person experiences. Tolerance or withdrawal symptoms that occur during medically supervised treatment are specifically excluded from an opioid use disorder diagnosis.

Partial agonist: A substance that binds to and activates the same nerve cell receptor as a natural neurotransmitter but produces a diminished biological response.

Physical dependence: An adaptive physiological state that occurs with regular drug use and results in a withdrawal syndrome when drug use stops.

Post-traumatic stress disorder (PTSD): A disorder that develops after exposure to a highly stressful event (e.g., wartime combat, physical violence, or natural disaster). Symptoms include sleeping difficulties, hyper-vigilance, avoiding reminders of the event, and re-experiencing the trauma through flashbacks or recurrent nightmares.

Psychosis: A mental disorder (e.g., schizophrenia) characterized by delusional or disordered thinking detached from reality; symptoms often include hallucinations.

Schizophrenia: A psychotic disorder characterized by symptoms that fall into two categories:

1. Positive symptoms, such as distortions in thoughts (delusions), perception (hallucinations), and language and thinking.
2. Negative symptoms, such as flattened emotional responses and decreased goal-directed behavior.

Self-medication: The use of a substance to lessen the negative effects of stress, anxiety, or other mental disorders (or side effects of their pharmacotherapy). Self-medication may lead to addiction and other drug- or alcohol-related problems.

Rush: A surge of euphoric pleasure that rapidly follows administration of a drug.

Tolerance: A condition in which higher doses of a drug are required to produce the same effect as during initial use; often leads to physical dependence.

Withdrawal: A variety of symptoms that occur after use of an addictive drug is reduced or stopped.

The definition of addiction

It is well documented that heroin is a highly addictive substance and addiction can occur with only one use. In order to fully understand the process of addiction, professionals must first understand heroin addiction, treatment, and prevention. The American Society for Addiction Medicine in their Public Policy Statement included the following short definition addiction [4]:

> **Addiction** is a primary, chronic disease of brain reward, motivation, memory and related circuitry. Dysfunction in these circuits leads to characteristic biological, psychological, social and spiritual manifestations. This is reflected in an individual pathologically pursuing reward and/or relief by substance use and other behaviors.
>
> Addiction is characterized by [4]:
> - Inability to consistently abstain.
> - Impairment in behavioral control.
> - Impairment in cognitive functioning.
> - Craving.
> - Diminished recognition of significant problems with one's behaviors and interpersonal relationships.
> - Dysfunctional emotional response.
> - Cycles of relapse and remission.
> - Progression that can result in disability or premature death.

As each stage of tolerance, dependence, and addiction progresses, the user requires increasing amounts of heroin to feel pleasure and combat the pain and sickness that now occurs as the body goes through withdrawal. This class of drugs is known by the name opioids or opiates. As defined by the DEA, heroin is a Schedule 1 substance under the Controlled Substances Act, which means it has high potential for abuse, no accepted medical use for treatment in the United States, and lacks accepted safety for use even under medical supervision [7].

Nursing consideration: Potential heroin users may think that using the drug only once or a few times poses no threat for addiction. Nurses must be prepared to explain that addiction can occur with only one use [4,7].

Today's heroin epidemic

Heroin was formerly viewed as a drug only found in back alleys of large urban areas. Today heroin addiction is found in every corner of the country and affects people of all ages in every socio-economic group in epidemic proportions. Heroin addiction still carries the stigma that it is a behavior or character flaw, though it affects a wide cross-section of America. No one is spared, from movie stars, such as Philip Seymour Hoffman who died from a heroin overdose after 20 years, to teenagers in suburbia and the homeless on inner-city streets.

The most alarming statistics show heroin addiction among youth is increasing in children as young as nine [6]. A number of factors contribute to this epidemic by making the drug inexpensive and readily available. As the use of heroin became more widespread in contemporary culture, it became more accepted among certain segments of society. Rock stars, actors, fashion models, photographers, and other celebrities in popular culture abuse heroin, and their deaths are almost commonplace today. In fact, the "heroin look" became popular in the fashion world in the mid 90s and was characterized by a thin, pale, emaciated appearance, blank expression, dark sunken eyes, dirty hair, and disheveled clothing. Popular music and advertising campaigns included references to heroin abuse and death had the effect of making the drug seem safe, exciting, glamorous, and mainstream in the eyes of impressionable youth. Young people who would never inject a drug can now find heroin that can be smoked or inhaled. This makes HEROIN seem easier, safer, and more desirable, thus increasing their willingness to try the drug [7]. Many youth have become addicted, comatose, or have died after only one dose of heroin. If individuals survive the first dose and continues to use heroin, they quickly develop a tolerance to the previous amount used and must have increasing amounts of the drug to replicate the high they experienced the first time. When the high from smoking and snorting is no longer enough, as tolerance develops, users may inject the drug to enhance the rush and get the most they can from the amount they have. As the amount used and the frequency of use escalates, so does the danger of overdose. Similarly, if drug use is curtailed through incarceration or time in rehabilitation, users may overdose and die when they return to using heroin at the previous level. Sadly, another factor in the increasing number of deaths from heroin abuse is that those around them are unable or unwilling to summon help when problems occur. Death usually occurs due to the drug's suppressive effects on the automatic breathing response of the victim, which can |be easily reversed through mechanical measures or medication to restore breathing [3].

Families, schools, health agencies, local, state and federal agencies across the country are now focused on addressing the epidemic rates of addiction and death caused by heroin.

Heroin today is very different from the drug initially developed and can be found in many multiple drug combinations. With continued use, these euphoric feelings become more difficult for users to reach, and over time, the body tries to adjust to the damage caused by the drug. Individuals become addicted to heroin quickly and their immune and body systems are damaged, leaving the individual weak, sick, malnourished, thin, and if untreated, they will die. One addict reported from the time she started using heroin she never stopped, and in a week she went from snorting it to injecting and was addicted in a month [5]. To support her habit, she sold everything she had, stole all she could from her family, ran her credit cards to the limit, sold her car, lost her job and house and became homeless. While living on the street she was raped, robbed, beaten, sick, and in constant fear for her life and desperate for her next heroin hit. She realized she would die and felt that living as a junkie was worse than death, so she sought help from a local agency and continues to struggle to end her addiction.

Research into treatment and prevention programs around the world produced promising results, but it has not kept pace with the rampant addiction and death caused by heroin. The frequency of overdose among youth has increased so drastically that some states now allow family members to administer antidotal drugs in cases of near death that were previously only used by medical personnel.

Why heroin, why today?

Heroin abuse and addiction has replaced other high-priced, commonly abused opiates and became the drug of choice in the United States, increasing rapidly since 2010 [6]. The general public was largely unaware of the epidemic until recent widespread media attention brought heroin addiction and death to the forefront and demands for solutions came from Vermont to California. The war against heroin must be fought on many fronts, and medical and mental health personnel must lead the charge.

Typically the drug is supplied by Mexican cartels, for just $10 a hit called a "stamp bag," and has gone up 600% in the last 10 years across the country [7]. As the United States cracks down on the sale of opiates such as Oxycodone by closing down pill mills throughout

the country, an 80 milligram Oxycontin dose now costs $100, which makes heroin cheaper and easier to obtain [7]. Manufacturers are also making opiates and other prescription drugs in formulas that are more difficult for users to snort or dissolve to inject. Another reason heroin use is thought to have doubled in five years relates to the high rate of addiction to prescription opiate painkillers now replaced by heroin, which is a natural opiate. Approximately 34,000 12 to 17-year-olds experiment with heroin each year due to lower costs of the drug and its availability [6].

Even though heroin abuse exists throughout the United States, large cities are reporting dramatic increases in the rates of heroin addiction and death. In large cities like Chicago, heroin can be found on the west side, often sold on the streets in plain sight. Addicts know where they can go to in any city, and with a phone call, they can receive the drug in a few minutes. Local police are aware of the problem but seem unable to get it under control. Addicts can be seen shooting up on the street, bleeding from their injuries as they attempt to find a vein. Special Agent Jack Riley, Regional Representative of the Drug Enforcement Agency (DEA) and Special Agent in charge of the DEA's Chicago Field Division, is familiar with the addicts on Lower Wacker Drive, a notorious drug-infested part of the community. Many addicts congregate under the overpass, injecting drugs or sleeping them off. Riley reports that the Mexican cartels supply 70% of the drugs used on Chicago's streets and that statistic is mirrored nationwide [7]. One of the addicts he encountered first took heroin as young as eleven years old and now lives on the street with two young children. Riley states," heroin addiction is probably at its all time high." "Heroin is the drug of choice for street gangs," says Riley, and he noted the increase started about three years ago, when Mexico's Sinaloa Cartel began importing heroin through Chicago. "We are seeing it in places like Indianapolis, Madison, and Milwaukee, places where traditionally we really did not see an uptick in heroin [7]." "The ability to smoke and snort today's pure form of heroin has made it accessible and acceptable to people who normally wouldn't come near it for fear of the needle," says Riley. "That's why it is spreading." Riley continues, "I've been doing this for 30 years in virtually every corner of this country and if anything can be likened to a weapon of mass destruction on a family, on a community, on society, it's heroin. I just don't understand why people across the board don't see its danger. Social services are overwhelmed, our healthcare services are overwhelmed, yet Mexican organized crime and street gangs make billions from it [7]."

Many youth come from suburban areas around Chicago and other large urban areas to buy the drug, and they may spend hundreds of dollars a day to feed their habit. The streets of Chicago are filled with stories of ruined lives caused by heroin addiction, including one from a college student who went from shooting up between classes to living homeless on the street, turning to prostitution to survive and stay high. In another tragic instance, a suburban high school girl tried it once, overdosed, and died. These stories are not unique to Chicago or large urban areas, and they are echoed through the farmlands of Wisconsin and Vermont.

Illinois is not alone in its fight against the heroin epidemic that has plagued that state. Over one weekend in February 2014, a drug raid in the New York City Bronx area resulted in seizure of $8 million worth of heroin. "Heroin is pummeling the northeast, leaving addiction, overdoses, and fear in its wake," said James Hunt, acting special agent in charge of the DEA's New York office [7]. DEA heroin investigations in suburban Rockland County have doubled, and agents note that use is increasing in all age groups and across all socio-economic levels. The Long Island Council on Alcoholism and Drug Dependence found an increase in families seeking assistance over the last five years from 100 to 850, and 80% of those were due to heroin addiction [7].

Dr. Wilson Compton, deputy director of the National Institute on Drug Abuse (NIDA), described heroin addiction as consuming the user. "The most common and important outcome of using heroin is that it can cause an addiction where people organize their lives around the drug," Dr. Compton said. "They use it to the exclusion of all other aspects of their lives. It just becomes about scoring the next hit [8]."

The following NIDA statistics describe a nationwide problem [6]:

- In Maryland, state health officials believe that heroin combined with other drugs is responsible for 30 or more deaths in the six months prior to March of 2014. They also note the number of deaths attributed to heroin rose 54% from 2011 to 2012 totaling 378 deaths.
- The U.S. Drug Enforcement Agency (DEA) notes that Baltimore has the highest per capita heroin addiction rate in the country. In a city of 645,000, the Baltimore Department of Health estimates there are 60,000 drug addicts, with as many as 48,000 of them hooked on heroin. A federal report released last month puts the number of heroin addicts alone at 60,000 [7].
- Virginia officials note 91 heroin deaths in the first nine months of 2012, up from 90 for all of 2011 and 70 for 2010.
- Vermont Governor Peter Shumlin spent his entire 34-minute State of the State address this year discussing a "full-blown heroin crisis." Heroin-related deaths in Vermont doubled in 2013 according to the governor, and there were twice as many federal indictments against heroin dealers than in the prior two years. Per capita, the heroin use in Vermont is second in the nation.
- Heroin overdose deaths in the Minneapolis/St. Paul metro area nearly tripled from 2010 to 2011, increasing from 16 to 46 deaths, and these new heroin users were considerably younger. In Minneapolis, for example, arrestees testing positive for heroin were much younger: 19.8% were less than 21 years of age, which is much younger than those testing positive for cocaine and methamphetamine, according to the Arrestee Drug Abuse Monitoring Report.
- In March 2014, Maryland, Vermont, New York, and Florida each reported an unprecedented number of deaths, according to the National Institute on Drug Abuse, which is still determining the numbers. NIDA reports these numbers could be the highest ever.
- In 2012, New Jersey saw more than 800 opioid overdoses, and half involved heroin.
- The DEA reports that drug seizures in New York comprise 20% of the total heroin confiscated each year. The amount seized by the DEA in New York City has increased 67 % over the past five years because heroin is now mass-produced in city apartments [7].
- The New York City Department of Health notes fatal heroin-related overdoses increased 84 % between 2010 and 2012, and 2012 showed a higher rate of heroin overdose deaths at 52% over deaths involving any other substance. The problem is particularly bad on Staten Island, where the death rate from overdoses is almost three times higher than the rest of New York City, according to the agency [7].
- Heroin is the most commonly found illicit substance in drug intoxication deaths in Philadelphia, PA. In 2011, 251 intoxication deaths involved heroin/morphine, a significant increase from 138 in 2010. Heroin is also the most commonly found substance in mortality cases where illicit drugs are present, with 32.4% in 2011.
- Dr. Karen Simone from the Northern New England Poison Center said the number of heroin-related calls doubled from 2007 to 2012.
- Only 20% of the estimated 810,000 heroin addicts seek or receive any form of treatment for their addiction.

EBP alert! Research shows that heroin addiction is a staggering problem throughout the United States and affects persons from all socioeconomic groups and in all geographic regions from large cities to small, rural communities. Healthcare professionals must be active in their communities' efforts to curtail this deadly epidemic [6,7,8].

Street names for heroin

It is important to know the street names of the drugs to help identify the user's drug of choice. There are many street names for heroin, including the following [7,37]:

- Big H, H.
- Black Pearl.
- Black Tar, Tar.
- Boy.
- Brown Crystal, Brown Sugar.
- Chiba, Chiva.
- Dope.
- Dragon (smoking heroin is called "Chasing the Dragon").
- H.
- Harry.
- Hell Dust.
- Horse.
- Junk.
- Mexican Mud.
- Negra.
- Nod.
- Nose Drops.
- Scag, Skag.
- Shit.
- Smack.
- Snowball.
- Stuff.
- Thunder.
- White, White Lady, China White.
- White Junk.
- White Stuff.

Heroin combinations

Heroin is often used in combination with other drugs that are known by specific names as follows:

Heroin and cocaine

- Speedball, Snowball.
- Belushi.
- Boy-Girl.
- H&C.
- Murder One, One and One.
- Smoking Gun.
- Whiz Bang.

Heroin and methamphetamine

- Meth Speedball.
- Heroin and Marijuana.
- Canade.
- Woolie.
- Woola.

Heroin, cocaine, methamphetamine, rohypnol. and alcohol

- The Five Way.

Heroin and fentanyl

- Theraflu.
- Bud Ice.

Heroin, cocaine, and tobacco

- Flamethrowers.

Heroin and cold medicine

- Cheese.
  Cheese heroin is a combination of Mexican black tar heroin and cold medicine obtained over the counter. It is a highly addictive substance, which is very inexpensive, only a few dollars, so it is often targeted at young people. Children as young as nine years old have been identified in emergency rooms with addiction, overdose, and withdrawal to this form of heroin which suppresses the central nervous system causing breathing and heartbeat to slow or stop. Since 2004, 40 deaths in North Texas are attributed to cheese heroin [7].

Nursing consideration: It is imperative that nurses be aware of just how young some children are when they begin heroin use and become addicted. Nurses may be the first to triage patients with signs and symptoms of heroin-related emergencies [7].

Facts and figures of increased heroin addiction, overdose and death

Statistics from the United States Government Substance Abuse and Mental Health Services Administration (SAMHSA) noted the following statistics [9]:

- Nearly a half million Americans are addicted to heroin, and this number is thought to be the highest in history.
- In 2011, 4.2 million Americans aged 12 or older (or 1.6 percent) had used heroin at least once in their lives. It is estimated that about 23% of individuals who use heroin become dependent.
- NSDUH reports the number of new heroin users increased from 142,000 in 2010 to 178,000 in 2011. Both numbers are a sizeable increase from the average annual estimates of 2002 to 2008 (ranging from 91,000 to 118,000).
- In 2012, there were 156,000 persons aged 12 or older who had used heroin for the first time within the past 12 months.
- A SAMHSA study from August of 2012 found that persons aged 12 to 49 who abused prescription pain killers were 19 times more likely to try heroin than those who abused pain killers in the previous year.
- In 2011, the average age at first use among heroin abusers aged 12 to 49 was 22.1 years and in 2010 it was 21.4 years, significantly lower than the 2009 estimate of 25.5 years.
- The 2012 average age at first use among recent heroin initiates aged 12 to 49 was 23.0 years, which was similar to the 2011 estimate (22.1 years).
- The annual Monitoring the Future survey of teens reported in 2012 that 20% of high school seniors felt that heroin was "easily available."
- From 2007 to 2012, the number of Americans using heroin nearly doubled, from 373,000 to 669,000, according to the federal government's most recent National Survey on Drug Use and Health, released fall 2013.
- One out of every four people who try heroin become addicted.
- The number of people meeting Diagnostic and Statistical Manual of Mental Disorders, 4th edition (DSM-IV) criteria for dependence or abuse of heroin doubled from 214,000 in 2002 to 467,000 in 2012 [10].
- When teens were surveyed to find out why they started using drugs in the first place, 55% replied that it was due to pressure from their friends. They wanted to be cool and popular.
- Heroin accounts for 18% of the admissions for drug and alcohol treatment in the United States.
- An estimated 9.2 million-use heroin worldwide.

The U.S. Drug Enforcement Agency (DEA) 2013 National Drug Threat Assessment Summary found that heroin smuggling is increasing across the United States border from Mexico and Mexican

cartels, called Transnational Criminal Organizations (TCOs) by the DEA [7]. The summary noted, "The availability of heroin continued to increase in 2012, likely due to high levels of heroin production in Mexico and Mexican traffickers expanding into white powder heroin markets in the eastern and Midwest United States." Previous to 2012, heroin from Mexico was predominantly west of the Mississippi River with heroin from Asia coming through the major airports east of the Mississippi River. Some heroin from South America is smuggled through Mexico to the United States. The DEA report noted a steady decrease in cocaine trafficking from Mexico to the U.S. during this time period and theorizes that the increase in heroin trafficking may be a push by the Mexican TCOs to make up for the loss of cocaine profits. The DEA 2013 National Drug Threat Assessment Report includes the following [7]:

- The availability of white powder heroin continued to increase in 2012 due to an increase in Mexican heroin production and trafficking which expanded into the Eastern and Midwest markets.
- There was an increased level of smuggling of both Mexican-produced heroin and South-American-produced heroin, which was smuggled through Mexico into the United States in 2012.
- According to National Seizure System (NSS) data from January 15, 2013, the amount of heroin seized each year at the Southwest Border increased 232% from 2008 (558.8 kilograms) to 2012 (1,855 kilograms).
- The increase in Southwest Border seizures appears to correspond with increasing levels of production of Mexican heroin and the expansion of Mexican heroin traffickers into new US markets.
- Heroin-related overdoses and deaths are increasing in certain areas, possibly due to high-purity heroin on the streets and increasing numbers of heroin abusers at a younger age because it can be smoked or inhaled. Inexperienced abusers, such as teens, college students, and those who would normally not inject a substance start by smoking or inhaling. Law enforcement officials reported an increase of high-purity heroin available at the street level.
- People are switching from abusing prescription drugs to abusing heroin. Law enforcement and treatment officials throughout the country report that many heroin abusers began using the drug after having first abused prescription opioids. These abusers turned to heroin because it was cheaper and/or more easily obtained than prescription drugs and because heroin provides a high similar to that of prescription opioids.
- According to treatment providers, many opioid addicts will use whichever drug is cheaper and/or available to them at the time. Several treatment providers report the majority of opioid addicts will eventually end up abusing heroin and will not switch back to another drug, because heroin is highly addictive, relatively inexpensive, and more readily available. Those abusers who have recently switched to heroin are at higher risk for accidental overdose.
- Unlike prescription drugs, heroin purity and dosage amounts vary, and heroin is often cut with other substances, all of which could cause inexperienced abusers to accidentally overdose.

ETIOLOGY OF HEROIN ADDICTION

Physical effects on the brain

The thorough study of the effects of heroin on the brain would require a separate course, but it is important to include an outline of the effects of heroin on the brain that lead to addiction. Whether heroin is smoked, snorted, or injected, it is rapidly absorbed and crosses the blood brain barrier. Addiction occurs due to specific effects on the brain caused by the drug that interfere with normal brain function in the following ways [4]:

- Addiction affects the transmission of neurons within the parts of the brain that control motivation and reward. These parts include the basal forebrain amygdala and the anterior cingulate cortex. This part of the brain affects the individual's ability to conduct routine behaviors related to healthcare, motivation, and normal reward-seeking behavior.
- Addiction interferes with cortical and hippocampal interactions that affect reward; memory of reward; and control of physical, mental, and behavioral response to stimuli that drives individuals' drug cravings and drug-related behaviors. These behaviors may include lack of judgment and impulse control, inability to delay gratification, poor decision-making and repeated inability to react appropriately despite patterns of repeated negative consequences.
- Addictive behaviors are exacerbated when younger individuals, whose brain systems have not fully matured, use heroin.
- Addiction causes changes in brain chemistry and function, which results in physical changes to the nerve cells that transmit messages in the brain. Damage to neuron transmission in the nerve cells may disrupt signals and cues that communicate a variety of messages affecting learning, perception, memory, impulse control, motivation, pleasure/pain sensations, and more critically, central nervous system function that controls breathing responses and heart rate.

Factors influencing addiction

Psychological factors

Individuals may have psychological disorders or mental illnesses that interfere with their ability to function normally. They may use heroin and other substances to deal with their psychological issues, which may be the only coping mechanism they know. Their self-medication to escape their negative feelings turns to addiction, which may mask an undiagnosed mental disorder. As the heroin addiction progresses, the underlying issues will be complicated by increasing psychological and physical changes cause by the damaging effects of the drug.

Genetic factors

Though genetics factors do not cause an addiction to heroin, they can indicate addictive behavior and were found to be significant in about 50% of addictions [8]. One or more immediate family members with an addictive disorder may be an indicator that the individual addicted to heroin has a genetic predisposition. Social and environmental influences may determine the impact of genetic factors on addiction. The individual's sense of security, stability, personality, motivation, emotional and mental well-being are influenced by their role models, early experiences, culture, health and behavior patterns as they mature. These factors can influence whether genetic indicators of addiction come into play.

EBP alert! Research indicates that although genetic factors do not cause heroin addiction one or more immediate family memers with an addictive disorder may be an indicator that the person addicted to heroin has a genetic predisposition to such behavior. It is important that both personal and family history of addiction be incorporated into patient assessment [8].

Environmental factors

Environmental factors include a complex set of interacting variables and may be difficult to measure initially. Issues related to the individual's upbringing, family dynamics, belief systems, educational level, peer group influences, cultural or religious beliefs, stress, trauma, community values, and group affiliations may influence an individual's decision to try heroin.

Screening

The two main ways to identify the presence of heroin is in either the blood or urine of a user. The analytical methods used are **gas chromatography-mass spectrometry** (GC-MS) and **liquid chromatography-mass spectrometry** (LC-MS) [11]. Both methods do the same thing, which is to separate a mixture of compounds present in the sample prepared from the urine or blood, followed by the detection of those compounds. The separation step allows for detection of any substance that has been used in combination with heroin. The urine is screened for 6-acetylmorphine (6-AM) by immunoassay and confirming the results by GC-MS analysis, which can take four to five days to complete. Heroin can be detected for one to two days after use. Heroin metabolizes into 6-AM, and this differentiates the use of heroin from other drugs such as codeine, morphine, and other prescription opiate drugs. Since October 1, 2010, the **Substance Abuse and Mental Health Services Administration (SAMHSA)** established mandatory guidelines that require 6-AM screening as part of the required screening for all federally mandated drug testing in the workplace [12]. The 6-AM screening can be done in house and one version can deliver results in 11 minutes with 98% accuracy when compared with GC-MS. The Supreme Court has approved this test as defensible technology [11].

In addition to the tests above, medical history, criminal records, and physical health/appearance typically identify chronic users. Chronic heroin abusers commonly have a lengthy arrest record for drug possession or theft; they may have overdosed one or more times and were brought to the hospital; and they will typically have "track marks" over the veins in their arms, which are small areas of contusions from injecting the drugs; along with other indicators of chronic use. Track marks may be found on any part of the body if larger veins are destroyed by repeated injection. A very lengthy, expensive way to identify chronic users would be hair analysis for the accumulation of small amounts of the drug. Extracting drugs from hair is extremely expensive and time consuming. The low amounts of the drugs that are present in the hair require highly sensitive instrumentation, and those techniques would typically not be done by a lab [13].

Signs and symptoms of heroin addiction

No two individuals who are addicted to heroin will present with the same signs and symptoms, which will vary due to the method of use, level of tolerance, dependency, addiction, frequency of use, form of the drug, and secondary illness and disease. HIV/AIDS is often the consequence of injecting heroin [8].

Common signs and symptoms of heroin use can be divided into the following categories [8]:

Psychological indicators

- Hallucinations, delusions.
- Paranoia.
- Depression.
- Disorientation.
- Sudden changes in behavior.
- Slurred, forced, or incoherent speech.
- Negative school or work performance.
- Distractibility.
- Frequent comments indicating low self-esteem, negativity.
- Insomnia or excessive sleep.
- Euphoria.
- Blaming others for their issues.
- Withdrawal from friends and family, association with new, unknown friends.
- Constant runny nose or bloody nose.
- Avoiding eye contact.
- Mood swings.
- Anxiety.
- Apathy, lack of motivation in interests and regular activities.
- Fatigue/exhaustion.
- Hostility toward others, agitation, and irritability.
- Lying about drug use.
- Stealing.
- Avoiding loved ones and others.

Physical indicators

- Cuts, contusions, bruises, and needle marks on the body, not just arms.
- Weight loss.
- Scabs or bruises as the result of picking at the skin.
- Decreased attention to personal hygiene and appearance.
- Shortness of breath.
- Frequent respiratory infections.
- Dry mouth, loss of teeth.
- Skin infections and abscesses.
- Warm, flushed skin.
- Drooping heavy extremities.
- Constricted pupils.
- Hyperactivity or hyper alertness followed by lethargy.
- Extreme itching.
- Loss of menstruation.
- Miscarriage.

Other indicators [7]

- Possession of burned spoons.
- Needles or syringes.
- Items to use as tourniquet such as a shoelaces or rubber bands.
- Evidence of drug residue in baggies or foil.
- Foil, straws or gum wrappers with burn marks.
- Glass pipes or water pipes.
- Wearing long pants and shirts, even in warm weather.
- Repeated borrowing of money, missing valuable items.
- Criminal activity.

Short term effects of heroin

Every addict will present with different side effects due to the type, amount, and frequency of heroin use, other substances used, co-existing physical and mental disorders ,and pre-existing conditions. In addition to the initial "rush" or feeling of euphoria, short-term side effects of heroin use include [3]:

- Dry mouth.
- Flushed skin.
- Poisoning due to contaminants or adulterants.
- Vomiting.
- Itching externally and feeling itchy sensation internally, picking at skin.

- Nausea.
- Breathing that is slow, shallow, or irregular.
- Slurred speech.
- "Nodding out," "crashing," lethargy, sleep/alert cycles.
- Confused cognition.
- Decreased sensations of pain, physical and emotional "numbness."
- Constipation.
- Stomach cramps.
- Overdose/death.

Long-term effects of heroin

Chronic abuse of heroin leads to severe medical complications, many irreversible, and may lead to death [3]:

- Heart problems such as infection of heart lining, infection of the heart's surface called endocarditis, valve prolapse, blockage, myocardial infarction and arrhythmia, congestive heart failure.
- Infectious diseases transmitted through needles (HIV/AIDS and Hepatitis B and C).
- Chronic pneumonia, pulmonary diseases.
- Collapsed veins, vascular blockages, clots, resulting tissue death due to lack of blood supply.
- Bacterial infections.
- Liver and kidney disease.
- Immune disorders.
- Pulmonary edema.
- Coma.
- Paralysis.
- Cognitive disorder.
- Seizures.
- Miscarriage.
- Birth defects.*
- Diseases and infections from sharing needles.
- Overdose/death.

*In addition to miscarriage, babies born to mothers using heroin suffer problems associated with malnutrition, drug toxicity, infection. These problems include low birth weight, developmental delays, prematurity, birth defects, failure to thrive, drug dependence, or addiction known as neonatal abstinence syndrome (NAS). NAS is drug withdrawal that the baby must endure under strict medical care in the hospital. Studies have shown that pregnant mothers with heroin addiction can be treated in the hospital with the drug buprenorphine, which treats the mother and baby and reduces their withdrawal symptoms. Heroin addicted mothers will often lose custody of their baby and many are charged with child neglect or abuse. Addicted mothers often abandon their babies after birth.

Nursing consideration: Nurses must be able to recognize signs and symptoms of heroin addiction as well as to be able to differentiate and teach about the short and long-term effects of heroin.

Heroin withdrawal

Heroin withdrawal symptoms can occur within an hour after the last drug dose, based on the level of abuse. Withdrawal symptoms may include [4]:

- Severe heroin cravings.
- Sweating.
- Severe muscle and bone aches.
- Nausea and vomiting.
- Heavy extremities.
- Muscle cramping.
- Crying.
- Insomnia.
- Edema.
- Chills.
- Runny nose.
- Diarrhea.
- Fever.
- Death.

Nursing consideration: Addicts facing withdrawal must receive medical care in a clinic, rehabilitation facility, or hospital from providers who are specifically trained to treat patients for heroin withdrawal. They should never attempt withdrawal alone [4].

Signs and symptoms of multiple substance abuse

Among persons with heroin addiction, multiple substance addiction is common. Cocaine and alcohol are the substances most often abused with heroin [14]. A trained professional should assess for abuse of other substances and determine the effects of the overlapping substances. The American Psychiatric Association (APA) suggests the following four approaches for assessing heroin dependent people for other substances:

- Screening instruments: MAST, DAST, CAGE-AID, AUDIT.
- Clinical assessments using interview with the patient, family of significant others.
- Structured interviews: DSM-V SCID-1, Structured Clinical Interview for DSM-V Axis 1 Disorders.
- Laboratory tests: Urine samples done onsite for immediate results that can be addressed with the patient.

Heroin addiction and co-occurring disorders

As with other substance abuse addictions, individuals with heroin addiction often have co-occurring mental disorders. Since psychological and emotional causative factors for heroin addiction exist, it may be critical to determine the primary and secondary disorder in planning a long-term treatment plan. Of course, chronic addiction to heroin and the physical ravages of the disease must be addressed immediately, which will require medical care and monitoring. Patients must be screened for suicide ideation and self-harm tendencies, which are often part of the heroin addict's coping or escape mechanism. The following co-occurring mental disorders are commonly seen among heroin addicts on the street and those in rehabilitation programs [4]:

- Depressive and/or anxiety disorder.
- Addiction to other drugs and/or alcohol.
- Personality disorder.
- Cutting, self-harm behaviors.
- Bipolar disorder.
- Eating disorders.
- Post traumatic stress disorder.
- Schizophrenia.
- Conduct disorder.
- Psychosis.

Treating heroin overdose

A new and controversial medication to reverse the effects of heroin overdose has been approved and released for sale by prescription by the Federal Food and Drug Administration (FDA) in April 2014 [15]. Naxalone comes in the form of a hand-held device, injection, or nasal spray, and is being hailed by government and health care leaders as a ground-breaking tool to address the epidemic of heroin overdoses across the nation. The states of New York and New Jersey are already mandating its use by first responders, and after training, the drug was saving lives in the first weeks of use.

The drug, also known as Narcan, is marketed under the name of Evzio [15]. A single dose of the drug, which acts as an antidote to heroin, has been successful in bringing back overdose victims from death due to respiratory failure and lack of blood pressure. Naloxone works by reversing the suppressive effects of heroin on the opioid receptors that signal respiration to bring back consciousness and normal breathing. The drug is not new and has been used by emergency medical personnel on the street and in the hospital for over 40 years in injectable form. The release of the drug is controversial, because some, believe it will give addicts a false sense of confidence that they can continue to use much heroin as they want and the drug will save them from death from overdose. Many also object on the grounds that it will drive up insurance costs. Proponents of the drug do not believe addicts will purposely take enough drugs to overdose just because the drug is available and feel the FDA has addressed a life threatening public health crisis that has reached epidemic proportions.

Evzio works like an Epipen, which counteracts anaphylactic shock, and can go into the muscle or the skin. New Jersey has approved the use of naloxone for law enforcement officers. "We think greater availability of immediate treatments like naloxone are important as New Jersey confronts this crisis in heroin and opioid overdoses," said Aline Holmes, a registered nurse and senior vice president of clinical affairs at the New Jersey Hospital Association [16]. In May 2013, New Jersey signed the Overdose Protection Act, which gives legal immunity to anyone using the drug to save a life.

The state of New York has also approved the use of the drug by all law enforcement agents, and 17 other states have followed suit, with some allowing prescriptions to family and friends of the addict. It comes in a nasal spray or injectable form and can be used by anyone without advanced training in an emergency situation. It is suggested for use after calling 911 and checking for breathing, though additional training is advisable.

One drawback of the drug is that if the heroin is adulterated with fentanyl, patients will need a larger dose over a longer period of time to combat longer-acting drug combinations, which may cause them to sink back into respiratory distress. Patients will also require emergency medical care and/or hospitalization despite receiving the drug and being revived.

The CDC reports local and state health departments fund the drug and provide it to hospitals and community-based clinics free of charge [22]. San Francisco's Drug Overdose Prevention and Education Project and Massachusetts' Overdose Education and Naloxone Distribution Program are examples of two community-based programs using the drug [15].

Nursing consideration: Nurses must be familiar with the use of Narcan and the pros and cons of using it [15].

MOVING FROM WITHDRAWAL TO TREATMENT

The American Society for Addiction Medicine (ASAM) provides a wealth of information about the changes faced by the person who is withdrawing or has withdrawn from addiction. Addiction by definition includes periods of withdrawal and relapse, and the journey will be different for each individual. It is important to remember that unlike the feelings of early heroin use, as time goes by, the euphoria, pleasure or "reward" felt when the individual gets high does not continue to escalate with each subsequent use. As outlined previously, users need more heroin to achieve the same high and actually builds tolerance to the "high." However, they continue to experience deeper and more painful "lows" as their addiction progresses. As explained by ASAM [4]:

> Persons with addiction compulsively use even though it may not make them feel good and in some cases long after the pursuit of "rewards" is not resulting in pleasurable feelings. Although people from any culture may choose to "get high" from one or another activity, it is important to appreciate that addiction is not solely a function of choice. Simply put, addiction is not a desired condition.

Addiction is classified as a chronic brain disorder or disease and not a behavioral one, which is important to remember when working with a person in recovery. As in any chronic disease there will be periods of relapse which will vary by frequency, duration or amount of use but ASAM points out that," the return to drug use or pathological pursuit of reward is not inevitable [4]." They provide the following information about the recovery process:

- Clinical interventions can help to alter the course of addiction.
- Close monitoring of the behaviors of the individual and contingency management, sometimes including behavioral consequences for relapse behaviors, can contribute to positive clinical outcomes.
- Engagement in health promotion activities that encourage personal responsibility and accountability, connection with others, and personal growth also contribute to recovery.
- The patient must be monitored and managed over time to decrease the frequency and intensity of relapses, to sustain remission and optimize functioning, and to minimize episodes of relapse and their impact.
- Medication management can improve treatment outcomes. Integration of psychosocial rehabilitation and ongoing care with evidence-based pharmacological therapy provides the best results.
- Recovery is best achieved through a combination of self-management, mutual support, and professional care provided by trained and certified professionals.

Nursing consideration: Nurses need to educate not only patients and families, but their healthcare colleagues as well, that heroin addiction is a chronic brain disorder or disease and not a behavioral problem. This is important to remember when providing treatment and counseling [4,37].

Treatment and recovery

The ultimate goal of treatment is recovery, because the person addicted to heroin has so many levels of life that have been damaged or destroyed. Some individuals have co-occurring mental disorders that may have preceded the addiction or occurred during drug use. Knowing that the individual is ready to enter treatment to move toward recovery, and developing a treatment plan to support them in reaching their goal are the first steps in the process. The recovering patients may face unresolved issues that initially led to their drug use. Therefore, patients may need to make total life changes with the assistance from their treatment team. According to the Substance Abuse and Mental

Health Services Administration (SAMHSA), "Recovery from Mental Disorders and Substance Use Disorders" is a process of change through which individuals improve their health and wellness, live a self-directed life, and strive to reach their full potential [17]. SAMHSA has delineated four major dimensions that support a life in recovery:

- **Health:** Overcoming or managing one's disease(s) as well as living in a physically and emotionally healthy way.
- **Home:** A stable and safe place to live.
- **Purpose:** Meaningful daily activities, such as a job, school, volunteerism, family caretaking, or creative endeavors, and the independence, income, and resources to participate in society.
- **Community:** Relationships and social networks that provide support, friendship, love, and hope.

Heroin addiction is a chronic disease that cannot be treated easily or quickly since it has been prevalent since the late 1880s . Scientific research and treatment trials conducted over decades have yielded the following guiding principals for treatment [18]:

- Addiction is a complex but treatable disease that affects brain function and behavior.
- No single treatment works for everyone.
- Treatment needs to be readily available.
- Effective treatment attends to multiple needs of patients, not just their drug abuse.
- Remaining in treatment for an adequate period of time is critical, sometimes continuing for years.
- Counseling, individual and/or group, along with behavioral therapies are the most commonly used forms of drug abuse treatment.
- Medications are an important element of treatment for many patients, especially when combined with counseling and other behavioral therapies.
- Patients' treatment and services plan must be assessed continually and modified as necessary to ensure that it meets their changing needs.
- Many drug-addicted individuals also have other mental disorders, which must be addressed.
- Medically assisted detoxification is only the first stage of addiction treatment and by itself does little to change long-term drug abuse.
- Treatment does not need to be voluntary to be effective.
- Drug use during treatment must be monitored continuously, as lapses during treatment do occur.
- Treatment programs should assess patients for the presence of HIV/AIDS, hepatitis B and C, tuberculosis, and other infectious diseases, as well as provide targeted risk-reduction counseling to help patients modify or change behaviors that place them at risk for contracting or spreading infectious diseases.

After the patient is stabilized and makes the decision to enter treatment, a long-term treatment plan is developed. There is no single method that works for all individuals, but practitioners need to review a variety of programs available in the vicinity of the patient and match the program to the patient's needs. This course outlines some current programs and provides resources for free training materials and program guides.

Nursing consideration: Nurses must remember that treatment is a long-term process and that support and counseling may very well be needed for the patient's lifetime.

Therapeutic communities for residential treatment: For individuals with severe drug and addiction problems, therapeutic communities (TC) are the next step after hospital or medical management of their withdrawal symptoms [18]. These programs provide a highly structured, strictly monitored program to meet the medical and psychological needs of patients. Patients may live in the facility for up to a year and receive treatment for their addiction as well as other therapy and services needed for recovery. They receive support and treatment to address behavior issues, including criminal behavior, social, communication and family issues. Specialized centers can accommodate pregnant women, children, and adolescents. The goal of the therapeutic community is to provide the treatment and skills necessary for individuals to return to the community as healthy, drug-free individuals who can successfully when re-enter society and live productive lives. After-care will continue through outpatient or support services in the community following successful release from residential care.

Pharmacological treatment

Heroin addiction changes the structure and function of specific parts of the brain, so for medication to be effective, it must work despite changes that occur in the short and long term. In the beginning stages of withdrawal, medication must curb the strong cravings for heroin and lessen the painful side effects of withdrawal to avoid a relapse. In later stages of recovery, individuals need medication to help them think clearly, gain control, make decisions, and focus on goals and skills for a healthy new life.

Pharmacological treatment of heroin addiction has proven to be successful by increasing time in treatment, decreasing rates of relapse, and reducing rates of infectious disease and illegal drug-seeking behaviors. Medications such as buprenorphine, methadone, and naltrexone can help people to escape the grip of heroin, because it reduces their cravings by blocking the euphoric effect. The medications used in this treatment work in the same manner as heroin by impacting the opioid receptors, but they do not cause the dangerous side effects or lead to addiction. The three types of medications interact with the opioid receptors in different ways as follows [19]:

1. **Agonist medication** such as Methadone, also known as Dolophine and Methadose, activates receptors by gradually reaching the brain slowly, preventing the euphoric feeling, and preventing withdrawal symptoms. These drugs are appropriate for use by certified physicians in outpatient treatment programs and are given to the patient orally each day. An estimated 200,000 people in correctional facilities each year are addicted to heroin. Therapy such as methadone maintenance treatment has been effective in prison populations and shown to increase time in treatment and diminish criminal activity if continued in the community upon release, because it eliminates the need to commit crime to buy heroin.
2. **Partial agonists,** such as Buprenorphine, also called Subutex, produce a small response in the brain, which relieves cravings with no euphoria or side effects when taken orally. The FDA approved buprenorphine in 2002 for prescription by certified physicians in their office, which extends the availability of this drug to a wider population of patients and makes it more accessible. Some critics theorize that the ease of obtaining this drug will encourage more individuals to enter and stay in pharmacologic treatment. In 2013, the FDA approved two generic forms of Suboxone, which is buprenorphine that contains naloxone, in 2013 [15]. This drug prevents attempts to get high by causing severe withdrawal symptoms if injected but no negative effects when taken orally as directed. Buprenorphine can be used effectively with prisoners and could be implemented through collaboration with health professionals and the juvenile justice system.

   Many governmental agencies are working together to address the heroin addiction epidemic. An example of one partnership, known as the Blending Initiative [20], combines the efforts of

SAMHSA and NIDA to fund and conduct research and clinical trials on a variety of therapies that can effectively treat heroin addiction. Currently, they are developing and disseminating protocols to educate multidisciplinary treatment professionals about buprenorphine. Information can be found at *(http://www.ctndisseminationlibrary.org/ display/85.htm)*. This information contains the following goals:

Blending teams of NIDA researchers, treatment practitioners, and trainers have completed two buprenorphine training packets [21]:

- To increase overall awareness of buprenorphine therapy.
- To instruct physicians and treatment practitioners in implementing a 13-day detoxification intervention for opiate-dependent patients.
- To change the mindset of many community treatment providers previously unwilling to consider the use of medications to treat drug addiction.
- To expand the programs now regularly use buprenorphine to assist in opiate detoxification and treatment maintenance.
- To work with SAMHSA's Addiction Technology Transfer Centers (ATTC), State Directors, and other stakeholders, to spread the word about buprenorphine to more proactively address the urgent needs of drug addiction.
- To continue clinical tests on the safety and efficacy of buprenorphine in other affected populations, including pregnant women, adolescents, and patients addicted to opiate analgesics.
- To increase the use of this and other addiction medications in different settings and locales, including in the U.S. criminal justice system and in countries where injection drug use is still a primary mode of HIV transmission [21]. Additional information on buprenorphine can be found at *http://www.ctndisseminationlibrary.org/display/85.htm.*

3. **Antagonists,** such as Naltrexone, also known as Depade and Revia, block opioid receptors that send pleasure signals, thus blocking the "high." They do not cause dependence, addiction, or sedation. Patients must take this drug daily, but the FDA recently approved a long-acting form called Vivitrol that can be administered once a month, which may increase compliance. Naltrexone does not suppress all drug craving, and many patients cannot remain abstinent and relapse in six months. According to Dr. George Woody, a professor of psychiatry at the University of Pennsylvania [22], "Drug abusers are notoriously ambivalent and just because they decide to quit using heroin one week doesn't mean they'll be motivated to quit a week later." Extended-release forms like Vivitrol can provide long-lasting protection over time, which can help patients in their resolve to stay drug-free. Patients taking a daily oral dose of naltrexone must make a daily decision to remain drug-free. Patients using Vivitrol will receive a sustained dose each month, so they have more time in treatment and recovery between doses and do not face a daily decision to use heroin when the naltrexone tapers every 24 hours. Clinical trials are being conducted on patients in Russia with extended release implants that last up to two months and can be refilled without having to be removed [22]. Early trials of these implants are proving to be three times more effective in some patients than the daily dose pill in preventing relapse. Dr. Woody continues, "Methadone and buprenorphine have helped hundreds of thousands of people around the world who are drug dependent, and they have helped reduce the spread of HIV. The new injectable and implantable naltrexone formulations are really the new kids on the block, but they're offering us more options in an area where we really need a lot of help."

Nursing consideration: Nurses must explain the use of all drugs used in the treatment process, their actions, appropriate administration, side effects, and what to do if side effects occur.

Urine testing for compliance

Treatment programs that include medication are only effective if they include strict monitoring to make sure patients comply with the program and have not relapsed. This is done through urine testing, patient interview, observation, and input from family and other significant parties in the patient's life. Drug treatment programs that are administered through outpatient or doctor's office settings may have limited contact with the patient and must rely on tightly controlled drug monitoring protocols. These testing protocols must contain the following components [12]:

Location: A decision must be made about whether testing will be on site or off site.

There are advantages to each setting, depending on the person's needs. On-site testing will give immediate, affirming results if positive. The sample will require less handling, and the patient may feel this testing is more confidential because it is kept on site. If the results are negative, the therapist can immediately address the issue with the person. In both cases, the samples may have to be confirmed off site depending on the lab, and additional tests may be required if the result is negative. Off-site testing allows for more comprehensive testing; a higher level of expertise among personnel, which may yield higher rates of accuracy; and admissibility in court.

Type of test: Different types of tests provide different levels of information. Immunoassay can test for heroin and other natural opioids, and it provides almost immediate results. Methadone is a synthetic opioid but specific immunoassay tests have been developed for this drug. Immunoassay tests will not detect the presence of other synthetic opioids, like fentanyl and buprenorphine, so it is not as comprehensive as other tests. Laboratory tests such, as GS-MS, will detect all types of opioids but take four to five days [11].

Current research in pharmacology – New medications

NIDA is committed to new treatments for heroin addiction, which include improved medication and other forms of therapy. When combined, they have proven to raise recovery rates. The NIDA is working to improve treatment for heroin addiction that they can implement to large numbers of patients across the country. A new drug called Probuphine is producing positive results in clinical trials. It is a long-acting form of buprenorphine that is administered as an implant under the skin to provide medication over a six-month period [23]. This drug is more convenient for the patient and eliminates daily dosing which increases adherence to treatment goals.

The heroin vaccine

Another exciting NIDA clinical trial currently underway is vaccine research that can effectively block addiction to heroin and other drugs. Dr. Ronald Crystal and Dr. George Koob and Dr. Kim Janda are among the many researchers around the world conducting research and clinical trials to develop a vaccine to address heroin addiction [24]. The vaccine acts to combat the effects of heroin as it enters the

bloodstream before it reaches the brain and the opioid receptors so the euphoric or reward sensation is not released. The medication would be part of a treatment plan that would increase the chance of recovery by lowering the risk of relapse. The vaccine works by interfering with the immune system's ability to conduct the action of heroin on the brain. The antibodies in the vaccine identify and attach to molecules of heroin and the together they are too big to cross the blood brain barrier to enter the brain. When the drug does not enter the brain, it cannot reach the opioid receptor and signal the pleasurable sensation that drivers the need for the drug.

Two parts must be present in the vaccine to accomplish this action [24]. The first is a protein that causes the immune system to produce sufficient antibodies to overtake the total molecules in the amount of heroin taken so they do not reach the brain. The second part of the drug, hapten, has molecules that are similar to heroin in structure. Hapten serves as the schematic for the development of the antibodies that identify and combine with the heroin molecules. Each person's immune system responds differently, and the system is often compromised from heroin addiction. The drug trials focus on identifying the effective combinations of the parts of the vaccine to elicit the immune response necessary to block the action of the heroin in the bloodstream.

Several concurrent trials are underway for the vaccine, which are in the early stages of development and have not yet been tested on humans. Researchers agree that vaccine treatment should be part of a comprehensive therapy plan [24]. Dr. Janda and Dr. Crystal note, "People have the misconception that a single vaccine can protect patients from substance abuse, that's not true." Dr. Crystal states, "A patient who has attained abstinence could be vaccinated to block the effects of the drug, thereby preventing relapse. Dr. Janda notes, "Our vaccine will not alleviate craving, but it could help patients maintain abstinence in weak moments."

"The vaccine approach provides an alternative strategy for treating drug addiction," says Dr. Nora Chiang of NIDA's Division of Pharmacotherapies and Medical Consequences of Drug Abuse. "There is much more work to be done on these vaccines, but the results so far are promising [25]."

EBP alert! All healthcare professionals must be sure to monitor vaccine research regarding heroin addiction. They need this knowledge to intervene effectively for persons facing the hazards of addiction.

Treatment for adolescents

Many biological factors, such as immature brain development in the frontal cortex, social and environmental factors, influence drug abuse and addiction in adolescents. Government health agencies, through their initiatives to blend the fields of study that research addiction, have combined neurobiology and social sciences to develop prevention and treatment programs that address the multiple and overlapping factors that influence heroin addiction in adolescents. NIDA explains this process as follows:

The resulting social neuroscience initiative will help us better understand how neurobiological mechanisms and responses, genetic, hormonal, and physiological, underlie, motivate, and guide social behaviors related to abuse and addiction. This perspective may help us understand adolescents' heightened sensitivity to social influences and decreased sensitivity to negative consequences, for example, that make them particularly vulnerable to drug abuse [20].

Pharmacology

None of the medications used with adults to treat addiction have been approved by the FDA for use with children and adolescents. At this time, clinical trials for additional medications are in development.

Behavioral treatment

Behavioral therapies are effective with children and adolescents and follow the same procedures noted in the section on therapy for adults. Contingencies and incentives help to motivate youth, and cognitive behavioral strategies work effectively when they are structured to meet the child's needs, age, developmental and maturity level. Any healthcare provider trained and certified to provide services to young clients can deliver behavioral treatment.

Family therapy

Children and adolescents can benefit from treatment using family therapy approaches, which include all significant people in their lives, including parents, guardians, mentors, siblings, and peers. Family therapy can address all areas of children's lives and increase communication and address problems in family dynamics, which may add to the stress of recovery. Therapy can build a wide circle of support for adolescents and help them gain confidence and self-esteem as they fight their addiction. Involving the family is a critical part of adolescent substance abuse treatment.

The following evidence-based family treatments programs work effectively to treat adolescent substance abuse [26].

Brief strategic family therapy (BSFT)

BSFT focuses on unhealthy family interactions that contribute to the young person's drug problem. The therapist works to establish rapport with each family member, while observing how each member interacts, to identify problem areas and strategies. During the course of 12 to 16 sessions, the therapist will work to address problems and guide the family members to work together to resolve them. This approach can target any family issue and can be conducted in any setting.

Family behavior therapy (FBT)

FBT includes strategies from behavioral therapy, including behavior contracts that include contingencies to motivate the young person, and build impulse control and appropriate behaviors. The therapist works with the adolescent and parent to develop behavior goals, treatment plans, behavior strategies, and treatment interventions. The therapist writes a contact based on the goals and treatment plan, with

contingencies based on measurable behaviors. The adolescent and parent work together to practice new behaviors and skills in the home, school, and community. Therapists and adolescents review the contract on a schedule that is appropriate for the child's age and maturity level to motivate and reinforce behavior. Professionals should reinforce appropriate behavior and goal mastery frequently in order for the program to work effectively.

Functional family therapy (FFT)

FFT is based on the premise that problem behaviors stem from dysfunctional family interactions. Therapy uses behavioral strategies to resolve conflict by improving skills for parenting, communication, and problem solving within the family involving all family members. Program goals include engaging and motivating all family members to work together to change their patterns of interaction through techniques of behavior therapy.

Multidimensional family therapy (MDFT)

The MDFT approach combines treatment components from all programs addicted youths encounters as a result of their addiction or conduct. At-risk or addicted youths can benefit from techniques of family therapy combined with treatment at school, juvenile justice, child protective services, clinics, family court, or other community agencies involved in their treatment plans. Often adolescents abusing drugs exhibited at-risk behavior, conduct disorder, family problems, or illegal behavior in the past that brought them in contact with special services in a number of organizations. MDFT goals work toward pooling resources and developing consistency and collaboration among all agencies involved in the child's care. Representatives from these agencies meet together with the adolescent and family to plan and implement goals and strategies consistently and hold the young person accountable on all fronts. According to NIDA, the MDFT program has been effective with severe substance-use disorders and can facilitate the reintegration of juvenile detainees into the community.

Multisystemic therapy (MST)

Similar to MDFT, this therapy uses a multidimensional approach that combines family therapy approaches with treatment strategies from a variety of treatment programs in the community. This approach is a natural out-growth of treatment for adolescents involved in severe drug addictions, violent behavior, and illegal activity. MST focuses on adolescents' personality, attitude, behavior, emotions, and peer influences related to their addiction and behavior. The second component includes a review of family interactions such as discipline, parenting skills, communication, and history of substance abuse among family members, and attitudes and values that influence them. The last variable looks to adolescents' performance and attitudes in the community at school, on the street, and membership in gangs or other groups in the community. The therapist works with the youth individually, with the family and youth together, and they coordinate and lead meetings with community agencies to coordinate services and build program consistency.

Recovery support for adolescents

If addiction treatment and recovery programs work effectively, there must be support services for aftercare to avoid relapse and support adolescents as they develop and apply skills to maintain a healthy, drug-free lifestyle. NIDA notes the following programs in clinical trials show promise in supporting recovery and lowering relapse among adolescent addicts [26].

Assertive Continuing Care (ACC)
ACC is a home-based continuing-care approach delivered by trained clinicians to prevent relapse, and is typically used after an adolescent completes therapy utilizing the Adolescent Community Reinforcement Approach (A-CRA). ACC combines A-CRA, behavior therapy, and assertive case management services using a multidisciplinary team of professionals, round-the-clock coverage, and assertive outreach to help adolescents and their caregivers acquire the skills needed to engage in positive social activities.

Peer recovery support services
Peer recovery support services connect youth with groups and individuals who have experienced addiction and recovery and act as peer mentors. They help individuals, based on their specific needs, support and coach the individual through treatment, and help them connect with community support groups and resources. More importantly, these services can provide new social connections so the adolescent can build positive social interactions with sober peers.

Recovery high schools
Recovery high schools can take different forms, but they are designed to meet the specific needs of students recovering from drug abuse. Students may attend a separate school or be part of a community school, but initially, they attend classes in a separate area with students who share their specific experiences and needs. The high school program may run concurrently with other treatment programs. Students benefit from specially trained teachers and counselors who support their treatment plan, which may address mental disorders as well as substance abuse. Students participate with peers who have experienced similar issues in a structured setting that promotes recovery.

BEHAVIORAL THERAPIES

Outpatient behavioral treatment provides therapy through individual and group settings based on the program that best meets the needs of the person. It can be designed to meet the needs of youth and adults and is often combines with pharmacological treatment to increase efficacy. The NIDA outlines the following types of outpatient behavioral treatment programs [27].

- **Cognitive behavioral therapy** aims to help patients recognize, avoid, and cope with the situations in which they are most likely to abuse drugs.
- **Motivational interviewing** capitalizes on the readiness of individuals to change their behavior and enter treatment.
- **Motivational incentives and contingency management** uses positive reinforcement to encourage abstinence from drugs.

Contingency programs and cognitive-behavioral therapy are commonly used forms of therapy to help patients take control and responsibility for their behavior and build coping and life skills to move toward long-term recovery and health. Behavior therapy uses strategies to address unwanted behaviors using learning theory,

conditioning, and reinforcement with the focus on the present and addicts' ownership and responsibility for their behavior. Therapy focuses on targeted behaviors to change and strategies to identify the triggers, or antecedents, and consequences of the behavior. The addict identifies behavior patterns to change and works toward healthy replacement behaviors. The therapist and client work to identify goals and barriers to those goals that may include habits, obsessions, compulsions, denial, procrastination, fear, depression, anxiety, dysfunctional inter-personal relationships, communication issues, and any other negative thought and behavior patterns. They work through these barriers together to build the client's awareness of the former thoughts, feelings, and behaviors that have a negative impact on recovery and must be changed. Behavior therapy has been around for decades, and many forms have proven effective with addiction. In the case of heroin addiction, this therapy works best when combined with pharmacological therapy.

Motivational incentives for enhanced drug abuse recovery: Promoting awareness of motivational incentives

The National Institute on Drug Abuse (NIDA) a division of the Substance Abuse and Mental Health Services Administration (SAMHSA) noted the challenge of helping patients avoid relapse while in a treatment program. They conducted research and clinical trials to develop an evidence-based approach called Promoting Awareness of Motivational Incentives (PAMI) to train other organizations to use incentive techniques, sometimes called contingencies, in programs to maintain abstinence from drug and alcohol use [30]. After testing the program, they developed a package of tools and training resources to replicate the program and share evidence-based research data behind the clinical use of motivational incentives. The strategies of the approach used low-cost incentives with patients that were successful in maintaining abstinence and program compliance to avoid relapse during treatment. PAMI is based on positive research outcomes from the NIDA Clinical Trials Network (CTN) study, Motivational Incentives for Enhanced Drug Abuse Recovery (MIEDAR), and uses strategies from Dr. Nancy Petry's Fishbowl Method of incentives [31]. "We use rewards as a clinical tool not as by bribery but for recognition; the really profound will come later."

The researchers used motivational incentives because they lead to higher rates of retention in treatment and abstinence from drug abuse. They found incentives that were motivating, low cost, and supported the patient's treatment plan included prices, vouchers, and clinic privileges. The patients earned reinforcers on the results of their on-site urine screening and completion of treatment goals. The study noted that patients who participated in incentive programs were more likely to submit urine samples that were negative than patients not receiving incentives. The average cost of incentives was $120 per patient [32]. PAMI is designed to build awareness of motivational incentives as a research-based therapeutic strategy for addiction treatment. The package, which is free of charge, reviews the research, provides support materials and resources along with suggestions for implementation, data collection, training and replication of the program and includes a video, *Successful Treatment Outcomes Using Motivational Incentives.*

The NIDA [31] reported data showing that approximately 25% of samples from both study groups tested negative for stimulants and alcohol at the first study visit. Overall, participants in the incentive group (54.4%) were significantly more likely to submit target drug-negative samples than were participants in the usual care group (38.7%).

The motivational incentives and interviewing techniques address patients' feelings and barriers about stopping drug use. Motivational interviewing is a therapeutic approach to help patients in recovery, and the incentives help patients modify and change specific behaviors. The incentives acted as a supplement to therapy were effective in the treatment of substance-use disorders. The study noted that the incentives improved therapeutic climate because they were based on positive, affirming, and celebratory strategies. Positive reinforcement incentives will be effective if they are valuable to the person and motivate them to work to change target behaviors. Patients received a menu of incentives to choose from, and therapists were consistent in the distribution of the incentives earned. Intermittent schedules of reinforcement were the most powerful, and the Fishbowl Method used this schedule to deliver low or no-cost incentives, such as coupons, vouchers, and privileges. Patients had a chance to earn and win prizes when they drew from the fishbowl. Target behaviors must be observable and measurable, and they should include abstinence and the successful completion of goals from the patient's treatment plan. The PAMI program outlines seven core principles of motivational incentive programs [30].

Seven core principles of motivational incentive programs:

1. Identification of target behavior.
2. Choice of target population.
3. Choice of reinforcer.
4. Incentive magnitude.
5. Frequency of incentive distribution.
6. Timing of the incentive.
7. Duration of the incentive.

The PAMI program materials include all the information needed to replicate the program and include supplemental software to track information about patients' participation and progress in the program. Information on these programs, and others to address the heroin addiction epidemic, can be obtained from the Motivational Incentives Web-Portal: *www.bettertxoutcomes.org*; National Institute on Drug Abuse: *http://www.drugabuse.gov/blending-initiative*; and SAMHSA ATTC: *http://www.attcnetwork.org/blendinginitiative.*

Prevention

Prevention programs to address heroin addiction have been researched for over 20 years, which is not very long, considering the heroin addiction goes back to the late 1800s.

To find a solution to the complex, epidemic disease of heroin addiction, the process must include the following components:

- Identification and definition of heroin addiction.
- Determine the scope of the problem, sequence of events and factors that lead to addiction.
- Review evidence-based programs proven to effectively break the cycle of addiction including prevention and treatment.
- Matching prevention and treatment programs to the individual needs of the individual and community.

There is a rush to implement these steps because of the public's awareness of the problem of heroin addiction and the number of overdose deaths in every community, large or small. For those in the field of medical and mental health, the work to eradicate this complex problem has been in progress for decades. It is clear to all who work in this field that there is no easy and quick solution because the predictors or heroin addiction are varied and there is no definitive "test" to determine who will become addicted. Instead, many factors overlap to increase the chance that a person will become addicted. Biology, genetics, age at onset of use, environment, personality, and social influences are a few of the factors that contribute to addiction but are impossible to unravel or measure. Researchers, therapists, medical personnel, school staff, and families know that addiction to

the substance may take hold quickly, but addiction is a developmental disease that begins long before the person becomes addicted to heroin. NIDA research shows that in some cases, the signs were there in childhood and adolescence while the brain is rapidly developing and changing. Brain research shows that the prefrontal cortex develops last, and that is the part of the brain that controls decisions and judgments, which explains why adolescents often engage in at risk behaviors. These factors correlate with statistics that show heroin addiction is rising among young people because they are open to experimentation with drugs, and therefore, vulnerable to heroin addiction.

These facts, established from evidence-based research, conclude that for prevention programs to work, they must begin early in order to address all the factors that lead to addiction, which often begin in childhood. NIDA identifies the following factors that can be addresses to prevent addiction at an early age [33]:

- Mental illness.
- Neurobiology.
- Physical or sexual abuse.
- Aggressive behavior.
- Academic problems.
- Poor social skills.
- Lack of motivation.
- Peer influences.
- Poor parent-child relations.

Effective prevention programs must have a multidimensional approach involving family, school staff, community health agencies, media, and other social and cultural modes of communicating prevention education, information, and early intervention. Because heroin addiction crosses all boundaries and excludes no one, community prevention outreach programs must speak directly to the intended audience in a way they can understand; therefore, the programs must encompass all languages, cultures, and educational levels. Community education for prevention must also address the relationship between at-risk behavior, addiction and the spread of HIV/AIDS, which is part of the heroin addiction epidemic.

The NIDA and other federal research organizations have included prevention as a primary goal. The principles outlined in this section focus on numerous, long-term, evidence-based studies of addiction behavior and combined concepts from many successful prevention programs. The prevention principles target children through young adults across the country with the goal of implementation at the community level. Prevention programs are geared to specific settings and specific needs of the participants and address the needs of all youth, whether they are drug-free, at-risk, or already experimenting with drugs. These principles can be implemented at home, school, community or all three.

The entire list and specific details on each principle, including research information, can be obtained on the NIDA website Prevention section at *http://www.drugabuse.gov/publications/preventing-drug-use-among-children-adolescents*. The following information and principles can guide the development of prevention programs for children and youth [35]:

> NIDA's prevention research program focuses on risks for drug abuse and other problem behaviors that occur throughout a child's development, from pregnancy through young adulthood. Research funded by NIDA and other federal research organizations – such as the National Institute of Mental Health and the Centers for Disease Control and Prevention – shows that early intervention can prevent many adolescent risk behaviors.

Principle 1 – Prevention programs should enhance protective factors and reverse or reduce risk factors. The risk of becoming a drug abuser involves the relationship among the number and type of risk factors, deviant attitudes and behaviors, and protective factors. Specific risk and protective factors change with age and stage of development. For example, risk factors within the family have greater impact on a younger child, while association with drug-abusing peers may be a more significant risk factor for an adolescent. Early intervention with risk factors, such as aggressive behavior and poor self-control, often has a greater impact than later intervention by changing a child's life path away from problems and toward positive behaviors. These factors can have a different effect depending on a person's age, gender, ethnicity, culture, and environment.

Principle 2 – Prevention programs should address all forms of drug abuse, alone or in combination, including the underage use of legal drugs and substances and the use of illegal drugs.

Principle 3 – Prevention programs should address the type of drug abuse problem in the local community, target modifiable risk factors, and strengthen identified protective factors.

Principle 4 – Prevention programs should address risks specific to population or audience characteristics, such as age, gender, and ethnicity, to improve program effectiveness.

Principle 5 – Family-based prevention programs should enhance family bonding and relationships including parenting skills and training in drug education and information. Family bonding is the bedrock of the relationship between parents and children. Family bonding can strengthen through skills training on parent supportiveness of children, parent-child communication, and parental involvement. Parental monitoring and supervision are critical for drug abuse prevention. Training on rule-setting; techniques for monitoring activities; praise for appropriate behavior; and moderate, consistent discipline that enforces defined family rules should be included. Drug education and information for parents or caregivers reinforces what children learn about the effects of drugs and opens opportunities for family discussions about the abuse of legal and illegal substances. Brief, family-focused interventions for the general population can positively change specific parenting behavior and reduce children's later risks of drug abuse.

Principle 6 – Prevention programs can be designed to intervene as early as infancy to address risk factors for drug abuse, such as aggressive behavior, poor social skills, and academic difficulties.

Principle 7 – Prevention programs for elementary school children should target academic and social-emotional skills to address risk factors for drug abuse. Education should focus on the following skills:

- Self-control.
- Emotional awareness.
- Communication.
- Social problem solving.
- Academic support, especially in reading.

Principle 8 – Prevention programs for middle or junior high and high school students should increase academic and social competence with the following skills:

- Study habits and academic support.
- Communication.
- Peer relationships.
- Self-efficacy and assertiveness.
- Drug resistance skills.
- Reinforcement of anti-drug attitudes.
- Strengthening of personal commitments against drug abuse.

Principle 9 – Prevention programs aimed at general populations at key transition points, such as the transition to middle school, can produce beneficial effects even among high-risk families and children.

Principle 10 – Community prevention programs that combine two or more effective programs, such as family-based and school-based programs, can be more effective than a single program.

Principle 11 – Community prevention programs reaching populations in multiple settings such as schools, clubs, faith-based organizations,

and the media, are most effective when they present consistent, community-wide messages in each setting.

Principle 12 – When communities adapt intervention programs to match their needs, community norms, or differing cultural requirements, they should retain core elements, which include the structure, content, and delivery of the program.

Principle 13 – Prevention programs should be long-term with repeated interventions to reinforce the original prevention goals. Benefits from middle school prevention programs diminish without follow-up programs in high school.

Principle 14 – Prevention programs should include teacher training on good classroom management practices, such as rewarding appropriate student behavior to foster students' positive behavior, achievement, academic motivation, and school bonding.

Principle 15 – Prevention programs work most effectively when they use interactive techniques, such as peer discussion groups and parent role-playing.

Principle 16 – Research-based prevention programs can be cost-effective. Research shows that for each dollar invested in prevention, a savings of up to $10 in treatment for alcohol or other substance abuse [28].

The community youth development study

This NIDA program offers assessment tools and technical trainings to communities so they can more accurately identify risk and protective factors for youth drug use and related behavior problems. This system allows communities to select appropriate evidence-based prevention programs based on their particular needs [29].

Future trends

In addition to the pharmacological and therapeutic models in clinical trials previously reviewed, additional research studies may prove effective in the identification, prevention, and treatment of heroin addiction.

High-resolution mapping of targeted brain areas

Research is currently underway that will increase knowledge of the brain systems and pathways taken by drugs and their effects on centers of the brain that influence drug-related behaviors involved in motivation, impulse control, pleasure, reward, compulsions, addiction, and relapse [34]. With this information, advances can be made to identify medications that interfere and block these drug behaviors to prevent drug addiction in persons at risk or assist in recovery and relapse prevention.

Blending initiative

Research and clinical trials are of no use if the results languish in a government publication and remain unused. The goal of the Blending Initiative of 2001 [20] was to address this problem of disseminating research-based addiction treatment information so that it could be implemented in clinical practice. NIDA explains the process as follows:

> NIDA and the Substance Abuse and Mental Health Services Administration (SAMHSA) joined together to create the Blending Initiative in 2001 to reduce the gap that exists between the publication of research results and impact on treatment delivery. This initiative incorporates collaboration between clinicians, scientists, and experienced trainers to catalyze the creation of user-friendly treatment tools and products and facilitate the adoption of research-based interventions into front-line clinical settings. Through this initiative, NIDA and SAMHSA's Addiction Technology Transfer Centers (ATTC) disseminate treatment and training products based on results from studies conducted by the National Drug Abuse Clinical Trials Network (CTN) as well as other NIDA-supported research.

Conclusion

It is the responsibility of all health care professional to advocate for their clients and promote access to health care for everyone. The disease of heroin addiction impacts all ages in all communities, so health professionals today must work to bring heroin addiction out of the shadows. They must educate others to remove the stigma and address heroin addiction as a brain disease that can affect anyone. As with many diseases, such as HIV/AIDS, heroin addiction causes fear and is widely misunderstood in the community. Scientists and researchers are collaborating on better screening, treatment, and prevention techniques, health professionals and the general public should be educated about what they can do in their daily lives to prevent heroin addiction from spreading. This course points to the need for a multiple disciplinary approach that must start early in life to address the complex factors that lead to at-risk behaviors that may lead to drug experimentation. Environmental, social, genetic, physical, and mental health factors that contribute to addiction have been identified and are critical in developing effective treatment and prevention programs. Addressing these factors among youth at an early age may be the only way to control the epidemic, while law enforcement tries to eradicate the source of the drug from Mexico, South America, and Asia.

Prevention begins by educating parents, teachers, and healthcare staff about early identification of risk factors in childhood as well as the early the signs and symptoms of drug use. Health care professionals, school staff, and community resource agencies can identify and refer at-risk individuals and struggling families to social services for prevention and treatment programs. Once identified, these families can benefit from early intervention programs, including, health care, counseling, assistance with parenting, and discipline to support healthy family interaction. Health care professionals must participate in prevention and treatment programs in the community through fundraising activities, lobbying local officials and state legislators, conducting community outreach activities to identify and offer services to young people and adults at risk, educating the public about the disease, and working with the media to develop effective campaigns to combat negative cultural influences.

By moving forward through a multi-disciplinary approach, health care professionals can close the heroin treatment gap and increase prevention efforts. As advocates, health professionals, government agencies, and politicians must collaborate to write policies and increase funding for heroin addiction prevention and treatment to stop the escalating cycle of addiction and relapse. NIDA research has demonstrated that prevention is cost effective in lowering expenditure in areas such as residential treatment, hospital and health care, incarceration, crime, and the justice system. Funds are necessary to increase the accessibility and ease of treatment to encourage families and individuals to seek help to stop the cycle of addiction and prevent it in the future. There is no way to put a price on the mounting death

toll from this epidemic, and health care professionals are the front line of defense. The epidemic of heroin addiction is a massive problem that requires effort on the part of every health care professional to identify what they can do today to break the cycle of addiction in their community.

Resources

- **Addiction Severity Index:** Provides a structured clinical interview designed to collect information about substance use and functioning in life areas from adult clients seeking drug abuse treatment, *triweb.tresearch.org/index.php/tools/download-asiinstruments-manuals.*
- **Blending Teams** web sites: *nida.nih.gov/blending* and *drugabuse.gov/blending-initiative.*
- **Center for Substance Abuse Treatment (CSAT): Substance Abuse and Mental Health Services Administration (SAMHSA)**, *www.samhsa.gov/about/csat.aspx,* and *http://www.samhsa.gov/data/NSDUH/2012SummNatFindDetTables/NationalFindings/NSDUHresults2012.htm.*
  Treatment locator: 1-800-662-HELP or search *www.findtreatment.samhsa.gov*. SAMHSA's Store has a wide range of products: *store.samhsa.gov.*
- **Clinical Trials:** For more information on federally and privately supported clinical trials, please visit *clinicaltrials.gov.*
- **Drugs, Brains, and Behavior: The Science of Addiction** (*Reprinted 2010*): This publication provides an overview of the science behind the disease of addiction. Publication #NIH 10-5605. Available online at *drugabuse.gov/publications/science-addiction.*
- Complete NSDUH findings are available at **National Institute for Drug Addiction,** *drugabuse.gov.*
- **National Institute of Drug Addiction** Website: *www.drugabuse.gov,* NIDA Public Information Office: 301-443-1124.
- **The National Institute of Justice:** The research agency of the **Department of Justice**. For information contact the **National Criminal Justice Reference Service** at 800-851-3420 or 301-519-5500; or visit *nij.gov.*
- **National Institute of Mental Health** *nimh.nih.gov.*
- **The National Registry of Evidence-Based Programs and Practices:** This database of interventions for the prevention and treatment of mental and substance use disorders is maintained by SAMHSA and can be accessed at *nrepp.samhsa.gov*.
- **NIDA DrugFacts: Treatment Approaches for Drug Addiction** (*Revised 2009*). This is a fact sheet covering research findings on effective treatment approaches for drug abuse and addiction. Available online at *drugabuse.gov/publications/drugfacts/treatment-approaches-drugaddiction.*
- **NIDA DrugPubs Research Dissemination Center:** NIDA publications and treatment materials are available from this information source. Staff provide assistance in English and Spanish, and have TTY/TDD capability. Phone: 877-NIDA-NIH (877-643-2644); TTY/TDD: 240-645-0228; fax: 240-645-0227; e-mail: *drugpubs@nida.nih.gov*; Website: *drugpubs.drugabuse.gov.*
- **Preventing Drug Use among Children and Adolescents: A Research-Based Guide for Parents, Educators, and Community Leaders**, Second Edition. This booklet lists over 20 examples of effective research-based drug abuse prevention programs and is available free on NIDA's website.
- **Principles of Drug Abuse Treatment for Criminal Justice Populations: A Research-Based Guide**, NIH Publication No.: 11-5316. Available online at *nida.nih.gov/PODAT_CJ.*
- **Research Report Series: Therapeutic Community.** This report provides information on the role of residential drug-free settings and their role in the treatment process. NIH Publication #02-4877. Available online at NIDA's National Drug Abuse Treatment Clinical Trials Network (CTN) *drugabuse.gov/CTN/Index.htm.*
- **Seeking Drug Abuse Treatment: Know What To Ask** NIDA Publication #12-7764. Available online at *drugabuse.gov/publications/seeking-drug-abuse-treatment.*
- The **"Find A Physician"** feature on the American Society of Addiction Medicine (ASAM) Web site: *http://community.asam.org/search/default.asp?m=basic.*
  Patient Referral Program on the American Academy of Addiction Psychiatry Website: *http://www.aaap.org/patient-referral-program.*
- **The Child and Adolescent Psychiatrist Finder** on the American Academy of Child and Adolescent Psychiatry Web site: *http://www.aacap.org/cs/root/child_and_adolescent_psychiatrist_finder/child_and_adolescent_psychiatrist_finder.*

References

1. Foundation for a Drug-Free World. (2014). Retrieved from *http://www.drugfreeworld.org/drugfacts/heroin.html*
2. What is Heroin and What is it For? (2014). Retrieved from *http://www.drugabuse.gov/publications/research-reports/heroin/what-heroin*
3. Drugs, Brains, and Behavior: The Science of Addiction (2014). Retrieved from *http://www.drugabuse.gov/publications/science-addiction*
4. The Definition of Addiction (2011). Retrieved from *http://www.asam.org/advocacy/find-a-policy-statement/view-policy-statement/public-policy-statements/2011/12/15/the-definition-of-addiction*
5. Panell, I. (2014). The Horrific Toll of America's Heroin Epidemic. BBC News Magazine. Chicago. Retrieved from *http://www.bbc.com/news/magazine-26672422*
6. National Survey on Drug Use and Health: Summary of National Findings (2012). Retrieved from *http://www.drugabuse.gov/publications/research-reports/heroin/scope-heroin-use-in-united-states*
7. The U.S. Drug Enforcement Administration (2012) National Drug Threat Assessment Report (FULL) Retrieved from *http://www.justice.gov/dea/resource-center/DIR-017-13%20NDTA%20Summary%20final.pdf*
8. Heroin Addiction. (2013). Retrieved from *http://report.nih.gov/nihfactsheets/viewfactsheet.aspx?csid=123*
9. Data, Outcomes and Quality (2012). Retrieved from *http://www.samhsa.gov/data/*
10. American Psychiatric Association (2013). Substance-Related and Addictive Disorders, in Diagnostic and Statistical Manual of Mental Disorders, 5th Edition. Washington, DC: American Psychiatric Publishing, 540–550, and 2013.
11. Mardis, C. (2011). Increased Opiate Use and the Need for Onsite Heroin Screening. Retrieved from *http://www.nadcp.org/sites/default/files/nadcp/Final%206AM%20Brief.pdf*
12. Department of Health and Human Services (2010). Mandatory Guidelines for Federal Workplace Drug Testing Programs. Retrieved from *http://www.gpo.gov/fdsys/pkg/FR-2010-04-30/pdf/2010-10118.pdf*
13. Harrison, L .D., Martin, S. S., Enev, T., Harrington, D. (2007). Comparing Drug Testing and Self-Report of Drug Use among Youths and Young Adults in the General Population Department of Health and Human Services Substance Abuse and Mental Health Services Administration Office of Applied Studies. Retrieved from *http://www.samhsa.gov/data/nsduh/drugtest.pdf*
14. Symptoms and Signs of Poly-substance Abuse (2014). Retrieved from *http://www.buppractice.com/howto/screen/polysubstance*
15. U.S. Foods and Drug Administration (2014). FDA Approves New Hand-Held Auto-Injector to Reverse Opioid Overdose. FDA News Release. April 3, 2014. Retrieved from *http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/ucm391465.htm.*
16. O'Brien, R. (2014) FDA Approves Potential Lifesaver in Heroin Epidemic: April 4, 2014. Retrieved from *http://www.northjersey.com/news/fda-approves-potential-lifesaver-in-heroin-epidemic-1.841414?page=all*
17. SAMHSA Announces a Working Definition of "Recovery" from Mental Disorders and Substance Use Disorders. Retrieved from *http://www.samhsa.gov/newsroom/advisories/1112223420.aspx*
18. Principles of Drug Addiction Treatment: A Research-Based Guide, Third Edition (2012). Retrieved from *http://www.drugabuse.gov/publications/principles-drug-addiction-treatment*
19. Neuropsychopharmacology. (2012) 2012 Apr; 37(5): 1083-91. doi: 10.1038/npp.2011.200. Epub 2011 Sep 14. Retrieved from *http://www.ncbi.nlm.nih.gov/pubmed/21918504*.
20. Topics in Brief: NIDA's Blending Initiative: Accelerating Research-Based Treatments into Practice (2007). Retrieved from *http://www.drugabuse.gov/publications/topics-in-brief/nidas-blending-initiative-accelerating-research-based-treatments-practice*
21. National Institute on Drug Abuse (2006) Buprenorphine: Treatment for Opiate Addiction Right in the Doctor's Office Retrieved from *http://www.drugabuse.gov/publications/topics-in-brief/buprenorphine-treatment-opiate-addiction-right-in-doctors-office*
22. Krupitsky, E.; Zvartau, E.; Blokhina, E.; Verbitskaya, E.; Wahlgren, V.; Tsoy-Podosenin, M.; Bushara, N.; Burakov, A.; Masalov, D.; Romanova, T.; Tyurina, A.; Palatkin, V.; Slavina, T.; Pecoraro, A.; Woody, G. E. (2013). Naltrexone Implant Outperforms Daily Pill in Russian Trial: Randomized Trial of Long-Acting Naltrexone Implant vs Oral Naltrexone or Placebo for Preventing Relapse to Opioid Dependence. Archives of General Psychiatry 69(9): 973–981, 2012. Retrieved from *http://www.drugabuse.gov/news-events/nida-notes/2013/11/naltrexone-implant-outperforms-daily-pill-in-russian-trial*
23. CDC (2002). Methadone Maintenance Treatment. Retrieved from *http://www.cdc.gov/idu/facts/MethadoneFin.pdf*
24. Substance Abuse and Mental Health Services Administration, Results from the 2011 National Survey on Drug Use and Health: Summary of National Findings (2012) NSDUH Series H-44, HHS Publication No. (SMA) 12-4713. Rockville, MD: Substance Abuse and Mental Health Services Administration, 2012. Retrieved from *http://www.drugabuse.gov/publications/research-reports/heroin/scope-heroin-use-in-united-states*

25. Wee, S., Hicks MJ, De BP, Rosenberg JB, Moreno AY, Kaminsky SM, Janda KD, Crystal RG, Koob GF. (2011). Novel Cocaine Vaccine Linked to a Disrupted Adenovirus Transfer Vector Blocks Cocaine Psychostimulant and Reinforcing Effects. Neuropsychopharmacology. Retrieved from *http://www.ncbi.nlm.nih.gov/pubmed/21918504*
26. Division of Pharmacotherapies and Medical Consequences of Drug Abuse (DPMCDA) (2011). Retrieved from *http://www.drugabuse.gov/about-nida/organization/divisions/division-pharmacotherapies-medical-consequences-drug-abuse-dpmcda/research-programs#ATDP*
27. Family Based Approach (2014). Retrieved from *http://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/evidence-based-approaches-to-treating-adolescent-substance-use-disorders/family-based-approaches*
28. Behavioral Therapies (2012). Retrieved from *http://www.drugabuse.gov/publications/principles-drug-addiction-treatment/evidence-based-approaches-to-drug-addiction-treatment/behavioral-therapies*
29. Mark TL, Woody GE, Juday T, Kleber HD. (2001) The Economic Costs of Heroin Addiction in the United States. Drug Alcohol Dependency. 2001; 61:195–206. Retrieved from *http://www.ncbi.nlm.nih.gov/pubmed/11137285*
30. Community Youth Development Study (2009). Retrieved from *www.drugabuse.gov/sites/default/files/nnvol23n4.pdf*
31. Promoting Awareness of Motivational Incentives NIDA (2006). Retrieved from *http://www.drugabuse.gov/sites/default/files/files/PAMI_Factsheet.pdf*
32. Petry, N. M., & Bohn, M. J. (2003). Fishbowls and candy bars: Using low-cost incentives to increase treatment retention. NIDA Science & Practice Perspectives, 2(1), 55–61. PDF] Successful Treatment Outcomes Motivational Incentives: Positive Reinforces to Enhance *http://www.drugabuse.gov/sites/default/files/files/MI-PRESTO_Factsheet.pdf*
33. Kellogg, S. H., Burns, M., Coleman, P., Stitzer, M., Wale, J. B., & Kreek, M. J. (2005). Something of Value: The Introduction of Contingency Management Interventions into the New York City Health and Hospital Addiction Treatment Service. Journal of Substance Abuse Treatment, 28, 57–65. Retrieved from *http://www.drugabuse.gov/sites/default/files/files/MI-PRESTO_Factsheet.pdf*
34. Principles of Adolescent Substance Use Disorder Treatment: A Research-Based Guide (2014). Retrieved from *http://www.drugabuse.gov/publications/principles-adolescent-substance-use-disorder-treatment-research-based-guide/principles-adolescent-substance-use-disorder-treatment*
35. High Resolution Brain Spectrum Imaging in a Clinical Substance Abuse Practice (2010). Retrieved from *http://www.ncbi.nlm.nih.gov/pubmed/20648911* J Psychoactive Drugs. 2010 Jun; 42(2): 153-60.
36. National Institute on Drug Abuse Preventing Drug Use among Children and Adolescents: A Research-Based Guide for Parents, Educators, and Community Leaders, Second Edition booklet. (2003). NIH Pub Number: 04-4212(A) Published: January 1997Revised: October 2003: Retrieved from *http://www.drugabuse.gov/publications/preventing-drug-use-among-children-adolescents*
37. Stuart, G. W. (2013). *Principles and Practice of Psychiatric Nursing* (10th ed.). St. Louis: Elsevier.

HEROIN USE IN AMERICA: IDENTIFICATION, TREATMENT, AND PREVENTION

Final Examination Questions

Choose the best answer for questions 21 through 30 and mark your answers on the Final Examination Sheet found on Page 141 or take your test online at **nursing.elitecme.com**.

21. NAS occurs only when the mother combines heroin with other drugs that pass through the placenta into the baby's bloodstream during pregnancy, allowing the baby to become addicted along with the mother.
    a. True.
    b. False.

22. There are increasing numbers of heroin abusers at a younger age, because the drug can be smoked and inhaled.
    a. True.
    b. False.

23. Heroin addiction does not actually change brain chemistry or function.
    a. True.
    b. False.

24. Genetic factors cause addiction in 60% of all addiction cases.
    a. True.
    b. False.

25. Severe muscle and bone aches can be symptoms of withdrawal.
    a. True.
    b. False.

26. Addiction is classified as a chronic brain disorder or disease.
    a. True.
    b. False.

27. Integration of psychosocial rehabilitation and ongoing care with evidence-based pharmacological therapy provides the best results.
    a. True.
    b. False.

28. Agonist medication activates receptors gradually, reaching the brain slowly.
    a. True.
    b. False.

29. Motivational incentives and contingency management use positive reinforcement to encourage abstinence from drugs.
    a. True.
    b. False.

30. The prefrontal cortex develops first, and that is the part of the brain that controls breathing and heart rate.
    a. True.
    b. False.

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Patient Safety: Implementation of National Safety Standards for Nurses

4 Contact Hours

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Faculty

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Content reviewer
Nancy J. Denke, DNP, ACNP-BC, FNP-BC, FAEN

Audience

National patient safety standards are a core competency for nursing practice. This course is for all nurses who are responsible for providing patient care.

Purpose statement

Safety comes first in patient care and in health care environments. This course presents the latest National Patient Safety goals as well as strategies for nursing.

Learning objectives

- Implement patient care designed to achieve National Patient Safety Goals.
- Describe how to prevent “never-ever” events.
- Explain how to reduce the occurrence of non-reimbursable hospital-acquired conditions.

How to receive credit

- Read the entire course online or in print which requires a 4-hour commitment of time.
- Depending on your state requirements you will asked to complete either:
  - An affirmation that you have completed the educational activity.
  - A mandatory test (a passing score of 70 percent is required). Test questions link content to learning objectives as a method to enhance individualized learning and material retention.
- Provide required personal information and payment information.
- Complete the MANDATORY Self-Assessment and Course Evaluation.
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Activity director

June D. Thompson, DrPH, MSN, RN, FAEN, Lead Nurse Planner

Disclosures

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Introduction

Safety first! There is not a practicing healthcare professional who would not agree that "safety first" is (or should be) the guiding principle of patient care services. Given that, why are medical errors the third leading cause of death in the United States? Why, according to recent research, do nearly 440,000 Americans die annually from preventable hospital errors [1]?

EBP alert! Research shows that an alarming number of healthcare consumers die from preventable medical errors. It is imperative that nurses and their healthcare colleagues comprehend safety mandates and safety research findings and then implement the recommendations into all aspects of their practice [1,2].

Clearly, it is essential for all healthcare providers to improve the safety of the environment in which patient care is delivered. Accrediting bodies and national organizations such as The Joint Commission and the Institute of Medicine have conducted research, published reports, and issued mandates regarding safety measures that should, and must, be implemented. But, how much is the average healthcare professional aware of such research and the rationale behind mandates and recommendations?

The purpose of this educational program is to discuss three critical topics related to essential safety standards:

- National Patient Safety Goals.
- "Never ever events."
- Centers for Medicare and Medicaid Services conditions that are not reimbursable if not present upon admission.

The educational program will also explain how nurses can implement the recommendations and mandates of these standards to improve patient safety as well as the quality and appropriateness of their practice.

National Patient Safety Goals

It is a typically hectic evening at one of the Hazelmoor Community Hospital medical units. A notice has been shared and posted that concerns the latest National Patient Safety Goals. Nurses are requested to familiarize themselves with these goals and how the hospital plans to achieve them. The nurses know that they must "eventually" make time to review this information, but that time is not tonight as it is just too busy, and patient care comes first. Nor is there time the next evening. Nor the next. Time goes by, and as one nurse puts it, "Our patients come first. We can't stop to read a bunch of stuff when we should be taking care of patients. That's why safety is compromised. All of this paper work and theory! The people that write these things should try being out here actually taking care of patients. Then maybe they'd see what it's like in the real world!"

Does the preceding situation sound familiar? Have you heard colleagues make similar statements? Have you made such comments yourself? You are not alone. Many healthcare professionals do not have a clear understanding of the National Patient Safety Goals, or how achieving these goals will improve patient care. It is not enough to distribute facts about these goals and what should be done to achieve them. Leaders of healthcare organizations have an obligation to explain how these goals were identified, how each organization developed a plan for achieving these goals, and most importantly, how the goal achievement will improve patient care.

History of the National Patient Safety Goals

The National Patient Safety Goals (NPSGs) are a set of standards which address the highest-priority patient safety issues that The Joint Commission promotes and utilizes to implement major changes in patient safety [3]. The NPSG program was established in 2002 and the first set of NPSGs was effective on January 1, 2003. The purpose of establishing such goals was to assist accredited organizations in addressing specific areas of concern regarding patient safety [4].

How are the NPSGs developed, and who develops them? According to The Joint Commission website, a panel of "widely recognized patient safety experts advise The Joint Commission on the development and updating of NPSGs" [4]. This panel is called the Patient Safety Advisory Group and is comprised of nurses, physicians, pharmacists, risk managers, clinical engineers, and other professionals who have hands-on experience in addressing patient safety issues in a wide variety of healthcare settings.

The Patient Safety Advisory Group works with staff from The Joint Commission to identify emerging patient safety issues, and advises The Joint Commission on how to address those issues in NPSGs, Sentinel Event Alerts, standards and survey processes, performance measures, educational materials, and/or in Center for Transforming Healthcare projects [4].

Large amounts of data are generated by the collaboration of The Joint Commission and the Patient Safety Advisory Group. How does The Joint Commission determine patient safety issue priorities for

NPSGs when faced with so much information? Input is solicited from practitioners, provider organizations, purchasers, consumer groups, and other stakeholders. Based on this input, The Joint Commission identifies priority patient safety issues, and how to best address them. The Joint Commission also determines if an NPSG is applicable to a specific accreditation program. If so, the goal is adapted to be program-specific [4].

Nursing consideration: Nurses may be concerned that the people who have input into the development of safety priorities lack current experience in patient care delivery. One way to alleviate these concerns, and to encourage staff nurses to become more involved in implementing NPSG recommendations is to encourage them to become more involved with The Joint Commission Perhaps they may even become a member of the Patient Safety Advisory Group or become active in another Joint Commission process. For more information about the Patient Safety Advisory Group, contact the Executive Vice-President and Chief Medical Officer of The Joint Commission at +1 (630) 792-5350, or access The Joint Commission website for more information (http://www.jointcommission.org).

NPSGs alert! What exactly are the responsibilities of the Patient Safety Advisory Group? As stated directly on the website, the group [5]:

- Annually recommends program-specific NPSGs for adoption by The Joint Commission Board of Commissions.
- Reviews draft patient safety recommendations for potential publication in The Joint Commission's periodic Sentinel Event Alert advisory, and advises Joint Commission staff as to the evidence for, and face validity of these recommendations as well as their practically and cost of implementation.
- Recommends potential future topics for Sentinel Event Alert.
- Assesses and facilitates learning initiatives about sentinel events, Sentinel Event Alerts, and the National Patient Safety Goals, including the implementation and effectiveness of the National Patient Safety Goals. Learning initiatives include: on-line tools such as Frequently Asked Questions and PowerPoint presentation;, tool kits to facilitate implementation of the National Patient Safety Goals; and education seminars and workshops.

Current National Safety Goal priorities

Samantha is a registered nurse who was recently appointed as a member of her hospital's Safety Advisory Council. She is preparing to attend her first meeting. The focus of the meeting will be a review of the newly published National Patient Safety Goals (NPSGs). Samantha is a bit uneasy about this focus as her role as a staff nurse has been to implement actions mandated by the hospital to comply with the goals. Now she is going to be in a position to help design actions that she and her colleagues must implement. This is a major responsibility, and Samantha is both excited and apprehensive about her new accountability as a leader.

Samantha and other stakeholders must not only follow organizational mandates in regards to compliance with NPSGs, but must become active participants in the decision-making process of how these goals can be achieved. Since their establishment in 2002, the NPSGs have evolved to become one of the most important methods of promoting and enforcing major safety changes in healthcare organizations. Recent changes, in addition to existing goals, have concentrated on preventing hospital-acquired infections and medication errors, promoting surgical safety, ensuring correct patient identification, enhancing communication between staff, and identifying patients at risk for suicide. The most recent 2016 goal is to reduce the harm associated with clinical alarm systems [3].

Before discussing the implications of the newest goal related to the safety of hospital alarm systems, we must review the other goals highlighted in the 2016 NSPGs. Each goal was developed to evaluate the safety and the quality of care provided for patients in the different care arenas which include hospitals, home-care, ambulatory care, behavioral health, critical-access hospitals, laboratories, long-term care, nursing-care centers, and office-based surgery. To access information about each 2016 NPSGs, go to this website link: http://www.jointcommission.org/standards_information/npsgs.aspx. For the purpose of this educational program, we will focus on the hospital, ambulatory care, and home-care goals.

2016 Hospital National Patient Safety Goals

The following summaries are based on information taken from The Joint Commission web site's easy-to-read version of the goals [6]. The easy-to-read version is intended for the general public as well. For the exact language of the goals, access: http://www.jointcommission.org.

Identify patients correctly.

- Use at least two ways to identify patients. For example, use the patient's name and date of birth. This will make sure that each patient gets the correct medications and treatments.
- Make sure that the correct patient gets the correct blood when receiving a blood transfusion.

Nursing consideration: Nurses must always be sure to identify patients in at least two ways prior to administering medications and blood products. Nurses may be tempted to ignore this simple safety mandate, especially if they know the patient well. But, ignoring the mandate even once makes it easier to ignore it again, and then again. Nurses also serve as role models for colleagues bound by the same mandate. Nurses must always use at least two methods to identify each patient [6].

Improve staff communication.

- Get important test results to the right staff person on time.

Nursing consideration: Communication is essential to reduce errors. Research shows that appropriate communication enhances patient safety [7]. Research shows that poor communication can contribute to medical errors while good communication can help to reduce their occurrence [7]. However, improving staff communication is not limited to just getting test results to the right person in a timely manner. Communication involves sharing information as a team about the patient's status and progress toward desired outcomes.

Use medicines safely.

- Before a procedure, label medicines that are not labeled, for example, medicines in syringes, cups and basins. Do this in the area where medicines and supplies are set up.
- Take extra care with patients who take medications to thin their blood.
- Record and pass along correct information about a patient's medicines. Find out what medicines the patient is taking. Compare those medicines to new medicines given to the patient. Make sure the patient knows which medicines to take when they are at home. Tell the patient it is important to bring their up-to-date list of medicines every time they visit a doctor.

Nursing consideration: In addition to complying with the preceding directives, nurses must ensure medication lists are reconciled each time a patient is transferred from or accepted from another healthcare facility or patient care area. Educate patients and families how to safely take their medications at home. Have them demonstrate safe self-medication practices. Do not ask them simple yes and no questions such as "Do you know what side effects your medication can cause?" Instead, ask them "Tell me what side effects your medicine can cause and what you should do if these happen." Be sure to assess their knowledge in a practical way.

Use alarms safely.

- Make improvements to ensure that alarms on medical equipment are heard and responded to on time.

This is a major addition to the 2016 NPSGs. It will be discussed in detail later in this program.

Prevent infection.

- Use the hand cleaning guidelines from the Centers for Disease Control and Prevention (CDC) or the World Health Organization (WHO). Set goals for improving hand cleaning, and use these goals to improve hand cleaning.
- Use proven guidelines to prevent infections that are difficult to treat.
- Use proven guidelines to prevent blood infection from central lines.
- Use proven guidelines to prevent infection after surgery.
- Use proven guidelines to prevent infections of the urinary tract that are caused by catheters.

EBP alert! Research shows that proper hand washing is the most effective way to prevent the spread of infections in hospitals [8]. Nurses have an obligation to share research findings that show that this and other infection control interventions really do help to prevent infection. Adults are more likely to apply knowledge in the work setting if they have evidence that specific interventions actually "work."

Identify patient safety risks.

- Find out which patients are likely to try to commit suicide.

Nursing consideration: The prevalence of mental illness makes it almost a certainty that nurses, no matter where they practice, will care for persons who are currently experiencing a mental illness. It is estimated that 25 percent of all adults in the United States will develop at least one mental illness during their lifetime [9]. Nurses must be aware of the signs and symptoms as well as information from the patient's personal and family history that indicate a patient is at risk for suicidal behavior.

Prevent mistakes in surgery.

- Make sure that the correct surgery is conducted on the correct patient, and at the correct location on the patient's body.
- Mark the correct place on the patient's body where the surgery is to be done.
- Pause before the surgery to make sure that a mistake is not being made.

Nursing consideration: It is essential that nurses be alert to the possibility of any potential errors in the surgical setting and act swiftly to prevent their occurrence.

2016 Home Care National Patient Safety Goals

This summary is taken directly from The Joint Commission's easy-to-read version [10].

Identify patients correctly.

- Use at least two ways to identify patients. For example, use the patient's name and date of birth. This ensures that each patient gets the correct medicine and treatment.

Use medicines safely.

- Record and pass along correct information about a patient's medicines. Find out what medicines the patient is taking. Compare those medicines to new medicines given to the patient. Make sure the patient knows which medicines to take when they are at home. Tell the patient it is important to bring their up-to-date list of medicines every time they visit a doctor.

Nursing consideration: Nurses should have patients or families demonstrate safe self-medication. It is not enough to simply give them information about their medications and ask "yes" or "no" questions such as, "Do you understand how to take your medicine?" Instead have them explain what side effects might occur and what to do about them, or have them actually demonstrate how to administer a specific medication.

Prevent infection.

- Use the hand cleaning guidelines from the Centers for Disease Control and Prevention (CDC) or the World Health Organization (WHO). Set goals for improving hand cleaning. Use these goals to improve hand washing.

Nursing consideration: Nurses must teach patients and friends appropriate hand washing techniques. This includes when and how to implement the techniques.

Prevent patients from falling.

- Find out which patients are most likely to fall. For example, is the patient taking any medicines that might make them weak, dizzy or sleepy? Take action to prevent falls for these patients.

Nursing consideration: Nurses must also be alert to other safety hazards or issues in the patient home that contribute to falls such as scatter rugs, highly polished floors, wet surfaces and mobility difficulties.

Identify patient safety risks.

- Find out if there are any risks for patients who receive oxygen. For example, are there fireplaces in the patient's home?

Nursing consideration: Nurses must teach patients and families how to avoid hazards associated with oxygen therapy. Increasing the awareness of contraindications when a family member is on oxygen therapy, such as smoking, must be communicated to persons visiting the home where oxygen is in use.

2016 Ambulatory Care National Patient Safety Goals

The following summary is taken from The Joint Commission's easy-to-read version [11].

The 2016 goals for ambulatory care are similar to those of hospitals and include:

- Identify patients correctly.
- Use medicines safely.
- Prevent infection(s).
- Prevention of mistakes in surgery.

Ben is an experienced cardiovascular care nurse. He is working on the "step-down" cardiac care unit, and has been one of the leaders on the unit for many years. A new nursing employee is touring the unit with the nursing director as part of her hospital orientation. She comments, "Isn't anyone worried about all of the alarms going off? Nobody seems to be concerned." Ben explains that, "Most alarms are actually false. You get to know what is 'real' and what isn't. For instance, we have one man whose alarm goes off all the time because he's a really restless sleeper." At that moment the code for cardiac arrest is heard coming from the room of the man who is a "restless" sleeper. His cardiac monitor alarm had been going off for several minutes. Unfortunately, the alarm had been ignored and now the patient is in cardiac arrest.

Alarm fatigue occurs when the daily number of alarm signals, such as bells, beeps, and tones from medical devices (especially physiological devices), overwhelms healthcare personnel with information. This can actually desensitize healthcare personnel to the alarms themselves. Nurses and other healthcare professionals may turn alarm volumes down in an effort to control noise levels. Turning down the volume may create an unsafe environment for the patient. After a period of time, clinicians may not respond to alarms simply because the alarms have become part of the "normal" background noise of a unit, and no longer trigger concern [12].

EBP alert! Research shows that 80 to 99 percent of alarms generated by devices such as ventilators, blood pressure monitors, and electrocardiograms are false and/or do not actually need any clinical intervention [13]. Clinicians are becoming desensitized to the sounds of alarms, and experiencing alarm fatigue. Nurses and other healthcare professionals must work with each other to make eliminating alarm fatigue a priority. This can be accomplished by avoiding unnecessary monitoring, and educating clinicians to the full potential of devices.

The extent to which alarm fatigue has adversely affected patients is not precisely known. The United States Food and Drug Administration's Manufacturer and User Facility Device Experience Database listed 566 alarm-related deaths between January 2005 and June 2010. This number is believed to under-represent the actual cases [12]. From 2009 to 2012, The Joint Commission reported 98 alarm-related events, 80 of which resulted in death, 13 resulted in permanent loss of function, and five resulted in unexpected additional care or extended stays. Since sentinel event reporting to The Joint Commission is voluntary, some experts believe that this number represents less than ten percent of such adverse occurrences [13].

Healthcare safety experts agree that alarm fatigue is becoming worse, and the consequences of this are perilous [4,12,13]. In June 2013, The Joint Commission approved a new NPSG on clinical alarm safety for hospitals and critical access hospitals. This goal was implemented in two phases. Phase one began on January 1, 2014 when hospitals were required to establish alarm safety as an organizational priority, and to identify the most important alarms to manage based on their internal situations. Phase two began on January 1, 2016 and hospitals are expected to develop and implement specific components of policies and procedures, and to educate staff in the organization of alarm system management [4].

The Joint Commission points out that "clinical alarm systems are intended to alert caregivers of potential patient problems, but if they are not properly managed, they can compromise patient safety" [14]. The Joint Commission also notes that the problem of alarm safety is multifaceted. Alarms may be difficult to detect. There may be numerous alarm signals that tend to desensitize staff and contribute to persons missing or even ignoring alarm sounds. Some staff members may even turn off alarms to decrease the amount of "noise" on a particular unit [14]. Desensitization to alarms may have serious or even fatal consequences for patients.

In addition to The Joint Commission, several organizations have compiled useful information about safely managing alarm systems. For example, the Advancement of Medical Instrumentation (AAMI) founded in 1967, is a nonprofit organization with a mission to develop, manage, and use safe and effective healthcare technology. On the organization's website, they are described as the primary source of national and international consensus standards for the medical device industry as well as a source of practical information, support, and guidance for healthcare technology and sterilization professionals [15]. More detailed information can be found at their website: http://www.aami.org/.

Another source of information is the ECRI Institute, an independent nonprofit organization whose mission is "to benefit patient care by promoting the highest standards of safety, quality, and cost-effectiveness in healthcare" [2]. The institute accomplishes its mission through research, publishing, education, and consultation. ECRI's goal is to "be the world's most trusted, independent organization providing healthcare information, research, publishing, education, and consultation to organizations and individuals in healthcare" [2].

The ECRI Institute compiles an annual top ten list of patient safety concerns based on its review of patient safety event reports, research requests, and root-cause analyses submitted to the ECRI Institute PSO. This is one of the first patient safety organizations (PSOs) to be federally certified under the provisions of the Patient Safety and Quality Improvement Act (PSQIA). The ECRI Institute's report is not simply a list. It recommends that healthcare organizations use the list of patient safety concerns as a starting point for their patient safety discussions and for establishing their patient safety priorities [2]. The ECRI Institute also provides some free safety resources on its website: https://www.ecri.org/Pages/default.aspx.

Since the ECRI Institute began publishing its list of top health technology hazards in 2007, "alarm hazards have been at or near the top of the list"[2]. Although the current Joint Commission emphasis is on alarm fatigue, the ECRI Institute is encouraging healthcare organizations to look beyond alarm fatigue, and investigate the incidence of alarms that do not activate when a patient is in distress. According to the senior project officer at the institute, alarm-related adverse events, whether due to missed alarms or unrecognized alarm conditions, can often be traced to alarm systems that were not configured appropriately. The ECRI Institute recommends that organizations examine their alarm configuration policies and procedures and ensure that they address the full range of factors that can lead to alarm hazards [2].

January 4, 2016: The Safety Council is meeting today, the first "regular" work day of the new year. Members of the council are reviewing their compliance with The Joint Commission's alarm safety goal. Compliance was to have been achieved on January 1, 2016. The Safety Council members are confident that the policies and procedures that have been in place since October 2015 adequately meet Joint Commission standards; however, they are not going to relax. Today, council members are going to review safety data, including adverse events reports, particularly those relating to alarm safety. They have also invited several staff nurses and therapists, who work daily on units that are sometimes bombarded by the constant "noise" of alarms, to attend the meeting. Members want to know how these healthcare professionals have been implementing policies and procedures, and what revision suggestions they may have to further enhance patient safety.

Nursing consideration: The preceding example of a fictional Safety Council demonstrates the importance of constantly reviewing actions undertaken to meet safety standards. It also emphasizes the importance of soliciting feedback from practitioners who work with these identified safety dilemmas every day.

Experts note, that in order to adequately address patient safety and clinical workflow, an overall plan must be developed to manage clinical interruptions. This plan must include [16]:

- Addressing alarms (e.g. physiological monitors).
- Responding to alerts (e.g. critical lab notification).
- Communicating with members of the healthcare team.

Nursing consideration: In order to effectively address the problem of alarm safety, nurses should also know what types of adverse events have occurred that are linked to problems with alarms.

What types of alarm-related adverse events have been reported? According to information from the U. S. Food and Drug Administration's Manufacturer and User Facility Device Experience database, falls, delays in treatment, ventilator use, and medication errors were causes of death or common injuries related to alarms [12]. Factors that contributed to these injuries or fatalities included [12]:

- Absent or inadequate alarm systems.
- Improper alarm settings.
- Alarm signals that were not audible in all areas.

Nursing consideration: Key recommendations from The Joint Commission and other safety experts regarding alarm safety include [12]:

- Establish a cross-disciplinary team to address the potential effect of alarm fatigue in all patient care areas.
- Create priorities for the adoption of alarm technology.
- Train clinical care teams on safe alarm management and response in high-risk areas and on the safe use of the devices.

Ronald Wyatt, MD, MHA, medical director of the division of healthcare improvement at The Joint Commission as of November 2015, suggests that healthcare organizations begin their alarm safety efforts by determining the baseline number of device alarms per day. They should then be able to answer the following questions [13]:

- How many alarms required a clinical intervention?
- How many alarms resulted in harm or death?
- What are the organization's current monitor alarm default parameters?
- How can we adjust alarms to indicate actionable alarms?

Nursing consideration: Nurses are all too well aware that many alarms do not actually indicate an actual patient problem or emergency. Some experts recommend that clinicians work with engineers and equipment manufacturers to customize the configuration of alarms and avoid the overlapping of redundant alarms. These changes must demonstrate a means for staff to quickly recognize alarms that need immediate attention. Additionally, some experts say that unnecessary patient monitoring results in excessive "nuisance alarms." Patients should be monitored only when it is clinically necessary. Alarms should be individualized for each patient to make the alarms most effective [13].

It is necessary for all healthcare organizations to have a documented and functional work plan to achieve the alarm National Patient Safety Goal [17], in addition to the specific requirements and explanations outlined in the 2016 Joint Commission National Patent Safety Goals [18]. The Joint Commission Sentinel Event Alert published on April 8, 2013 provides very helpful information to deal with the problem of alarms [19].

The Joint Commission Sentinel Event Alert of April 8, 2013 focuses on medical device alarm safety in hospitals. The Joint Commission's Sentinel Event database includes 98 alarm-related events (80 of which led to fatalities) reported from January 2009, to June 2012. The majority of events, 94 of 98, occurred in hospitals. The majority of the 94 events occurred in telemetry, intensive care, general medicine, and emergency department areas [19].

For the alarm-related events reported to The Joint Commission, major contributing factors included [19]:

- Absent or inadequate alarm system(s).
- Improper alarm settings.
- Alarm signals that were not audible in all areas.
- Alarm signals inappropriately turned off.

EBP alert! Research shows that the preceding factors have contributed to alarm-related problems. All nurses must be familiar with research findings related to this issue and be advocates for the reduction of alarm-related incidents [19].

Additional factors that contributed to alarm-related sentinel events have been identified by The Joint Commission. These include [19]:

- Alarm fatigue.
- Alarm settings that have not been customized to the individual patient or patient population.
- Inadequate staff training or education on the proper equipment use and functioning.
- Inadequate staffing to support or respond to alarm signals.
- Alarm conditions and settings that are not integrated with other medical devices.
- Equipment malfunction and failure.

EBP alert! Research shows that alarm fatigue is the most common contributing factor related to alarm-related sentinel events. Thus, all clinicians must take every possible action to resolve the problem of alarm fatigue [19].

So now we know the major factors that contribute to alarm-related adverse events. What do we do about them? The Joint Commission, the Association for the Advancement of Medical Instrumentation (AAMI), and ECRI Institute have compiled a number of recommendations for the reduction of patient harm related to alarm systems [2,19]:

- Organizational leadership must ensure that there is a process for safe alarm management and response in high-risk areas identified by the organization.
- Prepare an inventory of alarm-equipped medical devices used in high-risk areas and for high-risk clinical conditions. Identify the default alarm settings and the limits for such devices.
- Establish guidelines for alarm settings on alarm-equipped medical devices used in high-risk areas and for high-risk clinical conditions.

Alarm alert! When establishing such guidelines, include identification of situations when alarm signals are not clinically necessary [19].

- Establish guidelines for tailoring alarm settings, and limits for individual patients. These guidelines should address situations when limits can be modified to minimize alarm signals, and the extent to which alarms can be modified to minimize alarm signals.
- Inspect, check, and maintain alarm-equipped devices to provide accurate and appropriate alarm settings, proper operation, and detectability.

Alarm alert! The frequency of inspection, checking, and maintenance activities should be based on established criteria such as manufacturers' recommendations and risk levels [19].

- All members of the clinical care team should receive education and training on the organization's process for safe alarm management and response in high-risk areas, and on the safe use of the alarmed medical devices on which they rely.
- To help in the reduction of nuisance alarm signals, it is recommended that single-use sensors be changed according to manufacturer's recommendations, unless contraindicated.
- Assess the acoustics in the patient environments to determine if critical alarm signals are audible.
- Organizational leadership must re-establish priorities for the adoption of alarm technology. Note that the priority-setting process

should drive technology adoption rather than allowing technology to drive priority-setting.
- Establish a cross (interdisciplinary) team that includes representation from clinicians, clinical engineering, information technology, and risk management to address alarm safety and the potential impact of alarm fatigue in all patient care areas.
- Share information about alarm-related incidents with appropriate organizations such as The Joint Commission, the Food and Drug Administration, AAMI, and the ECRI Institute.

Nursing consideration: All staff nurses should be encouraged to contribute input to the development of safe alarm management. They must also be encouraged to seek membership on appropriate councils that address patient safety and quality.

Never ever events

What does the term "never ever event" mean? First introduced in 2001 by Ken Kizer, MD, former CEO of the National Quality Forum (NQF), the term "never ever event" is used to describe especially shocking medical errors (such as wrong-site surgery) that should never occur. The list of "never ever events" has grown over time to include adverse events that are unambiguous (clearly identifiable and measurable), serious (resulting in death or significant disability), and usually preventable [21].

The current list, revised in 2011, consists of 29 events, grouped into seven categories [21]:
- Surgical events.
- Product or device events.
- Patient protection events.
- Care management events.
- Environmental events.
- Radiologic events.
- Criminal events.

The "never ever" sentinel events most often reported to The Joint Commission are [21]:
- Wrong-site surgery (13.5 percent).
- Suicide (12 percent).
- Op/post-op complications (11 percent).
- Delay in treatment (8.3 percent).
- Medication error (8.2 percent).
- Patient fall (6.3 percent).

Surgical events

Carolyn is a young nurse who is about to begin her "dream job" as a surgical nurse in a prestigious operating theater at a major metropolitan medical center. She has had three years of experience as a staff nurse on a large post-operative surgical unit, and has recently completed her operating room orientation. Today she and her colleagues are dealing with a heavy caseload of outpatient surgeries. The next patient is scheduled to have a partial mastectomy of the right breast. Dr. Marlene Mason, the surgeon scheduled to perform the operation, has a reputation of being a bully and verbally abusive to the nurses working with her. One of Carolyn's colleagues whispers a warning to her, "Be alert today. This is Mason's fourth case today and she's in a horrible mood. One of her patients went downhill during surgery this morning and died soon after the surgery was completed." Dr. Mason enters the operating room and immediately begins complaining about the way the nurses have set up the room. She spots Carolyn and groans, "Don't tell me I have to deal with some new kid that doesn't know what she's doing. I need competent help in here! OK let's get this over with. It's a simple partial mastectomy of the left breast so even you should be able to deal with it." Carolyn is horrified and explains that the procedure is to be performed on the right, not the left, breast. The surgeon becomes agitated and accuses Carolyn of insubordination and orders her from the room. "Get out! Don't you think I know what I'm doing? It's the left breast!" She shoves Carolyn towards the exit as Carolyn's supervisor arrives. The supervisor clarifies that the surgery is to be performed on the right breast and tells the operating room team to take a time out until this situation is under control.

The preceding example is an example of a "never ever event" that is on the verge of occurring. Unfortunately, healthcare professionals are not strangers to circumstances that are out of control. The response to such circumstances is to ALWAYS act in the best interest of the patient. "Carolyn" acts appropriately in the best interest of the patient to avoid the tragic occurrence of a "never ever event."

Surgical "never ever events" include [21]:
- Surgery or other invasive procedure performed on the wrong body part.
- Surgery or other invasive procedure performed on the wrong patient.
- Wrong surgical or another invasive procedure performed on a patient.
- Unintended retention of a foreign object in a patient after a surgery or another procedure.
- Intra-operative or immediate postoperative/post-procedure death in an American Society of Anesthesiologists Class I patient.

Nursing consideration: All nurses, not just those who work in the surgical suite, must be aware of surgical "never ever events." All nurses contribute, to some extent, to the prevention of surgical "never ever events."

Fortunately, wrong-site, wrong-procedure, and wrong-patient surgery (WSPE) events are relatively rare. Research suggests that such errors occur once out of every 112,000 surgical procedures. To put this in perspective of individual hospitals, this statistic means that an individual hospital would only experience one such error every five to ten years. However, this estimate is based on procedures performed in the operating room. If procedures performed in other settings (such as ambulatory surgery centers) were included, the rate of such occurrences may be significantly higher [22].

The Joint Commission has developed a universal protocol for the prevention of WSPEs. The following is a summary of the critical factors of this protocol taken directly from the organization's website. For the complete protocol, access The Joint Commission website: https://www.jointcommission.org [23].

Conduct a pre-procedure verification process.
- Verify the correct procedure, for the correct patient, at the correct site.
- When possible, involve the patient in the verification process.
- Identify items that must be available for the procedure.
- Use a standardized list to verify the availability of items necessary for the procedure.
- Match the items that are to be available in the procedure area to the patient.

Mark the procedure site.
- For spinal procedures, mark the general spinal region on the skin. Special intraoperative imaging techniques may be used to locate and mark the exact vertebral level.
- Mark the site before the procedure is performed.
- If possible, involve the patient in the site marking process.
- The site is to be marked by a licensed independent practitioner who is ultimately accountable for the procedure and will be present when the procedure is performed.
- In limited circumstances, site marking may be delegated to some medical residents, physician assistants, or advanced practice registered nurses.
- Ultimately, the licensed independent practitioner is accountable for the procedure, even when delegating site marking.

- The mark must be unambiguous and used consistently throughout the organization.
- The mark is to be made at or near the procedure site.
- The mark should be sufficiently permanent to be visible after skin preparation and draping.
- Adhesive markers are not the sole means of marking the site.
- For patients who refuse site marking or when it is technically or anatomically impossible or impractical to mark the site, use your organization's written, alternative process to ensure that the correct site is operated on.

Perform a time-out.
Note that the procedure is not to start until all questions or concerns are resolved! Recall that a time-out was called in the sample scenario at the beginning of this section in order to resolve the conflicts that were occurring.

- Conduct a time-out immediately before starting an invasive procedure or making an incision.
- A designated team member starts the time-out.
- The time-out is to be standardized.
- The time-out involves the immediate members of the procedure team including the individual performing the procedure, the anesthesia providers, the circulating nurse, the operating room technician, and other active participants who will be participating in the procedure from the beginning.
- During the time-out, the team members must agree, at a minimum, on the correct patient identity, correct site, and the correct procedure to be conducted.
- When the same patient has two or more procedures, if the person performing the procedure changes, another time-out needs to be performed before starting each new procedure.
- Document the completion of the time-out. The amount and type of documentation is to be determined by the organization.

Surgical event alert! As of October 1, 2015 there were 92 wrong-patient/wrong-site/wrong-procedure errors reported to The Joint Commission for the 2015 calendar year [25].

Author's note: The remainder of the National Quality Forum's Healthcare "never ever events" are summarized in the following sections [21]. Because of, in part, their scope and number, generalized suggestions for achievement are provided.

Product or device events

A senior year nursing student is providing patient care to a woman who is on mechanical ventilation following a severe car wreck. The student notices that the safety inspection tag on the ventilator expired a few weeks ago. She also notices that her patient has developed a low-grade fever. Could there be some type of contamination of the ventilator? The student reports her findings to the staff nurse responsible for the patient who tells her, "Oh, it's not the ventilator. Bio-engineering is so busy that sometimes they can't check every single piece of equipment on time. It's only a couple of weeks late." Unfortunately, the patient's condition deteriorates, and it is determined that the ventilator was harboring bacteria that led to the patient developing pneumonia.

The preceding scenario is an example of a "never ever" that should have been prevented. According to the National Quality Forum's Health Care "Never Events," product or device events include [21]:

- Patient death or serious injury associated with the use of contaminated drugs, devices, or biologics provided by the healthcare setting.
- Patient death or serious injury associated with the use of or function of a device in patient care, in which the device is used for functions other than as intended.
- Patient death or serious injury associated with intravascular air embolism that occurs while being cared for in a healthcare setting.

Nursing consideration: Some suggestions for preventing the preceding never ever events include [21,24]:

- Remain alert to any drugs, devices, or biologics that have expired expiration or inspection dates, and take immediate action to remove/replace/check such items as appropriate.
- Monitor all equipment for any evidence of malfunction, and take immediate action to replace/repair such equipment.
- Monitor connections between catheter connections to prevent air embolism.

Patient protection events

Mr. Burns is 92 years old and is being discharged from the hospital today following treatment for pneumonia. He has had trouble understanding his discharge instructions. He also displays problems with short-term memory and the ability to perform self-hygiene. Mr. Burns is a widower and his only child, a daughter, lives nearly 700 miles away. Should Mr. Burns be discharged to his home? What obligations do his caregivers have to protect his safety after discharge?

This scenario is a good example of a potential patient protection event. Discharging Mr. Burns without further assessment of his ability to function safely at home, or an assessment of his home environment and resources would be negligent. His caregivers have an obligation to ensure his safety. Current assessment indicates Mr. Burns may be unable to make decisions and live safely in his home environment. Patient protection events are among the "never ever events" identified by the National Quality Forum. These include [21]:

- Discharge or release of a patient/resident of any age, who is unable to make decisions, to anyone other than an authorized person.
- Patient death or serious disability associated with patient elopement (disappearance).
- Patient suicide, attempted suicide, or self-harm resulting in serious disability, while being cared for in a health care facility.

Nursing consideration: Nurses must work collaboratively with all members of the healthcare team to develop and implement policies and procedures to ensure that patient protection events do not occur. These policies and procedures should include [21,24]:

- Assessment of a patient's ability to make decisions, including his/her ability to return to a safe environment after discharge.
- Implementing safeguards to avoid patient elopement from the healthcare setting.
- Assessment of a patient's mental health, including assessment for suicidal ideation. Such assessment should be conducted on all patients.

Care management events

The administrative team and members of the quality/risk management council are meeting under emergency circumstances. A patient has died as the result of a serious medication error. Some members of the council want to fire the nurse who made the error and "blame" the

entire tragic adverse event on her. Other council members point out that the error was not just one person's fault, but a combination of events resulting from a flawed medication administration process.

A true organizational culture of safety does not play the "blame game." An error is seldom the "fault" of one person. Persons who are interested in improving patient safety should look to improve the processes and systems that are the foundation of any healthcare organization functions.

"Never ever" care management events include [21]:

- Patient death or serious injury associated with a medication error.
- Patient death or serious injury associated with unsafe administration of blood products.
- Maternal death or serious injury associated with labor or delivery in a low-risk pregnancy while being cared for in a healthcare setting.
- Death or serious injury of a neonate associated with labor or delivery in a low-risk pregnancy.
- Artificial insemination with the wrong donor sperm or wrong egg.
- Patient death or serious injury associated with a fall while being cared for in a healthcare setting.
- Any stage 3, stage 4, or unstageable pressure ulcers acquired after admission/presentation to a healthcare facility.
- Patient death or serious disability resulting from the irretrievable loss of an irreplaceable biological specimen.
- Patient death or serious injury resulting from failure to follow up or communicate laboratory, pathology, and/or radiology test results.

Nursing consideration: The preceding care management "never ever" issues are broad in scope and numerous in number, and affect many aspects of patient care. Preventing these events includes following policies and procedures, improving patient/family education, assessing the effectiveness of patient/family education, ensuring excellent communication and collaboration among healthcare team members, and participating in continuing education and training to keep knowledge and skills current [2,21,24,26].

Environment events

Environmental "never events" include [21]:

- Patient death or serious injury associated with an electric shock while being cared for in a facility, excluding events involving planned treatments such as electric counter-shock.
- Any incident in which a line designated for oxygen or other gas to be delivered to a patient contains the wrong gas or is contaminated by toxic substances.
- Patient death or serious injury associated with a burn incurred from any source while being cared for in a facility.
- Patient death or serious injury associated with the use of or lack of restraints or bedrails while being cared for in a facility.

Nursing consideration: Prevention of environmental events involves teamwork among clinical and non-clinical staff members. If equipment is malfunctioning, it should be immediately removed from service, and the appropriate department notified for repair and/or replacement. If a piece of equipment has outdated safety check documentation, the appropriate department must be notified for repair and/or replacement. The use of any type of restraining device must strictly adhere to legal mandates and organizational policies and procedures [2,21,24,26].

Radiologic events

The specific factor identified in the radiologic event category is the introduction of a metallic object into the MRI area associated with the death or serious injury of a patient or staff member [21]. It is imperative that anyone working with a patient undergoing an MRI be alert to the introduction of any metallic objects in the MRI area. A checklist must be completed to assure patient eligibility for this procedure.

Criminal events

Criminal "never ever events" include [21]:

- Any incidence of care ordered by or provided by someone impersonating a physician, nurse, pharmacist, or other licensed healthcare provider.
- Abduction of a patient/resident of any age.
- Death or significant injury of a patient or staff member resulting from a physical assault that occurs in or on the grounds of a healthcare setting.

The leadership of all healthcare organizations must have policies and procedures in place to ensure that all persons working in or having privileges to work in a facility have the appropriate licenses and credentials to fulfill the roles for which they have been hired. Appropriate security must be in place to prevent patient/resident abduction and/or physical assault. Policies and procedures must also address what to do in the event of acts of (or threatened acts of) violence so that patients, visitors, and staff members are kept as safe as possible. Education and training should be provided regarding how to deal with violence in work settings [2,21,24,26].

Additional safety concerns identified by the ECRI Institute

As mentioned earlier, the ECRI Institute compiles an annual list of the top ten safety concerns for healthcare organizations. In 2015, the number one identified concern was alarm hazards, which has been discussed in detail. But what are the remaining nine concerns? A summary of the ECRI Institute's additional nine concerns follows. It is likely that these concerns are of importance to most, if not all, healthcare organizations.

1. **Data integrity: Incorrect or missing data in EHRs and other health IT systems.**
   Information technology (IT) can help to improve communication, provide swift access to essential data, and reduce errors for all members of the healthcare team. However, in order for IT to improve safety, a system must be in place to ensure that data in the electronic healthcare records (EHRs) are accurately and appropriately transferred to the various IT systems within an organization.

   According to the ECRI report, examples of data integrity failures include [2]:
   - Appearance of one patient's data in another patient's record.
   - Missing data or delayed data delivery.
   - Clock synchronization errors between medical devices and systems.
   - Default values used by mistake.
   - Fields pre-populated with erroneous data.
   - Inconsistencies in patient information when both paper and EMR are used.
   - Outdated information copied and pasted into a new report.

Nursing consideration: Nurses and their colleagues must remember to evaluate any IT issues that may and can contribute to an adverse event. Data entry is only as accurate as the person who is entering the information. The configuration of the IT system must also be evaluated. How easy is it to have multiple patient records open on a user's screen at one time? What, if any, are the identification checks to make sure that data is entered for the correct patient? How easy is it to cut and paste information? How can "old" or no longer accurate information be deleted from the active portion of a patient's record? These are just some of the questions that arise when reviewing the role IT may play in errors. Nurses must be vigilant in assisting in the evaluation of the IT process in their organizations and in the effectiveness of EHRs.

2. **Managing patient violence.**

EBP alert! Research shows that workers in healthcare and social assistance settings are five times more likely to be victims of nonfatal assaults or violent acts than average workers in all other occupations [27]. This makes managing workplace violence imperative, and a top priority in the healthcare setting.

A current review of the literature indicates that violence occurs in all healthcare settings, not just in the emergency department (ED) [2]. The ECRI Institute lists "Managing Patient Violence" as number three in their 2015 list of top ten patient safety concerns. The report suggests the following actions to help manage/prevent patient violence [2]:

- Acknowledge that the problem of violence is occurring in all healthcare organizations/facilities and is not limited to specific areas such as the ED.
- Provide all staff with training and education in de-escalation strategies, behavioral health, and management strategies when physical violence is threatened or actually occurring.
- Hire adequate security staff.
- Develop and implement a facility-wide safety plan that considers all levels of risk, from a single acute episode, to an active shooter, to a threat that requires evacuation of the facility.

3. **Mix-up of IV lines leading to misadministration of drugs and solutions.**
The risk of IV line mix-ups is more likely in critical care areas where multiple lines are often in place. However, the risk exists in all healthcare settings where patients or residents (e.g. long-term care residents) may need several types of medication [2].

The ECRI Institute recommends the following actions to prevent IV infusion-line confusion [2]:

- Trace all lines back to their origin before making connections.
- Develop and implement a policy and procedure for positioning different lines on different sides of the patient.
- Label each infusion line with the name of the drug or solution being infused.
- Do not force connections. If force is required, it should probably not be connected.

Nursing consideration: Since nurses are those who administer drugs or solutions via IV lines, this safety concern is especially critical to their practice. Incorporating ECRI Institute recommendations into applicable policies and procedures should help to avoid IV line mix-ups.

4. **Care coordination events related to medication reconciliation.**
The ECRI Institute has identified medication reconciliation as its fifth top ten patient safety concerns [2]. The prevention of medication errors is an ongoing healthcare concern, and medication reconciliation is of utmost importance.

The Agency for Healthcare Research and Quality has identified the following recommendations for accurate medication reconciliation [28]:

- Develop a single medication list that is shared by all disciplines for documenting the patient's current medications.
- Clearly define roles and responsibilities for each discipline involved in the medication reconciliation process.
- Standardize the medication reconciliation process throughout the organization.
- Simplify the medication reconciliation process as much as possible by eliminating unnecessary redundancies.
- Make the right thing to do the "easiest" thing to do within the parameters of normal legal practice.
- Develop effective prompts or reminders for consistent behaviors as they pertain to the medication reconciliation process.
- Educate patients, families, or other caregivers on the medication reconciliation process.
- Ensure that the medication reconciliation process meets all pertinent legal and regulatory requirements.

Nursing consideration: Note that medication reconciliation can be problematic upon admission to acute care or outpatient facilities unless the patient and/or family have kept accurate records of the patient's medications. It should be a top nursing priority to educate patient and family about the necessity of keeping thorough and accurate medication records. This includes not only prescription medications, but over-the-counter medications, vitamins, minerals, herbal preparations, and any other supplements being taken.

5. **Failure to conduct independent double checks independently.**
Failure to conduct truly independent double checks can, and does lead to errors. The ECRI Institute recommends the following recommendations to make sure that independent double checks are completed [2]:

- The second patient care provider who is performing the double check needs to look at all facets of the process including patient identity, indication and appropriateness, drug or blood type, dose, programmed infusion rate, and route.
- The second provider should not receive conclusions from the first provider. For example, suppose the first provider says to the second provider, "I get a dose of 5,000 units of heparin. What do you calculate?" The second provider already has a "clue" about what he or she thinks the answer should be. The second provider should calculate the dosage without hearing what the first provider calculated.
- Obtain staff buy-in for the independent double check process. Risk management and research findings regarding errors linked to the failure to adhere to independent double checks should be shared with clinical staff.
- Investigate systems processes and issues. The organization should be prudent when determining which processes require independent double checks.

6. **Opioid-related events.**

EBP alert! The use and prescription of opiates has increased dramatically in recent years. So has opioid misuse and abuse. In fact, in 2011, the number of ED visits related to opioid misuse and abuse were over 420,000. This is double the number of visits recorded in 2004. Therefore, nurses and other patient care providers must be alert to the likelihood of encountering patients who may be misusing or abusing opioids [2].

The ECRI Institute identified two issues of major concern regarding opioid prescriptions and the potential for opioid-related events. First, there is a concern that prescribers are ordering the same amount of hydromorphone as they would morphine, even though hydromorphone is about seven to

seven and one half times as potent as morphine. This can lead to overdose and dangerous adverse effects [2].

The second issue is that prescribers sometimes do not differentiate between patients who are opioid-tolerant (defined as patients who have been taking an opioid of a threshold dosage for at least one week) from those who are described as opioid-naïve (meaning patients who have not been taking an opioid of a threshold dosage for at least one week). Failure of prescribers to consider these two issues of major concern can lead to serious, even fatal consequences [2].

Nursing consideration: Research shows that patients may share their opioid medications with family members or friends. Research also shows that family members and friends may "help themselves" to such medications without the patient's knowledge or consent. It is imperative that nurses educate patients and families regarding the dangers of opioid misuse [2].

In order to reduce/avoid opioid-related events the ECRI Institute recommends that [2]:

- Prescribers participate in continuing education regarding safe opioid prescribing and the potential dangers of failing to adhere to safe-prescribing standards.
- All healthcare professionals should participate in continuing education regarding safe opioid prescribing as well as recognition of opioid use, misuse, and abuse, and strategies to intervene.
- Patients and families must be educated about opioid safety including how to properly store and dispose of opioids.
- Healthcare organizations must monitor their adverse events for evidence of opioid-related events, and take steps to prevent their occurrence.

7. **Inadequate reprocessing of endoscopes and surgical instruments.** Even though endoscopes and surgical instruments are extremely difficult to clean (requiring multiple steps to ensure cleanliness), healthcare organizations reprocess thousands of reusable surgical instruments and devices on a daily basis. Failure to thoroughly clean such devices may allow organisms to remain on the devices (i.e. "fomite"). Some organisms may not be affected by disinfection or even sterilization. Even if thorough cleaning is accomplished, organisms may grow if equipment is not thoroughly dried.2 In other words, reprocessing requires thorough cleaning, disinfection, sterilization (as appropriate), and drying.

   The Association for the Advancement of Medical Instrumentation (AAMI) suggests the following steps to improve the quality of medical device and surgical instrument reprocessing [29]:

   - Cleaning and disinfection/sterilization of reusable devices are separate but equally important actions that must be performed before each patient use according to manufacturer's written instructions for use of the device.
   - Follow the manufacturer's instructions for cleaning, disinfection, and/or sterilization of devices.
   - Create a multidisciplinary committee to review priorities and establish a plan for implementing them. Representatives should be sourced from the operating room, infection control, healthcare technology management endoscopy, risk management, quality improvement, safety, education, and materials management groups and teams.
   - Share "lessons learned" with other healthcare organizations and learn from other organizations as well.
   - Establish formal written procedures for reprocessing.
   - Know and implement the current standards, recommended practices, and manufacturer's written instructions for use.
   - Include central sterile processing in the act of purchasing decisions for medical devices.
   - Separate and standardize functions and locations. In other words, separate central service from reprocessing.
   - Train and educate staff regarding appropriate reprocessing.
   - Assess organizational compliance with standards and regulations. Examples of tools for assessment can be found at: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance.

8. **Inadequate patient handoffs related to patient transport.** Research shows that when a patient is transported within the healthcare facility to another clinical setting or between units within the facility, a risk for harm exists [2]. But transport does not pose the only danger as the change of shift report (also a form of "handoff"), if not performed correctly, also can endanger the patient [30].

   "Handoff" is defined as the process of transferring responsibility for patient care. "Sign-out" is the act of relaying information regarding the patient [30]. The risks involved with handoff and sign-out vary with the acuity of the patient. However, even so called "low-risk patients" are at risk if the processes of handoff and sign-out are not executed accurately.

   The Joint Commission requires that each patient handoff communication include a standardized interactive approach to promote safe transfers. The ECRI Institute's report on the 2015 top ten safety hazards identifies several recommendations to build a process that enhances safety and reduces risk during handoff and sign-out [2,30].

   - Include transport-related incidents (including handoff and sign-off information) as part of adverse event, and near-miss adverse event, reporting.
   - Identify units and areas that are most often involved in transport and safety hazards.
   - Establish criteria for determining the level of transport needed.
   - Ensure that the necessary equipment is available for transport and that responsibility has been assigned for maintenance of therapies, and troubleshooting of equipment problems during transport.
   - Determine the training, competency, and experience required of personnel performing the transport, and ensure that those personnel possess such training, competence, and experience.
   - Develop and implement tools, forms, and checklists that facilitate handoff communication among all team members.

9. **Medication errors related to pounds and kilograms.** Errors involving mix-ups between pounds and kilograms often occur in emergency departments, but can occur in any setting, including the home. These kinds of errors generally involve pediatric patients, whose small bodies often react quite adversely, even fatally, to an inaccurate mediation dose [2,31].

   Pediatric drug doses are weight-based, and the recommended doses are administered in relation to weight in kilograms. However, in many healthcare settings, children are weighed in pounds, and medication measurements must then be converted to kilograms. This conversion can be inaccurately calculated, thus leading to medication errors [31].

   The Emergency Nurses Association's (ENA) position statement in support of weighing pediatric patients only in kilograms includes the following information [31]:

   - Pediatric weights should be measured and documented in kilograms only.
   - Scales used to weigh pediatric patients should be configured to only record weights in kilograms.
   - Pediatric weights should be documented in a prominent place on the medical record.
   - Electronic medical records (EMR) should be standardized to allow only kilograms for pediatric weight entries.

- The actual weight of the pediatric patient should be considered to be part of the mandatory nursing assessment unless patients need resuscitation or emergent stabilization.
- For the pediatric patient needing resuscitation or emergent stabilization, there should be a standard method of estimating weight in kilograms.
- The pediatric patient's weight in kilograms must be included in an interdisciplinary or intradisciplinary patient handoff report.

Nursing consideration: Note that the weight in kilograms must be utilized as a function of all handoffs to facilitate safety, and decrease adverse effects related to handoffs and sign-outs.

The ECRI Institute offers these suggestions for reducing the risk of medication errors related to pounds and kilograms [2].

- Ensure that pediatric scales (calculated in kilograms) are readily available in all areas of the organization.
- Document and display weights only in kilograms in the electronic healthcare record (EHR).
- Integrate digital scales with the HER to eliminate or reduce the need for data entry.
- Use clinical decision support functions that compare recorded weights with expected weights.
- Purchase infusion pumps with dose error reduction components.
- Avoid storing any high-alert drugs or other medications that have the potential to cause patient harm if weight-based doses are miscalculated in clinical areas.

Hospital-acquired conditions

The phrase hospital-acquired condition (HAC) refers to conditions that patients acquire while receiving treatment for another condition in an acute care health setting [32]. On July 31, 2008, in the Inpatient Prospective Payment System (IPPS) Fiscal Year 2009 Final Rule, the Centers for Medicare and Medicaid Services (CMS) included ten categories of HACs that, if they occurred, were not reimbursable by Medicare [33].

These categories are, for most if not, all organizations, "never ever events" as well.

As of 2015, the list of categories has been expanded to 14 and include the following items [33]:

- Foreign object retained after surgery.
- Air embolism.
- Blood incompatibility.
- Stage III and IV pressure ulcers.
- Falls and trauma.
  - Fractures.
  - Dislocations.
  - Intracranial injuries.
  - Crushing injuries.
  - Burn(s).
  - Other injuries.
- Manifestations of poor glycemic control.
  - Diabetic ketoacidosis.
  - Non-ketotic hyperosmolar coma.
  - Hypoglycemic coma.
  - Secondary diabetes with ketoacidosis.
  - Secondary diabetes with hyperosmolarity.
- Catheter-associated urinary tract infection (CAUTI).
- Vascular catheter-associated infection.
- Surgical site infection, mediastinitis, following coronary artery bypass graft (CABG).
- Surgical site infection following bariatric surgery for obesity.
  - Laparoscopic gastric bypass.
  - Gastroenterostomy.
  - Laparoscopic gastric restrictive surgery.
- Surgical site infection following certain orthopedic procedures.
  - Spine.
  - Neck.
  - Shoulder.
  - Elbow.
- Surgical site infection following cardiac implantable electronic device (CIED).
- Deep vein thrombosis (DVT)/pulmonary embolism (PE) following certain orthopedic procedures.
  - Total knee replacement.
  - Hip replacement.
- Iatrogenic pneumothorax with venous catheterization.

Nursing consideration: Beginning in fiscal year 2015, the HAC reduction program mandated by the Affordable Care Act, requires the CMS to reduce hospital payments by one percent for hospitals that rank among the lowest-performing 25 percent in regards to HACs [32]. Thus, it is essential that all nurses be especially vigilant in preventing HACs. They must also appreciate where their organizations stand in regard to HAC performance.

It is important that nurses be familiar with policies and procedures established to prevent HACs in their organizations. This educational program provides information to support nurses in their efforts to reduce/prevent HAC occurrence.

Foreign object retained after surgery

The problem of surgical items accidentally left inside the body after surgery has existed since the beginning of the practice of surgery. The contemporary preferred term for this problem is Retained Surgical Items (RSI) rather than retained foreign bodies, or objects, or URFOs [35].

Nursing consideration: Retained objects are usually detected immediately after the procedure by X-ray, during routine follow-up medical visits, or from the patient's reports of pain or other forms of discomfort [34]. However, RSIs can be discovered hours to years after the initial operation [35]. Therefore, nurses must remain alert to the possibility of RSI and always ask patients about any history of surgical procedures during nursing assessment.

The most frequent retained surgical items are [34]:

- Soft goods, such as sponges and towels.
- Small miscellaneous items, including un-retrieved device components or fragments (such as broken parts of instruments), stapler components, parts of laparoscopic trocars, guidewires, catheters, and pieces of drains.
- Nails and other sharps.
- Instruments, most commonly malleable retractors.

Research shows that the retention of surgical items has significant monetary implications. The Pennsylvania Authority estimated that the average total cost of care related to the retention of such items is about $166,000, which includes legal defense, indemnity payments, and surgical costs not reimbursed by the CMS. Other studies estimate that the medical and liability costs are $200,000 or more per incident [34].

What are the most common root causes of RSIs reported to The Joint Commission? These causes are [34]:

- Absence of policies and procedures.
- Failure to comply with existing policies and procedures.
- Problems with hierarchy and intimidation.
- Communication failure with the physicians.
- Failure of staff members to communicate important patient information.
- Inadequate or incomplete staff education.

In the October 17, 2013 Sentinel Event Alert [34], The Joint Commission recommended a number of strategies to reduce RSIs and improve safety. A summary of some of the most essential information follows. For the complete report, access this online pdf: http://www.jointcommission.org/assets/1/6/SEA_51_URFOs_10_17_13_FINAL.pdf.

Establish effective processes and procedures.
- Establish a reliable and standardized counting system.
- Develop and implement effective evidence-based, organization-wide standardized policies and procedures for the prevention of RSIs.

Establish an effective counting procedure.
The Joint Commission directly recommends that a counting procedure should [34]:
- Be performed audibly and visibly by two persons engaged in the process. The surgical team should verbally acknowledge verification of the count.
- Include counts of items added to the surgical field throughout the surgery or procedure.
- Include counts of soft goods, needles/sharps, instruments, and small miscellaneous items. The team should document un-retrieved device fragments.
- Verify that counts printed on prepackaged sponges and instrument sets are correct. Handle any discrepancies according to the organization's policy.
- Be performed before the procedure begins in order to establish a baseline count; before the closure of a cavity within a cavity; before wound closure begins; at skin closure or end of procedure; and at the time of permanent relief of either the scrub person or the circulating registered nurse.
- Be applicable in all settings where invasive procedures are performed.
- Be reviewed periodically and revised as appropriate.

Establish effective wound opening and closing procedures.
Wound opening and closing procedures should include:
- Inspection of instruments for signs of breakage before and after use.
- Adherence to the organization's established counting procedure.
- Methodical wound exploration.
- Empowerment of any member of the operative team to call a "closing time-out" prior to the initial closing count to allow for an uninterrupted count.

Perform intra-operative radiographs.

Intra-operative radiographs should be performed:
- When the surgical count is incorrect [34].
- When the operative procedure is determined by the surgical team to be at high risk for retained surgical items.

Nursing consideration: If the counts remain unreconciled after initial radiologic examination, the surgical team should consider additional imaging or further wound exploration.

Effective communication.
Effective communication is essential. The Joint Commission recommends that an organization should institute team briefings and debriefings as a standard part of the surgical procedure. This allows any team member to express concerns regarding patient safety. Additionally, the surgeon should verbally verify the results of the counting procedure.

Appropriate documentation.
Document the results of counts of surgical items, instruments, or items intentionally left inside a patient (such as needle or device fragments deemed safer to remain than remove), and actions taken if count discrepancies occur.

Safe technology.
The Joint Commission suggests that organizations research the potential of using assistive technologies to supplement manual counting procedures and methodical wound exploration.

Air embolism

Intravascular air embolism is a preventable HAC that occurs when air enters the vascular system [36,37]. Air embolism is a serious, life-threatening event. It occurs when there is a direct connection between a source of air and the vascular system, and the pressure gradient allows the entry of this air into the bloodstream [37].

Common causes of air embolism include [36,38]:
- The entry of air through open intravenous (IV) and infusion systems. Examples include disconnection and open stop-cock.

EBP alert! Research shows that the amount of air that enters the vascular system is influenced by the patient's position, and the height of the vein in relation to the right side of the heart [36]. Thus, nurses must be aware of proper patient positioning at all times!

- Infusion lines that are not properly filled or completely vented.
- During parallel infusions where gravity and infusion pumps are connected together.
- Errors that occur during the performance of a pressure infusion.
- Air entering the intravascular system during surgical procedures that require the opening of the vascular system such as neurosurgical, vascular, gynecological, or orthopedic procedures.

The Pennsylvania Patient Safety Authority has published the following suggestions to prevent air embolism associated with central venous access devices (CVADs) [37].

During insertion [37]:
- Place the patient in Trendelenburg position with a downward tilt of 10 to 30 degrees during central line placement.
- Avoid CVAD insertion during patient inspiration. If the patient is able, ask him/her to hold his/her breath and perform a Valsalva maneuver.

After insertion [37]:
- Make sure that all catheters and connections are intact and secure.
- Occlude the catheter and/or the needle hub.
- Make sure that all self-sealing valves are functioning accurately.

Ensure proper care and maintenance of CVADs by: [36,37,62,63]
- Making sure that all lumens are capped and/or clamped.
- Using Luer-lock connections for needleless IV ports and self-sealing valves.
- Using infusion pumps with air-in-line sensors for all continuous infusions.
- Completely priming all infusion tubing, and expelling air from syringes before any injection or infusion.
- Using an air-eliminating filter on infusion tubing sets whenever necessary.
- Removing air from infusion bags when infusing fluids using inflatable pressure infusors.
- Fully priming contrast media injectors.
- Checking for air prior to each injection.
- Tracing lines and double-checking all connections.
- Taking all steps necessary to prevent misconnections.
- Inspecting the insertion site, catheter, and all connections regularly to assess for any breaks or openings that could allow air into the system.
- Ensuring the integrity of the central line dressing surrounding the insertion site.
- Using caution when moving or repositioning the patient to prevent pulling on the central line and compromising the integrity of the closed system.
- Teaching patients and/or families how to manage infusion therapy.

During removal of CVAD [37,62,63]:

- Place the patient in Trendelenburg position. If this is not possible the supine position may be used.
- Position the catheter exit site at a height that is lower than the height of the patient's heart.
- Cover the exit site with gauze. Apply gentle pressure while removing the catheter in a smooth, slow, and constant motion.
- Ask the patient to hold his/her breath and perform a Valsalva maneuver as the last portion of the catheter is removed. If the patient is unable to do this remove the CVAD during patient expiration.
- Place pressure on the site until hemostasis occurs. A time frame of one to five minutes is recommended.
- Apply a sterile occlusive dressing that remains in place for at least 24 hours. Change the dressing every 24 hours until the exit site has healed.
- Tell the patient to remain lying flat for 30 minutes after removal of the catheter.

Nursing consideration: For the latest information on central line devices and other infusion issues access:

- *The Infusion Nurses Society* at http://www.ins1.org/i4a/pages/index.cfm?pageid=1
- *The Association for Vascular Access* at http://www.avainfo.org/website/article.asp?id=280986

Blood incompatibility

It is 3PM, and the end of a particularly stressful eight-hour shift. Blood arrives from the blood bank for two patients: Mr. Robert Morino (who is Type A positive), and Mr. Roger Moran (who is Type A negative). Sandy, the RN responsible for the nursing care of both Mr. Morino and Mr. Moran is feeling stressed and anxious. It is snowing, and she wants to leave on time in order to be home before her young children arrive from their after-school activities. Without instituting the independent double check per hospital policy, Sandy begins administering the A positive blood to Mr. Moran, who quickly begins to have an adverse blood incompatibility reaction.

The preceding scenario is truly a disaster that was waiting to happen. What are some things that contributed to this adverse event?

- Sandy is anxious and stressed and not focused on her work.
- Sandy failed to institute the independent double check required by hospital policy.
- The two patients had similar first and last names.
- The two patients had similar (yet different!) blood types.

Blood incompatibility is preventable. What can nurses do to make sure that it does not occur? Let's start by reviewing what happens during an incompatibility reaction.

There are four types of blood [39,40,41]:

- Type A (red blood cells (RBCs) have A-antigen proteins attached to them).
- Type B (RBCs have B-antigen proteins attached to them).
- Type AB (RBCs have both A-antigen and B-antigen proteins attached to them).
- Type O (RBCs have neither A- nor B-antigens).

Blood is also classified by rhesus (Rh) factor. This is a specific RBC antigen in the blood. If this antigen is present, the blood type is Rh positive (e.g. such as in the case of Mr. Morino, who is A +). Absence of the antigen is classified as Rh negative.

Most occurrences of blood incompatibility are due to human error. During an incompatibility reaction, the patient's immune system reacts against the "wrong" blood. The patient's immune system produces antibodies against any blood antigens not present in his/her own blood. Such a reaction can have serious, even fatal, consequences [39,40,41].

EBP alert! Research shows that the most serious transfusion complications occur within the first 15 minutes before, and the 15 minutes after initiation of each unit of blood. Thus, nurses must be particularly alert for reactions during these time periods [42].

Here are some suggestions for nurses to implement in order to avoid blood incompatibility reactions [39,42,43]:

- Facilitate the establishment of an interdisciplinary transfusion committee. This committee should include a transfusion safety officer.
- Ensure that policies and procedures relating to blood transfusion are reviewed and updated on an ongoing basis.
- Review the prescriber blood product ordering process.
- Review the patient's consent for blood product transfusion and make sure that the right for refusal appears on the consent.
- Ensure that there is a process for monitoring, tracking, and trending all blood samples for type and cross, type and hold, wrong blood in tube, mislabeled tubes, and issued blood components from the blood bank.
- Transfuse the patient within 30 minutes of blood product pick-up from the blood bank.
- Always confirm the identity of the patient using two identifiers.
- Institute independent double check per hospital policy.
- Double check the blood type of patients and the blood packs before each transfusion.
- Double check that all information (full patient name, address, blood type, etc.) on the label of the blood product matches the patient's information. Note that this means that the nurse MUST know the patient's blood type and other relevant information.
- Double check the blood product's label for expiration dates.
- Implement a bar code patient identification system as appropriate.

Stage III and stage IV pressure ulcers

In addition to the physical and emotional toll on patients, stage III and stage IV pressure ulcers carry a significant monetary burden as well. It is estimated that the cost of one stage III or stage IV pressure ulcer may be between $5,000 and $50,000 [44].

How are stage III and stage IV pressure ulcers described? Here are their determining characteristics [45]:

- Category/stage III: Full thickness tissue loss, although subcutaneous fat may be seen. Bone, tendon, or muscles are not exposed. Sloughing may be present, but it does not obscure the depth of tissue loss. There may be undermining and tunneling.
  - The depth of this pressure ulcer depends on the anatomical location. For example, the bridge of the nose or the ear does not have (adipose) subcutaneous tissue and stage III ulcers in such locations can be shallow. However, in areas where there is significant adipose tissue, ulcers can be exceptionally deep. Bone and/or tendon are neither seen nor are directly palpable.
- Category/stage IV: Full thickness tissue loss where bone, tendon, and/or muscle are exposed. Sloughing or eschars may be present, often with undermining and tunneling.
  - The depth varies according to anatomical position. Ulcers may be shallow in areas that do not have (adipose) subcutaneous tissue (e.g. nose, ear). These types of pressure ulcers can extend into muscle and/or supporting structures such as fascia, tendon, or joint capsules, thus making osteomyelitis possible. Exposed bone or muscle is visible and/or directly palpable.

Which patients are at risk for the development of pressure ulcers? Here are some factors that increase such risk. These are divided into

three primary areas including mobility/activity, perfusion (including diabetes), and skin/pressure ulcer status [44,46].

- Advanced age: The elderly person's skin has less subcutaneous fat, which leads to decreased protection from pressure.
- Friction/shear: Decreases the epidermal layer, reducing protection of the skin.
- Hypotension: Decreases the perfusion of local tissues, making skin more vulnerable to breakdown.
- Immobility: Lack of mobility can lead to sustained pressure on bony prominences.
- Length of stay in critical care units: The longer the length of stay is indicative of critical conditions associated with decreased mobility and/or position change, and increased shear force, all of which increase the risk for skin breakdown.
- Length of time on mechanical ventilation: Indicates inadequate oxygenation and the need to provide ventilation mechanically. Decreased oxygen levels means decreased oxygen to body tissues, including the skin.
- Moisture: Moisture (e.g. incontinence, sweat, failure to dry skin after bathing) contributes to skin breakdown, and in many cases, poor wound healing.
- Nutrition: Inadequate nutrition and decreased protein intake alters the proper state of the skin, contributing to skin breakdown.
- Pressure: The longer pressure is sustained, the more likely local tissue ischemia, edema, and tissue death occurs.
- Pressure scale risk scores: The higher the score on a pressure scale score, the greater the risk of pressure ulcer development.
- Vasoactive medications: Vasoactive medications, given to improve blood pressure, increase vasoconstriction, thus decreasing the perfusion of skin tissue.

Nursing measures to decrease the risk for pressure ulcer development include [44,46]:

- Performing skin assessment upon admission and at least once per shift thereafter. Skin inspection should be conducted more often on patients at high risk for pressure ulcer development. Document the results of all skin assessments.
- Identify patients at high risk for pressure ulcer development using a risk-identification scale.
- Incorporate results of skin assessment in change-of-shift reports and at any handoffs and sign-offs.
- Incorporate a schedule of turning and body repositioning, and document these actions.

EBP alert! Research shows that shearing forces can be reduced by keeping the head of the bed no higher than 30 degrees [44,46].

- Use appropriate positioning devices according to hospital policy and procedure.
- Keep skin warm and dry. Dry thoroughly after bathing. Remove skin secretions such as sweat and barrier creams. Use non-irritating, non-drying cleansing agents. Use moisturizers as appropriate. Keep bed sheets, clothing, etc., dry and wrinkle free.
- Take measures to avoid spasticity and contracture prevention.
- Ensure proper nutritional intake, especially protein.
- Promote mobility and self-position changes as appropriate.
- Remain alert to any skin changes (such as redness) that may suggest impending skin breakdown.

Falls and trauma

Patient falls with serious injury are among the top ten sentinel events reported to The Joint Commission Sentinel Even Database. Since 2009, The Joint Commission has received 465 reports of patient falls with injuries. About 65 percent of those falls caused fatalities [47].

The Joint Commission reports that from January 2009 to October 2014, the most common contributing factors contributing to reported falls included [47]:

- Communication failures.
- Deficiencies in the physical environment.
- Failure to adhere to protocols and safety practices.
- Inadequate assessment.
- Inadequate staff orientation, supervision, staffing levels, or skills.
- Lack of leadership.

EBP alert! Research shows that major factors to reduce falls and other adverse events are effective communication and interdisciplinary work [48]. Thus, nurses must work with their interdisciplinary colleagues to reduce/prevent falls.

Suggestions for fall prevention include the following nursing interventions [47,48]:

- Establish an interdisciplinary fall team with representatives from all disciplines.
- Develop and implement policies and procedures to enhance safety and prevent falls.
- Implement a fall risk screening assessment. Assess patients on admission, and periodically throughout hospitalization.
- Determine if patient medications may cause dizziness, coordination problems, or other issues that may contribute to falls.
- Initiate fall prevention interventions such as providing the patients with no-slip socks, teaching them about the use of (and supervising the use of) mobility assistive devices, and making sure that the call bell is within reach, and that patients know how to use it.
- Create a culture of safety in which systems and process issues are evaluated as the primary causes of adverse effects, and in which open communication is supported.
- Initiate rounds at least hourly to evaluate the safety of the patients and their environments.

Nursing consideration: If and when a fall does occur, a post-fall huddle should be conducted. This is done to evaluate: what risk factors for the fall existed: the circumstances surrounding the fall: and what measures should be taken to prevent future falls, including the review and revision of existing policies and procedures. Such a huddle is not conducted to cast blame, but to improve the culture of safety within the organization.

Manifestations of poor glycemic control

Nurses are essential to managing glycemic control for hospitalized patients. They perform and act on the results of blood glucose monitoring and medication administration. They also provide much of the patient/family education pertaining to glycemic management [49].

Research indicates that there are several factors that increase the risk of poor glycemic control in hospitalized patients. These include [49]:

- Insufficient nurse staffing.
- Nursing staff with excessive workloads.
- Lack of effective and timely communication.
- Teaching hospitals in which inexperienced resident physicians may be providing care for complex, critically ill patients.

EBP alert! Low nurse staffing undermines the culture of safety critical to the provision of safe and appropriate patient care. The organization's nurse leaders must evaluate staffing in terms of a culture of safety [49].

Suggestions for ensuring proper glycemic control include [49,50]:

- Establishing a system of interdisciplinary collaboration and open communication.
- Providing continuing education for nurses and physicians regarding glycemic control.
- Providing adequate patient/family education regarding glycemic control.
- Establishing policies and procedures that effectively guide glycemic control.
- Monitoring blood glucose levels according to hospital policies and procedures, and intervening appropriately.
- Establishing an adequate system of nurse staffing to ensure adequate patient coverage.
- Ensuring that equipment used for blood glucose monitoring is in good working order and that all nurses know how to use such equipment.

Catheter-associated urinary tract infections

Clara is a junior nursing student. She is taking care of a patient who has had an indwelling urinary catheter for three days. Clara is concerned about the possibility of infection, and asks the staff nurse responsible for the patient when it would be removed. The staff nurse is extremely busy and tells the student not to worry about a catheter when there are more urgent matters to attend to. Clara knows that hospital policy is that the catheter should be removed as soon as possible. She decides to talk to her instructor, and the resident physician when he sees the patient that morning. Are Clara's concerns valid? Are her actions appropriate?

The answer to both questions is "yes." Clara knows, as should all nurses, that hospital acquired catheter-associated urinary tract infections (CAUTIs) are a serious problem.

A catheter-associated urinary tract infection (CAUTI) is considered to be a preventable complication by the Centers for Medicare and Medicaid Services and thus no additional payment is provided to hospitals for costs associated with CAUTIs. Unfortunately, CAUTIs are still the most common nosocomial infection. They account for up to 40 percent of infections reported by acute care hospitals. Such infections increases hospital costs and is linked to an increase in morbidity and mortality [51].

EBP alert! Research shows that [52]:

- 70 to 80 percent of CAUTIs are due to the presence of an indwelling urethral catheter.
- 12 to 16 percent of adult hospitalized patients will have a urinary catheter at some time during hospitalization.
- When an indwelling urethral catheter remains in place the daily risk of acquiring bacteria in the urinary tract varies from three to seven percent.

Nurses must do everything possible to find alternatives to insertion of indwelling catheters., If such catheterizations cannot be avoided, removal of indwelling catheters must be performed as soon as possible.

Additional research findings show that [51]:

- The major risk factor for CAUTIs is prolonged catheterization.
- 25 percent of hospital in-patients, and up to 90 percent of patients in a critical care unit have a urinary catheter at some point during hospitalization. Unfortunately, such catheters are often inserted without an appropriate indication or remain in place after the need is no longer present.
- Most hospitals do not have effective strategies for preventing CAUTIs.

Experts recommend the following actions to prevent CAUTIs [51,52]:

- Establish policies and procedures which include: indications for indwelling urinary catheterization, insertion guidelines, and limitation of insertion to those patients who meet criteria for use.
- All healthcare team members must document the indication for indwelling catheter placement upon admission, and daily. If the patient is admitted with a CAUTI, this must also be documented.
- Be sure that only trained, competent personnel insert urinary catheters. Provide education and training as needed.
- Ensure that supplies and equipment necessary for aseptic catheterization technique are readily available.
- Review the necessity of continuing indwelling catheters on a daily basis. Such catheters should be removed as soon as possible.
- Implement infection control surveillance programs which include the: development of any CAUTIs; and the development of appropriate action plans to reduce/prevent CAUTI occurrence.

Nursing consideration: Nurses should ensure that indwelling catheters are properly secured to prevent movement and urethral traction. They must also ensure that a sterile, continuously closed drainage system is maintained [52].

Vascular catheter-associated infection

More than five million patients require central venous access every year, and infection is the main complication of intravascular catheters in patients who are critically ill [53]. Every year, an estimated 250,000 cases of central venous catheter-associated blood stream infections occur in the United States. The cost per infection is an estimated $34,508-$56,000 [54]. Nurses and their interdisciplinary colleagues must make every effort to prevent such infections.

The following interventions are important to the prevention of vascular catheter-associated infections:

Hand hygiene.

Proper hand hygiene is the most important infection control measure and the most effective way to prevent the transmission of healthcare associated infections [54,55].

Nursing consideration: Patients and families should be taught to observe if healthcare workers are washing their hands before and after providing patient care. They should be told to ask their healthcare providers to wash their hands if they have not done so.

The Centers for Disease Control and Prevention (CDC) and the Institute for Healthcare Improvement (IHI) both advocate that hand hygiene be performed "before and after palpating the catheter insertion site; before and after inserting, replacing, accessing, repairing or dressing a venous access device; before donning and after removing gloves; when hands are visibly soiled or contaminated; before and after invasive procedures; and after using the bathroom. Palpation of the insertion site should not be performed after the application of skin antiseptics, unless aseptic technique is maintained" [54].

Maximum sterile barrier precautions.

Maximum sterile barrier precautions must be taken when inserting the venous catheter. These precautions include not only the person inserting the catheter, but anyone assisting with the procedure, and the patient as well [53,54].

Skin antisepsis.

The IHI advocates the use of chlorhexidine skin antisepsis. The CDC prefers the use of a two percent chlorhexidine solution but a tincture of iodine or 70 percent alcohol can be used [54]. Skin antisepsis should be performed at the time of insertion and with every dressing change [54,55].

Selection of catheter site.
The site of insertion is important to optimal outcomes. The use of the subclavian site is preferred to the jugular or femoral sites in adults to minimize infection risk [54,55].

Dressing change.
Dressings for insertion sites must be impermeable to water vapor. Use of sterile gauze, a sterile transparent, semipermeable dressing, or a chlorhexidine-impregnated sponge dressing that covers the catheter insertion site should be initiated. Topical antibiotic ointments or creams should not be applied to the insertion site because of the possibility of promoting fungal infections or pathogen resistance. Dressings are changed when they become wet, loose, or soiled. CVAD dressing are generally changed weekly for a transparent semipermeable dressing, and every 48 hours for a gauze dressing [54].

Assessment and removal.
The catheter should be removed as soon as it is no longer indicated. The risk for infection increases with the length of time the device is left in place, and decreases when the catheter is removed [54].

EBP alert! The risk for infection has declined with the standardization of aseptic care and the requirement that insertion and maintenance of catheters be performed by experienced staff members. Education of staff in the insertion and maintenance of intravascular catheters is required, and staff competency must be periodically evaluated. Nurses must demonstrate competency in the care of patients with vascular catheters [54,55].

Surgical site infections

The prevention of surgical site infections is imperative. In the operating room setting, breaks in sterility, and a failure to follow established protocols for infection control put the patients at risk for surgical site infections [56].

Some strategies to prevent surgical site infections include the following interventions [56,57]:

- Healthcare providers must cleanse their hands and arms up to their elbows with an antiseptic agent just prior to surgery.
- Healthcare providers must cleanse their hands with soap and water or an alcohol-based hand cleanser before and after caring for each patient.
- If hair needs to be removed from the surgical site, an electric clipper must be used. A razor should NOT be used.
- Patients and families should be educated to not touch the surgical wound or dressings.
- Healthcare providers caring for patients after surgery should adhere to strict hand hygiene standards. They should also change dressings according established policies and procedures.

Nursing consideration: As stated earlier in this education program hand hygiene is the most effective way to prevent infections. Nurses must help to ensure that all colleagues and visitors adhere to hand hygiene protocol.

Deep vein thrombosis

Deep vein thrombosis (DVT) affects about 350,000 Americans every year [59]. In the hospital setting DVT is listed as a preventable HAC.

Nurses and other healthcare providers must first be aware of factors that place patients at higher risk for the development of DVT. These include [58]:

- Using birth control pills or hormone therapy.
- Having blood clotting disorders.
- Some malignancies.
- Increasing age.
- Being overweight or obese.
- Immobility.
- Personal or family history of DVT or pulmonary embolism.
- Pregnancy.
- Smoking.
- Having vein disease(s).

Strategies for the prevention of DVT include [58,59]:

- Administrating anticoagulant therapy as indicated.
- Promoting early movement and mobilization.
- Facilitating position change in patients who have difficulty moving themselves.
- Applying compression stockings or pneumatic compression devices as ordered and indicated.
- Teaching patients and families about the importance of early movement and position change.

Nursing consideration: Most of the interventions to prevent DVT are easily implemented. However, busy nurses and other healthcare professionals may forget to implement tasks as simple as position change or teaching patients the importance of early movement and position changes. They must remain alert to the possibility of DVT development and how to prevent it!

Iatrogenic pneumothorax with venous catheterization

A pneumothorax is a collapsed lung, and the result of air leaking into the space between the lungs and the chest wall. In most cases of pneumothorax, only a portion of the lung collapses [60].

Pneumothorax can be due to [60,61]:

- Chest injuries.
- Underlying lung diseases.
- Ruptured lung air blisters.
- Mechanical ventilation.
- Certain invasive procedures, such as venous catheterization.

Certain risk factors for pneumothorax include [60]:

- Age: Pneumothorax due to ruptured air blisters is most likely to occur in patients between 20 and 40 years of age.
- Gender: Men are more likely to have a pneumothorax than women.
- Genetics: Some types of pneumothorax seem to run in families.
- History of pneumothorax: A previous pneumothorax event predisposes an individual to experience another pneumothorax.
- Lung disease: Patients with underlying lung disease, particularly chronic obstructive pulmonary disease (COPD) are more likely to suffer a pneumothorax.
- Mechanical ventilation: Patients requiring mechanical ventilation are at higher risk for pneumothorax.
- Smoking: The risk increases with the number of cigarettes smoked as well as the length of time the patient has been smoking.

Iatrogenic pneumothorax (iatrogenic means something that is accidentally caused during medical treatment or procedure) has been identified as a preventable HAC. Thus, it is important to be able to identify appropriate steps to take to prevent such occurrence during venous catheterization. Such steps include [61]:

- Identifying patients at higher risk for pneumothorax during catheterization and being especially alert for problems.
- Ensuring the use of a standardized method of venous catheter insertion according to established policies and procedures.

- Ensuring that insertion is performed by physicians who have adequate experience in catheter insertion.
- Using ultrasound during catheterization to guide catheterization.
- Using ultrasound, chest radiography, and CT scanning for early recognition of pneumothorax.

Nursing consideration: In the event of a pneumothorax during the procedure, a standardized treatment algorithm for management of pneumothorax has been shown to improve outcomes and decrease the length of hospitalization. Nurses must work with the healthcare team to develop such an algorithm and be familiar with the interventions identified in the algorithm [61].

In summary

Nurses must be familiar with HACs identified as preventable by the CMS and by organizations that emphasize safety and appropriateness of care. There are currently (as of this writing) 14 categories of HACs identified by the CMS. However, there may be additional categories identified in the future. There may also be additions to other "never-ever events" and these will most likely be revisions and additions to The Joint Commission National Patient Safety Goals.

Nurses have a professional responsibility and moral obligation to keep themselves informed about current and future safety issues such as National Patient Safety Goals, "never-ever events," and CMS identified preventable HACs. Thanks to modern technology, nurses can access such information on relevant internet websites such as the CMS and The Joint Commission websites.

Nurses also have a professional obligation to become involved in how their employing organizations address safety issues. They should volunteer for committees and task forces and act as patient advocates at all times.

Nurses must support their organization's efforts to enhance safety and well-being of patients, visitors, and employees. In addition to adhering to safety mandates, they should help teach their colleagues how to establish and maintain a culture of safety. All employees are responsible for patient safety. Nurses are on the front-line of all safety initiatives and should act as leaders in the safety process.

References

1. Hospital Safety Score. (2013). Hospital errors are the third leading cause of death in U.S., and new hospital safety scores show improvements are too slow. Retrieved November 7, 2015 from http://www.hospitalsafetyscore.org/newsroom/display/hospitalerrors-thirdleading-causeofdeathinus-improvementstooslow.
2. ECRI Institute. (2015). Top ten patient safety concerns for healthcare organizations. Retrieved October 28, 2015 from http:////C:/Users/Adrianne/Downloads/2015_Patient_Safety_Top10.pdf.
3. Patient Safety Network. (2014). National patient safety goals. Retrieved October 28, 2015 from https://psnet.ahrq.gov/resources/resource/2230/national-patient-safety-goals.
4. The Joint Commission (2015). Facts about the National Patient Safety Goals. Retrieved October 28, 2015 from https://www.ghresources.com/wp-content/uploads/2014/08/2014-NPSG-Reference-Material.pdf.
5. The Joint Commission (2015). Facts about the Patient Safety Advisory Group. Retrieved November 6, 2015 from http://www.jointcommission.org/facts_about_the_patient_safety_advisory_group/.
6. The Joint Commission (2015). 2016 Hospital Patient Safety Goals. Retrieved November 7, 2015 from http://www.jointcommission.org/assets/1/6/2016_NPSG_HAP_ER.pdf.
7. Nursezone.com. (2010). Nurses, communication and patient safety. Retrieved November 9, 2015 from http://www.nursezone.com/Nursing-News-Events/more-news/Nurses-Communication-and-Patient-Safety_34498.aspx.
8. Medline Plus. (2015). Infection control. Retrieved November 10, 2015 from https://www.nlm.nih.gov/medlineplus/infectioncontrol.html.
9. Centers Diseases Control and Prevention (CDC). (2011). CDC report: Mental illness surveillance among adults in the United States. Retrieved December 30, 2011 from http://www.cdc.gov/mentalhealthsurveillance/fact_sheet.html.
10. The Joint Commission (2015). Home care National Patient Safety Goals. Retrieved November 7, 2015 from http://www.jointcommission.org/assets/1/6/2016_NPSG_OME_ER.pdf.
11. The Joint Commission (2015). Ambulatory Care National Patient Safety Goals. Retrieved November 6, 2015 from http://www.jointcommission.org/assets/1/6/2016_NPSG_AHC_ER.pdf.
12. Pevtzow, L. (2013). New guidelines to reduce alarm fatigue. Retrieved November 11, 2015 from http://www.medscape.com/viewarticle/782597.
13. Appold, K. (2015). Noise complaint. The Hospitalist, 19(6), 20-22. Retrieved November 11, 2015 from http://www.medscape.com/viewarticle/846298.
14. The Joint Commission (2015). 2016 Hospital National Patient Safety Goals. Retrieved November 14, 2015 from http://www.jointcommission.org/assets/1/6/2016_NPSG_HAP.pdf.
15. Advancement of Medical Instrumentation (AAMI). (2015). About AAMI. Retrieved November 14, 2015 from http://www.aami.org/membershipcommunity/content.aspx?ItemNumber=1292&navItemNumber=1342&navItemNumber=2399.
16. Extension Health Care. (2015). The countdown is on: Complying with The Joint Commission alarm safety goal. Retrieved October 28, 2015 from http://www.extensionhealthcare.com/2015/07/countdown-complying-joint-commission-alarm-safety-goal//.
17. Hyman, W. A. (2014). A work plan for The Joint Commission Alarm National Patient Safety Goal. Journal of Clinical Engineering, 39(1), 23-27.
18. The Joint Commission (2015). 2016 National Patient Safety Goals. Retrieved November 15, 2015 from http://www.jointcommission.org/standards_information/npsgs.aspx.
19. The Joint Commission (2015). The Joint Commission Sentinel Event Alert. Issue 50, April 8, 2013. Retrieved November 14, 2015 from http://www.jointcommission.org/assets/1/18/SEA_50_alarms_4_5_13_FINAL1.PDF.
20. Patient Safety Network. (PSNET). (2014). Never events. Retrieved October 28, 2015 from https://psnet.ahrq.gov/primers/primer/3.
21. Patient Safety network (PSNET). (2015). Wrong-site, wrong-procedure, and wrong-patient surgery. Retrieved November 15, 2015 from https://psnet.ahrq.gov/primers/primer/18/wrong-site-wrong-procedure-and-wrong-patient-surgery.
22. The Joint Commission (no date given). The universal protocol for preventing wrong site, wrong procedure, and wrong person surgery. Retrieved November 16, 2015 from http://www.jointcommission.org/assets/1/18/UP_Poster1.PDF.
23. Minnesota Department of Health. (2013). Minnesota's 29 reportable adverse health events. Retrieved November 17, 2015 from http://www.health.state.mn.us/patientsafety/ae/adverse27events.html.
24. HCPro. (2015). Joint Commission: Procedure errors, retention of foreign body, suicide top sentinel event list. Accrditation Insider, November 16, 2015 Retrieved November 17, 2015 from http://www.hcpro.com/ACC-322803-4634/Joint-Commission-Procedure-errors-retention-of-foreign-body-suicide-top-sentinel-event-list.html.
25. McKeon, L. (2011). Preventing never events: What frontline nurses need to know. Nursing made Incredibly Easy, 9(1), 44-45. Retrieved November 18, 2015 from http://journals.lww.com/nursingmadeincrediblyeasy/Fulltext/2011/01000/Preventing_never_events__What_frontline_nurses.10.aspx.
26. Hospitals & Health Networks. (2015). Addressing violence in the health care workplace. Retrieved November 18, 2015 from http://www.hhnmag.com/articles/3365-addressing-violence-in-the-health-care-workplace.
27. Agency for Healthcare Research and Quality (AHRQ). (2012). Medications and clinical handoffs (MATCH) toolkit for medication reconciliation. Retrieved November 18, 2015 from http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/match/match3.html.
28. Pyrek, K. M. (2013). Improper reprocessing targeted as one of healthcare's most dangerous hazards. Retrieved November 19, 2015 from http://www.infectioncontroltoday.com/articles/2013/05/improper-reprocessing-targeted-as-one-of-healthcares-most-dangerous-hazards.aspx.
29. Patient Safety Network (PSNet). Handoffs and signouts. Retrieved November 27, 2015 from https://psnet.ahrq.gov/primers/primer/9/handoffs-and-signouts.
30. Sitko, E. R. (2013). Leading medication safety groups endorse position on weighing pediatric patients in kilograms. Retrieved November 30, 2015 from http://nurse-practitioners-and-physician-assistants.advanceweb.com/Features/Articles/Avoiding-Medication-Errors.aspx.
31. Lake Superior Quality Innovation Network. (2015). Understanding the hospital-acquired condition reduction program. Retrieved November 30, 2015 from https://www.stratishealth.org/documents/HAC_fact_sheet.pdf.
32. CMS.gov. (2015). Hospital-acquired conditions. Retrieved November 1, 2015 from https://www.cms.gov/medicare/medicare-fee-for-service-payment/hospitalacqcond/hospital-acquired_conditions.html.
33. The Joint Commission Sentinel Event Alert. (2013). Preventing unintended retained foreign objects. Retrieved November 30, 2015 from http://www.jointcommission.org/assets/1/6/SEA_51_URFOs_10_17_13_FINAL.pdf.
34. Nothing Left Behind. (2015). Retained surgical items. Retrieved November 30, 2015 from http://www.nothingleftbehind.org/.
35. [36] Safeinfustiontherapy.com. (2015). Causes of air embolism. Retrieved December 2, 2015 from http://www.safeinfusiontherapy.com/cps/rde/xchg/hc-safeinfusion-en-int/hs.xsl/7701.html
36. [37] Pennsylvania Patient Safety Authority. (2012). Reducing risk of air embolism associated with central venous access devices. Retrieved December 2, 2015 from http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2012/Jun;9(2)/Pages/58.aspx.
37. IV Infusion Home. (2015). Air embolisms and IV therapy. Retrieved December 2, 2015 from https://ivinfusion.wordpress.com/2015/03/23/air-embolisms-and-iv-therapy/.
38. Colledge, H., & Boskey, E. (2015). ABO incompatibility reaction. Retrieved December 3, 2015 from http://www.healthline.com/health/abo-incompatibility#Overview1.
39. Chen, Y.B. (2014). ABO incompatibility. Retrieved December 3, 2015 from https://www.nlm.nih.gov/medlineplus/ency/article/001306.htm.
40. Mesa, R. A. (2013). Blood transfusion: Is there a universal blood donor type? Retrieved December 3, 2015 from http://www.mayoclinic.org/tests-procedures/blood-transfusion/expert-answers/universal-blood-donor-type/faq-20058229?p=1.
41. American Society of Registered Nurses. (2008). Blood transfusion error prevention: Nurses role. Retrieved December 3, 2015 from http://www.asrn.org/journal-nursing/285-blood-transfusion-error-prevention-nurses-role.html.
42. Pennsylvania Patient Safety Authority. (2010). Improving the safety of the blood transfusion process. Retrieved December 3, 2015 from http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/2010/Jun7(2)/documents/33.pdf.
43. Cooper, K. L. (2013). Evidence-based prevention of pressure ulcers in the intensive care unit. Critical Care Nurse, 33(6), 57-67.
44. National Pressure Ulcer Advisory Panel (NPUAP). (2015). NPUAP pressure ulcer stages/categories. Retrieved November 4, 2015 from http://www.npuap.org/resources/educational-and-clinical-resources/npuap-pressure-ulcer-stagescategories/.
45. Kirman, C. N., et al. (2015). Pressure ulcers and wound care treatment & management. Retrieved December 4, 2015 from http://emedicine.medscape.com/article/190115-treatment#d16.
46. The Joint Commission (2015). New sentinel event alert focuses on preventing falls. Retrieved November 7, 2015 from http://www.jointcommission.org/new_sentinel_event_alert_focuses_on_preventing_patient_falls/.
47. Quigley, P. A., & White, S. V. (2013). Hospital-based fall program measurement and improvement in high reliability organizations. OJIN: The Online Journal of Issues in Nursing, 18,(2). Retrieved November 6, 2015 from http://nursingworld.org/MainMenuCategories/ANAMarketplace/ANAPeriodicals/OJIN/TableofContents/Vol-18-2013/No2-May-2013/Fall-Program-Measurement.html?css=print.
48. McHugh, M. D., Shang, J., Sloan, Dm. M., & Aiken, L. H. (2010). Risk factors for hospital-acquired "poor glycemic control": A case-control study. Retrieved December 7, 2015 from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3023952/.
49. Durkin, M. T. (Ed.). (2013). Professional guide to diseases (10th ed.). Philadelphia, PA: Wolters Kluwer Health/Lippincott Williams & Wilkins.
50. American Association of Critical Care Nurses (AACN). (2011). Catheter-associated urinary tract infections. Retrieved November 7, 2015 from http://www.aacn.org/wd/practice/content/practicealerts/cathassocuti-nov11.pcms?menu=practice.
51. Evelyn, L. et al. (2014). Strategies to prevent catheter-associated urinary tract infections in acute care hospitals. Retrieved November 8, 2015 from http://www.medscape.com/viewarticle/824790.
52. Frasca, D., Dahyot-Fizelier, C., & Mimoz, O. (2010). Prevention of central venous catheter-related infection in the intensive care unit. Retrieved November 8, 2015 from http://www.ccforum.com/content/14/2/212.
53. Siegel, M., & Kramer-Cain, J. (2013). Vascular catheter-associated infections. Retrieved November 8, 2015 from http://nursing.advanceweb.com/Article/Vascular-Catheter-Associated-Infections-2.aspx.
54. Busby, S. R. et al. (2015). Assessing patient awareness of proper hand hygiene. Nursing2015, May, 2015, 27-30.
55. Safety Monitor. (2014). Infection prevention practices in ambulatory surgery centers. AJN, 114(7), 64-67.
56. CDC et al. (no date given). FAQs: Surgical site infections. Retrieved December 9, 2015 from http://www.cdc.gov/HAI/pdfs/ssi/SSI_tagged.pdf.
57. American Academy of Orthopaedic Surgeons. (2015). Deep vein thrombosis. Retrieved December 9, 2015 from http://orthoinfo.aaos.org/topic.cfm?topic=a00219.
58. WebMD. (no date given). How to prevent deep vein thrombosis (DVT). Retrieved December 10, 2015 from http://www.webmd.com/dvt/deep-vein-thrombosis-prevent-dvt?page=2.
59. Mayo clinic. Pneumothorax. Retrieved December 10, 2015 from http://www.mayoclinic.org/diseases-conditions/pneumothorax/basics/definition/con-20030025.
60. Zarogoulidis, P. et al. (2015). Pneumothorax as a complication of a central venous catheter insertion. Retrieved December 10, 2015 from http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4356862/.
61. Agency for Healthcare Research and Quality (AHRQ). (2014). Appendix 3. Guidelines to prevent central line-associated blood stream infections. Retrieved February 15, 2016 from http://www.ahrq.gov/professionals/education/curriculum-tools/clabsitools/clabsitoolsap3.html.
62. Agency for Healthcare Research and Quality (AHRQ). (2015). Why focus on central line-related bloodstream infections (CLASBSIs) Retrieved February 15, 2016 from http://www.ahrq.gov/sites/default/files/wysiwyg/professionals/systems/hospital/qitoolkit/d4a-crbsi-bestpractice.pdf.

Final Examination Questions

Choose the best answer for questions 31 through 40 and mark your answers on the Final Examination Sheet found on Page 141 or take your test online at **nursing.elitecme.com**.

31. The Safety Council is establishing policies and procedures to reduce the threat of patient harm related to alarm systems. It is important that the council:
    a. Identify situations when alarm signals are not clinically necessary.
    b. Establish a system for frequency of inspection, checking, and maintenance activities based on hospital preferences.
    c. Mandate that all patients be monitored to some extent.
    d. Be composed primarily of members from the nursing department.

32. In order to prevent an adverse patient protection event, the nurse should take which of the following actions?
    a. Physically restrain patients to prevent them from leaving the hospital.
    b. Assess a patient's decision-making ability prior to discharge.
    c. Ask for a psychiatric evaluation of all inpatients.
    d. Refer all elderly patients to home health services.

33. Which of the following nursing actions shows compliance with the 2016 National Patient Safety Goals?
    a. A nurse prepares to administer insulin to a patient and identifies the patient by checking her identification bracelet.
    b. A nurse asks a nursing assistant to inform a physician about the results of critical blood work.
    c. A nurse asks a patient about to be discharged to home, "do you understand how to take your medication?"
    d. A nurse asks another nurse to perform an independent check before he administers blood to a patient.

34. Which of the following actions is appropriate to prevent never ever surgical events?
    a. Marking of the surgical site by a certified nursing assistant before the patient goes to the operating room.
    b. Using adhesive markers as the sole means of marking the surgical site.
    c. Conducting a time-out immediately before making the incision.
    d. Cancelling the surgery if the patient refuses to have his/her surgical site marked.

35. Which of the following is a never ever care management event?
    a. Artificial insemination with the wrong donor sperm or wrong egg.
    b. Maternal death or serious injury associated with the labor or delivery of a high-risk pregnancy.
    c. Any stage 2 pressure ulcer acquired after admission to a healthcare facility.
    d. Patient death or serious injury associated with unsafe administration of intravenous fluids.

36. A nurse manager is explaining the importance of adhering to National Patient Safety Goals. In an effort to encourage adherence to hospital mandates regarding goals the manager:
    a. Explains that the Patient Safety Advisory Group consists of a group of physicians who are safety experts.
    b. Tells her staff that the National Patient Safety Goals are mandated and enforced by federal law.
    c. Encourages nurses to become more involved in working with The Joint Commission.
    d. Explains that the national Patient Safety Goals are a critical method developed by the federal government.

37. When considering the 2016 Home Care National Safety Goals the nurse realizes that:
    a. Two patient identifiers are not necessary in the home since the home care patient is the only patient in the home and obviously identifiable.
    b. She/he must assess the home environment for safety hazards.
    c. Hand hygiene is important but adherence to the CDC and WHO guidelines for hand cleaning are not necessary.
    d. She/he must personally inform all of the patient's friends and family members that they must not smoke in the home if oxygen is in use.

38. Factors that contribute to errors associated with alarm fatigue include all of the following EXCEPT:
    a. Customizing alarm settings to the individual patient.
    b. Having the sounds of alarms become part of the normal background noise on a unit.
    c. Turning the volume of alarms down.
    d. Assuming that the alarms do not indicate a problem.

39. Which of the following statements is accurate regarding never ever events?
    a. The specific factor identified in the radiologic event category is death or serious injury of a patient due to an allergic response to contrast dye.
    b. Patient elopement, although serious, is not a component of an never ever event category.
    c. An example of a criminal never ever event is patient abduction.
    d. Responsibility for environmental never ever events is that of the safety officer.

40. When developing policies and procedures to enhance clinical alarm safety healthcare professionals must know that:
    a. 80 to 99 percent of alarms generated by devices such as ventilators are false.
    b. Alarm fatigue is improving thanks to the National Patient Safety Goals.
    c. Nurses have the primary responsibility for addressing the potential effects of alarm fatigue in all patient care areas.
    d. Determining a baseline number of device alarms per day is not necessary since there is little or no research concerning alarm fatigue available.

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10	○	○	○	○

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1-ANCCKS12BDE17[1-10] 2-ANCCKS10ESE17[11-20] 3-ANCCKS04HAE17[21-30] 4-ANCCKS04PSE17[31-40]

SELF-ASSESSMENT AND EVALUATION (Required)

Your feedback is vital for the planning and design of future educational activities and for continual process improvements. Thank you.

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Choose the appropriate answer for each course completed, mark your answers.

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4. Was the course well written, organized, and informative?
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8. Do you plan to make changes to your practice as a result of this activity?
9. The course information provided was: New, Review, or Both.
10. Will this activity have an impact on your knowledge, competence, performance and patient outcomes.

	Bugs and Drugs: Pharmacology of Infectious Disease Review 12 Contact Hours			**Disorders of the Endocrine System: Anatomy, Physiology and Current Treatment Initiatives 10 Contact Hours**			**Heroin Use in America: Identification, Treatment and Prevention 4 Contact Hours**			**Patient Safety: Implementation of National Safety Standards for Nurses 4 Contact Hours**		
	YES	NO		YES	NO		YES	NO		YES	NO	
1	❍	❍		❍	❍		❍	❍		❍	❍	
2	❍	❍		❍	❍		❍	❍		❍	❍	
3	❍	❍		❍	❍		❍	❍		❍	❍	
4	❍	❍		❍	❍		❍	❍		❍	❍	
5	❍	❍		❍	❍		❍	❍		❍	❍	
6	❍	❍		❍	❍		❍	❍		❍	❍	
7	❍	❍		❍	❍		❍	❍		❍	❍	
8	❍	❍		❍	❍		❍	❍		❍	❍	
	New	Review	Both	New	Review	Both	New	Review	Both	New	Review	Both
9	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍
	Yes	No	No Change	Yes	No	No Change	Yes	No	No Change	Yes	No	No Change
10	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍	❍

Fill in the circle below numbers **0=Not likely at all, 5=Neutral and 10=Extremely likely**

How likely is it that you would recommend Elite ..... 0 ○ 1 ○ 2 ○ 3 ○ 4 ○ 5 ○ 6 ○ 7 ○ 8 ○ 9 ○ 10 ○

Bugs and Drugs: Pharmacology of Infectious Disease Review: If you answered yes to question 8, how will you change your practice as a result of this activity and indicate any barriers you perceive in implementing these changes: _____

_____

Disorders of the Endocrine System: Anatomy, Physiology and Current Treatment Initiatives: If you answered yes to question 8, how will you change your practice as a result of this activity and indicate any barriers you perceive in implementing these changes: _____

_____

Heroin Use in America: Identification, Treatment and Prevention: If you answered yes to question 8, how will you change your practice as a result of this activity and indicate any barriers you perceive in implementing these changes: _____

_____

Patient Safety: Implementation of National Safety Standards for Nurses: If you answered yes to question 8, how will you change your practice as a result of this activity and indicate any barriers you perceive in implementing these changes: _____

_____

Please describe any clinical situations that you find difficult to manage or resolve that you would like to see addressed in future continuing education:

_____

_____

List other topics that you would like to see provided: _____

_____

❑I agree to allow Elite to use my comments. If you answered yes, please provide your name and title as you would like them to appear.

_____