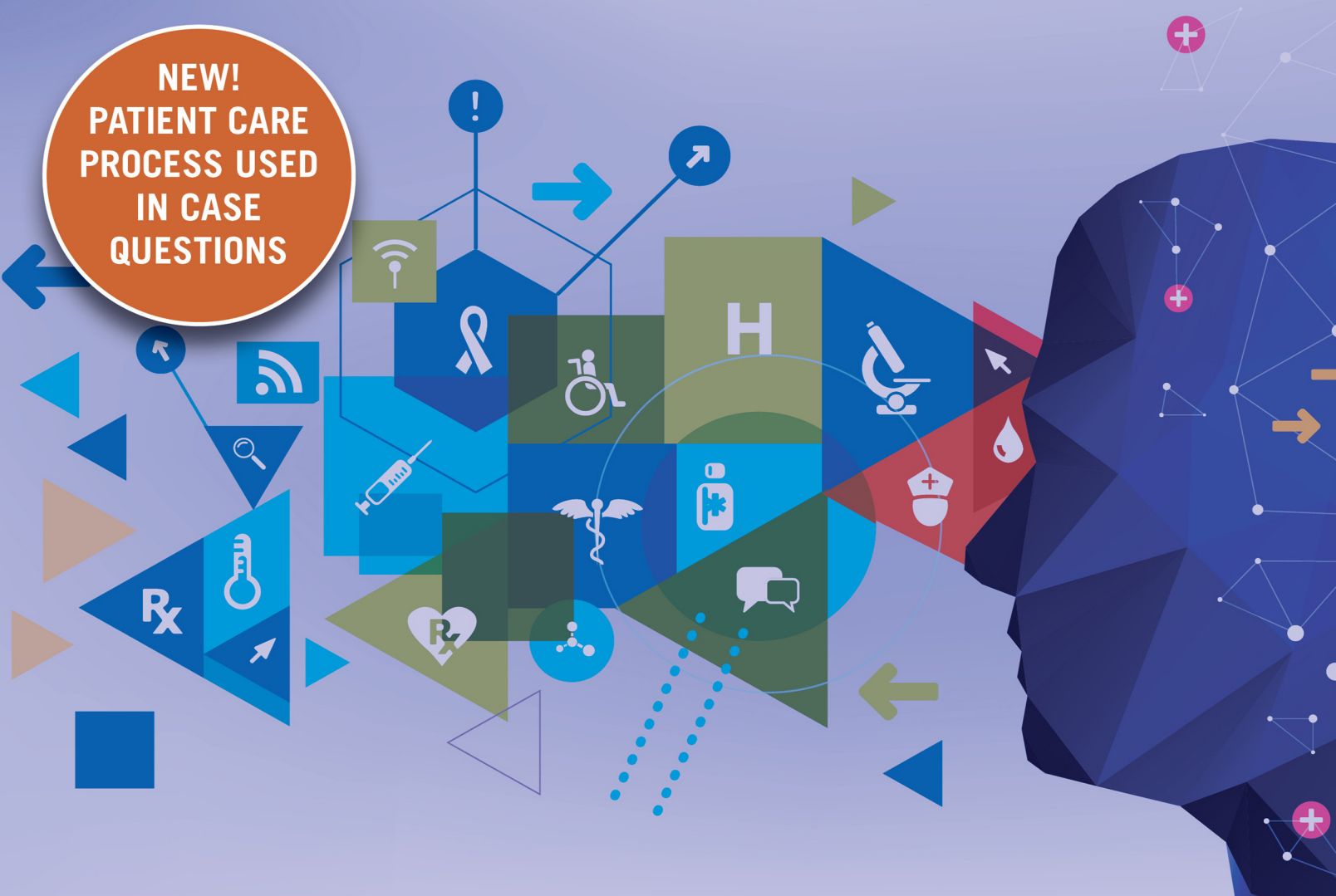


ELEVENTH EDITION

PHARMACOTHERAPY CASEBOOK

A Patient-Focused Approach

NEW!
PATIENT CARE
PROCESS USED
IN CASE
QUESTIONS



**Mc
Graw
Hill**

Terry L. Schwinghammer • Julia M. Koehler
Jill S. Borchert • Douglas Slain • Sharon K. Park

Pharmacotherapy Casebook

NOTICE

Medicine is an ever-changing science. As new research and clinical experience broaden our knowledge, changes in treatment and drug therapy are required. The authors and the publisher of this work have checked with sources believed to be reliable in their efforts to provide information that is complete and generally in accord with the standards accepted at the time of publication. However, in view of the possibility of human error or changes in medical sciences, neither the authors nor the publisher nor any other party who has been involved in the preparation or publication of this work warrants that the information contained herein is in every respect accurate or complete, and they disclaim all responsibility for any errors or omissions, or for the results obtained from use of the information contained in this work. Readers are encouraged to confirm the information contained herein with other sources. For example and in particular, readers are advised to check the product information sheet included in the package of each drug they plan to administer to be certain that the information contained in this work is accurate and that changes have not been made in the recommended dose or in the contraindications for administration. This recommendation is of particular importance in connection with new or infrequently used drugs.

Pharmacotherapy Casebook

A Patient-Focused Approach

Eleventh Edition

Editors

**Terry L. Schwinghammer, PharmD,
FCCP, FASHP, FAPhA**

Professor Emeritus
Department of Clinical Pharmacy
School of Pharmacy
West Virginia University
Morgantown, West Virginia

Julia M. Koehler, PharmD, FCCP

Professor and Associate Dean for External Affiliations
College of Pharmacy and Health Sciences
Butler University
Ambulatory Care Clinical Pharmacist, Pulmonary Rehabilitation
Methodist Hospital of Indiana University Health
Indianapolis, Indiana

**Jill S. Borchert, PharmD, BCACP,
BCPS, FCCP**

Professor and Vice Chair
Department of Pharmacy Practice
Chicago College of Pharmacy
Midwestern University
Downers Grove, Illinois

**Douglas Slain, PharmD, BCPS,
FCCP, FASHP**

Professor and Chair
Department of Clinical Pharmacy
School of Pharmacy
West Virginia University
Infectious Diseases Clinical Specialist
WVU Medicine and Ruby Memorial Hospital
Morgantown, West Virginia

Sharon K. Park, PharmD, MEd, BCPS

Associate Professor
Department of Clinical and Administrative Sciences
School of Pharmacy
Notre Dame of Maryland University
Clinical Pharmacy Specialist
Drug Information and Medication Use Policy
The Johns Hopkins Hospital
Baltimore, Maryland

A companion workbook for: *Pharmacotherapy: A Pathophysiologic Approach*, 11th ed.
DiPiro JT, Yee GC, Posey LM, Haines ST, Nolin TD, Ellingrod V, eds. New York, NY: McGraw-Hill, 2020.



New York Chicago San Francisco Athens London Madrid Mexico City
Milan New Delhi Singapore Sydney Toronto

Copyright © 2020 by McGraw Hill LLC. All rights reserved. Except as permitted under the United States Copyright Act of 1976, no part of this publication may be reproduced or distributed in any form or by any means, or stored in a database or retrieval system, without the prior written permission of the publisher.

ISBN: 978-1-26-011668-7

MHID: 1-26-011668-9

The material in this eBook also appears in the print version of this title: ISBN: 978-1-26-011667-0, MHID: 1-26-011667-0.

eBook conversion by codeMantra
Version 1.0

All trademarks are trademarks of their respective owners. Rather than put a trademark symbol after every occurrence of a trademarked name, we use names in an editorial fashion only, and to the benefit of the trademark owner, with no intention of infringement of the trademark. Where such designations appear in this book, they have been printed with initial caps.

McGraw-Hill Education eBooks are available at special quantity discounts to use as premiums and sales promotions or for use in corporate training programs. To contact a representative, please visit the Contact Us page at www.mhprofessional.com.

TERMS OF USE

This is a copyrighted work and McGraw-Hill Education and its licensors reserve all rights in and to the work. Use of this work is subject to these terms. Except as permitted under the Copyright Act of 1976 and the right to store and retrieve one copy of the work, you may not decompile, disassemble, reverse engineer, reproduce, modify, create derivative works based upon, transmit, distribute, disseminate, sell, publish or sublicense the work or any part of it without McGraw-Hill Education's prior consent. You may use the work for your own noncommercial and personal use; any other use of the work is strictly prohibited. Your right to use the work may be terminated if you fail to comply with these terms.

THE WORK IS PROVIDED "AS IS." McGRAW-HILL EDUCATION AND ITS LICENSORS MAKE NO GUARANTEES OR WARRANTIES AS TO THE ACCURACY, ADEQUACY OR COMPLETENESS OF OR RESULTS TO BE OBTAINED FROM USING THE WORK, INCLUDING ANY INFORMATION THAT CAN BE ACCESSED THROUGH THE WORK VIA HYPERLINK OR OTHERWISE, AND EXPRESSLY DISCLAIM ANY WARRANTY, EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO IMPLIED WARRANTIES OF MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE. McGraw-Hill Education and its licensors do not warrant or guarantee that the functions contained in the work will meet your requirements or that its operation will be uninterrupted or error free. Neither McGraw-Hill Education nor its licensors shall be liable to you or anyone else for any inaccuracy, error or omission, regardless of cause, in the work or for any damages resulting therefrom. McGraw-Hill Education has no responsibility for the content of any information accessed through the work. Under no circumstances shall McGraw-Hill Education and/or its licensors be liable for any indirect, incidental, special, punitive, consequential or similar damages that result from the use of or inability to use the work, even if any of them has been advised of the possibility of such damages. This limitation of liability shall apply to any claim or cause whatsoever whether such claim or cause arises in contract, tort or otherwise.

CONTENTS

Contributors.....	xi
Preface.....	xix
Acknowledgments.....	xxi

SECTION 1

Principles of Patient-Focused Therapy

Section Editor: **Terry L. Schwinghammer**

1. Introduction: How to Use This Casebook	1
<i>Terry L. Schwinghammer</i>	
2. Active Learning Strategies	11
<i>Rachel W. Flurie, Gretchen M. Brophy and Cynthia K. Kirkwood</i>	
3. Patient Communication: Getting the Most Out of That One-on-One Time.....	15
<i>Krista D. Capehart</i>	
4. Implementing the Pharmacists' Patient Care Process	21
<i>Erika L. Kleppinger</i>	
5. Documentation of Patient Encounters and Interventions.....	29
<i>Lori T. Armistead and Timothy J. Ives</i>	
6. Pediatrics.....	39
<i>Franklin R. Huggins</i>	
7. Geriatrics	41
<i>David P. Elliott</i>	
8. Palliative Care.....	44
<i>Jennifer L. Swank</i>	
9. Clinical Toxicology: Acetaminophen Toxicity	47
<i>Elizabeth J. Scharman</i>	
10. Cyanide Exposure	49
<i>Elizabeth J. Scharman</i>	
11. Chemical Threat Agent Exposure.....	52
<i>Elizabeth J. Scharman</i>	

SECTION 2

Cardiovascular Disorders

Section Editor: **Julia M. Koehler**

12. Hypertension	55
<i>Julia M. Koehler and James E. Tisdale</i>	
13. Hypertensive Crisis	57
<i>James J. Nawarskas</i>	
14. Dyslipidemia	60
<i>Joel C. Marrs</i>	
15. Stable Ischemic Heart Disease.....	62
<i>Alexander J. Ansara and Regan M. Wade</i>	
16. Acute Coronary Syndrome: ST-Elevation Myocardial Infarction.....	64
<i>Kelly C. Rogers and Robert B. Parker</i>	
17. Peripheral Arterial Disease.....	67
<i>Tracy J. Costello and Tracy L. Sprunger</i>	
18. Heart Failure With Reduced Ejection Fraction....	69
<i>Julia M. Koehler and Alison M. Walton</i>	
19. Heart Failure With Preserved Ejection Fraction...	71
<i>Joel C. Marrs and Sarah L. Anderson</i>	
20. Acute Decompensated Heart Failure	73
<i>Kena J. Lanham</i>	
21. Deep Vein Thrombosis.....	76
<i>Sally A. Arif and Tran Tran</i>	
22. Pulmonary Embolism.....	78
<i>Kristen L. Longstreth and Mary E. Fredrickson</i>	
23. Chronic Anticoagulation	81
<i>Mikayla L. Spangler and Beth Bryles Phillips</i>	
24. Stroke.....	84
<i>Alexander J. Ansara</i>	
25. Ventricular Arrhythmia	86
<i>Kwadwo Amankwa</i>	

- 26.** Atrial Fibrillation 88
Virginia H. Fleming
- 27.** Cardiac Arrest 91
Jennifer McCann and Sarah Hittle
- 28.** Hypovolemic Shock 93
*Brian L. Erstad, Brian J. Kopp, and
Yvonne C. Huckleberry*

SECTION 3

Respiratory Disorders

Section Editor: *Julia M. Koehler*

- 29.** Acute Asthma 97
Rebecca S. Pettit
- 30.** Chronic Asthma 99
*Julia M. Koehler, Meghan M. Bodenber, and
Jennifer R. Guthrie*
- 31.** Chronic Obstructive Pulmonary Disease 101
Sarah L. Anderson and Joel C. Marrs
- 32.** Pulmonary Artery Hypertension 103
Marta A. Miyares
- 33.** Cystic Fibrosis 105
Kimberly J. Novak

SECTION 4

Gastrointestinal Disorders

Section Editor: *Jill S. Borchert*

- 34.** Gastroesophageal Reflux Disease 109
Brian A. Hemstreet
- 35.** Peptic Ulcer Disease 111
Ashley H. Meredith
- 36.** NSAID-Induced Ulcer Disease 113
Carmen B. Smith and Jay L. Martello
- 37.** Stress Ulcer Prophylaxis/Upper GI Hemorrhage 115
Jay L. Martello and Lena M. Maynor
- 38.** Crohn Disease 117
Brian A. Hemstreet
- 39.** Ulcerative Colitis 119
Nancy S. Yunker
- 40.** Nausea and Vomiting 121
Kelly K. Nystrom and Amy M. Pick
- 41.** Diarrhea 124
Marie A. Abate and Charles D. Ponte

- 42.** Constipation 126
Michelle Fravel and Beth Bryles Phillips
- 43.** Irritable Bowel Syndrome 128
Nancy S. Yunker
- 44.** Pediatric Gastroenteritis 131
William McGhee and Laura M. Panko
- 45.** Ascites Management in Portal Hypertension and Cirrhosis 133
Laurel A. Sampognaro and Jeffery D. Evans
- 46.** Esophageal Varices 135
Vanessa T. Kline and Jonathan M. Kline
- 47.** Hepatic Encephalopathy 137
Jeffrey T. Wiczorkiewicz and Carrie A. Sincak
- 48.** Acute Pancreatitis 140
*Scott W. Mueller, Paul Reynolds, and
Robert MacLaren*
- 49.** Chronic Pancreatitis 142
Heather M. Teufel and Jaime L. Gray
- 50.** Viral Hepatitis A 144
Juliana Chan
- 51.** Viral Hepatitis B 147
Juliana Chan
- 52.** Viral Hepatitis C 149
Michelle T. Martin

SECTION 5

Renal Disorders

Section Editor: *Jill S. Borchert*

- 53.** Drug-Induced Acute Kidney Injury 153
Mary K. Stamatakis
- 54.** Acute Kidney Injury 155
Scott Bolesta
- 55.** Progressive Renal Disease 157
Christie Schumacher
- 56.** End-Stage Kidney Disease 159
Katie E. Cardone
- 57.** Syndrome of Inappropriate Antidiuretic Hormone Release 161
Sarah A. Nisly and Jane M. Gervasio
- 58.** Electrolyte Abnormalities in Chronic Kidney Disease 163
Lena M. Maynor and Mary K. Stamatakis
- 59.** Hypercalcemia of Malignancy 165
Laura L. Jung and Lisa M. Holle

- 60.** Hypokalemia and Hypomagnesemia 167
Denise M. Kolanczyk
- 61.** Metabolic Acidosis 169
Justin M. Schmidt and Megan E. Sands
- 62.** Metabolic Alkalosis 171
Natalie I. Rine

SECTION 6

Neurologic Disorders

Section Editor: **Sharon K. Park**

- 63.** Alzheimer Disease 175
Amie Taggart Blaszczyk and Rebecca J. Mahan
- 64.** Multiple Sclerosis 177
Sarah N. Fischer and Jacquelyn L. Bainbridge
- 65.** Complex Partial Seizures 180
James W. McAuley
- 66.** Generalized Tonic–Clonic Seizures 183
Jennifer A. Donaldson
- 67.** Status Epilepticus 185
Jennifer A. Donaldson
- 68.** Acute Management of the Traumatic Brain Injury Patient 187
Denise H. Rhoney and Dennis Parker, Jr.
- 69.** Parkinson Disease 191
Mary L. Wagner and Yuchen Wang
- 70.** Chronic Pain Management 194
Ernest J. Dole
- 71.** Acute Pain Management 197
Charles D. Ponte
- 72.** Migraine Headache 199
*Susan R. Winkler and
Brittany Hoffmann-Eubanks*

SECTION 7

Psychiatric Disorders

Section Editor: **Sharon K. Park**

- 73.** Attention-Deficit Hyperactivity Disorder 203
Laura F. Ruekert and Syed Khan
- 74.** Bulimia Nervosa 205
Laura F. Ruekert and Cheen T. Lum
- 75.** Alcohol Withdrawal 207
Kevin M. Tuohy

- 76.** Nicotine Dependence 209
Gabriella A. Douglass
- 77.** Schizophrenia 211
Leigh Anne Nelson
- 78.** Major Depression 214
Katelynn Mayberry and Brian L. Crabtree
- 79.** Bipolar Disorder 217
Jason M. Noel
- 80.** Generalized Anxiety Disorder 219
Sarah T. Melton and Cynthia K. Kirkwood
- 81.** Obsessive–Compulsive Disorder 222
Lindsey Miller and Chris Paxos
- 82.** Insomnia 224
Suzanne C. Harris and Rachel Marie E. Salas

SECTION 8

Endocrinologic Disorders

Section Editor: **Julia M. Koehler**

- 83.** Type 1 Diabetes Mellitus and Ketoacidosis 229
Holly S. Divine and Carrie L. Isaacs
- 84.** Type 2 Diabetes Mellitus: New Onset 231
*Nicole C. Pezzino, Scott R. Drab, and
Deanne L. Hall*
- 85.** Type 2 Diabetes Mellitus: Existing Disease 233
Sharon S. Gatewood and Margaret A. Landis
- 86.** Hyperthyroidism: Graves Disease 235
Kristine S. Schonder
- 87.** Hypothyroidism 237
Michael D. Katz
- 88.** Cushing Syndrome 239
*Scott G. Garland, Steven M. Smith, and
John Gums*
- 89.** Addison Disease 241
Zachary A. Weber
- 90.** Hyperprolactinemia 243
Amy Heck Sheehan

SECTION 9

Gynecologic and Obstetric Disorders

Section Editor: **Sharon K. Park**

- 91.** Pregnancy and Lactation 247
Sneha Baxi Srivastava and Ziemowit Mazur

- 92.** Contraception 249
Julia M. Koehler and Jennifer R. Guthrie
- 93.** Emergency Contraception 251
Rebecca H. Stone
- 94.** Premenstrual Dysphoric Disorder 253
Larissa N. H. Bossaer
- 95.** Endometriosis 255
Erin C. Raney
- 96.** Managing Menopausal Symptoms 257
Andrea S. Franks and Julie W. Jeter

SECTION 10

Urologic Disorders

Section Editor: **Terry L. Schwinghammer**

- 97.** Erectile Dysfunction 261
Cara Liday
- 98.** Benign Prostatic Hyperplasia. 263
*Kathryn Eroschenko, Michael Biddle,
and Kevin W. Cleveland*
- 99.** Urinary Incontinence 266
Mary W. L. Lee and Roohollah R. Sharifi

SECTION 11

Immunologic Disorders

Section Editor: **Terry L. Schwinghammer**

- 100.** Systemic Lupus Erythematosus 269
Nicole Paolini Albanese
- 101.** Allergic Drug Reaction 271
Lynne M. Sylvia
- 102.** Solid Organ Transplantation 274
Kristine S. Schonder

SECTION 12

Bone and Joint Disorders

Section Editor: **Sharon K. Park**

- 103.** Osteoarthritis 277
Christopher M. Degenkolb
- 104.** Rheumatoid Arthritis 279
Amie D. Brooks
- 105.** Osteoporosis 281
Mollie Ashe Scott and Lisa LaVallee
- 106.** Gout and Hyperuricemia 283
Erik D. Maki

SECTION 13

Eyes, Ears, Nose, and Throat Disorders

Section Editor: **Terry L. Schwinghammer**

- 107.** Glaucoma 287
Brian McMillan and Ashlee McMillan
- 108.** Allergic Rhinitis 289
Jon P. Wietholter

SECTION 14

Dermatologic Disorders

Section Editor: **Terry L. Schwinghammer**

- 109.** Acne Vulgaris 293
Rebecca M. Law and Wayne P. Gulliver
- 110.** Psoriasis. 295
Rebecca M. Law and Wayne P. Gulliver
- 111.** Atopic Dermatitis 297
*Rebecca M. Law, Poh Gin Kwa,
and Howard I. Maibach*
- 112.** Dermatologic Drug Reaction. 299
Rebecca M. Law and Howard I. Maibach

SECTION 15

Hematologic Disorders

Section Editor: **Terry L. Schwinghammer**

- 113.** Iron Deficiency Anemia 303
Matthew A. Cantrell and Elizabeth M. Bald
- 114.** Vitamin B₁₂ Deficiency 305
Jon P. Wietholter
- 115.** Folic Acid Deficiency 307
*Jonathan M. Kline and
Amber Nicole Chiplinski*
- 116.** Sickle Cell Anemia. 309
Jamal Brown

SECTION 16

Infectious Diseases

Section Editor: **Douglas Slain**

- 117.** Using Laboratory Tests in
Infectious Diseases 313
Anthony J. Guarascio and Branden Nemecek
- 118.** Bacterial Meningitis 315
S. Travis King and Elizabeth A. Cady

119.	Community-Acquired Pneumonia	317
	<i>Trent G. Towne and Sharon M. Erdman</i>	
120.	Hospital-Acquired Pneumonia	320
	<i>Kendra M. Damer</i>	
121.	Acute Bronchitis	322
	<i>Jessica Helmer Brady and Sherry Peveto</i>	
122.	Otitis Media	324
	<i>Rochelle Rubin and Lauren Camaione</i>	
123.	Rhinosinusitis.	326
	<i>Michael B. Kays</i>	
124.	Acute Pharyngitis	328
	<i>Anthony J. Guarascio and Autumn Stewart-Lynch</i>	
125.	Influenza	330
	<i>Christo L. Cimino and Douglas Slain</i>	
126.	Skin and Soft Tissue Infection	332
	<i>Jarrett R. Amsden</i>	
127.	Diabetic Foot Infection.	335
	<i>Renee-Claude Mercier and Paulina Deming</i>	
128.	Infective Endocarditis.	337
	<i>Ryan L. Crass, Manjunath (Amit) P. Pai, and Keith A. Rodvold</i>	
129.	Tuberculosis	340
	<i>Sharon M. Erdman and Kendra M. Damer</i>	
130.	<i>Clostridioides Difficile</i> Infection.	343
	<i>Michael J. Gonyeau and Brandon Dionne</i>	
131.	Intra-abdominal Infection	345
	<i>Paulina Deming and Renee-Claude Mercier</i>	
132.	Lower Urinary Tract Infection.	347
	<i>Melissa E. Badowski, Sharon M. Erdman, and Keith A. Rodvold</i>	
133.	Pyelonephritis	349
	<i>Elizabeth A. Coyle</i>	
134.	Pelvic Inflammatory Disease and Other Sexually Transmitted Infections	352
	<i>Neha Sheth Pandit and Christopher Roberson</i>	
135.	Syphilis	354
	<i>Craig Martin</i>	
136.	Genital Herpes, Gonococcal, and Chlamydial Infections	356
	<i>Jonathan C. Cho</i>	
137.	Osteomyelitis and Septic Arthritis	358
	<i>R. Brigg Turner and Gregory B. Tallman</i>	
138.	Sepsis.	361
	<i>Trisha N. Branan and Christopher M. Bland</i>	

139.	Dermatophytosis	363
	<i>Ilya Rybakov and Natalie R. Tucker</i>	
140.	Bacterial Vaginosis.	364
	<i>Charles D. Ponte</i>	
141.	<i>Candida</i> Vaginitis	366
	<i>Rebecca M. Law</i>	
142.	Invasive Fungal Infections	368
	<i>Douglas Slain</i>	
143.	Infection in an Immunocompromised Patient	370
	<i>Aaron Cumpston and Douglas Slain</i>	
144.	Antimicrobial Prophylaxis for Surgery.	373
	<i>Curtis L. Smith</i>	
145.	Pediatric Immunization	375
	<i>Jean-Venable “Kelly” R. Goode</i>	
146.	Adult Immunization	377
	<i>Jean-Venable “Kelly” R. Goode</i>	
147.	HIV Infection.	379
	<i>Rodrigo M. Burgos and Sarah M. Michienzi</i>	

SECTION 17

Oncologic Disorders

Section Editor: *Terry L. Schwinhammer*

148.	Breast Cancer	383
	<i>Jonathan W. Malara and Bonnie Lin Boster</i>	
149.	Non-Small Cell Lung Cancer	386
	<i>Michelle L. Rockey and Julianna V. F. Roddy</i>	
150.	Colon Cancer	389
	<i>Lisa E. Davis</i>	
151.	Prostate Cancer	391
	<i>Lisa M. Holle and Jessica M. Clement</i>	
152.	Non-Hodgkin Lymphoma	394
	<i>Keith A. Hecht</i>	
153.	Hodgkin Lymphoma	397
	<i>Cindy L. O'Bryant</i>	
154.	Ovarian Cancer	399
	<i>Amber E. Proctor and Alexis Jones</i>	
155.	Acute Lymphocytic Leukemia	402
	<i>Deborah A. Hass</i>	
156.	Chronic Myeloid Leukemia	406
	<i>Allison Martin and Aaron Cumpston</i>	
157.	Kidney Cancer	408
	<i>Daniel J. Crona and Jessica J. Auten</i>	

- 158.** Melanoma 411
Jessica Michaud Davis and Marina Kanos
- 159.** Hematopoietic Stem Cell Transplantation 413
Teresa C. Thakrar

SECTION 18

Nutrition and Nutritional Disorders

Section Editor: *Terry L. Schwinghammer*

- 160.** Parenteral Nutrition 417
Melissa R. Pleva and Michael D. Kraft
- 161.** Adult Enteral Nutrition. 419
Carol J. Rollins
- 162.** Obesity 422
Dannielle C. O'Donnell

SECTION 19

Complementary and Alternative Therapies (Level III) 427

Section Editor: *Terry L. Schwinghammer*

- Appendix A: Conversion Factors
 and Anthropometrics 437
- Appendix B: Common Laboratory Tests 441
- Appendix C:
 Part I: Common Medical Abbreviations 447
 Part II: Prevent Medication Errors by Avoiding
 These Dangerous Abbreviations, Symbols, and
 Dose Designations 455
- Appendix D: Sample Responses to Case Questions 457

FA

CONTRIBUTORS

Marie A. Abate, BS, PharmD

Professor of Clinical Pharmacy, Department of Clinical Pharmacy; Director, West Virginia Center for Drug and Health Information; Director of Programmatic Assessment, School of Pharmacy, West Virginia University, Morgantown, West Virginia

Nicole P. Albanese, PharmD, CDE, BCACP

Clinical Associate Professor, Department of Pharmacy Practice, School of Pharmacy and Pharmaceutical Sciences, University at Buffalo; Clinical Pharmacist in Ambulatory Care, Buffalo Medical Group, P.C., Buffalo, New York

Kwadwo Amankwa, PharmD, BCPS

Clinical Pharmacist, Advanced Heart Failure, Jewish Hospital Louisville, KentuckyOne Health, Louisville, Kentucky

Jarrett R. Amsden, PharmD, BCPS

Associate Professor, Department of Pharmacy Practice, College of Pharmacy and Health Sciences (COPHS), Butler University; Infectious Diseases Clinical Pharmacist, Department of Clinical Pharmacy, Community Health Network, Indianapolis, Indiana

Sarah L. Anderson, PharmD, FCCP, BCPS, BCACP

Associate Professor, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora; Clinical Pharmacy Specialist, Denver Health Medical Center, Denver, Colorado

Alexander J. Ansara, PharmD, BCPS (AQ Cardiology)

Associate Professor of Pharmacy Practice, Butler University College of Pharmacy and Health Sciences; Clinical Specialist, Advanced Heart Care, Indiana Health Methodist Hospital, Indianapolis, Indiana

Sally A. Arif, PharmD, BCPS (AQ Cardiology)

Associate Professor of Pharmacy Practice, Department of Pharmacy Practice, Midwestern University, Chicago College of Pharmacy, Downers Grove; Cardiology Clinical Pharmacist, Rush University Medical Center, Chicago, Illinois

Lori T. Armistead, MA, PharmD

Senior Research Associate and Clinical Coordinator, Center for Medication Optimization, UNC Eshelman School of Pharmacy, Chapel Hill, North Carolina

Jessica J. Auten, PharmD, BCPS, BCOP

Clinical Pharmacy Specialist—Malignant Hematology, Department of Pharmacy, UNC Medical Center; Assistant Professor of Clinical Education, UNC Eshelman School of Pharmacy, Chapel Hill, North Carolina

Melissa E. Badowski, PharmD, MPH, FCCP, BCIDP, BCPS, AAHIVP

Clinical Associate Professor, Section of Infectious Diseases Pharmacotherapy, Department of Pharmacy Practice, University of Illinois at Chicago, College of Pharmacy; Clinical Pharmacist in HIV/AIDS Telehealth, University of Illinois Hospital and Health Sciences, Chicago, Illinois

Jacquelyn L. Bainbridge, PharmD, FCCP, MSCS

Professor, Department of Clinical Pharmacy and Neurology, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Aurora, Colorado

Elizabeth M. Bald, PharmD, BCACP

Clinical Pharmacist, Madsen Family Health Clinic; Assistant Professor (Clinical), Department of Pharmacotherapy, University of Utah College of Pharmacy, Salt Lake City, Utah

Michael A. Biddle, Jr, PharmD, BCPS

Clinical Assistant Professor, Department of Pharmacy Practice and Administration, Kasiska Division of Health Sciences College of Pharmacy, Idaho State University, Meridian, Idaho

Christopher M. Bland, PharmD, FCCP, FIDSA, BCPS

Clinical Associate Professor, Department of Clinical and Administrative Pharmacy, College of Pharmacy, University of Georgia; Clinical Pharmacy Specialist, St. Joseph's/Candler Health System, Savannah, Georgia

Amie Taggart Blaszczyk, PharmD, BCGP, BCPS, FASCP

Associate Professor and Division Head—Geriatrics, Texas Tech University HSC School of Pharmacy, Dallas, Texas

Meghan M. Bodenberg, PharmD, BCPS

Associate Professor and Director of Advanced Experiential Education and Preceptor Development, Butler University College of Pharmacy and Health Sciences, Indianapolis, Indiana

Scott Bolesta, PharmD, BCPS, FCCM, FCCP

Associate Professor, Department of Pharmacy Practice, Nesbitt School of Pharmacy, Wilkes University; Visiting Investigator, Geisinger Heart Institute, Wilkes-Barre, Pennsylvania

Larissa N. H. Bossaer, PharmD, BCPS

Assistant Professor, Department of Pharmacy Practice, Bill Gatton College of Pharmacy, East Tennessee State University, Johnson City, Tennessee

Bonnie L. Boster, PharmD, BCOP

Clinical Pharmacy Specialist—Breast Medical Oncology, Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, Texas

Jessica H. Brady, PharmD, BCPS

Clinical Professor and Associate Director, School of Clinical Sciences, College of Pharmacy, University of Louisiana Monroe; Clinical Pharmacist in Internal Medicine, Ochsner-LSU Health Monroe Medical Center, Monroe, Louisiana

Trisha N. Branan, PharmD, BCCCP

Clinical Associate Professor, Department of Clinical and Administrative Pharmacy, College of Pharmacy, University of Georgia; Clinical Pharmacist in Critical Care, Piedmont Athens Regional Medical Center, Athens, Georgia

Amie D. Brooks, PharmD, FCCP, BCACP

Professor, Pharmacy Practice, Interim Director, Division of Ambulatory Care, St. Louis College of Pharmacy, St. Louis, Missouri

Gretchen M. Brophy, PharmD, BCPS, FCCP, FCCM, FNCS

Professor, Pharmacotherapy and Outcomes Science and Neurosurgery, School of Pharmacy, Virginia Commonwealth University, Richmond, Virginia

Jamal Brown, PharmD, BCGP

Assistant Professor of Pharmacy Practice, Florida A&M University, Tallahassee; Clinical Pharmacist in Ambulatory Care, Tampa General Medical Group, Tampa, Florida

Rodrigo M. Burgos, PharmD

Clinical Assistant Professor, Section of Infectious Diseases Pharmacotherapy, Department of Pharmacy Practice, College of Pharmacy, University of Illinois at Chicago; Clinical Pharmacist in HIV and ID, University of Illinois at Chicago Hospital and Health Sciences System, Chicago, Illinois

Elizabeth A. Cady, PharmD, BCPS

Clinical Assistant Professor, Department of Pharmacy Practice, School of Pharmacy, Southern Illinois University at Edwardsville; Clinical Pharmacist in Infectious Diseases, HSHS St. John's Hospital, Springfield, Illinois

Lauren Camaione, BS, PharmD, BCPPS

Pediatric Clinical Staff Pharmacist, The University of Rochester Medical Center, Rochester, New York

Matthew A. Cantrell, PharmD, BCPS

Clinical Associate Professor, Department of Pharmacy Practice and Science, University of Iowa College of Pharmacy, Iowa City, Iowa

Krista D. Capehart, PharmD, MS Pharm, BCACP, AE-C

Clinical Associate Professor, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University, Morgantown; Staff Pharmacist at the West Virginia Board of Pharmacy, Charleston, West Virginia

Katie E. Cardone, PharmD, BCACP, FNKF, FASN, FCCP

Associate Professor, Department of Pharmacy Practice, School of Pharmacy and Pharmaceutical Sciences, Albany College of Pharmacy and Health Sciences, Albany, New York

Juliana Chan, PharmD, FCCP, BCACP

Clinical Associate Professor, Colleges of Pharmacy and Medicine, University of Illinois at Chicago; Clinical Pharmacist, Gastroenterology/Hepatology, Illinois Department of Corrections Hepatology Telemedicine, Sections of Hepatology, Digestive Diseases and Nutrition, University of Illinois Hospital and Health Sciences Center, Chicago, Illinois

Amber N. Chiplinski, PharmD, BCPS

Clinical Pharmacy Specialist, Stroke/Neurology, WVU Medicine, J.W. Ruby Memorial Hospital, Morgantown, West Virginia

Jonathan C. Cho, PharmD, MBA, BCIDP, BCPS

Clinical Pharmacy Manager, Mountain View Hospital, Las Vegas, Nevada

Christo L. Cimino, PharmD, BCPS, BCIDP, AAHIVP

Clinical Pharmacy Specialist, Infectious Diseases, Department of Pharmaceutical Services, Vanderbilt University Medical Center, Nashville, Tennessee

Jessica M. Clement, MD

Associate Professor, University of Connecticut School of Medicine, Farmington, Connecticut

Kevin W. Cleveland, PharmD

Assistant Dean and Associate Professor of Pharmacy Practice, Department of Pharmacy Practice and Administration, Kasiska Division of Health Sciences College of Pharmacy, Idaho State University, Meridian, Idaho

Tracy J. Costello, PharmD, BCPS

Associate Professor of Pharmacy Practice, Butler University College of Pharmacy and Health Sciences; Clinical Pharmacy Specialist, Family Medicine, Community Health Network, Indianapolis, Indiana

Elizabeth A. Coyle, PharmD, FCCM, BCPS

Associate Dean for Academic Affairs and Clinical Professor, University of Houston College of Pharmacy, Houston, Texas

Brian L. Crabtree, PharmD, BCPP

Dean and Professor of Pharmacy Practice, Mercer University College of Pharmacy, Atlanta, Georgia

Ryan L. Crass, PharmD, BCIDP

Pharmacometrician, Ann Arbor Pharmacometrics Group, Ann Arbor, Michigan

Daniel J. Crona, PharmD, PhD, CPP

Tenure Track Assistant Professor, Division of Pharmacotherapy and Experimental Therapeutics, UNC Eshelman School of Pharmacy; Clinical Pharmacist Practitioner, Genitourinary Malignancies, Department of Pharmacy, UNC Hospitals and Clinics, Chapel Hill, North Carolina

Aaron Cumpston, PharmD, BCOP

Pharmacy Clinical Specialist, BMT/Hematological Malignancy, West Virginia University Medicine, Morgantown, West Virginia

Kendra M. Damer, PharmD

Associate Professor of Pharmacy Practice, Butler University College of Pharmacy and Health Sciences, Indianapolis, Indiana

Jessica Michaud Davis, PharmD, BCOP, CPP

Clinical Pharmacist Coordinator, Adult Hematology/Oncology, Levine Cancer Institute, Charlotte, North Carolina

Lisa E. Davis, PharmD, FCCP, BCPS, BCOP

Professor, Department of Pharmacy Practice and Science, College of Pharmacy, University of Arizona; Clinical Pharmacist in Oncology, Banner University Medical Center, Tucson, Arizona

Christopher M. Degenkolb, PharmD, BCPS

Clinical Pharmacy Specialist, Internal Medicine, Richard L. Roudebush Veterans Affairs Medical Center, Indianapolis, Indiana

Paulina Deming, PharmD, PhD

Clinical Associate Professor, Department of Pharmacy Practice, College of Pharmacy, University of New Mexico Health Sciences Center; Clinical Pharmacist, Center for Digestive Diseases HCV Clinic, University of New Mexico; Assistant Director, Viral Hepatitis Programs, Project ECHO, University of New Mexico Health Sciences Center, Albuquerque, New Mexico

Brandon Dionne, PharmD, BCPS-AQ ID, BCIDP, AAHIVP

Assistant Clinical Professor, Department of Pharmacy and Health Systems Sciences, School of Pharmacy, Northeastern University; Clinical Pharmacist, Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts

Holly S. Divine, PharmD, BCACP, BCGP, CDE, FAPhA

Clinical Professor, Department of Pharmacy Practice and Science, University of Kentucky College of Pharmacy, Lexington, Kentucky

Ernest J Dole, PharmD, PhD, FASHP, BCPS

Clinical Pharmacist, Pain Consultation and Treatment Center, University of New Mexico Hospitals; Clinical Associate Professor, College of Pharmacy, University of New Mexico Health Sciences Center, Albuquerque, New Mexico

Jennifer A. Donaldson, PharmD, BCPPS

Senior Content Management Consultant, Pediatric Pharmacist, Clinical Effectiveness, Wolters Kluwer, Indianapolis, Indiana

Gabriella A. Douglass, PharmD, BCACP, AAHIVP, BC-ADM

Assistant Professor, Department of Pharmacy Practice, Harding University College of Pharmacy, Searcy; Clinical Pharmacist in Ambulatory Care, ARcare, Augusta, Arkansas

Scott R. Drab, PharmD, CDE, BC-ADM

Associate Professor of Pharmacy and Therapeutics, School of Pharmacy, University of Pittsburgh; Director, University Diabetes Care Associates, Pittsburgh, Pennsylvania

David P. Elliott, PharmD, FASCP, FCCP, AGSF, BCGP

Professor and Associate Chair, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University Health Sciences Charleston Campus; Clinical Pharmacist in the Internal Medicine Clinic, Charleston Area Medical Center, Charleston, West Virginia

Sharon M. Erdman, PharmD, FIDSA

Clinical Professor, Department of Pharmacy Practice, College of Pharmacy, Purdue University, West Lafayette; Infectious Diseases Clinical Pharmacist, Eskenazi Health, Indianapolis, Indiana

Kathryn Eroschenko, PharmD

Clinical Associate Professor of Pharmacy Practice, Department of Pharmacy Practice and Administration, Kasiska Division of Health Sciences College of Pharmacy, Idaho State University, Meridian; Population Health Pharmacist, Saint Alphonsus Health Alliance, Boise, Idaho

Brian L. Erstad, PharmD, FCCP, MCCM, FASHP

Professor and Head, Department of Pharmacy Practice and Science, The University of Arizona College of Pharmacy, Tucson, Arizona

Jeffery D. Evans, PharmD

Director and Associate Professor, School of Clinical Sciences, College of Pharmacy, University of Louisiana Monroe, Monroe, Louisiana

Sarah N. Fischer, PharmD

Clinical Neurology Research Fellow, Department of Clinical Pharmacy and Neurology, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Aurora, Colorado

Virginia H. Fleming, PharmD, BCPS

Clinical Associate Professor, Department of Clinical and Administrative Pharmacy, College of Pharmacy, University of Georgia, Athens, Georgia

Rachel W. Flurie, PharmD, BCPS

Assistant Professor, Department of Pharmacotherapy and Outcomes Science, School of Pharmacy, Virginia Commonwealth University; Clinical Pharmacist in Internal Medicine, Virginia Commonwealth University Health System, Richmond, Virginia

Andrea S. Franks, PharmD, BCPS

Associate Professor and Vice Chair for Education, Department of Clinical Pharmacy and Translational Science; Associate Professor, Department of Family Medicine, College of Pharmacy and Graduate School of Medicine, University of Tennessee Health Science Center, Maryville, Tennessee

Michelle Fravel, PharmD, BCPS

Clinical Associate Professor, Department of Pharmacy Practice and Science, University of Iowa College of Pharmacy; Clinical Pharmacy Specialist in Ambulatory Care, University of Iowa Hospitals and Clinics, Iowa City, Iowa

Mary E. Fredrickson, PharmD, BCPS

Assistant Professor, Department of Pharmacy Practice, Director of Instructional Laboratories, College of Pharmacy, Northeast Ohio Medical University, Rootstown, Ohio

Scott G. Garland, PharmD

Postdoctoral Fellow, Departments of Pharmacotherapy and Translational Research and Community Health and Family Medicine, Colleges of Pharmacy and Medicine, University of Florida, Gainesville, Florida

Sharon S. Gatewood, PharmD, FAPhA, BCACP

Associate Professor, Department of Pharmacotherapy and Outcomes Science, School of Pharmacy, Virginia Commonwealth University, Richmond, Virginia

Jane M. Gervasio, PharmD, BCNSP, FCCP

Professor and Chair of Pharmacy Practice, Butler University College of Pharmacy and Health Sciences, Indianapolis, Indiana

Michael J. Gonyeau, BS, MEd, PharmD, FNAP, FCCP, BCPS

Clinical Professor, Department of Pharmacy and Health Systems Sciences, School of Pharmacy, Northeastern University; Clinical Pharmacist in Internal Medicine, Brigham and Women's Hospital, Boston, Massachusetts

Jean-Venable "Kelly" R. Goode, PharmD, BCPS, FAPhA, FCCP

Professor and Director, PGY1 Community-Based Pharmacy Residency Program, School of Pharmacy, Virginia Commonwealth University, Richmond, Virginia

Jaime L. Gray, PharmD, BCCCP

Clinical Pharmacy Specialist, Surgical Critical Care, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania

Anthony J. Guarascio, PharmD, BCPS

Associate Professor, Department of Pharmacy Practice, Duquesne University School of Pharmacy; Clinical Pharmacist in Infectious Diseases, Allegheny General Hospital, Pittsburgh, Pennsylvania

Wayne P. Gulliver, MD, FRCPC

Professor of Medicine and Dermatology, Faculty of Medicine, Memorial University of Newfoundland, Newfoundland, Canada

John G. Gums, PharmD, FCCP

Associate Dean for Clinical and Administrative Affairs; Professor of Pharmacy and Medicine, Department of Pharmacotherapy and Translational Research, Department of Community Health and Family Medicine, Colleges of Pharmacy and Medicine, University of Florida, Gainesville, Florida

Jennifer R. Guthrie, MPAS, PA-C

Director of Experiential Education, Physician Assistant Program; Assistant Professor of Health Sciences, College of Pharmacy and Health Sciences, Butler University, Indianapolis, Indiana

Deanne L. Hall, PharmD, CDE, BCACP

Associate Professor of Pharmacy and Therapeutics, University of Pittsburgh School of Pharmacy; Clinical Pharmacy Specialist, Ambulatory Care, UPMC Presbyterian/Shadyside, Pittsburgh, Pennsylvania

Suzanne C. Harris, PharmD, BCPP, CPP

Clinical Assistant Professor; Pharmacy Clinical Specialist, Psychiatry; Experiential Director, UNC Health Care, UNC Eshelman School of Pharmacy, University of North Carolina Hospitals and Clinics, Chapel Hill, North Carolina

Deborah A. Hass, PharmD, BCOP, BCPS

Associate Professor, Department of Pharmacy Practice, West Coast University School of Pharmacy, Los Angeles, California

Keith A. Hecht, PharmD, BCOP

Associate Professor of Pharmacy Practice, Southern Illinois University Edwardsville, School of Pharmacy, Edwardsville, Illinois

Brian A. Hemstreet, PharmD, FCCP, BCPS

Assistant Dean for Student Affairs, Professor of Pharmacy Practice, University of Colorado, Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, Colorado

Sarah Hittle, PharmD, BCCCP

Critical Care Clinical Pharmacy Specialist, St. Vincent Indianapolis Hospital, Indianapolis, Indiana

Brittany Hoffmann-Eubanks, PharmD, MBA

Pharmacy Manager, Jewel-Osco Pharmacy, South Holland, Illinois; Founder and Chief Executive Officer, Banner Medical LLC

Lisa M. Holle, PharmD, BCOP, FHOPA

Associate Clinical Professor, Department of Pharmacy Practice, University of Connecticut School of Pharmacy, Storrs; Associate Professor, University of Connecticut School of Medicine, Farmington, Connecticut

Yvonne C. Huckleberry, PharmD, BCPS, FCCM

Critical Care Pharmacist, Medical Intensive Care Unit, Banner, University Medical Center Tucson; Clinical Associate Professor, Department of Pharmacy Practice and Science, University of Arizona College of Pharmacy, Tucson, Arizona

Franklin Huggins, PharmD, BCPPS, BCCCP

Clinical Associate Professor, Department of Clinical Pharmacy, West Virginia University School of Pharmacy, Morgantown; Pediatric Clinical Specialist, CAMC Women and Children's Hospital, Charleston, West Virginia

Carrie L. Isaacs, PharmD, CDE, MLDE

Clinical Pharmacy Specialist in Primary Care, Lexington VA Medical Center, Lexington, Kentucky

Timothy J. Ives, PharmD, MPH, FCCP, CPP

Professor of Pharmacy and Adjunct Professor of Medicine, UNC Eshelman School of Pharmacy, Chapel Hill, North Carolina

Julie W. Jeter, MD

Associate Professor, Department of Family Medicine, Graduate School of Medicine, University of Tennessee, Knoxville, Tennessee

Alexis Jones, PharmD, BCOP

Clinical Pharmacist, Gynecologic Oncology, University of North Carolina Medical Center, Chapel Hill, North Carolina

Laura L. Jung, BS Pharm, PharmD

Medical Writer, ETHOS Health Communications, Mount Holly, North Carolina

Marina Kanos, MSN, RN, FNP-C

Advanced Clinical Practitioner, Adult Medical Oncology, Levine Cancer Institute, Charlotte, North Carolina

Michael D. Katz, PharmD

Professor, Department of Pharmacy Practice and Science; Director of International Programs; Director of Residency Programs, University of Arizona College of Pharmacy, Tucson, Arizona

Michael B. Kays, PharmD, FCCP, BCIDP

Associate Professor, Department of Pharmacy Practice, College of Pharmacy, Purdue University, West Lafayette and Indianapolis; Adjunct Associate Professor, Department of Medicine, Indiana University School of Medicine, Indianapolis; Clinical Specialist, Infectious Diseases, Eskenazi Health, Indianapolis, Indiana

Syed Khan, MD, MBA, FAPA

Chairman, Department of Psychiatry; Medical Director, Crisis and Inpatient Services; Core Faculty Member, Psychiatry Residency Program, Community Hospital North, Indianapolis; Adjunct Professor, Marion College of Osteopathic Medicine, Indianapolis, Indiana

S. Travis King, PharmD, BCPS-AQ ID

Clinical Pharmacy Specialist, Infectious Diseases, Ochsner Medical Center, New Orleans, Louisiana

Cynthia K. Kirkwood, PharmD, BCPP

Professor and Executive Associate Dean for Academic Affairs, School of Pharmacy, Virginia Commonwealth University, Richmond, Virginia

Erika L. Kleppinger, PharmD, BCPS

Associate Clinical Professor, Department of Pharmacy Practice, Harrison School of Pharmacy, Auburn University, Auburn, Alabama

Jonathan M. Kline, PharmD, CACP, BCPS, CDE

Director of Pharmacy, Jefferson Medical Center, WVU Medicine, Ranson, West Virginia

Vanessa T. Kline, PharmD, BCPS

Pharmacist, Winchester Medical Center, Winchester, Virginia

Julia M. Koehler, PharmD, FCCP

Associate Dean for External Affiliations; Professor of Pharmacy Practice, College of Pharmacy and Health Sciences, Butler University; Ambulatory Care Clinical Pharmacist, Pulmonary Rehabilitation, Indiana University Health, Indianapolis, Indiana

Denise M. Kolanczyk, PharmD, BCPS (AQ Cardiology)

Assistant Professor, Department of Pharmacy Practice, Midwestern University Chicago College of Pharmacy, Downers Grove; Clinical Pharmacist in Internal Medicine, Loyola University Medical Center, Maywood, Illinois

Brian J. Kopp, PharmD, BCCCP, BCPS, FCCM

Clinical Pharmacist, Surgical Trauma ICU, Banner-University Medical Center Tucson; Clinical Associate Professor, Department of Pharmacy Practice and Science, The University of Arizona College of Pharmacy, Tucson, Arizona

Michael D. Kraft, PharmD, BCNSP

Clinical Professor, Department of Clinical Pharmacy, College of Pharmacy, University of Michigan; Assistant Director, Education and Research, Department of Pharmacy Services, Michigan Medicine, Ann Arbor, Michigan

Poh Gin Kwa, MD, FRCPC

Pediatrician, Eastern Health, St. John's, Newfoundland and Labrador, Canada

Margaret A. Landis, PharmD

Staff Pharmacist, Kroger Pharmacy, Blacksburg, Virginia

Kena J. Lanham, PharmD, BCPS, BCGP, BCCP

Clinical Pharmacy Specialist, Cardiovascular, Tristar Centennial Medical Center, Nashville, Tennessee

Lisa LaVallee, MD

Clinical Associate Professor, UNC School of Medicine, Chapel Hill; Residency Director, MAHEC Family Practice Residency Program, Asheville, North Carolina

Rebecca M. T. Law, BS Pharm, PharmD

Associate Professor, School of Pharmacy and Faculty of Medicine, Memorial University of Newfoundland, St. John's, Newfoundland and Labrador, Canada; Visiting Research Scholar, Department of Dermatology, University of California San Francisco, San Francisco, California

Mary W. L. Lee, PharmD, BCPS, FCCP

Professor, Midwestern University Chicago College of Pharmacy, Downers Grove, Illinois

Cara Liday, PharmD, CDE

Associate Professor, Department of Pharmacy Practice and Administrative Sciences, Idaho State University; Clinical Pharmacist, Intermountain Medical Clinic, Pocatello, Idaho

Kristen L. Longstreth, PharmD, BCPS

Clinical Associate Professor, Department of Pharmacy Practice, College of Pharmacy, Northeast Ohio Medical University, Rootstown; Clinical Pharmacy Specialist, St. Elizabeth Youngstown Hospital, Youngstown, Ohio

Cheer T. Lum, PharmD, BCPP

Clinical Specialist in Behavioral Care, Community Hospital North; Ambulatory Care Pharmacist, Behavioral Care, Community Health Network, Indianapolis, Indiana

Robert MacLaren, BSc (Pharm), PharmD, MPH, FCCM, FCCP

Professor, Department of Clinical Pharmacy, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, Colorado

Rebecca J. Mahan, PharmD, BCGP, BCACP

Assistant Professor of Pharmacy Practice, Geriatrics, Texas Tech University HSC School of Pharmacy, Dallas, Texas

Howard I. Maibach, MD

Professor, Department of Dermatology, University of California San Francisco, San Francisco, California

Erik D. Maki, PharmD, BCPS

Associate Professor of Pharmacy Practice, Clinical Sciences Department, College of Pharmacy and Health Sciences, Drake University; Clinical Specialist in Internal Medicine, Mercy Medical Center, Des Moines, Iowa

Jonathan W. Malara, PharmD, BCOP

Clinical Pharmacy Specialist, Breast Medical Oncology, Division of Pharmacy, The University of Texas MD Anderson Cancer Center, Houston, Texas

Joel C. Marrs, PharmD, FAHA, FASHP, FCCP, FNLA, BCPS, BCACP, BCCP, CLS

Associate Professor, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora; Clinical Pharmacy Specialist, Denver Health Medical Center, Denver, Colorado

Jay L. Martello, PharmD, BCPS

Clinical Associate Professor, Department of Clinical Pharmacy, West Virginia University School of Pharmacy, Morgantown; Clinical Pharmacy Specialist in Internal Medicine, West Virginia University Medicine, Morgantown, West Virginia

Allison L. Martin, PharmD, BCOP

Pharmacist, Clinical Coordinator, Department of Hematologic Oncology and Blood Disorders, Levine Cancer Institute, Charlotte, North Carolina

Craig Martin, PharmD, BCPS, MBA

Professor and Associate Dean/Chief Operations Officer, University of Kentucky College of Pharmacy, Lexington, Kentucky

Michelle T. Martin, PharmD, FCCP, BCPS, BCACP

Clinical Pharmacist, University of Illinois Hospital and Health Sciences System; Clinical Associate Professor, University of Illinois at Chicago College of Pharmacy, Chicago, Illinois

Katelynn Mayberry, PharmD

Clinical Assistant Professor, Department of Pharmacy Practice, School of Pharmacy, Mercer University; Clinical Pharmacist in Psychiatry, Georgia Regional Hospital, Atlanta, Georgia

Lena M. Maynor, PharmD, BCPS

Director of Student Affairs and Academic Initiatives, Health Sciences Center; Associate Professor, Department of Clinical Pharmacy, West Virginia University, Morgantown, West Virginia

Ziemowit Mazur, EdM, MS, PA-C

Assistant Professor and Associate Director, Physician Assistant Program, Rosalind Franklin University of Medicine and Science, North Chicago, Illinois

James W. McAuley, RPh, PhD, FAPhA

Professor of Pharmacy Practice and Science and Neurology, The Ohio State University Colleges of Pharmacy and Medicine, Columbus, Ohio

Jennifer McCann, PharmD, BCCCP

State Director of Clinical Pharmacy Services, Ascension Indiana, St. Vincent Health, Indianapolis, Indiana

William McGhee, PharmD

Clinical Pharmacy Specialist, Transplantation, Department of Pharmacy, UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania

Ashlee McMillan, PharmD, BCACP

Clinical Associate Professor, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University, Morgantown, West Virginia

Brian McMillan, MD

Clinical Assistant Professor, Department of Ophthalmology, West Virginia University School of Medicine, Morgantown, West Virginia

Sarah T. Melton, PharmD, BCPP, BCACP, FASCP

Professor of Pharmacy Practice, Gatton College of Pharmacy, East Tennessee State University, Johnson City, Tennessee

Renee-Claude Mercier, PharmD, PhC, BCPS-AQID, FCCP

Professor of Pharmacy and Medicine, University of New Mexico Health Sciences Center; Co-Medical Director, Antimicrobial Stewardship Project ECHO, University of New Mexico Health Sciences Center, Albuquerque, New Mexico

Ashley H. Meredith, PharmD, FCCP, BCACP, BCPS, CDE

Clinical Associate Professor, Department of Pharmacy Practice, College of Pharmacy, Purdue University, West Lafayette; Clinical Pharmacy Specialist in Ambulatory Care, Eskenazi Health, Indianapolis, Indiana

Sarah M. Michienzi, PharmD, BCPS, AAHIVP

Clinical Assistant Professor, Section of Infectious Diseases Pharmacotherapy, Department of Pharmacy Practice, College of Pharmacy, University of Illinois at Chicago; Clinical Pharmacist in HIV and ID, University of Illinois at Chicago Hospital and Health Sciences System, Chicago, Illinois

Lindsey N. Miller, PharmD, BCPP

Associate Professor, Department of Pharmacy Practice, Lipscomb University College of Pharmacy; Clinical Psychiatric Pharmacist, Vanderbilt Psychiatric Hospital, Nashville, Tennessee

Marta A. Miyares, PharmD, BCPS, BCCP, CACP

Clinical Pharmacy Specialist, Internal Medicine and Anticoagulation, Jackson Memorial Hospital; Director, PGY1 Residency Program, Miami, Florida

Scott W. Mueller, FCCM, BCCCP

Associate Professor, Department of Clinical Pharmacy, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, Colorado

James J. Nawarskas, PharmD, BCPS

Associate Professor, Department of Pharmacy Practice and Administrative Sciences, College of Pharmacy, University of New Mexico, Albuquerque, New Mexico

Leigh A. Nelson, PharmD, BCPP

Professor, Division of Pharmacy Practice and Administration, School of Pharmacy, University of Missouri-Kansas City, Kansas City, Missouri

Branden D. Nemecek, PharmD, BCPS

Associate Professor, Department of Pharmacy Practice, Duquesne University School of Pharmacy; Clinical Pharmacist in Internal Medicine, UPMC Mercy Hospital, Pittsburgh, Pennsylvania

Sarah A. Nisly, PharmD, BCPS, FCCP

Associate Professor, School of Pharmacy, Wingate University, Wingate; Clinical Pharmacist in Internal Medicine, Wake Forest Baptist Health System, Winston Salem, North Carolina

Jason M. Noel, PharmD, BCPP

Associate Professor, Department of Pharmacy Practice and Science, University of Maryland School of Pharmacy, Baltimore, Maryland

Kimberly J. Novak, PharmD, BCPS, BCPPS, FPPAG

Advanced Patient Care Pharmacist, Pediatric and Adult Cystic Fibrosis, Nationwide Children's Hospital; Clinical Assistant Professor (Adjunct), The Ohio State University, College of Pharmacy, Columbus, Ohio

Kelly K. Nystrom, PharmD, BCOP

Associate Professor of Pharmacy Practice, School of Pharmacy and Health Professions, Creighton University; Oncology Clinical Specialist, CHI Health CUMC Bergan Mercy, Omaha, Nebraska

Cindy L. O'Bryant, PharmD, FCCP, FHOPA, BCOP

Professor, Department of Clinical Pharmacy, Skaggs School of Pharmacy and Pharmaceutical Sciences, University of Colorado, Aurora, Colorado

Dannielle C. O'Donnell, BS, PharmD

Clinical Assistant Professor, College of Pharmacy, The University of Texas; Principal Medical Science Liaison, Immunology, US Medical Affairs, Genentech, Austin, Texas

Manjunath (Amit) P. Pai, PharmD, FCP

Associate Professor of Clinical Pharmacy, Department of Clinical Pharmacy, College of Pharmacy, University of Michigan; Deputy Director, Pharmacokinetics and Mass Spectrometry Core Laboratory, University of Michigan, Ann Arbor, Michigan

Neha Sheth Pandit, PharmD, AAHIVP, BCPS

Associate Professor and Vice Chair for Research and Scholarship, Department of Pharmacy Practice and Science, University of Maryland School of Pharmacy, Baltimore, Maryland

Laura M. Panko, MD

Assistant Professor Pediatrics, University of Pittsburgh School of Medicine; Paul C. Gaffney Division of Pediatric Hospital Medicine, UPMC Children's Hospital of Pittsburgh, Pittsburgh, Pennsylvania

Dennis Parker, Jr, PharmD

Associate Professor of Pharmacy Practice, Eugene Applebaum College of Pharmacy and Health Sciences, Wayne State University, Detroit, Michigan

Robert B. Parker, PharmD, FCCP

Professor, Department of Clinical Pharmacy and Translational Science, University of Tennessee Health Science Center, Memphis, Tennessee

Chris Paxos, PharmD, BCPP, BCPS, BCGP

Associate Professor, Pharmacy Practice, Northeast Ohio Medical University, Rootstown; Pharmacotherapy Specialist, Psychiatry, Cleveland Clinic Akron General, Akron, Ohio

Rebecca S. Pettit, PharmD, MBA, BCPS, BCPPS

Pediatric Pulmonary Ambulatory Care Clinical Specialist, Riley Hospital for Children at IU Health, Indianapolis, Indiana

Sherry Peveto, DNP, WHNP-BC

Interim Associate Director Undergraduate Program, Kitty Degree School of Nursing, College of Health Sciences, University of Louisiana Monroe, Monroe, Louisiana

Nicole C. Pezzino, PharmD, BCACP, CDE

Assistant Professor of Pharmacy Practice, Wilkes University, School of Pharmacy, Wilkes-Barre; Clinical Pharmacist Community/Ambulatory Pharmacy, Weis Markets, Schnecksville, Pennsylvania

Beth Bryles Phillips, PharmD, FASHP, FCCP, BCPS, BCACP

Rite Aid Professor, University of Georgia College of Pharmacy; Clinical Pharmacy Specialist, Charlie Norwood VA Medical Center, Athens, Georgia

Amy M. Pick, PharmD, MS, BCOP

Professor of Pharmacy Practice, Creighton University, School of Pharmacy and Health Professions, Omaha, Nebraska

Melissa R. Pleva, PharmD, BCPS, BCNSP, BCCCP

Pharmacy Manager, CVC, Surgery and Cardiovascular Services, Michigan Medicine; Adjunct Clinical Assistant Professor, University of Michigan College of Pharmacy, Ann Arbor, Michigan

Charles D. Ponte, BS, PharmD, BC-ADM, BCPS, CDE, CPE, FAADE, FAPhA, FASHP, FCCP, FNAP

Professor of Clinical Pharmacy and Family Medicine, Department of Clinical Pharmacy, Schools of Pharmacy and Medicine, West Virginia University, Robert C. Byrd Health Sciences Center, Morgantown, West Virginia

Amber E. Proctor, PharmD, BCOP

Clinical Assistant Professor, Department of Pharmacotherapy and Experimental Therapeutics, UNC Eshelman School of Pharmacy, University of North Carolina; Clinical Pharmacist, Thoracic Oncology, University of North Carolina Medical Center, Chapel Hill, North Carolina

Erin C. Raney, PharmD, FCCP, BCPS, BC-ADM

Professor of Pharmacy Practice, College of Pharmacy-Glendale, Midwestern University, Glendale, Arizona

Paul M. Reynolds, PharmD, BCPS, BCCCP

Assistant Professor, Department of Clinical Pharmacy, University of Colorado Skaggs School of Pharmacy and Pharmaceutical Sciences, Aurora, Colorado

Denise H. Rhoney, PharmD, FCCP, FCCM, FNCS

Ron and Nancy McFarlane Distinguished Professor, Associate Dean for Curricular Innovation, UNC Eshelman School of Pharmacy, Chapel Hill, North Carolina

Natalie I. Rine, PharmD, BCPS, BCCCP

Clinical Pharmacy Specialist, Emergency Medicine/Critical Care, OhioHealth Riverside Methodist Hospital, Columbus, Ohio

Christopher Roberson, MS, AGNP-BC, AAHIVS

Nurse Practitioner, School of Medicine, University of Maryland, Baltimore, Maryland

Michelle L. Rockey, PharmD, BCOP, FHOPA

Hematology/Oncology Pharmacy Clinical Lead, Wake Forest Baptist Health, Winston-Salem, North Carolina

Julianna V. F. Roddy, PharmD, BCOP

Clinical Pharmacist Specialist, Hematology/Oncology; Assistant Professor, Clinical Practice, Arthur G. James Cancer Hospital, The Ohio State University, Columbus, Ohio

Keith A. Rodvold, PharmD, FCCP, FIDSA

Interim Chair and Professor of Pharmacy Practice, Department of Pharmacy Practice, Colleges of Pharmacy and Medicine, University of Illinois at Chicago, Chicago, Illinois

Kelly C. Rogers, PharmD, BCCP, FCCP, FACC

Professor, Department of Clinical Pharmacy and Translational Science, University of Tennessee Health Science Center, Memphis, Tennessee

Carol J. Rollins, MS, RD, PharmD, BCNSP, FASPEN, FASHP

Clinical Professor, Department of Pharmacy Practice and Science, College of Pharmacy, University of Arizona, Tucson, Arizona

Rochelle Rubin, PharmD, BCPS, CDE

Senior Clinical Pharmacy Coordinator, Family Medicine; Residency Program Director, PGY1 Pharmacy Residency, The Brooklyn Hospital Center, Brooklyn, New York

Laura F. Ruekert, PharmD, BCPP, BCGP

Clinical Specialist in Behavioral Care and Core Faculty Member, Psychiatry Residency Program, Community Hospital North; Associate Professor of Pharmacy Practice, Butler University, Indianapolis, Indiana

Ilya Rybakov, PharmD

Infectious Diseases Clinical Pharmacist, OPAT/Antimicrobial Stewardship, WVU Medicine, Morgantown, West Virginia

Rachel Marie E. Salas, MD, MEdHP, FAAN

Associate Professor, Neurology and Nursing; Director, Interprofessional Education and Interprofessional Collaborative Practice; Director, Neurology Clerkship; Director, PreDoc Program, Johns Hopkins Medicine, Baltimore, Maryland

Laurel Sampognaro, PharmD

Director of Student Success; Clinical Associate Professor, School of Clinical Pharmacy, College of Pharmacy, University of Louisiana Monroe, Monroe, Louisiana

Megan E Sands, PharmD

Clinical Pharmacist, Advocate Aurora Health, Aurora, Illinois.

Elizabeth J. Scharman, PharmD, DABAT, BCPS, FAAC

Professor, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University; Clinical Toxicologist and Director, West Virginia Poison Center, West Virginia University Health Sciences Center Charleston, Charleston, West Virginia

Justin M. Schmidt, PharmD, BCPS

Clinical Pharmacist in Internal Medicine, Edward Hines Jr. VA Hospital, Hines, Illinois; at the time of writing, she was also Associate Professor, Department of Pharmacy Practice, Chicago College of Pharmacy, Midwestern University, Downers Grove, Illinois

Kristine S. Schonder, PharmD

Assistant Professor, Department of Pharmacy and Therapeutics, University of Pittsburgh School of Pharmacy; Clinical Specialist, Transplant, Starzl Transplant Institute, UPMC, Pittsburgh, Pennsylvania

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE

Associate Professor, Pharmacy Practice; Director, PGY2 Ambulatory Care Residency Program, Midwestern University Chicago College of Pharmacy; Clinical Pharmacist, Advocate Medical Group, Southeast, Downers Grove, Illinois

Terry L. Schwinghammer, PharmD, FCCP, FASHP, FAPhA

Professor Emeritus, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University, Morgantown, West Virginia

Mollie A. Scott, PharmD, BCACP, CPP, FASHP

Regional Associate Dean, UNC Eshelman School of Pharmacy, Chapel Hill; Clinical Associate Professor, UNC School of Medicine and UNC Health Sciences at MAHEC, Asheville, North Carolina

Roohollah R. Sharifi, MD, FACS

Professor of Urology and Surgery, University of Illinois at Chicago College of Medicine; Section Chief of Urology, Jesse Brown Veterans Affairs Medical Center, Chicago, Illinois

Amy H. Sheehan, PharmD

Associate Professor, Department of Pharmacy Practice, Purdue University College of Pharmacy, West Lafayette; Drug Information Specialist, Indiana University Health, Indianapolis, Indiana

Kelly M. Shields, PharmD

Associate Dean and Professor of Pharmacy Practice, Ohio Northern University College of Pharmacy, Ada, Ohio

Carrie A. Sincak, PharmD, BCPS, FASHP

Associate Dean for Clinical Affairs, Professor of Pharmacy Practice, Chicago College of Pharmacy, Midwestern University, Downers Grove, Illinois

Douglas Slain, PharmD, BCPS, FCCP, FASHP

Professor and Chair, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University; Infectious Diseases Clinical Specialist, WVU Medicine and Ruby Memorial Hospital, Morgantown, West Virginia

Carmen B. Smith, PharmD, BCPS

Assistant Professor, Department of Pharmacy Practice, St. Louis College of Pharmacy; Clinical Pharmacist Internal Medicine, Mercy Hospital St. Louis, St. Louis, Missouri

Curtis L. Smith, PharmD, FCCP, BCPS

Professor, Department of Pharmacy Practice, College of Pharmacy, Ferris State University, Lansing, Michigan

Steven M. Smith, PharmD, MPH, BCPS, CHC, FCCP

Assistant Professor of Pharmacy, Departments of Pharmacotherapy and Translational Research, College of Pharmacy; Associate Director, Center for Integrative Cardiovascular and Metabolic Diseases, University of Florida, Gainesville, Florida

Mikayla L. Spangler, PharmD, BCPS

Associate Professor, Creighton University School of Pharmacy and Health Professions, Omaha, Nebraska

Tracy L. Sprunger, PharmD, BCPS

Associate Professor of Pharmacy Practice, Butler University College of Pharmacy and Health Sciences, Indianapolis, Indiana

Sneha Baxi Srivastava, PharmD, BCACP, CDE

Associate Professor, Department of Pharmacy Practice, Rosalind Franklin University of Medicine and Science, College of Pharmacy, North Chicago, Illinois

Mary K. Stamatakis, PharmD

Senior Associate Dean for Academic Affairs and Educational Innovation; Professor, Department of Clinical Pharmacy, School of Pharmacy; West Virginia University, Morgantown, West Virginia

Autumn Stewart-Lynch, PharmD, BCACP, CTS

Associate Professor, Department of Pharmacy Practice, Duquesne University School of Pharmacy, Pittsburgh; Clinical Pharmacist, Heritage Valley Family Medicine, Beaver Falls, Pennsylvania

Rebecca H. Stone, PharmD, BCPS, BCACP

Clinical Assistant Professor, Department of Clinical and Administrative Pharmacy, University of Georgia, Athens, Georgia

Jennifer L. Swank, PharmD, BCOP

Clinical Pharmacist Medical Oncology, H. Lee Moffitt Cancer Center, Tampa, Florida

Lynne M. Sylvia, PharmD

Senior Clinical Pharmacy Specialist, Cardiology, Department of Pharmacy, Tufts Medical Center, Boston, Massachusetts

Gregory B. Tallman, PharmD, MS, BCPS

Assistant Professor, School of Pharmacy, Pacific University, Hillsboro, Oregon

Heather M. Teufel, PharmD, BCCCP

Clinical Pharmacy Specialist, Emergency Medicine, Penn Medicine Chester County Hospital, West Chester, Pennsylvania

Teresa C. Thakrar, PharmD, BCOP

Clinical Pharmacist, Hematology/Stem Cell Transplant, Indiana University Health, Simon Cancer Center, Indianapolis, Indiana

James E. Tisdale, PharmD, BCPS, FCCP, FAPhA, FNAP, FAHA, FACC

Professor, College of Pharmacy, Purdue University, West Lafayette; Adjunct Professor, School of Medicine, Indiana University, Indianapolis, Indiana

Trent G. Towne, PharmD, BCPS

Associate Professor of Pharmacy Practice, Manchester University College of Pharmacy, Natural and Health Sciences; Infectious Diseases Clinical Pharmacist, Parkview Regional Medical Center, Fort Wayne, Indiana

Tran H. Tran, PharmD, BCPS

Associate Professor of Pharmacy Practice, Department of Pharmacy Practice, Chicago College of Pharmacy, Midwestern University, Downers Grove; Clinical Pharmacist, Substance Use Intervention Team (SUIT), Rush University Medical Center, Chicago, Illinois

Natalie R. Tucker, PharmD, BCPS, BCIDP

Director, PGY2 Infectious Diseases Pharmacy Residency Program, Antimicrobial Stewardship Pharmacist, HSHS St. John's Hospital, Springfield, Illinois

Kevin M. Tuohy, PharmD, BCPS

Associate Professor of Pharmacy Practice, Butler University College of Pharmacy and Health Sciences; Clinical Pharmacy Specialist, Internal Medicine, IU Health Methodist Hospital, Indianapolis, Indiana

R. Brigg Turner, PharmD, BCPS (AQ-ID)

Assistant Professor, School of Pharmacy, Pacific University, Hillsboro, Oregon

Regan M. Wade, PharmD, BCPS

PGY2 Pharmacy Resident, Indiana University Health Academic Health Center, Indianapolis, Indiana

Mary L. Wagner, PharmD, MS

Associate Professor, Earnest Mario School of Pharmacy, Rutgers, The State University of New Jersey, Piscataway, New Jersey

Alison M. Walton, PharmD, BCPS

Associate Professor of Pharmacy Practice, Department of Pharmacy Practice, College of Pharmacy and Health Sciences, Butler University, Indianapolis, Indiana

Yuchen Wang, PharmD, BCPP

Clinical Pharmacist, Fresno County Department of Behavioral Health and CCFMG, Fresno, California

Zachary A. Weber, PharmD, BCPS, BCACP, CDE

Director of Interprofessional Education; Clinical Associate Professor of Pharmacy Practice, Purdue College of Pharmacy; Assistant Dean for Programming, Indiana University Interprofessional Practice and Education Center, Indianapolis, Indiana

Jeffrey T. Wieczorkiewicz, PharmD, BCPS

Assistant Professor, Department of Pharmacy Practice, Midwestern University Chicago College of Pharmacy, Downers Grove, Illinois; Clinical Pharmacist in Internal Medicine, Hines VA Medical Center, Maywood, Illinois

Jon P. Wietholter, PharmD, BCPS

Clinical Associate Professor, Department of Clinical Pharmacy, School of Pharmacy, West Virginia University; Clinical Pharmacist in Internal Medicine, WVU Medicine J.W. Ruby Memorial Hospital, Morgantown, West Virginia

Susan R. Winkler, PharmD, BCPS, FCCP

Professor and Chair, Department of Pharmacy Practice, Midwestern University Chicago College of Pharmacy, Downers Grove, Illinois

Nancy S. Yunker, PharmD, FCCP, BCPS

Associate Professor of Pharmacy, Department of Pharmacotherapy and Outcomes Science, VCU School of Pharmacy; Clinical Pharmacy Specialist, Internal Medicine, VCU Health, Richmond, Virginia

PREFACE

The purpose of the *Pharmacotherapy Casebook* is to help students in the health professions and practicing clinicians develop and refine the skills required to identify and resolve drug therapy problems by using realistic patient cases. Case studies can actively involve students in the learning process; engender self-confidence; and promote the development of skills in independent self-study, problem analysis, decision-making, oral communication, and teamwork. Patient case studies can also be used as the focal point of discussions about pathophysiology, medicinal chemistry, pharmacology, and the pharmacotherapy of individual diseases. By integrating the biomedical and pharmaceutical sciences with pharmacotherapeutics, case studies can help students appreciate the relevance and importance of a sound scientific foundation in preparation for practice.

The patient cases in this book are intended to complement the scientific and clinical information in the 11th edition of *Pharmacotherapy: A Pathophysiologic Approach*. This edition of the casebook contains 157 unique patient cases, with case chapters organized into organ system sections corresponding to the *Pharmacotherapy* textbook. Students should read the relevant textbook chapter to become thoroughly familiar with the pathophysiology and pharmacotherapy of each disease state before attempting to identify and address the medication therapy problems of the patients described in this casebook. The *Pharmacotherapy* textbook, casebook, and other useful learning resources are also available on *AccessPharmacy.com* (subscription required). By using these realistic cases to practice creating, defending, and implementing pharmacotherapeutics care plans, students can begin to develop the skills and self-confidence that will be necessary to make the real decisions required in professional practice.

The knowledge and clinical experience required to answer the questions associated with each patient presentation vary from case to case. Some cases deal with a single disease, whereas others have multiple diseases and drug therapy problems. As a guide for instructors, each case is identified as being one of three complexity levels; this classification system is described in more detail in Chapter 1.

Casebook Section 1: Principles of Patient-Focused Therapy includes five chapters that provide guidance on use of the casebook and six patient cases related to managing special patient populations (pediatrics, geriatrics, palliative care) and toxicology situations.

Chapter 1 describes the format of case presentations and the means by which students and instructors can maximize the usefulness of the casebook. Previous editions of the casebook employed a systematic problem-solving approach to each case. Briefly, the steps involved in this approach include: (1) identifying drug therapy problems, (2) establishing therapeutic goals, (3) evaluating therapeutic options to achieve the goals, (4) designing an optimal patient care plan, (5) establishing monitoring parameters, and (6) providing patient education. A major innovation for the 11th edition is that the case questions and answers now use the Joint Commission of Pharmacy

Practitioners (JCPP) Pharmacists' Patient Care Process (PPCP; <https://jcnp.net/patient-care-process/>). The disease state chapters in the *Pharmacotherapy* textbook also include an outline of the PPCP for the relevant disorders. It is important for all clinicians to use a consistent process in delivering care so patients and other healthcare providers know what to expect from them. In addition, the PPCP is similar to the patient care process used by other healthcare professionals, and the Accreditation Council for Pharmacy Education (ACPE) requires schools/colleges of pharmacy to teach the PPCP in the curriculum.

Chapter 2 presents the philosophy and implementation of active learning strategies. This chapter sets the tone for the casebook by describing how these approaches can enhance student learning. The chapter provides useful active learning strategies for instructors and provides advice to students on how to maximize their learning opportunities in active learning environments.

Chapter 3 discusses the importance of patient communication and offers strategies to get the most out of the time that the clinician shares with the patient during each encounter. The information can be used as the basis for simulated counseling sessions related to the patient cases.

Chapter 4 describes in detail the steps involved in the PPCP: (1) Collect, (2) Assess, (3) Plan, (4) Implement, and (5) Follow-up: Monitor and Evaluate. The chapter includes example of patient case vignettes to demonstrate implementation of the PPCP. Implementing the PPCP profession-wide provides a common terminology for pharmacist patient care services and focuses on quality improvement, provider collaboration, improved patient outcomes, and cost savings. All pharmacists providing direct patient care should employ the PPCP, regardless of practice setting.

Chapter 5 describes the critically important process of documenting patient encounters and interventions to serve as a record of patient care services provided and to communicate effectively with other healthcare providers. The authors discuss documentation of medication therapy management (MTM) and comprehensive medication management (CMM) encounters as well as use of the traditional SOAP note for documenting the identification and resolution of drug therapy problems. A sample case presentation is provided to illustrate construction of a SOAP note with appropriate documentation of drug therapy problems.

Casebook Sections 2 through 18 contain patient cases organized by organ systems that correspond to those of the *Pharmacotherapy* textbook. Section 19 (Complementary and Alternative Therapies) contains patient vignettes that are directly related to patient cases that were presented earlier in this casebook. Each scenario involves the potential use of one or more dietary supplements. Additional follow-up questions are then asked to help the reader gain the scientific and clinical knowledge required to provide evidence-based recommendations about use of the supplement in that particular patient. Sixteen different dietary supplements are discussed: garlic, fish oil (omega-3 fatty acids), ginger, butterbur,

feverfew, St. John's wort, kava, melatonin, cinnamon, α -lipoic acid, black cohosh, soy, *Pygeum africanum*, glucosamine, chondroitin, and elderberry.

We are grateful for the broad acceptance that previous editions of the casebook have received. It has been adopted by many schools of pharmacy and nurse practitioner programs. It has also been used

in institutional staff development efforts and by individual pharmacists striving to upgrade their pharmacotherapy skills. It is our hope that this new edition will be even more valuable in assisting health-care practitioners to meet society's need for safe and effective drug therapy.

ACKNOWLEDGMENTS

The editors would like to thank the 215 case and chapter authors from more than 100 schools of pharmacy, healthcare systems, and other institutions in the United States and Canada who contributed their scholarly efforts to this casebook. We especially appreciate their diligence in meeting deadlines, adhering to the new Patient Care Process casebook format, and providing up-to-date pharmacotherapy information. The next generation of healthcare practitioners will benefit from their willingness to share their expertise.

We also thank the individuals at McGraw-Hill Education whose cooperation, guidance, and commitment were instrumental in maintaining the high standards of this publication, especially Michael Weitz, Peter Boyle, Richard Ruzicka, Laura Libretti, and

Melinda Avelar. We appreciate the meticulous attention to composition and pre-press detail provided by Garima Poddar of Cenveo Publisher Services. Finally, we are grateful to our spouses for their understanding, support, and encouragement during the preparation of this new edition.

Terry L. Schwinghammer, PharmD, FCCP, FASHP, FAPhA

Julia M. Koehler, PharmD, FCCP

Jill S. Borchert, PharmD, BCACP, BCPS, FCCP

Douglas Slain, PharmD, BCPS, FCCP, FASHP

Sharon K. Park, PharmD, MEd, BCPS

This page intentionally left blank

Pharmacotherapy Casebook

This page intentionally left blank

SECTION 1 PRINCIPLES OF PATIENT-FOCUSED THERAPY

CHAPTER

1

Introduction: How to Use This Casebook

TERRY L. SCHWINGHAMMER, PharmD, FCCP, FASHP, FAPhA

CASE STUDIES AS A MEANS OF ENHANCING STUDENT LEARNING

The case method can assist learners in developing the skills of self-learning, critical thinking, problem identification, and decision making. When case studies from this *Casebook* are used in the curricula of the healthcare professions or for independent study by practitioners, the focus should be on learning the *process* of identifying and resolving drug therapy problems rather than simply finding answers to the individual case questions. Students do learn scientific and clinical facts as they resolve case study problems, but they usually learn more from their own independent study and from discussions with their peers than they do from the instructor. Working through subsequent cases with similar problems reinforces information recall. Educational programs in the healthcare professions that rely heavily on traditional lectures tend to concentrate on dissemination of scientific and clinical content with rote memorization of facts rather than developing higher-order thinking and problem-solving skills.

Case studies in the health professions provide the personal history of an individual patient and information about one or more healthcare problems that require resolution. The learner's job is to collect the relevant patient information, assess that clinical data, develop hypotheses about the underlying cause of problems, consider possible solutions to problems identified, decide on and implement optimal solutions, perform follow-up to identify the consequences of one's decisions, and then make adjustments in the plan as needed.¹ The role of the teacher is to serve as coach and facilitator rather than as the source of "the answer." In fact, in many situations, there is more than one acceptable answer to a given case question. Because instructors do not necessarily need to possess the correct answer, they need not be experts in the field being discussed if they enter the learning environment prepared to participate as engaged coaches. The students also become teachers of themselves and others, and both instructors and students learn from each other through thoughtful discussion of the case.

PREPARATION FOR LEARNING WITH PATIENT CASES

The patient cases in this *Casebook* can be used for independent self-learning by individual students and for in-class problem-solving

discussions by student groups and their instructors. If meaningful learning and discussion are to occur, students must come to class sessions prepared to discuss the case material rationally, to make informed recommendations, and to defend their patient care plans. This requires a strong commitment to independent self-study prior to the session. The cases in this book were designed to correspond with the scientific and clinical information contained in the 11th edition of *Pharmacotherapy: A Pathophysiologic Approach*.² For this reason, thorough understanding of the corresponding textbook chapter is recommended as the principal method of student preparation. The McGraw-Hill online learning center *AccessPharmacy* (www.AccessPharmacy.com, subscription required) contains the *Pharmacotherapy* textbook, this *Pharmacotherapy Casebook*, and many other educational resources that can be beneficial in answering case questions. The patient cases in the *Casebook* can also be used with the textbook *Pharmacotherapy Principles & Practice*, 5th edition,³ or other therapeutics textbooks. Primary literature should also be consulted as necessary to supplement textbook readings.

Most of the cases in the *Casebook* represent common diseases likely to be encountered by generalist practitioners. As a result, not all of the medical disorders discussed in the *Pharmacotherapy* textbook have an associated patient case in the *Casebook*. On the other hand, *Pharmacotherapy* textbook chapters that discuss multiple diseases may have several corresponding cases in the *Casebook*.

LEVELS OF CASE COMPLEXITY

Each case is identified at the top of the first page as being one of the three levels of complexity. Instructors may use this classification system to select cases for discussion that correspond to the experience level of the student learners. These levels are defined as follows:

Level I—An uncomplicated case; only a single textbook chapter is required to complete the case questions. Little prior knowledge of the disease state or clinical experience is needed.

Level II—An intermediate-level case; several textbook chapters or other reference sources may be required to complete the case. Prior clinical experience may be helpful in resolving all of the issues presented.

Level III—A complicated case; multiple textbook chapters, additional readings, and substantial clinical experience may be required to solve all of the patient's drug therapy problems.

USING LEARNING OBJECTIVES TO FOCUS LEARNING

Learning objectives are included at the beginning of each case for student reflection. The focus of these outcomes is on eventually achieving clinical competence rather than simply learning isolated clinical and scientific facts. These objectives reflect some of the knowledge, skills, and abilities that students should possess after reading the relevant textbook chapter(s), studying the case, preparing a patient care plan, and defending their recommendations. Of course, true clinical competence can only be gained by direct interaction with real patients in various healthcare environments.

The learning objectives provided are meant to serve as a starting point to stimulate student thinking, but they are not intended to be all-inclusive. In fact, students should also generate their own personal ability outcome statements and learning objectives for each case. By so doing, students take greater control of their own learning, which serves to improve personal motivation and the desire to learn.

FORMAT OF THE CASEBOOK

PATIENT PRESENTATION

The format and organization of cases reflect those usually seen in actual clinical settings. The patient's medical history, physical examination findings, and laboratory results are provided in the following standardized outline format.

Chief Complaint

The chief complaint (CC) is a brief statement from the patient describing the symptom, problem, condition, or other reason for a medical encounter. The CC is stated in the patient's own words and forms the basis for the healthcare provider's initial differential diagnosis. Medical terms and diagnoses are generally not used in the CC, so the patient's symptoms are documented accurately. The appropriate medical terminology is used only after an appropriate evaluation (ie, medical history, physical examination, laboratory and other testing) leads to a medical diagnosis.

In the United Kingdom, the term "presenting complaint" (PC) may be used. Other synonyms include reason for encounter (RFE), presenting problem, problem on admission, or reason for presenting.

History of Present Illness

The history of present illness (HPI) (called the history of presenting complaint or HPC in the United Kingdom) is a more complete description of the patient's symptom(s). Items usually included in the HPI are:

- Date of onset
- Precise location
- Nature of onset, severity, and duration
- Presence of exacerbations and remissions
- Effect of any treatment given
- Relationship to other symptoms, bodily functions, or activities (eg, activity, meals)
- Degree of interference with daily activities

Past Medical History

The past medical history (PMH) includes serious illnesses, surgical procedures, and injuries the patient has experienced previously.

Minor complaints (eg, influenza, colds) are usually omitted unless they might have a bearing on the current medical situation.

Family History

The family history (FH) includes the age and health of parents, siblings, and children. For deceased relatives, the age and cause of death are recorded. In particular, heritable diseases and those with a hereditary tendency are noted (eg, diabetes mellitus, cardiovascular disease, malignancy, rheumatoid arthritis, obesity).

Social History

The social history (SH) includes the social characteristics of the patient as well as environmental factors and behaviors that may contribute to development of disease. Items that may be documented are the patient's marital status; number of children; educational background; occupation; physical activity; hobbies; dietary habits; and use of tobacco, alcohol, or other drugs.

Medication History

The medication history (Meds) should include an accurate record of the patient's current use of prescription medications, nonprescription products, dietary supplements, and home remedies. Because there are thousands of prescription and nonprescription products available, it is important to obtain a complete medication history that includes the names, doses, routes of administration, schedules, and duration of therapy for all medications, including dietary supplements and other alternative therapies.

Allergies

Allergies (All) to drugs, food, pets, and environmental factors (eg, grass, dust, pollen) are recorded. An accurate description of the reaction that occurred should also be included. Care should be taken to distinguish adverse drug effects ("upset stomach") from true allergies ("hives").

Review of Systems

In the review of systems (ROS), the examiner questions the patient about the presence of symptoms related to each body system. In a brief ROS, only the pertinent positive and negative findings are recorded. In a complete ROS, body systems are generally listed starting from the head and working toward the feet and may include symptoms related to the skin, head, eyes, ears, nose, mouth and throat, neck, cardiovascular, respiratory, gastrointestinal, genitourinary, endocrine, musculoskeletal, and neuropsychiatric systems. The purpose of the ROS is to identify patient complaints related to each body system and prevent omission of pertinent information. Findings that were included in the HPI are generally not repeated in the ROS.

Physical Examination

The exact procedures performed during the physical examination (PE) vary depending on the CC, medical history, and type of encounter. A complete physical examination may be performed for annual screening, employment, or insurance purposes. In most clinical situations, only a limited physical examination is performed that is focused on the reason for the encounter. In psychiatric practice, greater emphasis is usually placed on the type and severity of the patient's symptoms than on physical findings. Most of the cases in this *Casebook* include comprehensive physical examination data so students become familiar with common procedures and learn which findings are relevant to the CC and which are routine, normal findings. A suitable physical assessment textbook should be consulted

for the specific procedures that may be conducted for each body system. The general sections for the PE are outlined as follows:

General Appearance (Gen)

Vital Signs (VS)—blood pressure, pulse, respiratory rate, and temperature. In hospital settings in particular, the presence of acute and chronic pain should be assessed when appropriate, but pain is no longer referred to as “the fifth vital sign.”⁴ For ease of use and consistency in this *Casebook*, weight and height are included in the vital signs section, but they are not actually considered to be vital signs.

- **Skin** (or Integumentary)
- **Head, Eyes, Ears, Nose, and Throat (HEENT)**
- **Lungs/Thorax** (or Pulmonary)
- **Cardiovascular (Cor or CV)**
- **Abdomen (Abd)**
- **Genitalia/Rectal (Genit/Rect)**
- **Musculoskeletal and Extremities (MS/Ext)**
- **Neurologic (Neuro)**

Laboratory Data

The results of laboratory tests are included with most cases in this *Casebook*. **Appendix A: Conversion Factors and Anthropometrics** contains common conversion factors and anthropometric information that will be helpful in solving many case answers. Normal (reference) ranges for the laboratory tests used throughout the *Casebook* are included in **Appendix B: Common Laboratory Tests**. Values in the appendix are provided in both traditional units and SI units (*le système International d'Unités*). The reference range for a given laboratory test is determined from a representative sample of the general population. The upper and lower limits of the range usually encompass two standard deviations from the population mean, which includes a range within which about 95% of healthy persons would fall. The term *normal range* may therefore be misleading, because a test result may be abnormal for a given individual even if it falls within the so-called normal range. Furthermore, given the statistical methods used to calculate the range, about 1 in 20 normal, healthy individuals will have a value for a test that lies outside the range. For these reasons, the term *reference range* is preferred over normal range. Reference ranges differ among laboratories, so the values given in Appendix B should be considered only as a general guide. Institution-specific reference ranges should be used in actual clinical settings.

All of the cases include some physical examination and laboratory findings that are within normal limits. For example, a description of the cardiovascular examination may include a statement that the point of maximal impulse is at the fifth intercostal space; laboratory evaluation may include a serum sodium level of 140 mEq/L (140 mmol/L). The presentation of actual findings (rather than simple statements that the heart examination and the serum sodium were normal) reflects what will be seen in actual clinical practice. More importantly, listing both normal and abnormal findings requires students to carefully assess the complete database and identify the pertinent positive and negative findings for themselves. A valuable portion of the learning process is lost if students are only provided with findings that are abnormal and are known to be associated with the disease that is the focus of the patient case.

HUMANISTIC CONSIDERATIONS

The patients described in this *Casebook* have been given fictitious names to humanize the situations and to encourage students to remember that they will one day be caring for patients, not treating diseases or correcting laboratory values. However, in actual

clinical settings, patient confidentiality is of utmost importance, and real patient names should not be used during group discussions in patient care areas unless absolutely necessary. To develop student awareness and sensitivity to this issue, instructors may wish to avoid using these fictitious patient names during class discussions. In this *Casebook*, patient names are usually given in the initial presentation and are then used infrequently in subsequent questions or other portions of the case.

The issues of race, ethnicity, and gender also deserve thoughtful consideration. The traditional format for case presentations usually begins with a description of the patient's age, race, and gender, as in: “The patient is a 65-year-old white male....” Single-word racial labels such as “black” or “white” are actually of limited value in many cases and may actually be misleading in some instances.⁵ For this reason, racial descriptors are usually excluded from the opening line of each presentation in the *Casebook*. When ethnicity is pertinent to the case, this information is presented in the social history or physical examination. Adult patients in this *Casebook* are usually referred to as men or women, rather than males or females, to promote sensitivity to human dignity.

The patient cases in this *Casebook* include medical abbreviations and both generic and proprietary drug names, just as medical records do in actual practice. Although abbreviations and brand names are sometimes the source of clinical problems, the intent of their inclusion is to make the cases as realistic as possible. **Appendix C** lists the medical abbreviations used in the *Casebook*. This list is limited to commonly accepted abbreviations; thousands more exist, which can make it difficult for novice practitioners to efficiently assess patient databases. An accreditation standard of the Joint Commission International (JCI) mandates that health-care institutions ensure the standardized use of approved symbols and medical abbreviations across the hospital. In addition, use of abbreviations is prohibited in informed consent forms, patient rights documents, discharge instructions, and other documents that patients and families receive from the institution.⁶ Clinicians must be aware of this institutional document and use only approved symbols and abbreviations in the medical record system. Appendix C of this *Casebook* also lists abbreviations and designations that should be avoided. Given the immense human toll resulting from medical errors, this section should be considered “must” reading for all student learners. Medical abbreviations were ubiquitous throughout the paper medical charts used in physician offices, clinics, and hospitals prior to the advent of electronic health records. Fortunately, abbreviations are used less frequently now with the widespread adoption of electronic health records that have click boxes for sections of the medical history, PE, and other areas, along with physician dictation of progress notes.

The *Casebook* also contains some photographs of commercial drug products. These illustrations are provided as examples only and are not intended to imply endorsement of those particular products.

SOCIETAL NEED FOR COMPREHENSIVE MEDICATION MANAGEMENT SERVICES

Medication therapy plays a crucial role in improving human health by enhancing quality of life and extending life expectancy. The advent of biotechnology has led to the introduction of unique compounds for the prevention and treatment of disease that were unimaginable just a decade or two ago. Each year the US Food and Drug Administration (FDA) approves dozens of new drugs and biologic products containing molecular entities that have never before been marketed in the country. In 2017 the FDA reported approving 46 new drug therapies.⁷ According to the Patient-Centered Primary

Care Collaborative, more than 3.5 billion prescriptions are written annually, and medications are involved in 80% of all treatments in the United States.⁸ Although the cost of new therapeutic agents often receives intense scrutiny, appropriate drug therapy can be cost-effective and reduce total healthcare expenditures by decreasing the need for surgery, avoiding adverse drug reactions, preventing hospital admissions and readmissions, shortening hospital stays, and preventing emergency department and physician visits.⁹

Unfortunately, various types of drug therapy problems frequently interfere with the ability of healthcare providers and patients to achieve the desired health outcomes. The resulting cost of drug-related morbidity and mortality exceeds \$200 billion each year in the United States, which is more than the cost of the medications used.^{8,10} An analysis conducted by researchers at Johns Hopkins University concluded that more than 250,000 Americans die each year from medical errors, and that if medical error were a disease, it would rank as the third-leading cause of death in the United States.¹¹ Medical errors include not only drug therapy problems but also any unintended act (either of omission or commission) or an act that does not achieve its intended outcome, failure of a planned action to be completed as intended, use of a wrong plan to achieve a goal, or deviation from the process of care that may or may not cause harm to the patient. Considering the magnitude of this problem, there is a clear societal need for better medication use.

Comprehensive medication management (CMM) is the standard of care that ensures that each patient's medications (prescription, non-prescription, nutritional supplements, and other types) are assessed to determine that each one is appropriate for the patient, effective for the medical condition, safe given patient comorbidities and other medications being taken, and able to be taken by the patient as intended.⁸ When drug therapy problems are identified, pharmacists and other healthcare providers collaborate in a team-based approach to develop and implement an individualized care plan with specific therapeutic goals, drug therapy interventions, patient education, and follow-up evaluation to determine the actual patient outcomes achieved. Throughout this process, it is imperative that the patient understand, agree with, and participate actively in the treatment plan to optimize the medication experience and clinical outcomes.⁸ Widespread implementation of CMM in patient-centered medical homes (PCMHs) and other clinical settings has the potential to optimize medication use and improve healthcare for society.

CATEGORIES OF DRUG THERAPY PROBLEMS

A drug therapy problem has been defined as “any undesirable event experienced by a patient that involves, or is suspected to involve, drug therapy and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve.”¹² Seven distinct types of drug therapy problems have been identified that may potentially lead to an undesirable event that has physiologic, psychological, social, or economic ramifications.¹² These seven problem types relate to assessment of medication appropriateness, effectiveness, safety, or adherence:

Appropriate indication for the medication:

1. The medication is unnecessary because the patient does not have a clinical indication at this time.
2. Additional drug therapy is required to treat or prevent a medical condition.

Effectiveness of the medication:

3. The medication being used is not effective at producing the desired patient response.
4. The dosage is too low to produce the desired patient response.

Safety of the medication:

5. The medication is causing an adverse reaction.
6. The dose is too high, resulting in actual or potential undesirable effects.

Adherence to the medication:

7. The patient is not able or willing to take the drug therapy as intended.

These drug therapy problems are discussed in more detail in **Chapter 4**. Because this *Casebook* is intended to be used as a companion for the *Pharmacotherapy* textbook, one of its purposes is to serve as a tool for learning about the pharmacotherapy of disease states. For this reason, the primary drug therapy problem requiring identification and resolution for many patients in the *Casebook* is the need for additional drug treatment for a specific medical indication (problem 2 above). Other actual or potential drug therapy problems may coexist during the initial presentation or may develop during the clinical course of the disease.

APPLYING A CONSISTENT PATIENT CARE PROCESS TO CASE PROBLEMS

In this *Casebook*, each patient presentation is followed by a set of questions that are similar for each case. These questions are applied consistently to each case to demonstrate that clinicians should use a systematic patient care process for identifying, preventing, and resolving drug therapy problems regardless of the disease state being addressed. The 11th edition of the *Casebook* has adopted the Joint Commission of Pharmacy Practitioners (JCPP) *Pharmacists' Patient Care Process* (PPCP)¹³ as the framework for this purpose. The PPCP is the standard patient care process taught in schools and colleges of pharmacy in the United States. The Accreditation Council for Pharmacy Education (ACPE) Standard 10.8 states that “the curriculum prepares students to provide patient-centered collaborative care as described in the Pharmacists' Patient Care Process model endorsed by the Joint Commission of Pharmacy Practitioners.”¹⁴ Although the PPCP includes the word “pharmacists,” the process mirrors the patient care process used by other healthcare providers. Thus, teaching pharmacy students to employ this process in clinical practice will help ensure that they “speak the same language” as other healthcare providers when they become healthcare providers.

Prior to embarking upon the patient care process for a given individual, the clinician must establish an appropriate professional relationship with the patient, family, and caregivers that will support active engagement and effective communication. Throughout the process, the medication management expert must continually collaborate, document, and communicate with physicians, pharmacists, and other healthcare professionals to provide safe, effective, and coordinated care. See **Chapter 4, Fig. 4-1** for an illustration of how the PPCP is implemented in clinical practice. A description of how the case questions in this *Casebook* employ the steps of the PPCP is included in the following paragraphs.

1. COLLECT INFORMATION

1.a. What subjective and objective information indicates the presence of (the primary problem or disease)?

The first step is to collect the necessary subjective and objective information to understand the patient's medical and medication history and his/her clinical status. Therefore, the first case question in the *Casebook* asks the learner to identify the subjective and objective information that indicates the presence of the patient's primary

disease state that is associated with the reason for the patient encounter.

Subjective information is obtained by communicating with the patient and cannot usually be verified by the clinician. As examples, a patient may report having chest pain, palpitations, shortness of breath, dizziness, or feelings of depression. Subjective information usually begins with the CC, which includes one or more symptoms. Subjective information is also obtained from the ROS, as discussed previously.

Objective information can be measured and verified by the clinician using the physical examination procedures of inspection, auscultation, palpation, and percussion as well as vital signs (heart rate, blood pressure, respiratory rate, temperature). Laboratory data and other diagnostic test results also provide objective information.

For purposes of CMM in real patient situations, it is critically important to obtain accurate and complete information about all of the patient's medications, including prescription, nonprescription, alternative therapies, vitamins, nutritional supplements, and products used from family or friends, regardless of who prescribed them.⁷ It is also important to identify where the products were dispensed, purchased, or otherwise obtained. Even though not all of this information will be provided or known for the patient cases in the *Casebook*, it is important for students to realize the importance of collecting this information.

1.b. What additional information is needed to fully assess this patient's primary problem?

In many *Casebook* cases (just as in real life), some important pertinent information is missing from the patient presentation. A separate case question will ask the student to list other additional information that would be needed to fully assess the patient's main problem. Providing precise recommendations for obtaining the additional information needed to satisfactorily assess the patient's problems can be a valuable contribution to the patient's care. Therefore, it is important for students to have an in-depth understanding of the patient's medical conditions and medication therapy and be able to recognize the subjective and objective information that is available as well as the pertinent information that may be missing from the case presentation.

2. ASSESS THE INFORMATION

2.a. Assess the severity of the primary problem or disease based on the subjective and objective information available.

The next step is to review the information collected to assess the severity of the patient's clinical condition and determine whether drug therapy problems exist. Each medication should be assessed for its appropriateness, effectiveness, safety, and patient adherence. It is important to differentiate the process of identifying drug therapy problems from making a disease-related medical diagnosis. In fact, the primary medical diagnosis is often known for patients seen by pharmacists. However, pharmacists must be able to assess the patient's database to determine whether drug therapy problems exist that warrant a change in drug therapy. In the case of preexisting chronic diseases, such as asthma or rheumatoid arthritis, one must be able to assess information that may indicate a change in severity of the disease.

2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Novice student learners often struggle with writing statements of drug therapy problems. Simply put, a drug therapy problem statement must include a medical condition (disease) or health-related issue and a problem related to drug therapy. These statements should be clear, concise, and easily understood by other healthcare professionals. They must also contain sufficient detail so others can

understand the magnitude of the problem. Provided here are several examples of well-written drug therapy problem statements:

- Established rheumatoid arthritis (> 6 months duration) with high disease activity (DAS28 score > 5.1) inadequately treated with the current regimen of methotrexate monotherapy.
- Newly diagnosed stage IIIB classic Hodgkin lymphoma requiring treatment with pharmacotherapy that offers the best chance for cure.
- Dyslipidemia with need for change in statin therapy due to drug interaction (simvastatin and verapamil) and dose too low (inappropriate statin intensity).
- Allergic rhinitis treated with a medication (diphenhydramine) that is inappropriate for the patient and is likely causing an adverse reaction (excessive sedation).
- Recurrent falls, possibly related to medication use (diphenhydramine, metoprolol succinate, donepezil) and other factors.

The clinician should create a prioritized list of all of the drug therapy problems that were identified. Problems of the highest priority should be addressed first (immediately during the current encounter), whereas those of lower priority may be addressed later (eg, later in the course of a hospital stay or at subsequent follow-up visits). For many cases in the *Casebook*, the major drug therapy problem (highest priority) will be an untreated or inadequately treated indication. Other problems related to the primary or secondary diseases might be improper drug selection leading to ineffectiveness, subtherapeutic dosage, overdosage, failure to receive or take the drug(s) prescribed, adverse drug reactions, drug interactions, or drug use without indication.

2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Some patient cases will include a question related to these unique considerations that must be identified and addressed. For example, the patient may not have medical insurance or be able to afford high-cost biologic drug products for diseases such as inflammatory bowel disease, plaque psoriasis, or rheumatoid arthritis. Other patients may have family, social, or cultural issues that could interfere with effective drug therapy. The patient's race may have implications for precision medicine or appropriate medication selection for some diseases such as asthma and hypertension. Addressing these issues is an important part of developing an effective and comprehensive patient care plan.

3. DEVELOP A CARE PLAN

After all relevant patient information has been collected and assessed and the patient's drug therapy problems have been identified and prioritized, the pharmacist or other medication management expert develops an individualized patient-centered medication management plan in collaboration with other healthcare professionals and the patient (or caregiver). The plan must be evidence-based, cost-effective, and likely to be adhered to by the patient.

3.a. What are the goals of pharmacotherapy in this case?

The first step in designing a care plan is to establish treatment goals for each medical condition. The primary therapeutic outcomes include:

- Cure of disease (eg, bacterial infection)
- Reduction or elimination of symptoms (eg, pain from cancer)
- Arresting or slowing of the progression of disease (eg, rheumatoid arthritis, HIV infection)
- Preventing a disease or symptom (eg, coronary heart disease)

Other important outcomes of pharmacotherapy include:

- Not complicating or aggravating other existing disease states
- Avoiding or minimizing adverse effects of treatment
- Providing cost-effective therapy
- Maintaining the patient's quality of life

Sources of information for this step may include the patient or caregiver, the patient's physician or other healthcare professionals, medical records, and the *Pharmacotherapy* textbook or other literature references. Importantly, although national guidelines may stipulate population-level goals (eg, A1C <7% for type 2 diabetes), goals must be individualized for each patient based on potential risk, comorbidities, concomitant drug therapy, patient preference, and physician intentions.¹³

3.b. What nondrug therapies might be useful for this patient?

After the intended outcomes have been defined, attention can be directed toward identifying the types of treatments that might be beneficial in achieving those outcomes. The clinician should consider all feasible nondrug and pharmacotherapeutic alternatives available for achieving the predefined therapeutic outcomes before designing a regimen. Nondrug therapies that might be useful such as lifestyle measures (eg, diet, weight loss, and exercise), physical therapy, relaxation techniques, and surgical procedures should be included in the list of therapeutic alternatives.

3.c. What feasible pharmacotherapeutic alternatives are available for treating the disease or drug therapy problem?

Virtually all feasible drug therapy options should be considered while assessing the potential benefits and limitations of each one in light of the patient's particular situation. Some first-line agents may need to be avoided due to inadequate efficacy, potential for adverse effects, concomitant comorbidities or drugs, or high cost. For example, an asthma patient who requires new drug therapy for hypertension might better tolerate treatment with a thiazide diuretic rather than a β -blocker. On the other hand, a hypertensive patient with gout may be better served by use of a β -blocker rather than a thiazide diuretic. Useful sources of information on therapeutic options include the *Pharmacotherapy* textbook and other references, as well as the clinical experience of the healthcare provider and other healthcare professionals on the patient care team.

There has been a resurgence of interest in dietary supplements and other alternative therapies in recent years. The public spends billions of dollars each year on supplements for which there is little scientific evidence of efficacy, that are not standardized for potency and purity, and that are not regulated by the FDA as drug products. Furthermore, some products are hazardous, and others may interact with a patient's prescription medications or aggravate concurrent disease states. On the other hand, scientific evidence of efficacy does exist for some dietary supplements, and the National Institutes of Health Office of Dietary Supplements maintains fact sheets that give an overview of individual vitamins, minerals and other dietary supplements.¹⁵ Healthcare providers must be knowledgeable about these products and prepared to answer patient questions regarding their efficacy and safety.

The *Casebook* contains a separate section devoted to dietary supplements (see **Section 19**). This portion of the *Casebook* contains a number of fictitious patient vignettes that relate to patient cases that were presented earlier in the *Casebook*. Each scenario involves the potential use of one or more dietary supplements by the patient. Additional follow-up questions are then asked to help the reader gain the scientific and clinical knowledge required to provide an evidence-based recommendation about use of the supplement in that particular patient. The use

of 16 different dietary supplements for 13 different disorders is included in this section: α -lipoic acid (type 2 diabetes), black cohosh (menopausal symptoms), butterbur (migraine prevention, allergic rhinitis), cinnamon (diabetes), elderberry (influenza), feverfew (migraine prevention), fish oil (diabetes, dyslipidemia), garlic (dyslipidemia), ginger (nausea/vomiting), glucosamine/chondroitin (osteoarthritis), kava kava (anxiety), melatonin (insomnia), pygeum Africanum (benign prostatic hypertrophy), soy (menopausal symptoms), and St. John's wort (depression). Current reference sources are provided for all of the supplements.

3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's primary disease and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

The purpose of this step is to determine the specific drugs, dosage forms, doses, routes of administration, schedules, and durations of therapy that are best suited to resolve each drug therapy problem that has been identified. Each pharmacotherapy regimen should be evidence based and individualized for the specific patient. Thus, the learner should be prepared to defend the rationale for the regimens selected and provide logical reasons for avoiding specific regimens in the care plan. Some potential reasons for drug avoidance include drug allergy, drug-drug or drug-disease interactions, patient age, renal or hepatic impairment, adverse effects, inconvenient dosage schedule, likelihood of poor adherence, pregnancy, and high treatment cost.

The specific dose selected may depend on the severity of the medical condition. For example, the initial oral dose of the loop diuretic furosemide for edema ranges from 20 to 80 mg per day and may be titrated up to 600 mg per day for severe edematous states.¹⁶ Appropriate dosage also may vary depending on the indication for the drug; for example, the analgesic effect of the nonsteroidal anti-inflammatory drug ibuprofen may be achieved at lower doses than those required for anti-inflammatory activity.¹⁷ The likelihood of adherence with the regimen and patient tolerance come into play in the selection of dosage forms. For example, some patients receiving the tumor necrosis factor inhibitor golimumab for rheumatoid arthritis may prefer to self-administer the medication subcutaneously at home; others may require golimumab intravenous infusions because they are either unwilling or unable to use subcutaneous injections. The economic, psychosocial, and ethical factors that are applicable to the patient should also be given due consideration in designing the pharmacotherapeutic regimen.

In many clinical situations, there is more than one acceptable drug regimen, so it is important for the healthcare team to agree on all drug therapy regimens selected for a given patient.

3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

This optional question is included only for select patients in the *Casebook*. However, it is a good idea to always have an appropriate backup plan in place if the initial therapy fails or cannot be used.

4. IMPLEMENT THE CARE PLAN

In real-life clinical situations, the care plan that was agreed upon by the healthcare team and patient then requires thoughtful, collaborative implementation. Steps to be taken during the implementation process include¹³:

- Addressing medication- and health-related problems that exist or may arise
- Performing preventive care strategies, including administering vaccines

- Initiating, modifying, discontinuing, and administering medication therapy as authorized
- Providing education and self-management training to the patient or caregiver
- Contributing to coordination of care, including patient referral or transition to another healthcare professional
- Scheduling follow-up care as needed to achieve goals of therapy

4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

As described previously, CMM requires that healthcare providers establish a professional and personal relationship with the patient. Patients are our partners in healthcare, and our efforts may be for naught without their informed participation in the process. For chronic diseases such as diabetes mellitus, hypertension, and asthma, patients may have a greater role in managing their diseases than do healthcare professionals. Self-care is becoming widespread as increasing numbers of prescription medications receive over-the-counter status. For these reasons, patients must be provided with sufficient information to enhance compliance, ensure successful therapy, and minimize adverse effects. **Chapter 3** describes patient interview techniques that can be used efficiently to determine the patient's level of knowledge. Additional information can then be provided as necessary to fill in knowledge gaps.

In the questions posed with individual cases, students are asked to provide the kind of information that should be given to the patient who has limited knowledge of his or her disease. The information should be provided with the intent of improving adherence, ensuring successful therapy, and minimizing adverse effects. Under the Omnibus Budget Reconciliation Act (OBRA) of 1990, for patients who accept the offer of counseling, pharmacists should consider including the following items¹⁸:

- Name and description of the medication (which may include the indication)
- Dosage, dosage form, route of administration, and duration of therapy
- Special directions and precautions for preparation, administration, and use
- Common and severe adverse effects, interactions, and contraindications (with the action required should they occur)
- Techniques for self-monitoring
- Proper storage
- Prescription refill information
- Action to be taken in the event of missed doses

Instructors may wish to have simulated patient-interviewing sessions for new and refill prescriptions during case discussions to practice medication education skills. Factual information should be provided as concisely as possible to enhance memory retention. Various online and print resources are available for consumer information about individual drug products. MedlinePlus is the National Institute of Health's free website for consumers that contains information on prescription and nonprescription drugs, dietary supplements, medical conditions, wellness, diagnostic tests, and other medical information.¹⁹

4.b. Describe how care should be coordinated with other healthcare providers.

As part of the team-based approach, patient care must be coordinated among healthcare providers and the patient, family, and caregivers.

Learner responses to this *Casebook* question should include more than simple descriptions of the roles of other healthcare professionals. More importantly, learners should be able to thoughtfully express how each unique professional role is integrated with others in providing collaborative, team-based care.

For pharmacists and some other providers, their roles includes (in part) initiating, modifying, discontinuing, and administering medication therapy as authorized. Others involved in team-based care might include primary care physicians, specialist physicians, surgeons, nurses, physical therapists, occupational therapists, social workers, dentists, dietitians, psychologists, and others. Consider which of them should be involved in the patient's care and how their efforts serve to coordinate and optimize care. For example:

- Who will educate the patient about their primary disease(s), and the impending changes in care?
- Who will discuss the disease prognosis with the patient?
- Who will counsel the patient about new medications, nondrug therapies, and lifestyle changes?
- Who will provide an updated medication list to the patient?
- Who will discuss options for surgical intervention or discharge to an assisted-care facility?
- If referrals to specialists or other transitions of care are needed, how will this be accomplished? For example, should the patient be referred to a diabetes or anticoagulation management expert for chronic care? Does the patient need dental care? Is a social worker needed to manage the patient's social/home situation?
- Who will be involved in follow-up visits, and who will communicate with the patient about them?
- How will team members communicate with each other during this patient encounter and in planning and conducting future visits?
- Who will document treatment plans in the record?

Documenting the medication therapy plan in the medical record is necessary to ensure accurate communication among practitioners. Oral communication alone can be misinterpreted or transferred inaccurately to others. This is especially true because there are many drugs that sound alike when spoken but have far different therapeutic uses.

The SOAP (Subjective, Objective, Assessment, and Plan) format has been used by clinicians for many years to assess patient problems and to communicate findings and plans in the medical record. Writing SOAP notes may not be the optimal process for learning to solve drug therapy problems because several important steps taken by experienced clinicians are not always apparent and may be overlooked. For example, the precise therapeutic outcome desired is often unstated in SOAP notes, leaving others to presume what the desired treatment goals are. Healthcare professionals using the SOAP format also commonly move directly from an assessment of the patient (diagnosis) to outlining a diagnostic or therapeutic plan, without conveying whether careful consideration has been given to all available feasible diagnostic or therapeutic alternatives. The plan itself as outlined in SOAP notes may also give short shrift to the monitoring parameters required to ensure successful therapy and to detect and prevent adverse drug effects. Finally, SOAP notes often do not include the treatment information that should be conveyed to the most important individual involved: the patient. If SOAP notes are used for documenting drug therapy problems, consideration should be given to including each of these components.

In **Chapter 5**, the SOAP note is presented as the usual method for documenting care plans in the patient's health record. Although

preparation of written communication notes is not included in written form with each set of case questions in the *Casebook*, instructors are encouraged to include the composition of a SOAP note as one of the requirements for successfully completing each case study assignment. A well-written SOAP note focusing on drug therapy problems should provide a clear statement of the drug therapy problem, the clinician's findings relevant to the problem, assessment of the findings, an actual or proposed plan for resolving the problem, and the clinical and laboratory parameters required for follow-up and monitoring.

Clinicians responsible for the outcomes of drug therapy should create and maintain a record of each patient's drug therapy problem list, the plans for resolving each problem, the interventions actually made, and the subsequent therapeutic outcomes achieved.

5. FOLLOW-UP: MONITOR AND EVALUATE

Monitoring the effectiveness of the care plan and modifying it in collaboration with other healthcare professionals and the patient (or caregiver) is performed to assess¹³:

- Medication appropriateness, effectiveness, and safety
- Patient adherence
- Clinical endpoints that contribute to the patient's overall health
- Outcomes of care achieved

The outcome parameters are evaluated against the predetermined goals of therapy to determine the progress made toward achieving the therapeutic goals and to determine if any new drug therapy problems have developed that could interfere with safe and effective medication use.⁸ Patient follow-up should occur at intervals that are appropriate for the patient's clinical situation, the medical conditions being treated, and the drug therapy being used. Follow-up should be carefully coordinated with members of the healthcare team and the patient to avoid interfering with other ongoing patient care activities.⁸

5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

Clinicians must identify the clinical and laboratory parameters necessary to assess the therapy for achievement of the therapeutic goals and to detect and prevent adverse effects. Each outcome parameter selected should be specific, measurable, achievable, directly related to the therapeutic goals, and have a defined endpoint. As a means of remembering these points, the acronym SMART has been used (Specific, Measurable, Achievable, Related, and Time bound). If the goal is to cure bacterial pneumonia for a patient described in this *Casebook*, learners should outline the subjective and objective clinical parameters (eg, relief of chest discomfort, cough, and fever), laboratory tests (eg, normalization of white blood cell count and differential), and other procedures (eg, resolution of infiltrate on chest X-ray) that provide evidence of bacterial eradication and clinical cure of the disease. The intervals at which data should be collected are dependent on the outcome parameters selected and should be established prospectively. Some expensive or invasive procedures may not be repeated after the initial diagnosis is made.

Adverse effect parameters must also be well defined and measurable. For example, it is insufficient to state that one will monitor for potential drug-induced "blood dyscrasias." Rather, one should identify the likely specific hematologic abnormality (eg, anemia, leukopenia, or thrombocytopenia) and outline a prospective schedule for obtaining the appropriate parameters (eg, obtain

monthly hemoglobin/hematocrit, white blood cell count, or platelet count).

Monitoring for adverse events should be directed toward preventing or identifying serious adverse effects that have a reasonable likelihood of occurrence. For example, it is not cost-effective to obtain periodic liver function tests in all patients taking a drug that causes mild abnormalities in liver injury tests only rarely, such as omeprazole. On the other hand, the antipsychotic drug clozapine requires therapy-long periodic monitoring of white blood cell counts and absolute neutrophil counts to enable early detection of drug-induced leukopenia and agranulocytosis.

5.b. Develop a plan for follow-up that includes appropriate time-frames to assess progress toward achievement of the goals of therapy.

The care plan should outline the intervals at which the patient should return for team-based follow-up to ensure that progress is being made toward achieving the desired health outcomes. The return time may be short when there is a patient safety concern when a new potent medication is started that may have serious adverse effects. Longer intervals may be needed to allow a suitable time frame for new medications to exert either partial or full therapeutic effect, such as medications for dyslipidemia or depression.

CLINICAL COURSE

The patient care process requires assessment of the patient's progress to ensure movement toward achieving the desired therapeutic outcomes. A description of the patient's clinical course is included with many cases in this *Casebook* to reflect this process. Some cases follow the progression of the patient's disease over months to years and include both inpatient and outpatient treatment. Follow-up questions directed toward ongoing evaluation and problem solving are included after presentation of the clinical course.

SELF-STUDY ASSIGNMENTS

Each case concludes with several study assignments related to the patient case or the disease state that may be used as independent study projects for students to complete outside class. These assignments may require students to obtain additional information that is not contained in the corresponding *Pharmacotherapy* textbook chapter.

LITERATURE REFERENCES AND INTERNET SITES

Literature references relevant to the patient case are included at the end of each presentation. References selected for inclusion will be useful to students for answering the questions posed. Most of the citations relate to major clinical trials or meta-analyses, authoritative review articles, and clinical practice guidelines. The *Pharmacotherapy* textbook contains a more comprehensive list of references pertinent to each disease state.

Some cases list internet sites as sources of drug therapy information. The sites listed are recognized as authoritative sources of information, such as the FDA (www.fda.gov) and the Centers for Disease Control and Prevention (www.cdc.gov). Students should be advised to be wary of information posted on the internet that is not from highly regarded healthcare organizations or publications. The uniform resource locators (URLs) for internet sites sometimes change,

and it is possible that not all sites listed in the *Casebook* will remain available for viewing.

DEVELOPING ANSWERS TO CASE QUESTIONS

The use of case studies for independent learning and in-class discussion may be unfamiliar to many learners. For this reason, students may find it difficult at first to devise complete answers to the case questions. **Appendix D** contains the answers to two cases in order to demonstrate how case responses might be prepared and presented. The authors of the cases contributed the recommended answers provided in the appendix, but they should not be considered the sole “right” answer. Thoughtful students who have prepared well for the discussion sessions may arrive at additional or alternative answers that are also appropriate.

With diligent self-study, practice, and the guidance of instructors, students will gradually acquire the knowledge, skills, and self-confidence to develop and implement patient care plans for their own future patients in collaboration with other members of the healthcare team. The goal of the *Casebook* is to help students progress along this path of lifelong learning.

REFERENCES

1. Herreid CF. Case studies in science: a novel method of science education. *J Coll Sci Teach*. 1994;23:221–229.
2. DiPiro JT, Yee GC, Ellingrod VL, Haines ST, Nolin TD, Posey LM, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 11th ed. New York, NY: McGraw-Hill, 2020.
3. Chisholm-Burns MA, Schwinghammer TL, Malone PM, Kolesar JM, Bookstaver PB, Lee KC, eds. *Pharmacotherapy Principles & Practice*. 5th ed. New York, NY: McGraw-Hill, 2019.
4. Baker DW. The Joint Commission's pain standards: origins and evolution. Oakbrook Terrace, IL: The Joint Commission; 2017. https://www.jointcommission.org/assets/1/6/Pain_Std_History_Web_Version_05122017.pdf. Accessed October 15, 2018.
5. Caldwell SH, Popenoe R. Perceptions and misperceptions of skin color. *Ann Intern Med*. 1995;122:614–617.
6. Joint Commission International. Use of codes, symbols, and abbreviations. Oak Brook, IL; 2018. <https://www.jointcommissioninternational.org/use-of-codes-symbols-and-abbreviations/>. Accessed October 11, 2018.
7. United States Food and Drug Administration. Novel drug approvals for 2017. <https://www.fda.gov/drugs/developmentapprovalprocess/druginnovation/ucm537040.htm>. Accessed October 11, 2018.
8. Patient-Centered Primary Care Collaborative. The patient-centered medical home: integrating comprehensive medication management to optimize patient outcomes resource guide. Second Edition, June 2012. <https://www.pcpcc.org/sites/default/files/media/medmanagement.pdf>. Accessed October 11, 2018.
9. Dalton K, Byrne S. Role of the pharmacist in reducing healthcare costs: current insights. *Integr Pharm Res Pract*. 2017;6:37–36. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5774321/>. Accessed October 11, 2018.
10. Ernst FR, Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. *J Am Pharm Assoc*. 2001;41:192–199.
11. Makary MA, Daniel M. Medical error—the third leading cause of death in the US. *BMJ*. 2016;353:i2139. doi: 10.1136/bmj.i2139.
12. Cipolle RJ, Strand LM, Morley PC. Drug therapy problems. In: Cipolle RJ, Strand LM, Morley PC, eds. *Pharmaceutical Care Practice: The Patient-Centered Approach to Medication Management Services*. 3rd ed. New York, NY: McGraw-Hill, 2012:chap5. <https://accesspharmacy.mhmedical.com/book.aspx?bookid=491>. Accessed October 15, 2018.
13. Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. May 29, 2014. <https://jcphp.net/patient-care-process/>. Accessed October 15, 2018.
14. Accreditation Council for Pharmacy Education. Professional program in pharmacy leading to the doctor of pharmacy degree standards. <https://www.acpe-accredit.org/pdf/Standards2016FINAL.pdf>. Accessed October 15, 2018.
15. National Institutes of Health Office of Dietary Supplements. <https://ods.od.nih.gov/>. Accessed October 16, 2018.
16. Drug monographs: furosemide. www.accesspharmacy.com. Accessed October 16, 2018.
17. Drug monographs: ibuprofen. www.accesspharmacy.com. Accessed October 16, 2018.
18. Martin S. What you need to know about OBRA '90. *J Am Pharm Assoc*. 1993; NS33(1):26–28.
19. MedlinePlus: Trusted Health Information for You. U.S. National Library of Medicine, Department of Health and Human Services, National Institutes of Health; Bethesda, MD: 2018. <https://medlineplus.gov/>. Accessed October 16, 2018.

This page intentionally left blank

Active Learning Strategies

RACHEL W. FLURIE, PharmD, BCPS
 GRETCHEN M. BROPHY, PharmD, BCPS, FCCP, FCCM, FNCS
 CYNTHIA K. KIRKWOOD, PharmD, BCPP

Healthcare practitioners face situations that require the use of effective problem solving, critical thinking, and communication skills on a daily basis. Therefore, providing students with knowledge alone is insufficient to equip them with the tools needed to be valuable contributors to patient care. Students must understand that it is imperative to provide more than just drug information, which is readily obtained in today's world from internet sites, smartphone apps, and online reference texts. They must be able to evaluate, analyze, and synthesize information, and apply their knowledge to prevent and resolve drug-related problems. As clinicians, they will be required to contribute their expertise to team discussions about patient care, ask appropriate questions, integrate information, and develop action plans.

Professional students must also recognize that learning is a lifelong process. Scores of new drugs are approved every year, drug use practices change, and innovative research alters the way that diseases are treated. Students must be prepared to proactively expand their knowledge base and clinical skills to adapt to the changing profession.

Warren identified several traits that prepare students for future careers: analytic thinking, polite assertiveness, tolerance, communication skills, understanding of one's own physical well-being, and the ability to continue to teach oneself after graduation.¹ To prepare students to become healthcare professionals who are essential members of the healthcare team, many healthcare educators are using active learning strategies in the classroom.^{2,3}

ACTIVE LEARNING VERSUS TRADITIONAL TEACHING

Active learning has numerous definitions, and various methods are described in the educational literature. Simply put, *active learning is the process of having students engage in activities that require reflection on ideas and how students use them.*³ Most proponents of active learning strategies agree that compared with passively receiving lectures, active engagement of students promotes deeper learning, enhances critical thinking skills, provides feedback to students and instructors, and promotes social development. Learning is reinforced when students are actively engaged and apply their knowledge to new situations.³ Active learning is learner-focused and helps students take responsibility for their own learning.²

In contrast, traditional teaching involves a teacher-centered approach. At the beginning of the course, students are given a course syllabus packet that contains "everything they need to know" for the semester. In class, the teacher lectures on a predetermined topic that does not require student preparation and allows students to be passive recipients of information. The testing method is usually a written examination that employs a multiple-choice or short-answer format, which focuses on the student's ability to recall isolated facts

that the teacher has identified as being important. They do not learn to apply their knowledge to situations that they will ultimately encounter in practice. The reward is an external one (ie, exam or course grade) that may or may not reflect a student's actual ability to use the knowledge they have to improve patient care.

To teach students to be lifelong learners, it is essential to stimulate them to be inquisitive and actively involved with the learning that takes place in the classroom. This requires that teachers move away from more comfortable teaching methods and learn new techniques that will help students "learn to learn." In classes with active learning formats, students are involved in much more than listening. The transmission of information is deemphasized and replaced with the development of skills and application of knowledge. Active learning shifts the control of learning from the teacher to the students; this provides an opportunity for students to become active participants in their own learning.²

ACTIVE LEARNING STRATEGIES

Teachers implement active learning exercises into classes in a variety of ways. While some strategies engage individual students with the material, such as giving students the opportunity to pause and recall information, other active learning strategies involve the use of student groups, such as problem-based learning (PBL), team-based learning (TBL), or cooperative or collaborative learning whereby students work together to perform specific tasks in a small group (ie, solve problems, discuss case studies).^{2,4-6} Technology is increasingly used in active learning in numerous ways to maximize the use of class time for higher-order thinking tasks such as analysis, synthesis, and evaluation.⁷⁻⁹ The following are the examples of active learning strategies that involve students in the learning process.

EXERCISES FOR INDIVIDUAL STUDENTS

These exercises can complement lectures and are easily implemented. Quick writing tasks can assess student understanding of (or reaction to) material. Writing helps students to identify knowledge deficits, clarify understanding of the material, and organize thoughts in a logical manner. The "minute paper" or "half-sheet response" has students provide written responses to a question asked in class.¹⁰ Example questions might be, "What was the main point of today's class session?" or "What was the muddiest point of today's class session?" In-class quizzes can be strategically placed to break up lecture time and engage students. Quizzes given at the beginning of class on pre-class readings help stimulate students to review information they did not know and listen for clarification during class. Quizzes can also be given throughout class (eg, using electronic audience response systems [ARS]) and may or may not be graded. ARS can help instructors engage students in lecture content,

promote interactivity, identify misconceptions, and stimulate discussion.⁸ ARS questions posed immediately after presentation of the content will more likely test immediate recall than substantive knowledge. Quizzes at the end of class allow students to use their problem-solving skills by applying what they have just learned to a patient case or problem.

QUESTIONS AND ANSWERS

Active learning strategies that involve questions and answers can increase student involvement and comprehension. “Wait time” is a method whereby the instructor poses a question and asks students to think about it.¹¹ After a brief pause, the instructor can ask for volunteers or randomly call on a student to answer the question. This wait time forces every student to think about the question rather than relying on those students who immediately raise their hands to answer questions. With the “fish bowl” method, students are asked to write questions related to the course material for discussion at the end of class or at the beginning of the next class session.¹¹ Instructors then draw several questions out of the “fish bowl” to discuss or ask the class to answer. Questions can also be submitted electronically, using a learning management system or programs such as Google Forms or Poll Everywhere. In classes that use active learning, much of the learning will come from class discussion. However, many students may not pay attention to their classmates, but rather wait for instructors to either repeat or clarify what one of their classmates has said. To promote active listening, after one student has volunteered to answer a question, instructors could ask another student if they agree with the previous response and why.

THINK-PAIR-SHARE

The “think-pair-share” exercise involves providing students with a question or problem to solve.² After working on the assignment individually (think) for 2–5 minutes, they discuss their ideas for 3–5 minutes with the student sitting next to them (pair). Finally, student pairs are chosen to share their ideas with the whole class (share). By sharing ideas with a partner first, students are kept on task and can have a more intimate discussion to work out problems before sharing with others. This method provides immediate feedback and can lead to productive class discussion. Another type of sharing involves small-group discussions. Preassigned small groups of three to four students work together throughout the course to complete activities. Groups may have 20–30 minutes for discussion and apply a topic presented in class to a new situation. To create heterogeneity for discussion, one example is to group students with different experiences (eg, community vs hospital IPPE).¹² Assigning functional roles and role-playing can create multiple perspectives.

CONCEPT MAPPING

Concept maps are diagrams used to visually connect concepts. This strategy can be used to link new information to previously learned material, critically think through a process, or simply describe ideas in a pictorial form. Concept mapping can reveal how students organize their knowledge, understand relationships between various concepts, and display their creativity in incorporating new information.¹³ This may be particularly useful in clinical therapeutics courses where foundational theories are connected with pharmacotherapy. The activity can help students organize information about a disease state and focus on relevant information for clinical decision making.¹⁴ There are several free web-based programs available to build concept maps, but paper or any computer-based drawing tool is equally acceptable. Many different topics can be visualized using a concept map; therefore, detailed instructions and clear expectations are necessary for

successful implementation of the activity. In the classroom, concept maps work best when used during group activities to facilitate collaborative and cooperative learning.¹⁵

PROBLEM-BASED LEARNING

Problem-solving skills can be developed during a class period by applying knowledge of pharmacotherapy to a patient case. Application reinforces the previously learned material and helps students understand the relevance of the topic in a real-life situation. PBL is a teaching and learning method in which a complex problem is used as the stimulus for developing critical thinking and problem-solving skills, group skills, and investigative techniques. The process of PBL starts with the student identifying the problem in a patient case. The student spends time either alone or in a group exploring and analyzing the case and identifying learning resources needed to solve the problem. After acquiring the knowledge, the student applies it to solve the problem.¹⁶ Small or large groups can be established for case discussions to help students develop communication skills, respect for other students’ opinions, satisfaction for contributing to the discussion, and the ability to give and receive constructive feedback.¹⁶ Interactive PBL computer tools and the use of real patient cases also stimulate learning both outside and inside the classroom.^{17,18} Computer-assisted PBL can provide instant feedback throughout the process and incorporate other methods of active learning such as quizzes.¹⁹ Programs that create virtual patients can be used creatively in PBL cases to simulate actual patient outcomes based on student recommendations.²⁰

COOPERATIVE OR COLLABORATIVE LEARNING

Cooperative or collaborative learning strategies involve students in the generation of knowledge.⁵ Students are randomly assigned to groups of four to six at the beginning of the school term. Several times during the term, each group is given a patient case and a group leader is selected. Each student in the group volunteers to work on a certain portion of the case. The case is discussed in class, and each member receives the same grade. After students have finished working in their small groups or during large-group sessions, the teacher serves as a facilitator of the discussion rather than as a lecturer. Students actively participate in the identification and resolution of the problem. The integration of this technique helps with development of skills in teamwork, interdependency, and communication.¹² Group discussions help students formulate opinions and recommendations, clarify ideas, and develop new strategies for clinical problem solving. These skills are essential for lifelong learning and will be used by the students throughout their careers.

TEAM-BASED LEARNING

Team-based learning (TBL) is a learner-centered, instructor-directed, small-group learning strategy that can be implemented in large-group educational settings. The course is structured around the activity of teams of five to seven students who work together over an entire semester. TBL focuses on deepening student learning and enhancing team development. This is accomplished by the TBL structure, which involves: (1) pre-class preparation, (2) assurance of readiness to apply learned concepts, and (3) application of content to real-world scenarios through team problem-solving activities in class. A peer-review process provides important feedback to help team members develop the attitudes, behaviors, and skills that contribute positively to individual learning and effective teamwork.^{6,21,22} A growing number of schools are adopting this strategy, resulting in various combinations and permutations of TBL. Guidance documents describing the core elements of TBL that should be

incorporated to maximize student engagement and learning within teams have been published.^{22,23}

CASE-BASED LEARNING

Case-based learning (CBL) is used by a number of professional schools to teach pharmacotherapy.^{2,17,24} CBL involves a written description of a real-world problem or clinical situation. Only the facts are provided, usually in chronologic sequence similar to what would be encountered in a patient care setting. Many times, as in real life, the information given is incomplete, or important details are not available. When working through a case, the student must distinguish between relevant and irrelevant facts and realize that there is no single “correct” answer. CBL promotes self-directed learning because the student is actively involved in the analysis of the facts and details of the case, selection of a solution to the problem, and defense of his or her solution through discussion of the case.^{25,26} In CBL, students use their recall of previously learned information to solve clinical cases.²⁷

During class, active participation is essential for the maximum learning benefit to be achieved. Because of their various backgrounds, students learn different perspectives when dealing with patient problems. Some general steps proposed by McDade²⁶ for students when preparing cases for class discussion include:

- Skim the text quickly to establish the broad issues of the case and the types of information presented for analysis.
- Reread the case very carefully, underlining key facts as you go.
- Note on scratch paper the key issues and problems. Next, go through the case again and sort out the relevant considerations and decisions for each problem.
- Prioritize problems and alternatives.
- Develop a set of recommendations to address the problems.
- Evaluate your decisions.

ADVICE ON ACTIVE LEARNING FOR STUDENTS AND INSTRUCTORS

The use of active learning strategies provides students with opportunities to take a dynamic role in the learning process. Willing students, innovative teachers, and administrative support within the school are required for active learning to take place and be successful.²⁷

ADVICE FOR STUDENTS

Students may have concerns about active learning. Some students may be accustomed to passively receiving information and feel uncomfortable participating in the learning process. Taking initiative is the key to deriving the benefits of active learning.

Prepare for class. Assigned readings and homework must be completed before class in order to use class time efficiently for questions and discussion. Time management is important. Use time between classes wisely, identify the times of day when you are most productive, and focus on the results rather than the time to complete an activity.¹ When reading assignments, take notes and summarize the information using tables or charts. Alternatively, make lists of questions from class or readings to discuss with your colleagues or faculty or try to answer them on your own.

Seek to understand versus memorize. To develop appropriate therapeutic recommendations or answers to a question, you may have to look beyond the required reading materials. You may need to

review notes from previous courses or perform literature searches and use the library or the internet to retrieve additional information. It is important that you understand “why” and “how” and not just memorize “what.” Memorizing results in short-term retention of knowledge, whereas understanding results in long-term retention and will enable you to better justify your clinical recommendations. In active learning, much of what you learn you will learn on your own. You will probably find that you read more, but you will gain understanding from reading. At the same time, you are developing a critical lifelong learning skill. Your reading will become more “depth processing” in which you focus on:

- The intent of the reading
- Actively integrating what you read with previous parts of the text or previous courses
- Using your own ability to make a logical construction
- Thinking about the functional role of the different parts of an argument

During class, take an active role in the learning process. Be an active participant in class or group discussions; lively debates about pharmacotherapy issues allow more therapeutic options to be discussed. Discussing material helps you to apply your knowledge, verbalize the medical and pharmacologic terminology, engage in active listening, think critically, and develop interpersonal skills. When working in groups, all members should participate in problem solving because teaching others is an excellent way to learn the subject matter.¹ Listen carefully to and be respectful of the thoughts and opinions of classmates. Writing about a topic develops critical thinking, communication, and organization skills. Stopping to write allows you to reflect on the information you have just heard and reinforces learning. Although many options for digital note-taking are available, it is not known whether these enhance or deter learning.²⁸ Taking an active role through team discussions, note-taking, identifying connections between patient cases, and applying what you have learned to the current cases will promote development of self-directed and autonomous learning skills.

ADVICE FOR INSTRUCTORS

Instructors may also have concerns about incorporating active learning strategies. They may feel that their class is too large to accommodate active learning, have concerns that they will not be able to cover all the content or that it will take too much time to change their course, or even fear that students may be resistant to active learning strategies. Some of the hesitation may lie in the belief that active learning is an alternative to lecture. Rather, active learning strategies can be incorporated into didactic lectures to enhance learning sessions. Educators can move some course content online by assigning pre-class mini-lectures or quizzes.² Several strategies can be used to increase the successful implementation of active learning.

Discuss course expectations. Take time to describe teaching, learning, and assessment methods and how students can be successful in the course. Help students to understand the benefits of active learning.²⁹

Consider slowly implementing a change in the classroom. To implement active learning strategies, teachers must overcome the anxiety that change often creates. Experiment with simple active learning methods (ie, the pause technique) and slowly implement other active learning approaches.

Consider techniques to maximize student discussion. Allowing students to discuss content in pairs or small groups before asking them to share their ideas with the entire class can help minimize student

anxiety about engaging in classroom discussions. Consider moving around the room during discussions, if possible, and make an effort to learn student names.

Take a stepwise approach. Learners become self-directed in stages, not in one single moment of transformation. Sequence activities and assignments that gradually develop all three stages: learning, intellectual development, and interpersonal skills.³⁰

Prepare students for group learning. Group learning is not intuitive. Instructors who use group learning should create a workable environment, ensure that expectations of students are understood, and structure the learning sessions to maximize student engagement and learning within teams.

Have a preconceived plan for how the learning session will go and stick to it. Determine what learning objectives you would like to achieve during the session. Consider developing an outline for the learning session, estimating the time that will be spent on each active learning activity.²

USING THE CASEBOOK

The *Casebook* was prepared to assist in the development of each student's understanding of a disease and its management as well as problem-solving skills. It is important for students to realize that learning and understanding the material is guided through problem solving. Students are encouraged to solve each of the cases individually or with others in a study group before discussion of the case and topic in class. These cases can be used as an active learning strategy by allowing time for students to work on the cases during class as an application exercise for TBL.²¹ Teams or individuals can then report verbally on the questions and debate various treatment options.

SUMMARY

The use of case studies and other active learning strategies will enhance the development of essential skills necessary to practice in any setting. The role of the healthcare professional is constantly changing; thus, it is important for students to acquire the knowledge, skills, behaviors, and attitudes to develop the lifetime skills required for continued learning. Teachers who incorporate active learning strategies into the classroom are facilitating the development of lifelong learners who will be able to adapt to change that occurs in their profession.

REFERENCES

- Warren G. *Carpe Diem: A Student Guide to Active Learning*. Landover, MD: University Press of America, 1996.
- Gleason BL, Peeters MJ, Resman-Targoff BH, et al. An active-learning strategies primer for achieving ability-based educational outcomes. *Am J Pharm Educ*. 2011;75(9):186.
- Michael J. Where's the evidence that active learning works? *Adv Physiol Educ*. 2006;30:159–167.
- Bonwell CC, Eison JA. *Active Learning: Creating Excitement in the Classroom*. Washington, DC: George Washington University, School of Education and Human Development, 1991. ASHE-ERIC Higher Education Report No. 1.
- Shakarian DC. Beyond lecture: active learning strategies that work. *JOPERD*. 1995;May–June:21–24.
- Michaelsen LK, Parmelee DX, McMahon KK, Levine RE. *Team-Based Learning for Health Professions Education: A Guide for Using Small Groups to Improve Learning*. Sterling, VA: Stylus Publishing, 2008.
- Moore AH, Fowler SB, Watson CE. Active learning and technology: designing change for faculty, students, and institutions. *EDUCAUSE Rev*. 2007;42:42–61.
- Cain J, Robinson E. A primer on audience response systems: current applications and future considerations. *Am J Pharm Educ*. 2008;72(4):Article 77, 1–6.
- DiVall MV, Hayney MS, Marsh W, et al. Perceptions of pharmacy students, faculty members, and administrators on the use of technology in the classroom. *Am J Pharm Educ*. 2013;77(4):Article 75, 1–7.
- Stead DR. A review of the one-minute paper. *Active Learn Higher Educ*. 2005;6(2):118–131.
- Paulson DR, Faust JL. Active Learning for the College Classroom. <http://www.calstatela.edu/dept/chem/chem2/Active/main.htm>. Accessed November 13, 2018.
- Sylvia LM, Barr JT. *Pharmacy Education: What Matters in Learning and Teaching*. Sudbury, MA: Jones & Bartlett, 2011.
- Hill LH. Concept mapping in a pharmacy communications course to encourage meaningful student learning. *Am J Pharm Educ*. 2004;68(5):Article 109, 1–9.
- Carr-Lopez SM, Galal SM, Vyas D, Patel RA, Gnesa EH. The utility of concept maps to facilitate higher-level learning in a large classroom setting. *Am J Pharm Educ*. 2014;78(9):1–7.
- Roth W, Roychoudhury A. The concept map as a tool for the collaborative construction of knowledge: a microanalysis of high school physics students. *J Res Sci Teach*. 1993;30:503–534.
- Walton HJ, Matthews MB. Essentials of problem-based learning. *Med Educ*. 1989;23:542–558.
- Raman-Wilms L. Innovative enabling strategies in self-directed, problem-based therapeutics: enhancing student preparedness for pharmaceutical care. *Am J Pharm Educ*. 2001;65:56–64.
- Dammers J, Spencer J, Thomas M. Using real patients in problem-based learning: students' comments on the value of using real, as opposed to paper cases, in a problem-based learning module in general practice. *Med Educ*. 2001;35:27–34.
- McFalls M. Integration of problem-based learning and innovative technology into a self-care course. *Am J Pharm Educ*. 2013;77(6):Article 127, 1–6.
- Benedict N. Virtual patients and problem-based learning in advance therapeutics. *Am J Pharm Educ*. 2010;74(8):Article 143, 1–6.
- Conway SE, Johnson JL, Ripley TL. Integration of team-based learning strategies into a cardiovascular module. *Am J Pharm Educ*. 2010;74(2):35.
- Haidet P, Levine RE, Parmelee DX, et al. Guidelines for reporting team-based learning activities in the medical and health sciences education literature. *Acad Med*. 2012;87:292–299.
- Parmelee D, Michaelsen LK, Cook S, Hudes PD. Team-based learning: a practical guide: AMEE guide no. 65. *Med Teach*. 2012;34:e275–e287.
- Hartzema AG. Teaching therapeutic reasoning through the case-study approach: adding the probabilistic dimension. *Am J Pharm Educ*. 1994;58:436–440.
- Thistlethwaite JE, Davies D, Ekeocha S, et al. The effectiveness of case-based learning in health professional education. A BEME systematic review: BEME guide no. 23. *Med Teach*. 2012;34:e421–e444.
- McDade SA. *An Introduction to the Case Study Method: Preparation, Analysis, Participation*. New York, NY: Teachers College Press, 1988.
- Williams B. Case-based learning—a review of the literature: is there scope for this educational paradigm in prehospital education? *Emerg Med J*. 2005;22:577–581.
- Stacy EM, Cain J. Note-taking and handouts in the digital age. *Am J Pharm Educ*. 2015;79(7):Article 107, 1–6.
- Prince M. Does active learning work? A review of the research. *J Eng Educ*. 2004;93:223–231.
- Weimer ME. *Learner-Centered Teaching*. 1st ed. San Francisco, CA: Jossey-Bass, 2002:167–183.

Patient Communication: Getting the Most Out of That One-on-One Time

KRISTA D. CAPEHART, PharmD, MSPHarm, BCACP, AE-C

Talking with patients is a crucial component of the medication use process. Regardless of practice area, healthcare providers have the opportunity to teach and learn from people they interact with each day. In addition to having a wealth of scientific knowledge and clinical skills, providers must also possess excellent communication skills. This chapter focuses on key elements of communication in various practice settings. The intricacies of interpersonal communication can be found in other resources.¹⁻³

PATIENT-CENTERED CARE AND THE ROLE OF COMMUNICATION

With the movement toward value-based, accessible, high-quality care, provision of interprofessional, team-based care is vital. The Patient Protection and Affordable Care Act of 2010 fostered development of accountable care organizations (ACOs) and patient-centered medical homes (PCMHs). The National Center for Quality Assurance defines a PCMH as “a way of organizing primary care that emphasizes care coordination and communication to transform primary care into ‘what patients want it to be.’”⁴ A team-based approach that includes pharmacists with medication expertise and good communication skills can optimize the medication use process and ensure that the patient truly is at the center of care.

In patient-centered care, the patient participates in his/her own healthcare through shared decision making with healthcare providers. Shared decision making involves decision aids or a process to facilitate patient understanding when multiple treatment options could be used.⁵ Shared decision making increases knowledge and improves patient understanding of the risks of their care and makes patients more likely to receive care that is consistent with their values and beliefs.⁶

Consequently, the patient-clinician interaction must involve more than simply collecting information during a medication history interview or conveying verbal or written information about a prescription. Active listening skills must be employed to understand the patient's concerns about medication therapy, engage the patient in his/her care, and develop the trust required for a positive long-standing relationship. Establishing a trusting relationship is necessary for effective communication, but trust does not come quickly or easily. In the community pharmacy, it may result from a caring pharmacist always taking the time to ask how a patient's medications are working. In an ambulatory clinic, it could come from a nurse practitioner or pharmacist teaching about diabetes care and improving A1C levels. Pathways to a trusting relationship may vary, but the ultimate goal is for patients to feel that they can confide in and rely on their healthcare providers about medication-related needs.

Patient interactions vary depending on the practice setting, clinician training, the purpose of the interaction, and other factors.

In 2015, the Joint Commission of Pharmacy Practitioners (JCPP) published the Pharmacist's Patient Care Process, which is similar to the patient care process used daily by other healthcare providers and is intended to standardize the patient's experiences in each encounter with the pharmacist.⁷ The steps of the Pharmacists' Patient Care Process include (1) Collect, (2) Assess, (3) Plan, (4) Implement, and (5) Follow-up: Monitor and Evaluate (see **Chapter 4, Fig. 4-1**).

Optimal communication is necessary in the *Collect*, *Implement*, and *Follow-up* parts of the process. During the *Collect* portion, the pharmacist gathers information about the patient and the present medical situation. The information available may vary by practice site, but the process remains the same. During the *Implement* stage, the pharmacist has the opportunity to educate the patient about the care plan. This may include new medications, lifestyle modifications, changes in therapy, or referrals to other healthcare providers. *Monitor* and *Evaluate* can involve gathering information from the patient regarding how the medication is working, whether any adverse events have occurred, and vital adherence data. The key to successful use of the patient care process is collaboration with the patient and other healthcare team members.

IMPROVING THE PATIENT ENCOUNTER

Talking with a patient and collecting information require patience, empathy, and the ability to direct the conversation. The clinician should use open-ended questions, which start with *who*, *what*, *when*, *where*, *why*, or *how*. Close-ended questions are those that permit the patient to respond with a simple *yes* or *no* and tend to leave much unsaid. With a close-ended question, the patient may not provide complete information. For example, if a provider asks, “Have you been taking your warfarin as the doctor prescribed?” the patient may simply respond, “Yes.” However, it could be that the patient understood and adhered to the one-tablet-daily directions that were initially prescribed but did not realize that the directions were recently changed to one tablet Monday, Wednesday, Friday, and Saturday, and one-half tablet the other days of the week. An open-ended question such as, “How are you taking your warfarin each day?” requires more explanation from the patient, allowing the clinician to collect more accurate information to assess the patient's medication/medical history and status. There is a place for close-ended questions; after most of the information has been collected, close-ended questions can be used to narrow down the details about the patient's situation.

Healthcare providers must be exceptional listeners, open to what the patient is sharing and not sharing. Becoming an active listener is not always easy in busy patient care environments. It includes removing distractions, empathizing with the patient, acknowledging the patient's individuality, and recognizing nonverbal signals from the patient.

TABLE 3-1 Nonverbal Cues to Demonstrate Good Listening

Letter	Meaning
S	Squarely face the patient (do not have your body angled in another direction)
O	Open posture (do not cross your legs and arms)
L	Lean toward the patient (not encroaching on personal space) to show interest
E	Eye contact
R	Relax

Regardless of practice setting, distractions should be minimized to ensure that the patient is the primary focus of the provider's attention. In community pharmacies, separate counseling rooms may be used, if available. Attempts to maintain privacy help demonstrate the pharmacist's focus on the patient.

Empathy and sympathy are often confused. Empathy is the ability to understand the patient's feelings and share them, whereas sympathy is feeling sorry for the patient. Acknowledging emotions, reassuring the patient, and providing answers to questions helps to improve the interaction and outcomes. Each patient enters the medical encounter with a set of experiences, beliefs, and expectations; understanding them through active listening facilitates creation and implementation of the therapeutic plan.

Nonverbal communication can be as important as what the patient relates verbally, and clinicians must recognize these as well. Nonverbal cues may include body language, use of time, tone of voice, touch, distance, and physical environments. Body language clues include crossing the arms (a sign the patient is closing themselves off) or nodding the head (an indication the listener is paying attention or agreeing). Time can be used to delay (as with dramatic pauses) or to rush through situations that may be uncomfortable. Tone of voice is revealing because it includes pitch and intonation and can relate anger, fascination, confusion, and a variety of other emotions. Touch, distance, and physical environment are specific to the individual. Some patients are comfortable with a touch on the arm for reassurance or to show concern, whereas others require much greater personal space and shy away from physical contact. Generally, people prefer approximately 2 ft of personal space when having a one-on-one encounter. Maintaining an appropriate distance that makes the patient comfortable may take time to master, and it's important to maintain awareness of the patient's reaction to your proximity to them. The physical environment the clinician creates for the encounter serves as a nonverbal cue. For example, an open room with chairs arranged in a circle creates a welcoming space for individuals to gather for conversation. A lecture-style setup creates a more formal setting where the focus is on the presenter with less individual sharing. The clinician must be aware of the nonverbal cues he or she is giving as well. Egan developed a mnemonic to assist in demonstrating nonverbal cues for good listening (SOLER), which can help build a trusting patient relationship (Table 3-1).⁸

EXAMPLES OF COMMUNICATION WITHIN THE PHARMACIST-PATIENT RELATIONSHIP

Although the principles discussed in this section are directed toward pharmacy practice, many of them can also be used by other health-care providers in any environment in which medication counseling and education occur. The opportunities to talk with patients vary with practice settings and expectations. For example, hospital pharmacists or nurses may perform counseling on all discharge medications or discuss injectable medications being started with the

patient. The community pharmacist may counsel on new or refill medications or help select an over-the-counter (OTC) medication for a particular problem. Pharmacists communicate with patients to undertake medication therapy management, participate in collaborative drug therapy management, and perform medication reconciliation.

THE MEDICATION AND MEDICAL HISTORY

It is important to collect comprehensive information when conducting a patient medication interview. Using the tips presented previously, information can be gathered from the patient to improve patient care and safety.

Initially, collect demographic information about the patient, including name, address, and date of birth, unless this information is already available. Use an open-ended question to inquire about the patient's allergies (medication, environmental, and food), such as, "What medication allergies have you experienced in the past?" Be sure to document what happened when the patient experienced the reaction. It may be necessary at some point in the future to evaluate risk versus benefit and determine if a true allergy exists. Query the patient regarding social history related to drug and substance use, including tobacco use, alcohol consumption, recreation and medical marijuana use, illicit drug use, and caffeine intake. Asking about social history can sometimes make both the clinician and the patient uncomfortable. One method to ease tension is to advise the patient that some medications interact with alcohol or tobacco, and that it is important for information to be complete to evaluate drug-drug interactions. Remember to identify the type of substance, quantity, and frequency of use as well.

When verifying the patient's current prescription medications, it is helpful to start by asking whether the patient has either brought their medications or a written list to the visit. This is a good practice in the emergency department and many other clinical settings. Regardless of whether the patient has a list, ask, "What prescription medications do you take?" For each medication, specifically document the name, strength, route of administration, prescriber, and how he or she takes the medication. The way the patient actually takes each medication can be compared to the label directions to assess patient adherence. Remember that nonadherence could be due to misunderstanding the correct directions, attempting to save money, or any of a number of reasons other than simply choosing **not** to take the medication as directed. Also, be sure to ask the patient why each medication was prescribed. Remind each patient about nonoral routes of administration also. This could be a close-ended question followed up by an open-ended one, such as, "Do you use any medications that you apply to your skin? What other medications do you use that you don't swallow by mouth?" This may prompt the patient to remember some medications they may have forgotten.⁹

Patients should be asked about nonprescription items used, including OTC medications, herbals, vitamins, and dietary supplements. Patients may have the misconception that OTC or "natural" substances do not interact with prescription medications or medical conditions. This is an opportunity to educate the patient about the potential dangers of incorrect use of these products.

Pharmacists and other providers conducting medication interviews must also have or collect information on diagnosed medical conditions, but there is flexibility in when this occurs. One option is to address medical conditions after asking about allergies and before beginning questions on medications. This gives the interviewer an idea of the therapeutic categories of medications the patient may be taking. The other option is to cover diagnosed medical conditions after collecting the list of prescription and nonprescription medications. Using this order of questioning enables the interviewer to ask the patient "What are you taking X medication for?" if the patient fails to list an indication for a medication named earlier.

The comprehensive medication interview is optimal for the provision of medication reconciliation, medication therapy management, and collaborative drug therapy management. However, it is not always feasible to perform an interview directly with the patient. Sometimes, the information may need to be collected from the pharmacy dispensing record, a family member, or another source. Information not obtained personally from the patient may need to be reconfirmed later.

COUNSELING ON A NEW PRESCRIPTION

The Omnibus Budget Reconciliation Act of 1990 (OBRA 90) was passed, in part, to help ensure safe medication use for Medicaid patients. While OBRA 90 is often considered to be the law that mandated the offer to counsel on medications, it also gave rise to new record-keeping requirements and mandated that pharmacists complete a prospective drug utilization review for all Medicaid patients. Requirements vary by state regarding what must be done for drug counseling, but OBRA 90 required making an offer to counsel, not that counseling must actually be performed.¹⁰ Since 1990, some states have passed various additional requirements for patient counseling and education from merely complying with OBRA 90 to not permitting a patient to decline the offer of counseling. It is important to be familiar with your state's patient counseling requirements.

Counseling on medications increases the patient's knowledge and comfort level in using their medication correctly.¹¹ Part of the patient's comfort can derive from the process as well as from the information. The counseling should occur in a private area, if possible. If a separate room is not available, use a divider or area that makes the counseling space relatively easy to maintain patient confidentiality and privacy. A patient may be uncomfortable receiving counseling on certain types of medication, such as a medication for a vaginal infection; speaking in a confidential tone in a private area will improve patient satisfaction with the encounter.

Educating the patient on new medications should start by assessing what the patient already knows about the medication that has been prescribed. The Indian Health Service (IHS) began providing patient medication counseling services in the 1970s and 1980s.¹² The IHS would go on to develop a commonly used method for counseling on new and refill prescriptions. The method is referred to as the Three Prime Questions technique (Fig. 3-1).¹³

Asking "What did your doctor tell you the medicine was for?" is an excellent way to begin the session. After determining the patient's knowledge about the medication, state the medication name (including whether it is generic) and strength. Then ask, "How did the doctor tell you to take the medicine?" Next, provide

information about the route of administration, dosing schedule, duration of treatment, storage, and administration. Inquire about the patient's daily activities and attempt to incorporate the schedule into routine daily activities to increase adherence. Finally, the third question enables the pharmacist to provide information regarding adverse effects and how to monitor effectiveness. Explain the medication in terms of what condition it is intended to treat, what the expected action is, and how the patient can self-monitor for efficacy. The patient should realize if and when he/she should "feel different." For example, with medications for hypertension and dyslipidemia, the patient may not notice a difference in how they feel and should be counseled about the importance of laboratory testing or other monitoring. Potential side effects can be discussed by dividing them into two categories: (1) those that are more likely to occur but are not serious, and (2) those that are rare but serious. Provide guidance on how the patient can avoid some of the most common side effects, if possible, and what should be done if a serious one occurs. Also inform the patient about other drugs or conditions that interact with the medication and how to manage the interaction. In finishing this portion of the session, discuss storage information, what to do if a dose is missed, and any pertinent refill information.

As the counseling session is concluding, verify the patient's understanding of the information covered during the session. One of the best methods for this is the "teach-back method," which is used to determine what the patient understands and to correct any misunderstandings.¹⁴ To avoid the impression that you are testing the patient, a good approach is to say, "I have covered quite a bit of information about your new medication. Just to make sure that I did not forget anything, how are you going to take the medication when you get home?" This places the appearance of responsibility for remembering everything on the healthcare provider and reduces stress for the patient. Studies have compared lecture-based counseling and interactive counseling similar to the Three Prime Questions style for preference and retention of information. Approximately two-thirds of standardized patients who experienced both types preferred interactive counseling over lecture-based counseling.¹³ Another study examined retention among actual patients and found them to be four times more likely to correctly answer how to take their medication than those who received traditional lecture based counseling.¹⁵ The style of counseling may need to be individualized to a particular patient by picking up on nonverbal cues and the patient interaction.

COUNSELING ON A REFILL

Counseling on a medication refill is an abbreviated process of counseling for a new medication. The IHS has an additional three prime questions for refills (see Fig. 3-1). The purpose of the medication and how to take it is reviewed, but the focus changes from how to take the medication to monitoring the patient with queries such as, "What kinds of problems are you having?" Counseling on refills is especially important when use of a device is involved. For example, metered-dose inhalers are difficult to use correctly. Correct inhaler use decreases over time, even in as little as 2–3 months, and studies show that pharmacist counseling improves correct inhaler technique and adherence.¹⁶ Additionally, it is important to follow up with the patient to answer any questions that have arisen since the last fill and to provide contact information for any future questions that arise.

OVER-THE-COUNTER MEDICATION SELECTION

Assisting a patient with selection of self-care products also requires effective communication skills. The first steps are to assess the patient's complaints and evaluate whether self-management with OTC medications is appropriate or whether referral is needed.

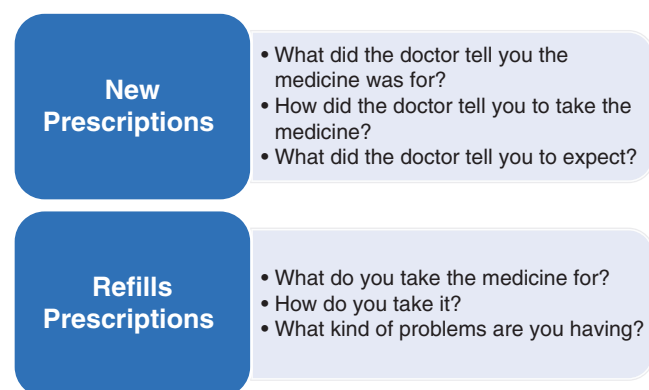


FIGURE 3-1. Indian Health Service Three Prime Question counseling method. (Lam N, Muravez S, Boyce RW. A comparison of the Indian Health Service counseling technique with traditional, lecture-style counseling. *J Am Pharm Assoc.* 2015;55(5):503–510.)

There are a variety of mnemonics to assist clinicians in asking all necessary questions before recommending a product. These include (1) CHAPS-FRAPS (Chief complaint, History of present illness, Allergies, Past medical history, Social history, Family history, Review of systems, Assessments, Plans, and SOAP); (2) The Basic Seven (location, quality, severity, timing, context, modifying factors, and associated symptoms); and (3) PQRST (Palliation and provocation, Quality and quantity, Region and radiation, Signs and symptoms, Temporal relationship).^{17–19} The most comprehensive mnemonic is the QuEST/SCHOLAR approach.²⁰ This method enables the clinician to evaluate the patient and most accurately select the best nonprescription product. The QuEST/SCHOLAR process includes:

1. Quickly and accurately assess the patient: Ask about the current complaint (SCHOLAR), other medications, and allergies.
 - ✓ Symptoms
 - ✓ Characteristics
 - ✓ History
 - ✓ Onset
 - ✓ Location
 - ✓ Aggravating factors
 - ✓ Remitting factors
2. Establish that the patient is a self-care candidate.
 - ✓ No severe symptoms, symptoms do not persist or return, patient is not using self-care to avoid medical care
3. Suggest appropriate self-care strategies.
 - ✓ Recommend the medication and nonpharmacologic therapy
4. Talk with the patient.
 - ✓ How the drug is going to work, when it should be taken, expected adverse events

For example, Joe comes into your pharmacy requesting assistance in selecting an OTC product for heartburn. Utilizing the QuEST/SCHOLAR process, you could:

1. Quickly and accurately assess the patient: “Let’s talk a little about the type of problems you have been having.”
Ask about the current complaint (SCHOLAR), other medications, and allergies:
 - ✓ Symptoms: “What symptoms are you having?”
 - ✓ Characteristics: “How would you describe the pain...burning, sharp, shooting?”
 - ✓ History: “Have you experienced this before? What have you tried already? Did it work?”
 - ✓ Onset: “When did the symptoms start?”
 - ✓ Location: “Where is the pain you are describing as heartburn?”
 - ✓ Aggravating factors: “What makes it worse?”
 - ✓ Remitting factors: “What makes it better?”
2. Establish that the patient is a self-care candidate.
 - ✓ “Based on this information, I think it would (or would not) be appropriate for you to use OTC treatment.”
3. Suggest appropriate self-care strategies.
 - ✓ “I would recommend _____ and some non-medication strategies, too.”
4. Talk with the patient
 - ✓ “You can take ____ tablet(s) every ____ hours to help with symptoms. This medication will work by _____. You

should start to notice improvement in _____ minutes. Also, try lifestyle changes like avoiding spicy foods and raising the head of the bed. If your symptoms persist for more than 2 weeks or do not improve, see your doctor. The OTC medications can cover up symptoms that need to be checked out further by your doctor.”

The QuEST/SCHOLAR method provides a technique for systematically assessing patients in the pharmacy and providing a thorough but efficient evaluation. It is vital to maintain the patient’s privacy (using a private area, if possible) and be cognizant of topics that make patients uncomfortable. These occur with OTC items, too; recognizing this and being prepared will help put the patient at ease. Try to employ the teach-back method with OTCs, herbals, and dietary supplements to ensure patient understanding of the information discussed.

BARRIERS TO COMMUNICATION

Patient communication does not always happen the way we plan. There are common barriers to communication, and knowing them can help you to be prepared. Communication barriers can be divided into three common categories: (1) patient barriers, (2) clinician barriers, and (3) healthcare setting barriers. Patient barriers may include the patient literacy level, misconceptions regarding the purpose of the visit, aging, or visual/hearing difficulties. A clinician may lack training with certain types of patient encounters or have a negative attitude about patient counseling. Healthcare setting barriers posing communication issues can include lack of privacy, space, or resources to serve their specific patient population.

Because the patient is ultimately in charge of his/her healthcare, patient barriers can be some of the most difficult to overcome. Lack of education and poor health literacy can be substantial barriers. The aging patient brings unique challenges to communication, such as changes in physical health, depression, cognitive decline, and changes in hearing, vision, voice, and speech processes.²¹ Also, you may be communicating with the caregiver and not the patient, and he/she may be in a rush or may not have all of the patient information needed.

HEALTH LITERACY

Health literacy is defined as the degree to which individuals have the capacity to obtain, process, and understand basic health information and services needed to make appropriate health decisions. It is not enough for patients to simply “understand” information about their health. They must be able to make decisions about what to do—to be able to navigate the healthcare system and be somewhat confident about it. Health literacy may or may not be tied to the level of education completed. For example, a patient with an MBA degree who is highly educated and very successful in the corporate world may not realize that it is unsafe to take OTC acetaminophen and an OTC cough and cold product also containing acetaminophen. On the other hand, a woman who only completed the 10th grade and has a young child with a pediatric cancer may be well versed in the healthcare system and able to tell you more about her child’s medications and medical needs than some members of the healthcare team. Simply put, clinicians cannot determine the level of health literacy by looking at a patient and making assumptions about his/her education or social status.

A sense of shame often accompanies a patient’s low health literacy. Because patients do not typically volunteer their lack of knowledge, identifying low health literacy is important, especially in light of its association with medication nonadherence.²² Some indicators

that health literacy may be a problem with a given patient are leaving forms partially filled out, referring to medications by their color (instead of by name), opening the bottle to look at the medication rather than the label, making excuses like “I forgot my glasses,” postponing appointments, chronic nonadherence, failing to look at written materials, or bringing someone with them.

Once you recognize that a patient presents health literacy concerns, it is vital to remain respectful, considerate, and maintain privacy. Failure to be sensitive to the needs of these patients can result in loss of the relationship that was forming and loss of an opportunity to impact the patient’s health outcomes. Recognizing that time is a limitation, there are some tips to help with patient understanding. First, limit the number of main counseling points to two or three. Covering too many topics can be overwhelming. Second, demonstrate the procedure or technique. One example of this is to show the patient how to use an inhaler and spacer device. Then ensure that understanding is complete with the teach-back method discussed previously. Pictures can also be used to convey information about medication instructions and safety. Standard pictograms created by the United States Pharmacopeia are available for download at <http://www.usp.org/usp-healthcare-professionals/related-topics-resources/usp-pictograms/download-pictograms>. Finally, summarize the information and be positive, communicating in an open manner while maintaining eye contact.

Using plain language is one of the most important tenets for working with patients with low health literacy. This involves using common words instead of medical jargon to improve understanding of complex situations. An example is to use “water pill” instead of “diuretic,” “a medication that helps open the airways” instead of “bronchodilator,” and “sore” instead of “abscess.” Additional examples can be found at http://www.plainlanguage.gov/populartopics/health_literacy/index.cfm under the Plain Language Thesaurus.

AGING

The aging patient may experience many physiologic changes such as cognitive decline and dementia that can make communication more difficult. Sensory loss, including both hearing and vision, may also occur with aging.²¹ Because these are challenging in their own right, living with them while navigating the healthcare system can be frustrating for patients.

Some general techniques can make the encounter with these patients more effective. Know the patient’s strengths and weaknesses and cater to them. Select educational materials that are most appropriate for that patient. Be prepared to take some extra time with the patient to ensure full understanding and buy-in of the information. Use an environment that is conducive to the conversation—a place with minimal distractions. If the patient has difficulty hearing, speaking louder will not help; it will only distort the sound. Speak slowly and simplify your sentences. Use plain language when speaking, making sure to avoid medical jargon that can be confusing and overwhelming. Finally, if the patient has visual difficulties, ensure that they have their glasses and be prepared to provide the materials in a larger font. You may also want to determine whether your prescription filling software can print prescription label information in a larger font for easier reading.

TEAM-BASED CARE AND PATIENT COMMUNICATION IN THE FUTURE

With the widespread implementation of electronic health records, more patients requiring chronic care management, and a value-based reimbursement system, a clinician’s ability to develop masterful patient communication skills is becoming essential. Employing a collaborative, team-based approach to patient care and the tips

for patient communication can help to ensure optimal health outcomes. Maximizing use of technology such as the electronic health record for referral to and communication with other clinicians who provide necessary services can meet needs that may seem impossible in a single clinic or pharmacy. Each healthcare team member brings special skills and communicates with the patient to obtain additional information. The best care is provided when providers come together at the same location (or virtually) to collaborate and meet the overall needs of each patient. In some settings, this may be collaborative drug therapy management working with the healthcare team to optimize medication therapy and overall health outcomes. In other settings, it may include clinicians working to coordinate with health educators in the community to provide services such as diabetes self-management classes.

CONCLUSION

Effective patient communication is a mandatory skill for all healthcare providers. Good communication involves developing a positive clinician–patient relationship, demonstrating a real interest in the patient’s health, listening carefully to the patient’s complaints, involving the patient in the decision-making process, and providing education in a way that the patient can understand. The ultimate goal is to improve the patient’s health, and effective communication is the key to making this happen.

REFERENCES

1. Patterson K, Grenny J, McMillan R, Switzler A. *Crucial Conversations*. 2nd ed. New York, NY: McGraw Hill, 2012.
2. Rantucci M. *Pharmacists Talking With Patients: A Guide to Patient Counseling*. 2nd ed. Philadelphia, PA: Lippincott, Williams, & Wilkins, 2007.
3. Berger B. *Communication Skills for Pharmacists: Building Relationships, Improving Patient Care*. 3rd ed. Washington, DC: American Pharmacists Association, 2009.
4. Ncqa.org. Patient-Centered Medical Home (PCMH). 2018. Available at: <http://www.ncqa.org/Programs/Recognition/Practices/PatientCenteredMedicalHomePCMH.aspx>. Accessed August 30, 2018.
5. Shafir A, Rosenthal J. *Shared-Decision Making: Advancing Patient-Centered Care through State and Federal Implementation*. 1st ed. Washington, DC: National Academy for State Health Policy, 2012. Available at: <http://www.nashp.org/sites/default/files/shared.decision.making.report.pdf>. Accessed October 28, 2018.
6. Stacey D, Bennett C, Barry M. Decision aids for people facing health treatment or screening decisions. *Cochrane Database Syst Rev*. 2011; 10:CD001431.
7. Bennett M, Kliethermes M. *How to Implement the Pharmacists’ Patient Care Process*. Washington, DC: American Pharmacist Association, 2015.
8. Egan G. *The Skilled Helper*. Belmont, CA: Brooks Cole, Cengage Learning, 2010.
9. Ahrq.gov. Figure 9: Tips for Conducting a Patient Medication Interview. Agency for Healthcare Research & Quality. 2012. Available at: <http://www.ahrq.gov/professionals/quality-patient-safety/patient-safety-resources/resources/match/matchfig9.html>. Accessed October 28, 2018.
10. Drug Diversion Toolkit. *Controlled Substance Integrity—Documentation from Drop-off to Pickup* 1st ed. Baltimore, MD: Center for Medicare and Medicaid Services, 2016. Available at: <https://www.homestatehealth.com/content/dam/centene/home-state-health/pdfs/drugdiversion-controlled-substancedoc-booklet.pdf>. Accessed October 28, 2018.
11. Erickson S, Kirking D, Sandusky M. Michigan Medicaid recipients perceptions of medication counseling as required by OBRA 90. *J Am Pharm Assoc*. 1998;38(3):333–338.
12. Fisher R, Brands A, Herrier R. History of the Indian Health Service Model of Pharmacy Practice: Innovations in Pharmaceutical Care. *Pharmacy in History*. 1995;37(3):107–122.

13. Lam N, Muravez S, Boyce RW. A comparison of the Indian Health Service counseling technique with traditional, lecture-style counseling. *J Am Pharm Assoc.* 2015;55(5):503–510.
14. Schillinger D, Piette J, Grumbach K, et al. Closing the loop: physician communication with diabetic patients who have low health literacy. *Arch Intern Med.* 2003;163(1):83–90.
15. Guirguis LM, Nusair MB. Standardized patients' preferences for pharmacist interactive counseling style: a mixed method approach. *J Am Pharm Assoc.* 2016;56(2):123–128.
16. Mehuys E, Van Bortel L, De Bolle L, et al. Effectiveness of pharmacist intervention for asthma control improvement. *Eur Respir J.* 2008;31(4):790–799.
17. McCallian DJ, Cheigh NH. The pharmacist's role in self-care. *J Am Pharm Assoc.* 2002;42(5 Suppl 1):S40S41.
18. Boyce R, Herrier R. Obtaining and using patient data. *Am Pharm.* 1991;31:65–71.
19. Bates B, Bates B, Northway D. PQRST: a mnemonic to communicate a change in condition. *J Am Med Direct Assoc.* 2002;3(1):23–25.
20. Leibowitz K, Ginsburg D. Counseling self-treating patients quickly and effectively. In: APhA Inaugural Self-Care Institute. Washington, DC: American Pharmacist Association, 2002.
21. Yorkston K, Bourgeois M, Baylor C. Communication and aging. *Phys Med Rehab Clin North Am.* 2010;21(2):309–319.
22. Ngoh L. Health literacy: a barrier to pharmacist–patient communication and medication adherence. *J Am Pharm Assoc.* 2009;49(5):e132–e149.

Implementing the Pharmacists' Patient Care Process

ERIKA L. KLEPPINGER, PharmD, BCPS

INTRODUCTION

Historically, the profession has referred to pharmacist patient care services by a variety of titles, such as pharmaceutical care, medication therapy management (MTM), comprehensive medication management (CMM), and individualized medication assessment and planning. While a pharmacist's activities generally focus on (1) identifying, resolving, and preventing drug therapy problems, (2) improving medication use, and (3) optimizing a patient's pharmacotherapeutic outcomes,¹ terminology tends to be inconsistent among practice settings, making it difficult to communicate the role of a pharmacist clearly with other healthcare providers. Without a clear, consistent patient care process, we cannot demonstrate to patients, caregivers, or other healthcare professionals our contributions to improved medication-related outcomes. The Pharmacists' Patient Care Process (PPCP), as published by the Joint Commission of Pharmacy Practitioners (JCPP), provides a standardized process applicable to a wide variety of patient care services and highlights a pharmacist's medication expertise.² While a consistent process of care applied to every patient is a foundational principle of most healthcare professions, the PPCP differs from processes in other professions because of a pharmacist's unique approach to assessing a patient's medication regimen to ensure that medications are appropriately indicated, effective, safe, and able to be taken by the patient as intended. The JCPP states that the goals of the PPCP are to (1) promote consistency across the profession, (2) provide a framework for delivering patient care in any practice setting, (3) be a contemporary and comprehensive approach to patient-centered care delivered in collaboration with other members of the healthcare team, and (4) be applicable to a variety of patient care services delivered by pharmacists, including medication management.³ Pharmacists in different practice settings have varying levels of intensity in implementing the PPCP. In some situations, pharmacists may not be responsible for all steps in the process or share responsibility with other pharmacists, yet all pharmacists will follow these basic steps to some degree. This chapter summarizes the steps in the PPCP and application of those steps to various patient care situations.

DRUG THERAPY PROBLEMS

The primary role of pharmacists when participating in the patient care process is to identify, resolve, and prevent drug therapy problems.⁴ A drug therapy problem is defined as "any undesirable event experienced by a patient which involves, or is suspected to involve, drug therapy and that interferes with achieving the desired goals of therapy and requires professional judgment to resolve."⁴ Pharmacists must assess patient factors, drug therapy, and information on the patient's medical conditions to thoroughly assess the

appropriateness of medication regimens and identify potential drug therapy problems. This process involves a logical sequence of steps. It begins with evaluating each medication regimen for appropriateness of indication, then optimizing the drug and dosage regimen to ensure maximum effectiveness, and finally, individualizing drug therapy to make it as safe as possible for the patient. After completing these three steps, the practitioner considers other issues such as cost, adherence, and convenience.

As described in **Chapter 1**, drug therapy problems can be separated into seven distinct categories related to medication appropriateness, effectiveness, safety, or adherence:

Appropriate indication for the medication:

1. The medication is unnecessary because the patient does not have a clinical indication at this time.
2. Additional drug therapy is required to treat or prevent a medical condition.

Effectiveness of the medication:

3. The medication being used is not effective at producing the desired patient response.
4. The dosage is too low to produce the desired patient response.

Safety of the medication:

5. The medication is causing an adverse reaction.
6. The dose is too high, resulting in actual or potential undesirable effects.

Adherence to the medication:

7. The patient is not able or willing to take the drug therapy as intended.

See Table 4-1 for a more comprehensive list of factors to consider in identifying drug therapy problems.⁴

To resolve or prevent a drug therapy problem, the underlying cause of the problem must be clearly understood. Table 4-2 provides a list of potential causes of drug therapy problems based on each category described previously.⁴

STEPS IN THE PHARMACISTS' PATIENT CARE PROCESS (PPCP)

The core of the PPCP is patient-centered care and establishing a relationship with the patient.² Including the patient, his/her family, and caregivers in the process allows for open communication and engagement in managing their own health problems. Communication, collaboration, and documentation are also key components incorporated into many if not all of the steps in the process. Collaboration among patients, pharmacists, physicians, and other healthcare providers is essential in providing optimal

TABLE 4-1 Drug Therapy Problems to Be Resolved or Prevented

Assessment	Drug Therapy Problem
Indication	Unnecessary drug therapy
	No medical indication
	Duplicate therapy
	Nondrug therapy indicated
	Treating avoidable adverse drug reaction
Effectiveness	Addictive/recreational use
	Needs additional drug therapy
	Untreated condition
	Preventive/prophylactic
	Synergistic/potentiating
Safety	Ineffective drug
	More effective drug available
	Condition refractory to drug
	Dosage form inappropriate
	Not effective for condition
Adherence	Dosage too low
	Wrong dose
	Frequency too long
	Duration too short
	Drug interaction
Safety	Incorrect administration
	Adverse drug reaction
	Undesirable effect
	Unsafe drug for patient
	Drug interaction
Adherence	Dose administered or changed too rapidly
	Allergic reaction
	Contraindications present
	Dosage too high
	Wrong dose
Adherence	Frequency too short
	Duration too long
	Drug interaction
	Incorrect administration
	Nonadherence
Adherence	Directions not understood
	Patient prefers not to take
	Patient forgets to take
	Drug product too expensive
	Cannot swallow or administer
Adherence	Drug product not available

Adapted with permission from Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care Practice: A Clinician's Guide*. 2nd ed. New York, NY: McGraw-Hill, 2004:168.

patient care. These topics are covered in more detail in **Chapters 3 and 5**.

The steps of the PPCP include *Collect, Assess, Plan, Implement*, and *Follow-up: Monitor and Evaluate*, and are illustrated as a circle to indicate the cyclical nature of the process, with *Follow-up* leading back to *Collect* at a future patient encounter (Fig. 4-1).² Each of the steps is summarized below followed by a short patient case vignette example.

COLLECT

Collection of subjective and objective information provides the basis for identifying drug therapy problems. This information can be obtained directly from the patient or caregiver, through review of existing health records, or communicating with other healthcare professionals. In all practice settings, a primary function of pharmacists is to conduct a medication history as the initial step in identifying drug therapy problems. This is especially important during patient transitions of care. A complete medication history includes all of the prescription and nonprescription medications the patient is currently taking; dietary supplements, herbal products, and complementary medicine approaches; and recent previous medications

TABLE 4-2 Causes of Drug Therapy Problems

Drug Therapy Problem	Possible Causes of Drug Therapy Problems
Unnecessary drug therapy	No valid medication indication for the drug at this time Multiple drug products are used when only single-drug therapy is required The condition is better treated with nondrug therapy Drug therapy is used to treat an avoidable adverse drug reaction associated with another medication The medical problem is caused by drug abuse, alcohol use, or smoking
Need for additional drug therapy	A medical condition exists that requires initiation of new drug therapy Preventive therapy is needed to reduce the risk of developing a new condition A medical condition requires combination therapy to achieve synergism or additive effects
Ineffective drug	The drug is not the most effective one for the medical problem The drug product is not effective for the medical condition The condition is refractory to the drug product being used
Dosage too low	The dosage form is inappropriate The dose is too low to produce the desired outcome The dosage interval is too infrequent A drug interaction reduces the amount of active drug available
Adverse drug reaction	The duration of therapy is too short The drug product causes an undesirable reaction that is not dose related A safer drug is needed because of patient risk factors A drug interaction causes an undesirable reaction that is not dose related The regimen was administered or changed too rapidly The product causes an allergic reaction The drug is contraindicated because of patient risk factors
Dosage too high	The dose is too high for the patient The dosing frequency is too short; the duration of therapy is too long A drug interaction causes a toxic reaction to the drug product
Nonadherence	The dose was administered too rapidly The patient does not understand the instructions The patient prefers not to take the medication The patient forgets to take the medication Drug product is too expensive The patient cannot swallow or self-administer the medication properly The drug product is not available for the patient

Adapted with permission from Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care Practice: A Clinician's Guide*. 2nd ed. New York, NY: McGraw-Hill, 2004:178–179.

the patient has taken. Other relevant health data such as a medical history, health and wellness information, biometric test results, and physical assessment findings may also be collected. Beyond conducting medication and health histories, other important factors to gather include lifestyle habits, a patient's preferences and/or beliefs, health and functional goals, and socioeconomic factors. This additional information can help to provide a holistic approach to patient care. A sample of specific types of information to collect is provided as follows.^{2,4}

Patient Information

- Name, address, and phone number (for future contact and follow-up evaluation)
- Primary care physician

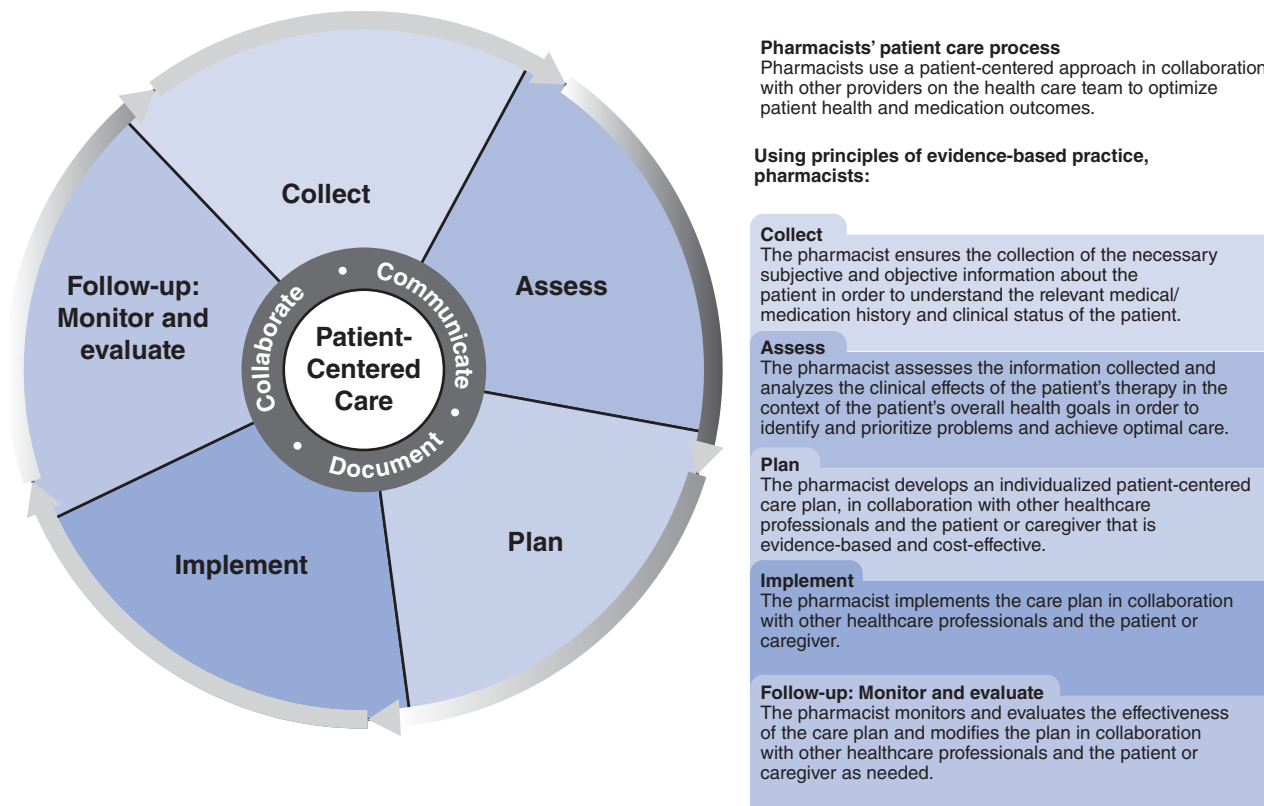


FIGURE 4-1. The pharmacists' patient care process. (Adapted with permission from the Joint Commission of Pharmacy Practitioners Pharmacists' Patient Care Process, May 29, 2014. <https://jcph.net/patient-care-process/>. Accessed March 29, 2019.)

- Demographic and background information: age (date of birth), gender, sexual orientation, gender identity, race, height, weight (important for weight-based dosing)
- Social history (SH): living arrangements, occupation, tobacco, alcohol, substance use (include name of substance, amount, and frequency when possible)
- Family history (FH): relevant health histories of parents and siblings
- Insurance information: name of health plan and policy number (important for accurate billing of services)

Disease Information

- Past medical history (PMH)
- Current medical problems
- History of present illness (HPI)
- Pertinent information from the review of systems (ROS), physical examination, laboratory results, and x-ray/imaging results
- Medical diagnoses
- Immunization history

Drug Information

- Allergies and side effects (include the name of the medication and the reaction that occurred)
- Current prescription medications; for each medication include start date, indication for use, drug name, strength, dosage regimen, and how the patient is actually taking it. The *actual* regimen may differ from the *prescribed* regimen because patients do not always take medications as directed. Also ask about effectiveness, adverse effects, and patient

questions or concerns about current medications for a complete medication history.

- Current nonprescription medications, vitamins, dietary supplements, and alternative/complementary therapies
- Recent past prescription and nonprescription medications (include the stop date)

The amount and type of information collected by pharmacists will vary based on the patient care service or practice setting. For example, in a community pharmacy there will be excellent data on a patient's refill history, but laboratory tests are not as readily available. The pharmacist will rely mostly on communicating with the patient to obtain information but may also conduct point-of-care testing, blood pressure measurement, or other screening tests when available. In hospital and clinic settings, pharmacists have access to laboratory and test results, physician physical exam information, and other objective data; however, they still rely on interviewing the patient to obtain subjective data to fully describe the problem.

Example Case Vignette

Martin Roberts is a 32-year-old Caucasian man who presents to the pharmacy today for a refill of his alprazolam. He states that he only has a few tablets left and doesn't want to run out. He was recently diagnosed with generalized anxiety disorder and started on sertraline and lorazepam. A review of the patient profile in the computer system reveals the following:

- Sertraline (Zoloft) 50 mg, takes one tablet daily, quantity #30 (started 2 weeks ago by Dr Johnson)
- Lorazepam (Ativan) 0.5 mg, takes one tablet daily as needed for anxiety, quantity #30 (started 2 weeks ago by Dr Johnson)
- Acetaminophen (Tylenol) 500 mg, takes one to two tablets as needed for headaches (OTC medication)

What additional information is needed to identify potential drug therapy problems in Mr Roberts?

First, it is important to ask Mr Roberts about his medications, specifically what he takes his medications for, how he takes his medications, and any problems he may be experiencing with them. A brief medication history can also be obtained. These questions reveal the following information: *He takes lorazepam twice a day most days because his doctor told him he could take it more often if he needed it for anxiety. He has only three tablets remaining. He takes sertraline as prescribed and is not experiencing any adverse effects; however, he doesn't think it is working very well. He does not use any other prescription or nonprescription medications and uses the acetaminophen about four to five times per month.*

After learning about his medications, it is important to determine what he knows about his generalized anxiety disorder, especially since it is a recent diagnosis. *He is seeing a therapist to help him with nonpharmacologic strategies for dealing with anxiety. He wasn't told a lot about the medications when he started them 2 weeks ago, so he wonders why he still needs to take the lorazepam.*

ASSESS

A great deal of time is spent analyzing the drug therapy in the context of the patient's overall health goals. Assessment of a patient's health and medications helps to identify and prioritize drug therapy problems. To identify potential drug therapy problems, pharmacists can ask five questions when assessing a patient's drug therapy:

1. Is there an appropriate indication for each medication?
2. Is the drug therapy effective?
3. Is the drug therapy safe for this patient?
4. Can the patient comply with the drug therapy and other aspects of their care plan?
5. Is there an untreated indication that needs drug therapy?

Asking these questions will allow the pharmacist to determine if the patient's drug therapy is appropriate, effective, safe, and convenient for the patient. When asked in this order, pharmacists can systematically assess for potential drug-related problems. For example, if a medication is not appropriate for the patient, one does not need to ask about its effectiveness, safety, or patient adherence because these questions would not be applicable. Additionally, pharmacists can identify drug therapy problems that may interfere with goals of therapy or other potential problems that could be prevented.

After a drug therapy problem is identified, it is also important to determine the severity of the medical condition or problem. This will help in prioritizing the problem list, which is the final portion of the Assess step. The most urgent or severe problem should be listed first, with the remaining problems listed in order of severity. In addition to assessing drug therapy problems, pharmacists may also assess a patient's health literacy, the patient's willingness and ability to make changes, barriers to follow-up (eg, transportation difficulties, insurance limitations), vaccination status, and other preventive care needs. The Collect and Assess steps are often conducted simultaneously because pharmacists evaluate the information as it is being collected. The assessment process is similar across practice settings, but the type and quantity of information available may vary.

Example Case Vignette (continued)

Prioritized problem list for Martin Roberts:

1. Generalized anxiety disorder: early refill of lorazepam (effectiveness problem—prescribed dose is too low). Mr Roberts is 2 weeks early in refilling his lorazepam. He is regularly taking more medication than prescribed, which has led to running out of his 30-day

supply of medication in 2 weeks. In taking 0.5 mg twice per day, he is still below the maximum daily dose of 10 mg. A new prescription will be needed for the increased dose.

2. Generalized anxiety disorder: lack of understanding of sertraline effects (adherence problem). Mr Roberts does not seem informed that the sertraline may take some time to be fully effective.
3. Headaches: potential for acetaminophen overuse (safety problem—dose too high): Mr Roberts is currently taking less than the maximum daily dose of acetaminophen (4000 mg/day). However, he should be educated on the maximum daily dose and reminded of other acetaminophen-containing products to avoid duplication of therapy and potential adverse events.

PLAN

Once a problem list has been identified and prioritized, pharmacists must then develop an individualized, patient-centered care plan specific for the patient's needs. Collaboration with other healthcare providers may be necessary if the plan goes beyond the pharmacist's scope of practice. When formulating a care plan, it is important to include the medical condition for which the patient has drug-related needs, the specific drug therapy problems identified, clear goals of therapy, proposed interventions (nonpharmacologic and pharmacologic), and a follow-up plan. A plan should be created for all problems identified in the assessment step.

Goals of therapy for each medical condition should indicate one of the primary therapeutic outcomes as described in **Chapter 1**: cure of disease, reduction or elimination of symptoms, arresting or slowing of the progression of disease, or preventing a disease or symptom. To create clear goals, the SMART acronym can be used. Each goal should be *Specific, Measurable* (or observable), *Achievable, Related* to the drug therapy problem, and include a *Timeline* for achievement. A patient-centered approach includes the patient in setting goals of therapy that are most important to them and seeking patient input in the prioritization of nonacute problems. Involving the patient in the care plan allows the pharmacist to address the patient's unique concerns, needs, and preferences, and empowers patients to take more responsibility in implementing their portion of the plan.

Specific drug therapy recommendations should include the drug name, dosage form, dose, route of administration, schedule, and duration of therapy. Nonpharmacologic approaches to treatment and preventive strategies (such as screenings or vaccinations) should also be included as appropriate. A plan for monitoring and care continuity is also essential in this step, including specific monitoring parameters for the patient's medical conditions and recommended medications, a specific timeframe for follow-up appointments, and information on referrals if needed.

As with *Assessment*, the process of creating a care plan is similar across practice settings and varies based on the information available for collection and assessment. Hospital and insurance formularies must be considered when developing patient care plans. In the community setting, pharmacists can recommend nonprescription products and self-care strategies but must contact a prescriber if prescription drug therapy needs to be changed, unless a collaborative practice agreement is in place. Pharmacists in all settings can address many drug therapy problems regarding patient adherence issues.

Example Case Vignette (continued)

Plan for Martin Roberts:

1. Generalized anxiety disorder: early refill of lorazepam. Goal of therapy is to alleviate acute anxiety symptoms. Contact

Dr Johnson for a new prescription for lorazepam 0.5 mg; take one tablet twice daily.

2. *Generalized anxiety disorder: lack of understanding of sertraline effects. Goal of therapy is to reduce anxiety symptoms. Educate Mr Roberts on sertraline, specifically its onset of action and the time needed to experience maximal effectiveness.*
3. *Headaches: potential for acetaminophen overuse. Goal is to prevent acetaminophen overdose. Educate Mr Roberts on the maximum dose of acetaminophen. Provide examples of other products that contain acetaminophen, such as over-the-counter cold medications and sleep aids.*

IMPLEMENT

A pharmacist's ability to implement care plans depends on the scope of activities allowed by state laws and regulations or through a collaborative practice agreement. Collaborative practice agreements can be broad or limited to a specific condition, such as anticoagulation. In clinical settings, pharmacists may also be a part of a health-care team conducting collaborative patient visits or rounding. When a plan requires expertise outside a pharmacist's scope of practice, it is important to provide a referral to the appropriate healthcare provider (eg, physician, podiatrist, dietician) and explain to the patient the importance of follow-up. A main component of implementation is providing education and self-management training for the patient and/or caregiver. When counseling patients, a pharmacist can discuss reasons for drug therapy, medication actions, administration, adverse effects, what to expect from treatment (eg, when the medication will begin working, if it provides a cure or just relieves symptoms, if it relieves symptoms completely or just improves them), and appropriate follow-up (eg, proper duration of therapy, when to see a physician if the problem continues).

If authorized, implementation may include initiating, modifying, discontinuing, or administering medication therapy. Under a collaborative practice agreement, pharmacists may be able to implement these changes directly with the patient. Preventive care strategies are also important, such as vaccinations, diabetic foot exams, diet and exercise counseling, and various screenings (eg, blood pressure, cholesterol, depression, blood glucose, HIV, osteoporosis). Many of these strategies could be implemented and patients referred to appropriate providers if abnormal results are found. Communication and documentation of the plan are also important to ensure that care is coordinated with other healthcare providers.

Example Case Vignette (continued)

You call and speak with Dr Johnson about Mr Martin's management of his anxiety. The physician confirms that Mr Martin was instructed to take the lorazepam more often if he needed it in the next few weeks. He provides you with a verbal prescription for lorazepam 0.5 mg, with instructions to take one tablet up to three times per day as needed for anxiety, Quantity #45, two refills. He states that this should be an adequate supply until Mr Martin's next appointment in 4 weeks. You then speak with Mr Martin and summarize your conversation with Dr Johnson. You also counsel Mr Martin on his sertraline and inform him that it may take up to 4–6 weeks to see the full effects of the medication, and that he should notice some effects soon and not need as much lorazepam. You counsel him on the importance of taking his medications as prescribed and contacting his physician if he needs more lorazepam than prescribed. You also discuss his acetaminophen use and educate him that the maximum daily dose is 4000 mg. While he is well under this dose currently, he should be aware of other medications that contain acetaminophen, including over-the-counter cold medications and sleep aids. He agrees to talk with you if he is unsure if

a medication contains acetaminophen. You document your conversation with the patient in his profile in the computer system.

FOLLOW-UP: MONITOR AND EVALUATE

The final step in the PPCP clearly delineates a continual process because at some future time subjective and objective data will again need to be collected and assessed. During follow-up, the pharmacist evaluates the positive and negative impact of the care plan on the patient, identifies new drug therapy problems, and takes action to address new problems or adjust therapy. It is also important to determine an appropriate follow-up time frame to ensure that efficacy and safety parameters can be evaluated appropriately. In some settings, patients may have scheduled visits at predetermined intervals while others may be conducted primarily as a walk-in. In these situations, patient no-shows for visits can make follow-up problematic. With follow-up, various outcomes can also be tracked and reported such as:

- *Clinical outcomes:* blood pressure, A1C, medication problem resolution, adverse drug events, adherence
- *Humanistic outcomes:* patient medication knowledge, patient functioning, self-management capability, satisfaction, patient concerns about the treatment
- *Economic outcomes:* hospitalizations, emergency department visits, medication costs

When evaluating the care plan, a pharmacist should compare the goals of therapy with the patient's current status. Cipolle et al developed terminology to describe the patient's status, the medical condition, and the comparative evaluation of that status with the previously determined therapeutic goals.⁴ These terms also describe the actions taken as a result of the follow-up evaluation:

Status	Definition
Resolved	Therapeutic goals achieved for the acute condition; discontinue therapy
Stable	Therapeutic goals achieved; continue the same therapy for chronic disease management
Improved	Progress is being made in achieving goals; continue the same therapy because more time is required to assess the full benefit of therapy
Partial improvement	Progress is being made, but minor adjustments in therapy are required to fully achieve the therapeutic goals before the next assessment
Unimproved	Little or no progress has been made, but continue the same therapy to allow additional time for benefit to be observed
Worsened	A decline in health is observed despite an adequate duration using the optimal drug; modify drug therapy (eg, increase the dose of the current medication, add a second agent with additive or synergistic effects)
Failure	Therapeutic goals have not been achieved despite an adequate dose and duration of therapy; discontinue current medication(s) and start new therapy
Expired	The patient died while receiving drug therapy; document possible contributing factors, especially if they may be drug related

Example Case Vignette (continued)

Mr Martin returns to the pharmacy in 2 weeks to pick up his sertraline prescription. You ask him how he is doing, and he reports that he is feeling better and his anxiety has improved. He expresses appreciation for the help you provided during his last visit to the pharmacy. He admits using less lorazepam in the past week and feels like the

sertraline is starting to have some positive effects. He has an appointment with Dr Johnson in 2 weeks for follow-up. You evaluate your care plan as follows:

1. *Generalized anxiety disorder: early refill of lorazepam. Goal of therapy is to alleviate acute anxiety symptoms, and symptoms are improving.*
2. *Generalized anxiety disorder: lack of understanding of sertraline effects. Goal of therapy is to reduce anxiety symptoms. Symptoms are improving, and the patient understands the current therapy.*
3. *Headaches: potential for acetaminophen overuse. The goal is to prevent acetaminophen overdose. The patient understands the need to avoid other acetaminophen-containing drug products; thus, this potential drug therapy problem was prevented at this time, but ongoing monitoring is advised.*

EXAMPLES OF PATIENT CARE PROCESS IMPLEMENTATION

The PPCP can be applied in a variety of patient care situations such as CMM, IV-to-oral dosing in the hospital setting, medication reconciliation during a care transition, disease state management, and provision of immunization services, to name a few. To assist pharmacists with implementing the PPCP, organizations have published resource guides for specific conditions such as immunization services⁵ and managing high blood pressure.⁶ In more general terms, many pharmacists use the PPCP in providing MTM, assisting patient's with self-care needs, and chronic disease state monitoring.

MEDICATION THERAPY MANAGEMENT

The American Pharmacists Association (APhA) and the National Association of Chain Drug Stores (NACDS) published core elements of MTM to assist pharmacists in providing these services consistently for patients, regardless of the setting.⁷ Medication therapy management (MTM) focuses on the identification and resolution of drug therapy problems, similar to the main purpose of the PPCP. Therefore, the steps of the PPCP can be easily seen in MTM's five core elements⁷:

1. **Medication therapy review (MTR):** Involves discussing the full list of the patient's medications (*Collect*), identifying and prioritizing potential drug therapy problems (*Assess*), and creating a plan to resolve the identified drug therapy problems (*Plan*). This could be conducted in person or via the telephone.
2. **Personalized medication record (PMR):** A complete record of the patient's medications including dosages and directions for use is provided for the patient (*Implement*). All prescription and nonprescription medications should appear on this list in addition to dietary supplements and herbal products. This record may also include demographic information, a complete list of allergies, the name of pharmacy, emergency contact information, and the date it was last updated.
3. **Medication-related action plan (MAP):** A document provided to the patient that includes any action items derived from the full medication therapy review (*Plan, Implement*). This plan is used by the patient to track their progress for self-management (*Follow-up*).
4. **Intervention and/or referral:** Completing any needed action steps (eg, calling a physician, making written instructions to the patient, counseling on proper inhaler use). The pharmacist either addresses the drug therapy problems directly or refers the patient to a physician or other healthcare provider. (*Implement*)

5. **Documentation and follow-up:** All interventions should be documented; however, the format may vary depending on the specific area of practice. Documentation may include a full SOAP note or something as simple as documenting a brief note in the pharmacy patient profile (*Implement*). Follow-up appointments are scheduled based on the patient's needs (*Follow-up*).

SELF-CARE MANAGEMENT

Pharmacists in many settings assist patients with various self-care needs. In this capacity, pharmacists perform functions similar to a primary care provider, specifically gathering and evaluating information about the patient's problems, differentiating between self-treatable conditions and conditions requiring medical intervention, and advising and counseling the patient about the proposed course of action. To assist pharmacists with these types of encounters, the QuEST/SCHOLAR tool was developed.⁸ In addition to patients presenting with a self-care complaint, the SCHOLAR-MAC questions could also be helpful to organize a patient interview for any patient presenting with a particular symptom complaint. The steps of the PPCP are clearly evident in QuEST, as described below⁸:

- **Quickly and accurately assess the patient using SCHOLAR-MAC questions (*Collect, Assess*)**
 - ✓ Symptoms: the main and associated symptoms
 - ✓ Characteristics: a description of the situation and evolution of the symptoms
 - ✓ History: previous experience with the problem; what has been tried so far
 - ✓ Onset: when the problem began
 - ✓ Location: where the problem is located
 - ✓ Aggravating factors: aspects that make the problem worse
 - ✓ Remitting factors: aspects that make the problem better
 - ✓ Medications: prescription and nonprescription medications, dietary supplements, herbal products, complementary therapies
 - ✓ Allergies: to medications and other substances
 - ✓ Conditions: all current medical conditions
- **Establish that the patient is an appropriate self-care candidate (*Assess*)**
- **Suggest appropriate self-care strategies (*Plan, Implement*)**
- **Talk with the patient about the suggested self-care strategies (*Implement, Follow-up*)**

CHRONIC DISEASE STATE MONITORING

In ambulatory settings, pharmacists often participate in chronic disease state monitoring in collaboration with other healthcare professionals. For example, a community pharmacist may have a collaborative practice agreement with a physician to manage their patients on chronic anticoagulation therapy. After starting anticoagulation, the physician may refer patients to the pharmacist for follow-up appointments. At these appointments the pharmacist interviews the patient, conducts point-of-care INR testing, makes adjustments in anticoagulant therapy, and communicates those changes to the patient's physician. Pharmacists also participate in chronic disease state monitoring in clinic settings, where they would have full access to the patient's medical record. While a patient may be referred to pharmacy services for a particular indication, such as diabetes management, it is important for the pharmacist to explore all potential drug-related problems that may arise, even if they go beyond the original intent of the consult. An illustration of how the

PPCP may be implemented during a chronic disease state monitoring situation is provided below:

Example case vignette

As part of a diabetes care clinic, pharmacists manage patients under a collaborative practice agreement and work collaboratively with other healthcare providers. Harper Johnson is a 62-year-old woman with diabetes, hypertension, and dyslipidemia. She presents to the pharmacy clinic today for follow-up of her diabetes management.

Collect: Because this patient has been seen previously in clinic, her medical record contains a wealth of information for the pharmacist to identify and assess Ms Johnson's medical and drug therapy problems. The encounter begins by interviewing the patient with a focus on what has changed since the last visit. It is important to assess the patient holistically and not focus exclusively on her diabetes management. Collect relevant patient information, disease information, and medication information as described previously. This information is organized similar to a medical record:

- **Chief complaint (CC):** "I don't think this new medication for my diabetes is working any better than the last one."

Asking the CC up front allows the pharmacist to elicit factors that are most important to the patient and may give some idea of potential drug therapy problems.

- **HPI:** Last month the physician started Ms Johnson on exenatide because her blood glucose readings were not controlled on metformin monotherapy. Exenatide is an injectable drug, so Ms Johnson thought that it worked like insulin and she no longer needed to take the metformin. She checks her fasting blood glucose every morning. Her daily log indicates fasting blood glucose readings of 145–155 mg/dL, which is about the same as when she was taking metformin monotherapy.

The HPI provides more information about the CC and is a summary of the patient interview. It provides a story describing the situation from the patient's perspective. When patients present with specific symptom complaints, SCHOLAR questions can be asked as part of the HPI.

- **PMH:** type 2 diabetes (diagnosed 2 years ago), HTN (diagnosed 5 years ago), dyslipidemia (diagnosed 2 years ago).
- **FH:** mother has type 2 diabetes and dyslipidemia; father has hypertension and history of an MI at age 68.
- **SH:** (–) tobacco; (+) alcohol – one glass of wine or beer 2–3 times per week.

A complete list of the patient's medical conditions (including when they were diagnosed), relevant family history, and relevant social history are helpful in identifying and assessing drug therapy problems.

- **Medications:** Ms Johnson takes all medications as prescribed except she stopped taking metformin 1 month ago when the exenatide was started. She does not use any nonprescription medications, dietary supplements, or herbal products. At this time, she is not experiencing any adverse effects with her medication.

✓ Metformin 1000 mg, take one tablet twice daily with meals (started 2 years ago and titrated up to the current dose, patient has not been taking for the past month)

✓ Exenatide 5 mcg, inject subcutaneously twice daily 60 minutes before meals (started 1 month ago)

✓ Lisinopril 10 mg, take one tablet daily (started 5 years ago)

✓ Chlorthalidone 25 mg, take one tablet daily (started 3 years ago)

✓ Atorvastatin 40 mg daily, take one tablet daily (started 2 years ago)

Documenting all of the medications the patient is currently taking, how the patient is taking them, adverse effects experienced, and adherence information is important to assist in identifying actual or potential drug therapy problems.

- **Allergies:** none
- **ROS:** No complaints of hypoglycemic symptoms, shortness of breath, or chest pain. No recent reports of polyuria, polyphagia, or polydipsia. Reports good sensation in lower extremities.

Pertinent positive and pertinent negative information related to the patient's medical conditions and drug therapy problems should be collected and documented.

- **Vital signs:** BP 142/74 mm Hg, HR 68 bpm, weight 85 kg

A targeted physical examination could also be conducted and included if pertinent to the situation. Review of the physician's previous physical exam information could also be included.

- **Laboratory results:**

✓ Fasting blood glucose 152 mg/dL (today)

✓ A1C 7.9% (1 month ago)

✓ Lipid panel: TC 164 mg/dL, LDL 98 mg/dL, HDL 42 mg/dL, TG 120 mg/dL (1 month ago)

✓ Electrolytes and liver function tests WNL (1 month ago)

Document all laboratory results relevant to the patient's medical conditions and drug therapy. This information is helpful in assessing the patient's drug therapy problems.

- **Preventive care:** eye exam 6 months ago, foot exam last month in clinic, urine albumin screening 6 months ago (negative results).
- **Immunizations:** All childhood vaccines, flu vaccine annually, Tdap 5 years ago, hepatitis B vaccine 2 years ago.

Relevant preventive care tests and a complete list of vaccinations allow the pharmacist to fully assess the patient to identify additional drug therapy problems that would otherwise have been missed.

Assess: Evaluate each of the patient's medical conditions and medications to identify and prioritize all drug therapy problems. An assessment of Ms Johnson's problems is provided below. Diabetes is the problem with highest priority not only because it is the reason for the patient's clinic visit, but also because it was the patient's primary concern. Any medical condition that is currently under control (such as dyslipidemia) is prioritized at the end of the list.

1. **Type 2 diabetes:** A1C above goal of <7.0% and fasting glucose above goal 80–130 mg/dL.⁹ No improvement since previous appointment. No reported episodes of hypoglycemia. Exenatide 5 mcg twice daily is an appropriate dose for this patient, and she is tolerating it well. However, she stopped taking metformin when she began using exenatide. Patient is up to date with preventive care measures for diabetes.
2. **Hypertension:** BP elevated above goal of <130/80 on lisinopril and chlorthalidone therapy.¹⁰ Patient reports adherence with medications and good tolerability. Lisinopril is not at the maximum dose and could be increased.
3. **Vaccination status:** The recombinant zoster vaccine (RZV) is recommended for all patients 50 years of age and older.¹¹ The vaccine is given as a two-dose series 2–6 months apart. The patient is up to date on all other vaccinations.
4. **Dyslipidemia:** Stable. Lipid panel is controlled on atorvastatin monotherapy (high-intensity statin therapy).¹²

Plan and implement: When documenting the plan, the problem list should appear in the same order as the assessment. All problems identified in the assessment should be provided with a plan.

In addition to specific medication changes, goals of therapy and needed referrals can be included. Implementation often occurs simultaneously with the plan. Counseling provided for the patient should be documented in the medical record. Medication therapy can be adjusted if a collaborative practice agreement is in place and it is within the pharmacist's scope of practice. Any referrals should be clearly specified and communicated with the patient.

1. *Type 2 diabetes: Goal of therapy—HbA1c <7.0% without episodes of hypoglycemia⁹ and improved medication adherence. Restart metformin 500 mg twice daily and titrate up to 1000 mg twice daily after 2 weeks if tolerated (new prescription called in to pharmacy for patient). Continue exenatide 5 mcg twice daily. Counsel patient on mechanism of action and adverse effects of medications for diabetes. Emphasized importance of checking with the clinic before stopping any medication.*
2. *Hypertension: Goal of therapy—BP <130/80.¹⁰ Increase lisinopril to 20 mg daily for improved BP control (new prescription called in to pharmacy for patient). Continue chlorthalidone 25 mg daily.*
3. *Vaccination status: Goal of therapy – up to date on all recommended vaccinations. Have nursing give one dose of RZV intramuscularly today. A second dose is needed in 2–6 months.*
4. *Dyslipidemia: Continue atorvastatin 40 mg daily. Patient does not need refills at this time.*

Follow-up: Plans for follow-up are often included when documenting plans for the identified drug therapy problems but could also be specified separately. It is important to be clear and specific not only with the monitoring parameters, but with a timeline for follow-up.

1. *Type 2 diabetes: Continue checking daily fasting glucose and recommended checking 2-hour postprandial glucose every other day. Schedule follow-up appointment with the pharmacist in 1 month. Call patient in 2 weeks to check on metformin tolerability and remind patient to increase the dose. Check A1C in 3 months.*
2. *Hypertension: Recheck BP at next clinic visit in 1 month. Encourage patient to check BP at home using an automatic monitor. Check kidney function (serum creatinine) in 1 month.*
3. *Vaccination status: Monitor for any soreness in the arm post-injection. Schedule an appointment for a second dose of RZV in 2 months.*
4. *Dyslipidemia – Recheck lipid panel in 1 year. Monitor for adverse effects of statin therapy, particularly myalgia.*

CONCLUSION

Implementing the PPCP throughout the profession of pharmacy provides a common terminology for pharmacist patient care services and allows the focus of the profession to shift to quality improvement, provider collaboration, improved patient outcomes, and cost

savings. This process should be incorporated into the thought process for all pharmacists providing direct patient care, regardless of the practice setting.

REFERENCES

1. Harris IM, Phillips B, Boyce E, et al. Clinical pharmacy should adopt a consistent process of direct patient care. *Pharmacotherapy*. 2014;34(8):e133–e148.
2. Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process. May 29, 2014. Available at: <https://jcphp.net/wp-content/uploads/2016/03/PatientCareProcess-with-supporting-organizations.pdf>. Accessed March 29, 2019.
3. Joint Commission of Pharmacy Practitioners. Pharmacists' Patient Care Process Presentation. Available at: https://jcphp.net/wp-content/uploads/2015/09/Patient_Care_Process_Template_Presentation-Final.pdf. Accessed March 29, 2019.
4. Cipolle RJ, Strand LM, Morley PC, eds. *Pharmaceutical Care Practice: The Patient-Centered Approach to Medication Management Services*. 3rd ed. New York, NY: McGraw-Hill, 2012.
5. American Pharmacists Association. *Applying the Pharmacists' Patient Care Process to Immunization Services: A Resource Guide for Pharmacists*. Washington, DC: American Pharmacists Association, 2017.
6. Centers for Disease Control and Prevention. *Using the Pharmacists' Patient Care Process to Manage High Blood Pressure: A Resource Guide for Pharmacists*. Atlanta, GA: Centers for Disease Control and Prevention, U.S. Department of Health and Human Services, 2016. Available at: <https://www.cdc.gov/dhdp/pubs/docs/pharmacist-resource-guide.pdf>. Accessed March 29, 2019.
7. American Pharmacists Association, National Association of Chain Drug Stores Foundation. *Medication Therapy Management in Pharmacy Practice: Core Elements of an MTM Service Model (version 2.0)*. J Am Pharm Assoc. 2008;48(3):341–353.
8. Divine H, McIntosh T. Pharmacists' patient care process in self-care. In: Krinsky DL, Ferreri SP, Hemstreet BA, Hume AL, Newton GD, Rollins CJ, Teitze KJ, eds. *Handbook of Nonprescription Drugs: An Interactive Approach to Self-Care*. 19th ed. Washington, DC: American Pharmacists Association, 2018:24.
9. American Diabetes Association. Glycemic Targets: Standards of Medical Care in Diabetes—2019. *Diabetes Care*. 2019;42(Suppl 1):S61–S70.
10. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018;71:e127–e248.
11. Centers for Disease Control and Prevention. *Recommended Adult Immunization Schedule, United States, 2019*. Available at: <https://www.cdc.gov/vaccines/schedules/downloads/adult/adult-combined-schedule.pdf>. Accessed March 31, 2019.
12. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2018. doi: <https://doi.org/10.1016/j.jacc.2018.11.002>.

Documentation of Patient Encounters and Interventions

LORI T. ARMISTEAD, MA, PharmD
TIMOTHY J. IVES, PharmD, MPH, FCCP, CPP

To ensure high-quality patient care, especially in the current environment of increasingly complex care, all healthcare providers must generate and maintain clear and concise records of each patient's health and medical conditions.^{1,2} Documentation is also required for providers to receive accurate and timely payment for services. Documentation outlines the care the patient received in a chronological and organized manner and serves as a form of communication among practitioners, which is an important element that contributes to the quality of care provided. Each practitioner involved knows what evaluation has occurred, what the patient's treatment plan is, and who will provide it. Furthermore, third-party payers may require documentation from practitioners that ensures that the services provided are consistent with the insurance coverage.^{1,2} General components of documentation include:

- A complete and legible record
- Date of service, site of service, and identity of the practitioner
- Documentation for each encounter with a rationale for the encounter, relevant history, physical findings, prior test results, and identified health risk factors
- An easily inferred rationale for ordering diagnostic tests or ancillary services, assessment, clinical impression (or diagnosis), and plan for care
- Patient progress, response to and changes in treatment, and revision of the original diagnosis/assessment
- Applicable diagnostic and treatment codes

Traditionally, this documentation was paper based; however, such records are often inaccessible at the point of care, not easily transferable or transportable, illegible, poorly organized, and missing key information. Due to these limitations, many academic centers and healthcare systems have developed and implemented electronic health records (EHRs), which have greatly enhanced workflow, usability, and patient safety.² Further, the 2001 Institute of Medicine report *Crossing the Quality Chasm* identified the EHR as a key component in improving provider access to medical information, facilitating decision support and data collection, and reducing medical errors and associated costs.³ The EHR may also improve documentation with reduced clinical variation, better provision of quality preventive and chronic care, and increased security of confidential patient information.⁴⁻⁷ Furthermore, EHRs are associated with higher performance on certain quality measures.^{1,8}

PRINCIPLES OF DOCUMENTATION

Documentation includes pertinent facts, findings, and observations about a patient's health history, including past and present illnesses, examinations, tests, treatments, and outcomes. With the growth of EHRs, additional benefits have been identified^{14,7,9-11}:

- Enhanced ability of providers across the continuum of care to evaluate care, plan immediate treatment, and monitor care over time
- Easier communication and continuity of care among providers involved in the patient's care
- New modes of communicating with patients and providing them information about their care
- More accurate and timely claims review and payment
- Improvement in the quality of care provided
- Increased time efficiency
- Greater adherence to practice guidelines and access to reference information
- Fewer medication errors and adverse drug events
- More appropriate utilization review and quality of care evaluations
- Improved ability to measure and track clinical, financial, humanistic, and process of care outcomes
- Greater clarity of coding (ie, Current Procedural Terminology [CPT] and International Statistical Classification of Diseases and Related Health Problems, Tenth Revision, Clinical Modification [ICD-10-CM], from the World Health Organization) on health insurance claim forms, which must be supported by documentation in the patient record

Much of this documentation is derived from a systematic patient care process that is standardized within each discipline. For example, physicians perform a history and physical examination based on a standardized review of body systems and document their results, using a universally accepted, standardized, and systematic process. Nurses document their observations and assessments of patient clinical parameters and outcomes, administration of patient medications, and order implementation according to guidelines set by the institutions for which they work.⁷ Pharmacist documentation typically focuses on medication-related parameters and appropriateness of medication therapies utilized.

Several evaluation/documentation systems have been suggested for healthcare professionals. More than 50 years ago, the use of a Problem-Oriented Medical Record was proposed,¹² and most physicians, nurse practitioners, physician associates, and other healthcare practitioners write progress notes using the Subjective, Objective, Assessment, Plan (SOAP) format. The elements of SOAP are as follows:

S = Subjective: Chief complaint; history of present illness; why the patient is being seen

O = Objective: Physical findings and measurable data such as laboratory values, drug levels, and imaging studies

A = Assessment: Analysis or conclusion about the patient's current health status, evidence of progress, response to intervention or medication, and change in functional status

P = Plan: Interventions or actions taken in response to assessment, collaboration with others, plan for follow-up, change in diagnosis, and documentation that the patient was informed of changes in interventions and/or medications.

Institutional consultant notes often use an abbreviated version of the SOAP format, often organized by pertinent disease states. This abbreviated version includes key subjective and objective information, assessments, and recommendations. In most cases, the EHR has embraced many of the key components of the above formats. HER documentation is tailored to documenting medical encounters and history, and also to maximizing billing by meeting requirements established by the US Centers for Medicare & Medicaid Services. Traditionally, this documentation was performed by dictation and transcription. Today, most EHRs use predetermined templates to accept automated insertion of clinical data to facilitate the documentation process.

DOCUMENTING PHARMACIST-PROVIDED PATIENT CARE

The provision of healthcare is evolving into team-based, patient-centered care, with each team member contributing in ways that best reflect their training and areas of specialty. Pharmacists are increasingly serving as accountable and integral members of healthcare teams and members of patients' broader medical neighborhoods.¹³ Where pharmacists are recognized as partners in care and have access to patients' full medical records, they have been shown to identify medication therapy problems with greater confidence and are better able to offer efficient and comprehensive medication management services.¹⁴ Due to the growth in pharmacists' clinical acumen, a standardized patient care process for pharmacists that is applicable to all practice settings has been adopted.¹⁵ In 2013, the Joint Commission of Pharmacy Practitioners (JCPP) adopted a vision for pharmacy practice in which patients achieve optimal health and medication outcomes with pharmacists as essential and accountable providers within patient-centered, team-based healthcare.¹⁶ In 2014, the JCPP promulgated a process of care for the delivery of patient care services provided by pharmacists in any practice setting called the Pharmacists' Patient Care Process (PPCP).¹⁷ In 2018, the American College of Clinical Pharmacy (ACCP) further defined the pharmacist's process of patient care by delineating the essential functions and operational definitions of each step of the process.¹⁸ The PPCP is the standard process taught in US schools and colleges of pharmacy and is included in the current Standards of the Accreditation Council for Pharmacy Education (ACPE).

Regardless of each clinician's perspective and role on the team, collaboration, communication, and documentation are key components for the provision of high-quality care. The need for interoperable information technology systems to facilitate efficient documentation and effective communication among all healthcare practitioners has been identified and is key for optimal communication and continuity of patient care.^{4,10}

As described in **Chapter 1**, the PPCP framework is used in this *Casebook* to identify and resolve the drug therapy problems of patients. The steps can be summarized as follows:

Collect Information

- 1.a. Identify subjective and objective information that indicates the presence of the primary problem or disease.

- 1.b. Identify additional information needed to fully assess the patient's problems.

Assess the Information

- 2.a. Assess the severity of the patient's problem based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. Define the goals of pharmacotherapy for the patient.
- 3.b. Identify nondrug therapies that might be useful.
- 3.c. Identify the feasible pharmacotherapeutic options available for treating the patient's problem(s).
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for the patient.

Implement the Care Plan

- 4.a. Outline information that should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects.
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. Define the clinical and laboratory parameters that should be used to evaluate the therapy for achieving the desired outcomes and to detect or prevent adverse effects.
- 5.b. Develop a plan for follow-up that includes appropriate timeframes to assess progress toward achievement of the goals of therapy.

Steps 4.a. and 4.b. are crucial. Clinicians must document the actual or potential drug therapy or medical problems identified, as well as the associated interventions that they desire to implement or have implemented. All clinicians must adequately communicate their recommendations and actions to other healthcare practitioners, patients, and caregivers (eg, parents). The goal is to provide a clear, concise record of the actual/potential problem,¹⁹⁻²¹ the thought process that led the clinician to select an intervention, and the intervention itself. Additionally, the ability to receive remuneration for services provided also necessitates an acceptable documentation strategy.

MEDICATION THERAPY MANAGEMENT

Medication Therapy Management (MTM) has been defined as a distinct service or group of services that optimize therapeutic outcomes for individual patients.²¹ Pharmacists are the largest provider of MTM services,²² which are independent of, but can occur in conjunction with, provision of a medication product. MTM encompasses a broad range of professional activities and responsibilities within the scope of practice of the licensed pharmacist or other qualified healthcare providers. MTM services can be provided in diverse healthcare settings and can be targeted or comprehensive in approach.²² The most comprehensive form of MTM has been termed Comprehensive Medication Management (CMM). CMM is a patient-centered approach to optimizing medication use and improving patient health outcomes, is delivered by a pharmacist or other clinician working in collaboration with the patient and other

healthcare providers, and assesses a patient's medications comprehensively, not in a targeted manner.¹⁸

MTM interventions include, but are not limited to, the following patient-focused activities²³:

- Performing or obtaining necessary assessments of the patient's health status
- Formulating a medication treatment plan
- Selecting, initiating, modifying, or administering medication therapy
- Monitoring and evaluating the patient's response to therapy, including safety and effectiveness
- Performing a medication review to identify, resolve, and prevent medication-related problems, including adverse drug events
- Documenting the care delivered and communicating essential information to the patient's other primary care providers
- Providing verbal education and training designed to enhance patient understanding and appropriate use of his or her medications
- Providing information, support services, and resources designed to enhance patient adherence with his or her therapeutic regimens
- Coordinating and integrating MTM services within the broader healthcare management services being provided to the patient

CMM includes all of the functions of MTM, but also includes the following¹⁸:

- Utilization of a patient's medical record for collecting patient information and documenting the findings, assessments, and interventions of each patient encounter
- A comprehensive review of *all* of a patient's medications, assessing the indication, effectiveness, and safety of each medication as well as the patient's adherence to their medications
- Documentation of all drug therapy problems identified, with planned interventions, monitoring, and follow-up
- Provision of adequate patient follow-up, in the context of the larger healthcare team, for the achievement of clinical and patient goals of therapy

When delivering MTM/CMM services, the clinician is responsible for documenting services in a manner appropriate for evaluating patient progress and sufficient for billing purposes. The use of core documentation elements helps create consistency in documentation and information sharing among members of the healthcare team, while facilitating practitioner, organization, and regional variations.²¹ Documentation of MTM/CMM services includes the following information categories:

- Patient demographics
- Known allergies, diseases (eg, heart failure), or conditions (eg, pregnancy)
- A record of all medications, including prescription, nonprescription, herbal, and other dietary supplement products
- Assessment of drug therapy problems and plans for resolution
- Therapeutic monitoring performed or needed
- Interventions or referrals made
- Education provided to the patient
- Feedback provided to providers and patients
- Schedule and plan for follow-up appointment

- Amount of time spent with the patient
- Appropriate billing codes

Similarly, the American Society of Health-System Pharmacists (ASHP) has suggested the following categories of information that may need to be documented in the patient medical record (PMR)²⁴:

- A summary of the patient's medication history on admission, including medication allergies and their manifestations
- Oral and written consultations provided to other healthcare professionals regarding the patient's medication therapy selection and management
- Physicians' oral orders received directly by the pharmacist
- Clarification of medication orders
- Adjustments made to medication dosage, dosage frequency, dosage form, or route of administration
- Medications, including investigational drugs, administered
- Actual and potential drug therapy problems that warrant surveillance
- Pharmacotherapy monitoring findings, including:
 - ✓ Therapeutic appropriateness of the patient's medication regimen, including the route and method of administration
 - ✓ Therapeutic duplication in the patient's medication regimen
 - ✓ The degree of patient compliance with the prescribed medication regimen
 - ✓ Actual and potential drug–drug, drug–food, drug–laboratory test, and drug–disease interactions;
 - ✓ Clinical and pharmacokinetic laboratory data pertinent to the medication regimen
 - ✓ Actual and potential medication toxicity and adverse effects
 - ✓ Physical signs and clinical symptoms relevant to the patient's pharmacotherapy
- Medication-related patient education and counseling provided

THE SOAP NOTE FORMAT FOR DOCUMENTATION

As discussed previously, in the SOAP note format subjective (S) and objective (O) data are recorded and then assessed (A) to formulate a plan (P). Subjective data include patient symptoms (eg, pain), clinician observations (eg, agitation), or information obtained about the patient (eg, history of smoking). By its nature, subjective information is descriptive and generally cannot be confirmed by diagnostic tests or procedures. Much of the subjective information is obtained by speaking with the patient while obtaining the medical history, as described in **Chapter 1** (ie, chief complaint, history of present illness, past medical history, family history, social history, medications, allergies, and review of systems). Important subjective information may also be obtained by direct interview with the patient after the initial medical history has been performed (eg, a description of an adverse drug effect, rating of pain severity using standard scales).

A primary source of objective information (O) is the physical examination. Other relevant objective information includes laboratory values, serum drug concentrations (along with the target therapeutic range for each level), and the results of other diagnostic tests (eg, electrocardiogram [ECG], X-rays, culture, and sensitivity tests). Risk factors that may predispose the patient to a particular problem should also be considered for inclusion. The communication

note should include only the pertinent positive and negative findings. Pertinent negative findings are signs and symptoms of the disease or problem that are not present in the particular patient being evaluated.

The assessment (A) section outlines what the practitioner thinks the patient's problem is, based on the subjective and objective information acquired. This assessment often takes the form of a diagnosis or differential diagnosis. This portion of the SOAP note should include all of the reasons for the clinician's assessment. This helps other healthcare providers reading the note to understand how the clinician arrived at his or her particular assessment of the problem.

The plan (P) may include ordering additional diagnostic tests or initiating, revising, or discontinuing treatment. If the plan includes changes in pharmacotherapy, the rationale for the specific changes recommended should be described. The drug, dose, dosage form, schedule, route of administration, and duration of therapy should be included. The plan should be directed toward achieving a specific, measurable goal or endpoint, which should be clearly stated in the note. The plan should also outline the efficacy and toxicity parameters that will be used to determine whether the desired therapeutic outcome is being achieved and to detect or prevent drug-related adverse events. Ideally, information about the therapy that should be communicated to the patient should also be included in the plan. The plan should be reviewed and referred to in the note as often as necessary.

IDENTIFICATION AND DOCUMENTATION OF DRUG THERAPY PROBLEMS

All clinicians, including pharmacists, have long adopted and adapted modes of documentation of other healthcare providers (eg, SOAP notes), which has been helpful for communicating findings and recommendations to other clinicians. However, there is no universally accepted, standardized documentation system that is specific to drug therapy problems (DTPs).²⁵ In attempts to better emphasize the medication-centric expertise within pharmacy and to track the clinical and financial impact of pharmacist-delivered patient care, the identification and documentation of DTPs have been increasingly implemented in practice.

The first step in documenting DTPs is to clearly state the nature of problem(s), including the medication and associated medical condition to which the DTP applies. Each DTP should be addressed separately and prioritized by level of urgency. Understanding the types of pharmacotherapeutic problems that may occur facilitates identification of DTPs. As described in **Chapter 1**, seven distinct types of problems have been identified that relate to assessment of medication appropriateness, effectiveness, safety, and adherence^{26,27}:

Appropriate indication for the medication:

1. The medication is unnecessary because the patient does not have a clinical indication at this time.
2. Additional drug therapy is required to treat or prevent a medical condition.

Effectiveness of the medication:

3. The medication being used is not effective at producing the desired patient response.
4. The dosage is too low to produce the desired patient response.

Safety of the medication:

5. The medication is causing an adverse reaction.
6. The dose is too high, resulting in actual or potential undesirable effects.

Adherence to the medication:

7. The patient is not able or willing to take the drug therapy as intended.

Use of a classification system such as the PQA Medication Therapy Problem Categories Framework for various types of medication-related problems offers at least two advantages. First, it presents a framework, applicable in any practice setting, to ensure that the clinician has considered each possible type of DTP. Second, categorization allows optimal data analysis and retrieval capabilities. Thus, problems as well as the interventions to resolve them can be stored in a standardized format electronically. When an analysis of this information is needed at a later date, such as determining how much money was saved through an intervention, how outcomes were improved by the intervention, or how many problems of a certain type have occurred, the problems and interventions can be reviewed by groups rather than individually. Documentation of DTPs can be stand-alone or included within the Assessment and Plan portions of a SOAP note. Regardless of the form of documentation, inclusion of the following components are critical:

- Pertinent patient identifiers, subjective, and objective information
- Patient's current medications, allergies, and medical conditions
- Medication and associated medical condition for each DTP identified
- Category and rationale for each DTP identified
- Prioritization of DTPs identified
- Planned intervention for each DTP identified (eg, discontinue medication, change medication dose, recommend lab monitoring, provide medication education)
- Rationale for each recommended intervention
- Individual responsible for implementing each intervention (patient, provider, pharmacist, or other clinician)
- Desired therapeutic endpoint or outcome for each intervention. This may include both short-term goals (eg, lower blood pressure [BP] to <140/90 mm Hg in a patient with primary hypertension [HTN] [therapeutic endpoint]) and long-term goals (eg, prevent cardiovascular complications in that patient [therapeutic outcome])
- Details of planned follow-up
- Resolution of each DTP, when known

MONITORING FOR ENDPOINTS AND OUTCOMES

It is not enough to only provide a clear, concise record of the nature of a problem, the assessment that led to the conclusion that a problem exists, and the selection of a plan for resolution of the problem. To truly "close the loop" of patient care, follow-up on the plan must occur to ensure that the intended outcome was achieved. A plan for follow-up monitoring of the patient must be documented and adequately implemented. This process should include questioning the patient, gathering laboratory data, and performing the ongoing physical assessments necessary to determine the effect of the plan that was implemented to ensure that it results in an optimal outcome for the patient.

Monitoring parameters to assess efficacy generally include improvement in or resolution of the signs, symptoms, and laboratory

abnormalities that were initially assessed. The monitoring parameters used to detect or prevent adverse reactions are determined by the most common and most serious events known to be associated with the therapeutic intervention. Potential adverse reactions should be precisely described along with the method of monitoring. For example, rather than stating “monitor for gastrointestinal (GI) complaints,” the recommendation may be to “question the patient about the presence of dyspepsia, diarrhea, or constipation.” The frequency, duration, and target endpoint for each monitoring parameter should be identified. The points at which changes in the plan may be warranted should be included. For example, in the case of a patient with type 2 diabetes mellitus (DM), one may recommend to “return to clinic (RTC) in 2 weeks to check blood glucose (BG) levels; recheck lipids in 4–6 weeks and recheck A1C in 3 months. If the goal A1C of <7% is not achieved with good adherence at 3 months, increase metformin from 500 mg by mouth twice daily to metformin 1000 mg by mouth twice daily. If the A1C goal is achieved, maintain metformin 500 mg by mouth twice daily and repeat A1C in 6 months.”

SUMMARY

A progress note constructed in the manner described identifies each DTP and states the clinician's findings, an assessment of the findings, the actual or proposed intervention for resolving the problem, and the parameters for follow-up and monitoring. Whether the note follows a strict SOAP format or not, it should provide a clear, logical, concise record of process, activity, and projected follow-up, clearly stating the medication therapy problems identified.

Based on recommendations from organizations such as the Institute of Medicine, Centers for Medicare & Medicaid Services, and researchers involved in the provision of quality of care, EHRs will continue to proliferate and change the way pharmacists and other healthcare providers document patient care encounters. Although the format of the documentation may not strictly follow the SOAP format, the common principles of documentation will remain.

SAMPLE CASE PRESENTATION

The following case presentation illustrates how such a system can be used in practice.

JS is a 71-year-old woman seen Monday morning in clinic for her first visit.

CHIEF COMPLAINT

“I get a little short of breath working around the house sometimes, and my feet have been bothering me recently.”

HISTORY OF PRESENT ILLNESS

JS states that she has mild heart failure and had a heart attack 4 years ago. She lives alone and has maintained a good level of activity and self-care over the years. She reports watching more television recently and feels as though she's not getting out and about as much as previously. She complains of some fatigue and shortness of breath while cleaning her house or when climbing stairs. She also complains of occasional pain and tingling in her feet, which she says has become bothersome over the past few months.

PAST MEDICAL HISTORY

JS has just moved to town to be near her son following the death of her husband. In addition to her heart failure (HF) and myocardial

infarction (MI) history, she has a history of atrial fibrillation and type 2 DM. She is maintained on metformin 500 mg PO BID, omeprazole 20 mg PO daily, digoxin 0.125 mg PO Q AM, warfarin 5 mg PO Q AM, enteric-coated (EC) aspirin 81 mg PO Q AM, furosemide 40 mg PO daily, and metoprolol XL 100 mg PO Q AM.

FAMILY HISTORY

Her husband died unexpectedly recently. She has one son alive and well living in the area and had one son who died by suicide 8 years ago.

SOCIAL HISTORY

JS denies illicit drugs and quit smoking 15 years ago. She has a 35 pack-year history of cigarette smoking. She drinks alcohol rarely on social occasions and denies excessive use. She is insured under her state's Medicare Advantage health plan, which includes drug coverage. She uses a pill box to organize her medications and reports missing her morning doses rarely and her evening doses no more than once weekly.

MEDICATIONS

Metformin 500 mg PO BID
Omeprazole 20 mg PO daily
Digoxin 0.125 mg PO Q AM
Warfarin 5 mg PO Q AM
EC aspirin 81 mg PO Q AM
Furosemide 40 mg PO Q AM
Metoprolol XL 100 mg PO Q AM

ALLERGIES

Penicillins (rash).

REVIEW OF SYSTEMS

General: Denies weight loss, fevers, or chills. Complains of occasional fatigue/SOB upon exertion.

HEENT: Last eye exam was less than 1 year ago; no hearing loss, tinnitus, mouth sores; sees dentist regularly; no voice change, sinus congestion.

Pulmonary: No cough, pneumonia, tuberculosis exposure, orthopnea, paroxysmal nocturnal dyspnea.

Cardiac: No known murmur, rheumatic fever, palpitations, chest pressure/pain.

GI: No dysphagia, odynophagia, nausea, vomiting, abdominal pain, diarrhea, constipation, melena, hematochezia, or change in stool caliber.

Genitourinary: No h/o STI; no urinary pain, burning, blood, or nocturia; no sexual dysfunction/dissatisfaction.

Hematologic: No bruising, bleeding problems.

Endocrine: No thyroid disease, hot/cold intolerance, polyuria/polydipsia.

Vascular: No leg pain with walking.

Neurologic: Pain/tingling in feet. Denies dizziness, weakness, balance, or gait problems.

Dermatologic: No rashes, skin lesions.

Psychiatric: No anxiety or depression; notes she had a difficult time adjusting to her husband's untimely death but now feels she is doing fine.

PHYSICAL EXAMINATION

General

The patient is a 71-year-old Caucasian woman whose appearance is consistent with her stated age. She appears well developed, well nourished, and in no acute distress.

Vital Signs

BP 169/88, HR 62 bpm and regular, RR 13/min, T 99°F; weight 184 lb, height 5'4".

Skin

Unremarkable.

HEENT

Slight arteriovenous (AV) nicking, otherwise unremarkable.

Neck/Lymph Nodes

Neck supple, thyroid normal with no mass, nodules, or tenderness; JVP 6 cm; normal carotid pulsations; no carotid bruits.

No cervical, supraclavicular, axillary, or inguinal lymphadenopathy.

Chest/Lungs

Slight crackles at the right and left bases; no rales, e-to-a changes, or tactile fremitus.

Breasts

Normal breasts without pain, swelling, discharge, or masses.

Cardiovascular

No murmurs or rubs. (+) S₃ gallop; PMI in the fifth intercostal space 3 cm to the left of the midclavicular line. (+) Hepatojugular reflux. Mild neck vein distention at 45°.

Abdomen

Soft, nontender, nondistended, bowel sounds normal. No hepatosplenomegaly.

Genital/Rectal

Unremarkable.

Musculoskeletal/Extremities

1–2+ pedal edema bilaterally. Ankle brachial index (ABI) 1.02 (negative). Strength 5/5.

Neurologic

Cranial nerves II–XII grossly intact bilaterally.

Semmes–Weinstein monofilament is unremarkable

Deep tendon reflexes brisk and 3/4 bilaterally.

Laboratory Values

Laboratory values are unremarkable with the following exceptions:

INR 3.5

FBG 198 mg/dL

A1C 9.5% = eAG 226 mg/dL

Serum creatinine 1.3 mg/dL

TC 183 mg/dL, LDL 128 mg/dL, HDL 38 mg/dL, TG 150 mg/dL

Digoxin level 1.0 ng/mL

Imaging

Chest X-ray demonstrates some diffuse patchiness at the bases. Enlarged cardiac silhouette.

Echo reveals no valvular abnormalities with an ejection fraction of 40%.

Electrocardiogram

Normal sinus rhythm. Changes are consistent with left ventricular hypertrophy.

Medical Assessment

1. Mild, class II–III HF with pedal edema and mild pulmonary congestion; taking digoxin, furosemide, and metoprolol.
2. Atrial fibrillation, currently rate-controlled on digoxin and metoprolol. Warfarin anticoagulation per guidelines above target (target INR 2–3).
3. Type 2 DM, not optimally controlled with metformin.
4. Peripheral neuropathy symptoms, currently untreated.
5. HTN not optimally managed with metoprolol.
6. Clinical ASCVD (s/p MI); taking aspirin and metoprolol; no statin therapy.
7. Moderate renal insufficiency stage 3: SCr 1.3, estimated ClCr 29 mL/min, glomerular filtration rate (GFR by MDRD)²⁸ 43 mL/min.
8. Obesity: BMI 31.6 kg/m².
9. Medication with no indication: Omeprazole.
10. Adverse medication effects associated with β -blocker use.
11. Inconsistent patient adherence with medication use.

PLAN

1. HF: Increase furosemide to 40 mg PO BID. Consult cardiology for evaluation of HF.
2. Type 2 DM: Continue metformin 500 mg PO BID. Initiate a GLP-1 receptor agonist for improved A1C control and the potential for weight loss. Provide education and review of injection technique for GLP-1 receptor agonist.
3. Peripheral neuropathy: Initiate gabapentin therapy at 100 mg PO Q HS.
4. Atrial fibrillation: Decrease warfarin dose per clinic algorithm. Continue digoxin and metoprolol.
5. Hypertension: Add an ACE inhibitor or ARB for BP reduction and renal protection.
6. Clinical ASCVD (s/p MI): Continue metoprolol and aspirin; add a high-intensity statin.
7. Consult Nephrology for evaluation of renal insufficiency.
8. Obesity: Counsel on lifestyle modifications for weight reduction.
9. Discontinue omeprazole.
10. Clinic appointment for follow-up in 2 weeks. Will reassess medication adherence at that time, and offer recommendations to enhance medication use.

CONSTRUCTION OF A SOAP NOTE WITH DRUG THERAPY PROBLEM DOCUMENTATION

Subjective

This 71-year-old woman recently moved to the area after the death of her husband. The patient complains of slight shortness of breath when walking up stairs and long distances as well as occasional pain and tingling in her feet. She has a history of atrial fibrillation, type 2 DM, mild–moderate HF, and s/p MI 4 years ago. She lives alone and maintains a good level of self-care but reports few outings and a lot of television watching at home. She reports that she takes metformin, omeprazole, digoxin, warfarin, aspirin, furosemide, and metoprolol. She states that she takes her medications as prescribed, missing morning doses rarely and evening doses no more than once weekly. She uses a pill box to organize her medications but has some difficulty describing the indication for each medication.

Objective

VS: BP 169/88, HR 62 and regular, RR 13, T 99.0°F; weight 184 lb, height 5'4"

Cardiac: S₃ gallop, PMI in the fifth intercostal space 3 cm to the left of the midclavicular line

Chest: Slight crackles at the right and left bases

Extremities: 1–2+ pedal edema bilaterally, ABI negative

HEENT: Slight AV nicking, otherwise unremarkable

Medications (per labels on vials):

Metformin 500 mg PO BID

Omeprazole 20 mg PO daily

Digoxin 0.125 mg PO Q AM

Warfarin 5 mg PO Q AM

EC aspirin 81 mg PO Q AM

Furosemide 40 mg PO Q AM

Metoprolol XL 100 mg PO Q AM

Labs:

INR 3.5

Fasting BG 198 mg/dL

A1C 9.5% (eAG 226 mg/dL)

Serum creatinine 1.3 mg/dL

TC 183 mg/dL, LDL 128 mg/dL, HDL 38 mg/dL, TG 150 mg/dL

Serum digoxin 1.0 ng/mL

Chest X-ray: Diffuse patchiness at the bases. Enlarged cardiac silhouette.

ECG: LVH

Assessment

1. Mild heart failure, class II, as suggested by pedal edema, DOE, symptoms on engaging in ordinary activities, cardiomegaly on chest X-ray, and diminished EF. Maintained with a β -blocker and digoxin (level within target range), not currently prescribed an ACE inhibitor.
2. Atrial fibrillation:
 - a. Rate control: Rate currently under control with metoprolol and digoxin. Digoxin level acceptable. No adjustment indicated.
 - b. Anticoagulation: INR above target range of 2.0–3.0, without clinical complications at this time. No cause could be

identified; although a change in diet associated with recent life events is possible, the patient provides no information to substantiate that idea. Decreased warfarin dose may be appropriate.

3. Type 2 DM, not well controlled with the current metformin dose. A1C above goal of <7%. Taking the maximum metformin dose for her current renal function. Not prescribed either an ACE inhibitor or an ARB for renal protective effects.
4. The patient experiencing symptoms of peripheral neuropathy: pain and tingling in her feet.
5. Hypertension, not optimally controlled on metoprolol, as suggested by increased BP, elevated serum creatinine, and AV nicking. Renal findings are suggestive of significant, sustained hypertension. Addition of an ACE inhibitor may improve control.
6. Clinical ASCVD (s/p MI): Taking low-dose aspirin and metoprolol; no statin therapy.
7. Possible moderate renal insufficiency as indicated by increased SCr/decreased GFR by MDRD. Renal dose adjustments evaluated. No changes necessary at this time. Addition of ACE inhibitor therapy may be beneficial to slow rate of GFR decline.
8. Obesity: Classified as obese with BMI 31.6 kg/m².
9. Medication without indication (omeprazole 20 mg): On further questioning, the patient recalls being started on it while hospitalized for MI 4 years ago. She was given a prescription upon discharge. She has no complaints related to GERD or PUD. No need for omeprazole can be identified.
10. Adverse medication effects: Although metoprolol may be considered appropriate for both the post-MI and HF indications and is a β_1 -selective β -blocker, its β_2 -blocking properties may contribute to worsening HF due to negative inotropic effects.
11. Nonoptimal adherence to medications; lack of knowledge about purpose of each medication.

Plan

1. Mild HF: Continue both the β -blocker metoprolol and digoxin, pending evaluation by the cardiology service to determine appropriateness. Suggest initiation of an ACE inhibitor: Lisinopril 10 mg daily titrating to 40 mg daily as tolerated. Increase furosemide to 40 mg PO BID because of persistent pedal edema and pulmonary congestion. No added dietary salt. Reassess medications at follow-up in 2 weeks.
2. Atrial fibrillation:
 - a. Rate control: Suggest continuing metoprolol and digoxin unless cardiology recommends otherwise. No adjustment indicated at this time.
 - b. Anticoagulation: INR is above target range of 2.0–3.0. Recommend warfarin 2.5 mg today and then resume 5 mg PO daily Monday–Saturday and 2.5 mg on Sunday (decrease in total weekly dose by 7.1%). Recheck INR in 2 weeks; adjust dose as needed to maintain INR between 2.0 and 3.0.
3. Type 2 DM:
 - a. Medications: Start lisinopril 10 mg daily as above per current ADA guidelines. Maintain metformin at 500 mg PO BID due to renal insufficiency. Initiate Victoza 0.6 mg SubQ once daily for 1 week, then increase to 1.2 mg once daily. Continue to follow serum creatinine and monitor BG readings. Educate patient on the proper injection technique for Victoza administration.

- b. Diet: Encourage three meals and bedtime snack, with no concentrated carbohydrate (CHO) choices. Limit CHO intake per meal to 60 g; snacks 15–20 g of CHO. No added salt. Check BG daily. Refer to dietitian for nutrition review.
4. Peripheral neuropathy: Start gabapentin 100 mg PO Q HS. If necessary, titrate dose over several weeks to 300 mg PO BID for better symptom control, as tolerated.
5. Hypertension: Present BP is $\geq 160/100$ mm Hg; goal is $<140/90$ mm Hg per ADA 2015 Standards of Medical Care in Diabetes. Start lisinopril 10 mg PO daily as recommended above. If repeated measurements confirm HTN diagnosis, titrate dose to maintain BP control (and improve HF symptoms); target dose 40 mg daily.
6. Clinical ASCVD (s/p MI): Recommend continuation of EC aspirin 81 mg PO Q AM. Suggest initiation of lisinopril 10 mg PO daily as noted above and a high-intensity statin (atorvastatin 40 mg PO daily). Continue metoprolol, if acceptable to cardiology.
7. Renal insufficiency: Repeat serum creatinine. No medication dosage adjustments are indicated currently. Begin low-dose ACE inhibitor (lisinopril 10 mg PO daily as above) for renal protective effects with diabetes to slow rate of GFR decline.
8. Obesity: Counsel on lifestyle modifications for weight reduction. Adding GLP-1 receptor agonist (Victoza as noted above) for potential for weight loss in addition to improved A1C control.
9. Medication without indication: Discontinue omeprazole 20 mg.
10. Adverse medication effects: As noted above, will await cardiology opinion on need for/appropriateness of β -blocker and digoxin to manage HF.
11. Assess and reinforce adherence/concordance with recommended therapy. Educate on purpose of each medication. Recommend use of an alarm or mobile device app to improve adherence.

Monitoring

1. Lab tests (orders entered):
 - a. Baseline electrolytes today (K, Na, Ca, and Mg levels in light of unopposed furosemide therapy of unknown duration and use of digoxin)
 - b. Serum creatinine today
 - c. INR at next clinic visit
2. The patient was instructed to monitor BG once daily and to bring information on RTC.

Follow-Up

1. RTC in 2 weeks to review lab results, recheck INR, and assess implementation of medication changes.
2. Consultations:
 - a. Cardiology consultation/education. Appointment made with Dr Welford's office.
 - b. Dietary consultation. Appointment made with Mary Ann Stamos, RD.
3. Prescribed medications after this visit:
 - ✓ Digoxin 0.125 mg PO Q AM for HF symptoms and rate control (maintain dose)
 - ✓ Furosemide 40 mg PO BID for HF (dose increase)
 - ✓ Warfarin 5 mg PO Q AM Monday–Saturday, 2.5 mg on Sunday for s/p MI and CVA prevention (dose decrease)

- ✓ EC aspirin 81 mg PO daily for secondary cardiovascular prevention (maintain dose)
- ✓ Metoprolol XL 100 mg PO Q AM for s/p MI and rate control (maintain dose)
- ✓ Lisinopril 10 mg PO daily for CHF, HTN, and type 2 DM (new medication)
- ✓ Atorvastatin 40 mg PO daily for secondary ASCVD prevention (new medication)
- ✓ Metformin 500 mg PO BID for type 2 DM (maintain dose)
- ✓ Victoza 0.6 mg SubQ daily for 1 week, then increase to 1.2 mg SubQ daily (new medication)
- ✓ Gabapentin 100 mg PO Q HS for peripheral neuropathy, with a 2-week titration to 300 mg PO BID (new medication)
- ✓ D/C omeprazole

REFERENCES

1. McNally ME. The importance of detailed documentation in ICD-10. *Bull Am Coll Surg*. 2015;100(8):63–64.
2. Patterson ES, Lowry SZ, Ramaiah M, et al. Improving clinical workflow in ambulatory care: implemented recommendations in an innovation prototype for the Veteran's Health Administration. *EGEMS (Washington, DC)*. 2015;3(2):1149.
3. Institute of Medicine. *Crossing the Quality Chasm: A New Health System for the 21st Century*. Washington, DC: National Academy Press; 2001.
4. Bates DW, Gawande AA. Improving safety with information technology. *N Engl J Med*. 2003;348:2526–2534.
5. Wright A, McCoy AB, Hickman TT, et al. Problem list completeness in electronic health records: a multi-site study and assessment of success factors. *Int J Med Inform*. 2015;84(10):784–790.
6. Jamoom E, Beatty P, Bercovitz A, et al. *Physician Adoption of Electronic Health Record Systems: United States, 2011*. NCHS Data Brief, No. 98. Hyattsville, MD: National Center for Health Statistics, 2012.
7. American Nurses Association. 2010. *Principles of Nursing Documentation: Guidance for Registered Nurses*. Available at: <https://www.nursingworld.org/~4af4f2/globalassets/docs/ana/ethics/principles-of-nursing-documentation.pdf>. Accessed October 6, 2018.
8. Poon EG, Wright A, Simon SR, et al. Relationship between use of electronic health record features and health care quality: results of a statewide survey. *Med Care*. 2010;48:203–209.
9. *Evaluation and Management Services Guide*. Washington, DC: Centers for Medicare & Medicaid Services; August 2017. Available at: www.cms.gov/Outreach-and-Education/Medicare-Learning-Network-MLN/MLNProducts/Downloads/eval-mgmt-serv-guide-ICN006764.pdf. Accessed October 6, 2018.
10. Campanella P, Lovato E, Marone C, et al. The impact of electronic health records on healthcare quality: a systematic review and meta-analysis. *Eur J Public Health*. 2016;26(1):60–64.
11. American Pharmacists Association. 2007. *Medication Therapy Management Services: Documenting Pharmacy-Based Patient Care Services*. Available at: https://www.pharmacist.com/sites/default/files/files/mtm_documenting_pc_services.pdf. Accessed October 6, 2018.
12. Weed LL. Medical records that guide and teach. *N Engl J Med*. 1968;278:593–600, 652–657.
13. Adams AJ, Clark DR, DeLander GE, et al. Report of the AACP task force on patient-centered medical homes and accountable care organizations. *Am J Pharm Educ*. 2013;77(7):Article 142.
14. van Lint JA, Sorge LA, Sorensen TD. Access to patients' health records for drug therapy problem determination by pharmacists. *J Am Pharm Assoc*. 2015;55:278–281.
15. American College of Clinical Pharmacy. *Standards of practice for clinical pharmacists*. *Pharmacotherapy*. 2014;34(8):792–795.
16. Bennett MS, Kliethermes MA, Derr S, Irwin A. APHA academics reflect on the pharmacists' patient care process of the joint commission of pharmacy practitioners. *J Am Pharm Assoc*. 2015;55:230–236.

17. Joint Commission of Pharmacy Practitioners. 2014. Pharmacists' patient care process. Available at: <http://www.pharmacist.com/sites/default/files/files/PatientCareProcess.pdf>. Accessed October 6, 2018.
18. American College of Clinical Pharmacy. 2018. The Patient Care Process for Delivering Comprehensive Medication Management (CMM): Optimizing Medication Use in Patient-Centered, Team-Based Care Settings. CMM in Primary Care Research Team. Available at: http://www.accp.com/cmm_care_process. Accessed October 6, 2018.
19. Donnelly WJ. The language of medical case histories. *Ann Intern Med*. 1997;127:1045–1048.
20. Voytovich AE. Reduction of medical verbiage. *Ann Intern Med*. 1999;131:146–147.
21. Bluml BM. Definition of medication therapy management: development of professionwide consensus. *J Am Pharm Assoc*. 2005;45:566–572.
22. Center for Medicare and Medicaid Services. 2015. Medication Therapy Management (MTM) Fact Sheet. Available at: <https://www.cms.gov/medicare/prescription-drug-coverage/prescriptiondrugcovcontra/mtm.html>. Accessed October 6, 2018.
23. American Pharmacists Association, National Association of Chain Drug Stores Foundation. Medication therapy management in pharmacy practice: core elements of an MTM service model (version 2.0). *J Am Pharm Assoc*. 2008;48(3):341–353.
24. American Society of Health-System Pharmacists. ASHP guidelines on documenting pharmaceutical care in patient medical records. *Am J Health Syst Pharm*. 2003;60:705–707.
25. Canaday BR, Yarborough PC. Documenting pharmaceutical care: creating a standard. *Ann Pharmacother*. 1994;28(11):1292–1296.
26. Cipolle RJ, Strand LM, Morley PC. *Pharmaceutical Care Practice: The Clinician's Guide*. 3rd ed. New York, NY: McGraw-Hill, 2012.
27. Pharmacy Quality Alliance. 2017. Medication Therapy Problem Categories Framework for PQA Measures document for a framework of MRPs and detailed description of categories and rationale. Available at: https://www.pqaalliance.org/index.php?option=com_content&view=article&id=109:medication-therapy-management&catid=32:measures. Accessed October 6, 2018.
28. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med*. 1999;130:461–470.

This page intentionally left blank

6

PEDIATRICS

The Case of Baby's Busted Belly Level III

Franklin R. Huggins, PharmD, BCPPS, BCCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Use age-appropriate assessment parameters to recognize septic shock in a pediatric patient.
- Design an evidence-based pharmacotherapy plan for the child in septic shock, including medications, dosing, and monitoring.
- Determine the pediatric patient's fluid and electrolyte requirements and make therapeutically sound recommendations for repletion.
- Use appropriate metrics to monitor the progress of the sick child and adjust therapy as indicated.
- Employ specific techniques to ensure that medications are deployed safely for pediatric patients.
- Recommend age-appropriate vaccinations for children.

PATIENT PRESENTATION

■ Chief Complaint

Mother reports vomiting, poor feeding, and fever in her 15-month-old adopted son.

■ HPI

David Williams is a 15-month-old boy who weighs 5.6 kg. He presents today with his foster mother, who reports poor oral intake, vomiting, and fever for 1 day. The patient underwent reversal of a colostomy and placement of a gastrostomy tube 5 days ago and was discharged home with foster mother 2 days ago. Yesterday he had four episodes of vomiting and was unable to retain any of the G-tube feedings. The foster mother took him to the PCP where he was found to be lethargic, ill appearing, and febrile, which prompted his admission directly to the pediatric intensive care unit.

■ PMH

Vaginal delivery at 35 weeks' gestation

No prenatal care

Intrauterine growth restriction

Birth hypoxia

Imperforate anus requiring colostomy on second day of life

Single kidney

Bilateral undescended testes

Neonatal abstinence syndrome requiring a 12-day morphine taper

Colostomy reversal and gastrostomy tube placement 5 days PTA

Failure to thrive

Immunizations: hepatitis B immune globulin and hepatitis B vaccine administered at birth; DTaP, IPV, HepB, Hib, PCV13 administered 2 months PTA

■ FH

Unavailable

■ SH

The patient was referred to Child Protective Services at birth because of lack of prenatal care and prenatal drug exposure. He was lost to follow-up by them until 2 months ago when he presented to the PCP for the first time since birth with severe failure to thrive (weight and weight-for-height below 1% of expected). He was transferred to the custody of the current foster family at that time who, by report of the PCP, are appropriately attentive and have addressed the patient's healthcare needs appropriately. Foster mother at bedside and appropriately concerned.

■ Current Meds

Omeprazole suspension 10 mg GT daily

Pediatric multivitamin with iron 1 mL GT daily

■ All

NKDA

■ ROS (as reported by foster mother)

Constitutional

Foster mother affirms that the child, although normally nonverbal, is more lethargic and unresponsive than normal. The patient has not walked but rolls himself.

HEENT

Oral secretions well controlled. Denies history of rhinitis, allergies, or ear infections. The patient ordinarily tracks visually and responds to verbal cues.

Respiratory

Denies SOB, coughing

Cardiovascular

Echocardiogram and ECG normal at birth

Gastrointestinal

G-tube feeding dependent. Prior to G-tube placement oral feeds attempted with very limited success, usually less than an ounce per feeding, leading to failure to thrive. The patient tolerated continuous G-tube feeds of 30 kcal/oz formula at 25 mL/hr in the hospital on the day prior to discharge but vomited repeatedly at home leading to current admission. Stooled during previous admission but not at home.

Genitourinary

No wet diapers since yesterday. Follows with nephrology for single kidney. Evaluated by pediatric endocrinology for undescended testes and small penis who proposed a trial of β -hCG. If fails, will require orchiopexy.

■ Physical Examination

Gen

Ill appearing, mottled child who is floppy, lethargic, and barely responsive to painful stimuli

VS

BP 114/66, HR 148, RR 36, current temperature 40.2°C, O₂ saturation 95%, height 69 cm, weight 5.6 kg

Skin

Cool, pale, mottled, and dry

HEENT

Eyes sunken, PERRLA, tympanic membranes normal, mucous membranes dry

Neck/Lymph Nodes

Supple, nontender, no masses, no lymphadenopathy, no bruit, no JVD

Chest

Tachypneic, clear to auscultation and percussion

CV

Tachycardic, monitor shows NSR, no murmur, gallop or edema, no peripheral pulses, central pulses weak, capillary refill 6 seconds

Abd

Soft, nondistended, no masses, (+) rebound tenderness globally, no bowel sounds appreciated. G-tube in place with no erythema or drainage. Surgical scar in LLQ.

Genit/Rect

Tanner stage I, bilateral undescended testes

Ext

Flaccid, pale, cold extremities

Neuro

Lethargic, responds to painful stimuli, cranial nerves intact, reflexes intact

Laboratory Values

Na 135 mEq/L	Total protein 5.9 g/dL	WBC $1.6 \times 10^3/\text{mm}^3$
K 4.7 mEq/L	Albumin 2.1 g/dL	Neutrophils 8%
Cl 101 mEq/L	Total bilirubin 0.7 mg/dL	Immature neutrophils 36%
CO ₂ 20 mEq/L	Alk phos 365 U/L	Lymphocytes 51%
BUN 39 mg/dL	ALT 192 U/L	Monocytes 5%
SCr 0.3 mg/dL	AST 521 U/L	Hgb 10.5 g/dL
Glu 53 mg/dL		Hct 30%
Calcium		Plt $62 \times 10^3/\text{mm}^3$
7.6 mg/dL		

Imaging

- Radiograph abdomen two view: Nonspecific gaseous distention of stomach and loops of bowel in the lower abdomen and right upper quadrant. No discernible evidence of free air. No acute osseous abnormalities. G-tube.
- Ultrasound abdomen limited: Focused ultrasound of the left hemiabdomen identifies complicated extraluminal fluid in the upper abdomen, particularly the left upper quadrant. It is seen adjacent to the spleen and likely insinuating itself around the stomach. Internal debris and septations are noted. Stool-filled portions of the colon are seen in the left hemiabdomen. While there is no definite fluid collection or sonographic abnormality in the right hemiabdomen, the patient was very tender in the right hemiabdomen during real-time imaging.

Assessment

Critically ill child with sepsis and septic shock secondary to presumptive peritonitis, failure to thrive secondary to malnutrition, and underimmunization.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of septic shock?
- What additional information is needed to fully assess this patient?

Assess the Information

- Assess the severity of septic shock based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- How does the evidence supporting a diagnosis of septic shock in this patient differ from an adult patient?

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible therapeutic alternatives are available for treating pediatric septic shock?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.
- What pediatric-specific medication practices should be applied in this case to prevent adverse outcomes of medication therapy?

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects for the regimen you recommended?
- Develop a plan for follow-up that includes appropriate timeframes to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

After initial stabilization, the patient was taken to the operating room for an exploratory laparotomy that revealed failure of the colostomy repair from 5 days ago. The abdomen was found to be filled with fluid, stool, and pus. The abdomen was extensively irrigated and cultures sent. The colostomy was recreated, and the patient returned to the ICU with the abdomen open to facilitate further surgical intervention.

Current medications:

Famotidine 2.8 mg IV Q 12 H (1 mg/kg/day)
 Piperacillin-tazobactam 560 mg IV Q 8 H (300 mg/kg/day)
 Acetaminophen 80 mg GT Q 6 H PRN fever $>38^\circ\text{C}$ or pain score 4–6 (14 mg/kg/dose)
 Morphine 0.6 mg IV Q 4 H PRN pain score 7–10 (0.1 mg/kg/dose)
 TPN 10% dextrose + 2 g/kg/day amino acid IV
 Lipid emulsion 1 g/kg/day IV

On hospital day 2, the following laboratory results were obtained:

Na 141 mEq/L	Total protein 5.1 g/dL	WBC $1.4 \times 10^3/\text{mm}^3$
K 3.1 mEq/L	Albumin 1.7 g/dL	Neutrophils 17%
Cl 108 mEq/L	Total bilirubin	Immature neutrophils 23%
CO ₂ 21 mEq/L	0.8 mg/dL	Lymphocytes 53%
BUN 31 mg/dL	Alk phos 304 U/L	Monocytes 7%
SCr 0.6 mg/dL	ALT 239 U/L	Hgb 7.4 g/dL
Glu 140 mg/dL	AST 600 U/L	Hct 22%
Calcium 8.0 mg/dL		Plt $37 \times 10^3/\text{mm}^3$

Anaerobic Culture—Final

Source: Peritoneal cavity
 Gram stain: many WBC, many gram-negative rods, few gram-positive rods
 Light growth *Klebsiella pneumoniae*
 Light growth *Proteus mirabilis*
 Light growth *Bacteroides fragilis*

Antimicrobial Susceptibility (mcg/mL)

	Klebsiella Pneumoniae		Proteus Mirabilis	
Amikacin	S	≤16	S	≤16
Ampicillin	R	>16	S	≤8
Ampicillin/Sulbactam	S	8/4	S	N/A
Aztreonam	S	≤4	S	≤4
Cefazolin	S	≤4	S	4
Cefepime	S	≤2	S	≤2
Cefotaxime	S	≤2	S	≤2
Ceftazidime	S	≤1	S	≤1
Ceftriaxone	S	≤1	S	≤1
Cefuroxime	S	≤4	S	≤4
Ciprofloxacin	S	≤1	S	≤1
Ertapenem	S	≤0.5	S	≤0.5
Gentamicin	S	≤1	S	≤1
Imipenem	S	≤0.5	N/A	N/A
Levofloxacin	S	≤0.25	S	≤0.25
Meropenem	S	≤1	S	≤1
Piperacillin/Tazobactam	S	≤4	S	≤4
Tetracycline	S	≤4	R	>8
Tigecycline	S	≤2	N/A	N/A
Tobramycin	S	≤1	S	≤1
Trimethoprim/Sulfa	S	≤2/38	R	>2/38

FOLLOW-UP QUESTIONS

1. What is the likely cause of the elevated liver enzymes, increasing creatinine, and cytopenia in this patient?
2. Now that the patient is fully fluid resuscitated and hemodynamically stable, calculate the appropriate maintenance fluid rate.
3. What changes should be made to the patient's medication therapy based on the most recent results?

SELF-STUDY ASSIGNMENTS

1. Describe the challenges involved in managing parenteral nutrition in this patient.
2. Write an evidence-based paper outlining the role of corticosteroid therapy in pediatric septic shock.

CLINICAL PEARL

Children remain normotensive until very late in shock making blood pressure an unreliable indicator of perfusion status. Clinicians should carefully evaluate children for other signs of shock such as tachycardia,

decreased or weak pulses, altered mental status, oliguria, pale mottled skin, and slow capillary refill. If clinical signs of poor perfusion are present, appropriate fluid resuscitation and inotropic therapy should be initiated immediately. Hypotension in a septic child is a sign of impending cardiovascular collapse and must be addressed emergently.

REFERENCES

1. Davis AL, Carcillo JA, Aneja RK, et al. American College of Critical Care Medicine Clinical Practice Parameters for Hemodynamic Support of Pediatric and Neonatal Septic Shock. *Crit Care Med* 2017;45(6):1061–1093.
2. Sterling SA, Miller WR, Pryor J, Puskarich MA, Jones AE. The impact of timing of antibiotics on outcomes in severe sepsis and septic shock: a systematic review and meta-analysis. *Crit Care Med* 2015;43(9):1907–1915.
3. Solomkin JS, Mazuski JE, Bradley JS, et al. Diagnosis and management of complicated intra-abdominal infection in adults and children: guidelines by the Surgical Infection Society and the Infectious Diseases Society of America. *Clin Infect Dis* 2010;50(2):133–164.
4. American Academy of Pediatrics. Tables of Antibacterial Drug Doses. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Elk Grove Village, IL: American Academy of Pediatrics 2018:914–932.
5. Ventura AM, Shieh HH, Bouso A, et al. Double-blind prospective randomized controlled trial of dopamine versus epinephrine as first-line vasoactive drugs in pediatric septic shock. *Crit Care Med* 2015;43(11):2292–2302.
6. Centers for Disease Control and Prevention. Recommended immunization schedule for children and adolescents aged 18 years or younger, United States, 2018. Available at: <https://www.cdc.gov/vaccines/schedules/downloads/child/0-18yrs-child-combined-schedule.pdf>. Accessed November 29, 2018.
7. Levine SR, Cohen MR, Blanchard NR, et al. Guidelines for preventing medication errors in pediatrics. *J Pediatr Pharmacol Ther* 2001;6:426–442.
8. Meyers RS. Pediatric fluid and electrolyte therapy. *J Pediatr Pharmacol Ther* 2009;14(4):204–211.
9. Schwartz GJ, Work DF. Measurement and estimation of GFR in children and adolescents. *Clin J Am Soc Nephrol* 2009;4(11):1832–1843.
10. Aronoff GR, Bennett WM, Berns JS, et al. *Drug Prescribing in Renal Failure*. 5th ed. Philadelphia, PA: American College of Physicians; 2007.

7

GERIATRICS

Falling Frannie Level II

David P. Elliott, PharmD, FASCP, FCCP, AGSF, BCGP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify medications an older adult is taking that may not be suitable for that person and determine if a change in therapy should be considered.
- Recognize common geriatric syndromes, including falls, urinary incontinence, cognitive impairment, and frailty and identify medications that may precipitate or worsen these conditions.

- Evaluate a patient's response to therapy for osteoporosis as well as the benefits and risks of continuing therapy.
- Evaluate a patient's medication use system and recommend changes for reasons related to medication regimen effectiveness, safety, adherence, and caregiver stress or burden.
- Describe the screening, assessment, and prevention of falls in older adults.
- Recommend changes in pharmacotherapy for an older adult with multiple chronic conditions based on person-centered considerations such as patient preferences, remaining life expectancy, applicability of published evidence, and treatment complexity and feasibility.

PATIENT PRESENTATION

■ Chief Complaint

"My mother has been having dizzy spells and wets her underwear almost every day."

■ HPI

Mrs Fran Jones was referred by her PCP for a pharmacotherapy consult and adverse drug event review. Mrs Jones is an 87-year-old woman who presents with her daughter, who reports that her mother often complains of feeling dizzy and wets her underwear almost daily. The daughter reports that Mrs Jones fell last night after getting out of bed to use the bathroom, and Mrs Jones states that her hip hurts where she fell on it. The daughter reports that Mrs Jones often seems to be "very blue" and has crying spells when she discusses her husband who she says passed away recently.

■ PMH

Osteoporosis, diagnosed 7 years ago
Nonvalvular atrial fibrillation, no h/o VTE
Allergic rhinitis
Major neurocognitive disorder due to Alzheimer disease, diagnosed 2 years ago

■ PSH

Cesarean section

■ FH

Noncontributory

■ SH

Mrs Jones' daughter reports administering *Ginkgo biloba* to help with her mother's memory. The daughter also says that her mother has been requesting Tylenol frequently since her fall and suspects that her mother has been taking additional doses when the daughter is away from the home. Mrs Jones does not remember the other medications she is taking and says that her daughter helps her. Mrs Jones denies using any tobacco or alcohol. She moved in with her daughter 6 months ago after the death of her husband, and her daughter assists the patient with her daily needs. The patient's Medical Power of Attorney (MPOA) names her daughter as the party authorized to participate in medical decisions and speak on the patient's behalf when necessary. Her daughter works fulltime outside the home so Mrs Jones is alone in the house between about 8 AM and 5:30 PM each day. Mrs Jones is very concerned about paying for medications although her daughter says that the costs are manageable for them.

■ Meds

Warfarin 2 mg Mon-Wed-Fri-Sun and 4 mg Tue-Thu-Sat
Alendronate 70 mg PO once weekly for the last 7 years
Diphenhydramine 25 mg PO TID PRN allergy symptoms
Acetaminophen OTC Extra Strength 1-2 PO PRN pain
Metoprolol succinate 50 mg PO every morning
Donepezil 5 mg PO every evening started 2 years ago
Multiple vitamin every morning
Ginkgo biloba PO every morning started a few weeks ago

■ All

Donepezil: Developed nausea and diarrhea with donepezil 10 mg daily. Patient's family declines further attempts at dose increases or adding other drugs to enhance cognitive function.

■ ROS

Daughter reports that her mother needs to change her underwear at least once daily because they are wet with urine. Patient complains of hip pain where she fell as well as a runny nose from allergies; denies heartburn, chest pain, or shortness of breath.

■ Physical Examination

Gen

WDWN Caucasian woman who appears her stated age; NAD

VS

BP 118/72 mm Hg sitting, 100/60 mm Hg standing; HR 76 bpm (irregularly irregular), RR 18/min, T 98.4°F (36.8°C), Ht 5'4" (163 cm), Wt 55 kg, G3P3

HEENT

NCAT; PERRLA, EOMI, fundi benign; TMs intact; mildly inflamed nasal mucosa, watery nasal discharge consistent with allergic rhinitis

Neck

Neck supple without thyromegaly or lymphadenopathy

Lungs

Lung fields CTA bilaterally

Heart

Rhythm is irregularly irregular; no murmurs or bruits.

Abd

Soft, NT/ND; no masses, bruits, or organomegaly; normal BS

Genit/Rect

Deferred

Ext

No CCE, normal ROM

Neuro

Motor, sensory, CNs, cerebellar, and gait normal. MoCA (Montreal Cognitive Assessment. <https://www.mocatest.org/>) score 17/30 (normal ≥ 26), compared with a score of 17/30 and 19/30 last year and at the initial diagnosis, respectively. Disoriented to month, date, and day of week. Good registration but impaired attention and very poor short-term memory. Abnormal clock drawing. Able to recall

only one of three items after 5 minutes. Able to follow commands. Displayed irritability during administration of the MoCA.

■ Labs

Na 139 mEq/L	Hgb 13.5 g/dL	T. bili 0.9 mg/dL	Ca 9.7 mg/dL
K 3.7 mEq/L	Hct 39.0%	D. bili 0.3 mg/dL	Phos 4.5 mg/dL
Cl 108 mEq/L	AST 25 IU/L	T. prot 7.5 g/dL	TSH 3.8 mIU/L
CO ₂ 25.5 mEq/L	ALT 24 IU/L	Alb 4.5 g/dL	Free T4 1.2 ng/dL
BUN 16 mg/dL	Alk phos	Chol 212 mg/dL	Uric acid
SCr 1.1 mg/dL	81 IU/L	INR 3.1	6.8 mg/dL
Glu 78 mg/dL	GGT 22 IU/L	A1C 5.8%	25-OH vitamin D
	LDH 85 IU/L		21 ng/mL

■ Radiology

CT scan (head, 2 years ago): Mild to moderate generalized cerebral atrophy.

DXA scan results (last year): T scores in the spine and hip were −1.8 and −2.2, respectively.

■ ECG

Atrial fibrillation.

■ Assessment

1. Falls, secondary to multiple factors including medications
2. Urinary incontinence
3. Atrial fibrillation, rate controlled
4. Allergic rhinitis
5. Osteopenia

QUESTIONS

Collect Information

- 1.a. What additional information from the patient's history is needed to determine whether drug therapy should be considered for urinary incontinence?
- 1.b. What additional information is needed to assess whether the patient's medications are being administered in a safe and consistent manner?
- 1.c. What additional details about the patient's medication list are needed to evaluate current therapy?
- 1.d. What additional information would be helpful to evaluate the patient's drug therapy with respect to her fall history and treatment for atrial fibrillation and osteoporosis?

Assess the Information

- 2.a. Which one of the patient's chronic medical problems has the greatest impact on her independent function and life expectancy?
- 2.b. Which of the patient's medications is/are included in the Beers criteria as being potentially inappropriate based on her age or underlying conditions?
- 2.c. What are the patient's known risk factors for falls?
- 2.d. What are potential reasons why the patient is experiencing episodes of incontinence?
- 2.e. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of treatment for this patient?
- 3.b. What nondrug therapies should be implemented to prevent falls, fractures, and episodes of urinary incontinence?
- 3.c. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What strategies should be implemented with the patient and caregiver to reduce the medication-related burden, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be monitored after initiating this regimen and throughout the treatment course?
- 5.b. Develop a plan for follow-up that includes appropriate time-frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Review the 2019 AGS Beers criteria for potentially inappropriate use of medications in older adults, and consider your first-line recommendations for optimal treatment of depression, insomnia, and diabetes in the older adult.
2. Outline the changes that you would make to the pharmacotherapeutic regimen for this patient if she had each of the following comorbidities or characteristics:
 - Creatinine clearance <30 mL/min
 - Severe Alzheimer disease
3. For atrial fibrillation in this patient:
 - Based on the CHA₂DS₂-VASc, what is Mrs Jones' risk of stroke due to atrial fibrillation?
 - What tools may be used to assess the patient's risk of bleeding from anticoagulation?
 - What therapy should be offered to reduce the patient's risk of stroke? Provide a rationale for the decision. How should the different options be discussed with the patient and her daughter?

CLINICAL PEARL

When managing drug therapy in older persons, make as few changes to the regimen at one time as possible due to the unpredictability of outcomes in older adults with multiple chronic conditions.

REFERENCES

1. American Geriatrics Society Expert Panel on the Care of Older Adults With Multimorbidity. Patient-centered care for older adults with multiple chronic conditions: a stepwise approach from the American Geriatrics Society: American Geriatrics Society Expert Panel on the Care of Older Adults with Multimorbidity. *J Am Geriatr Soc* 2012; 60(10):1957–1968.

2. The 2019 American Geriatrics Society Beers Criteria® Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. *J Am Geriatr Soc* January 2019. doi:10.1111/jgs.15767.
3. Make STEADI part of your medical practice. STEADI (Stopping Elderly Accidents, Deaths & Injuries)—Older Adult Fall Prevention; CDC Injury Center Available at: <https://www.cdc.gov/steady/index.html>. Accessed November 17, 2018.
4. Carlson C, Merel SE, Yukawa M. Geriatric syndromes and geriatric assessment for the generalist. *Med Clin North Am* 2015;99(2):263–279.
5. Qaseem A, Forciea MA, McLean RM, Denberg TD; Clinical Guidelines Committee of the American College of Physicians. Treatment of low bone density or osteoporosis to prevent fractures in men and women: a clinical practice guideline update from the American College of Physicians. *Ann Intern Med* 2017;166(11):818–839.
6. Burns RB, Rosen H, Berry S, Smetana GW. How would you manage this patient with osteoporosis? Grand rounds discussion from Beth Israel Deaconess Medical Center. *Ann Intern Med* 2018;168(11):801–808.
7. Ashburner JM, Go AS, Chang Y, et al. Influence of competing risks on estimating the expected benefit of warfarin in individuals with atrial fibrillation not currently taking anticoagulants: the Anticoagulation and Risk Factors in Atrial Fibrillation Study. *J Am Geriatr Soc* 2017;65(1):35–41.
8. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation: CHEST Guideline and Expert Panel Report. *Chest* 2018;154(5):1121–1201.
9. Drug Interactions: Ginkgo Biloba–Warfarin. Micromedex Solutions. Truven Health Analytics, Inc., Ann Arbor, MI. Available at: <http://www.micromedexsolutions.com>. Accessed December 11, 2018.
10. Centers for Disease Control and Prevention. Adult Immunization Schedules and Tools for Providers. Available at: <https://www.cdc.gov/vaccines/schedules/hcp/adult.html>. Published April 24, 2018. Accessed November 21, 2018.
11. Fazio S, Pace D, Maslow K, Zimmerman S, Kallmyer B. Alzheimer's Association Dementia Care Practice Recommendations. *Gerontologist* 2018;58(Suppl 1):S1–S9.

8

PALLIATIVE CARE

Helpful Hospice Level III

Jennifer L. Swank, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Define the goals for pain management in a patient with chronic malignant pain with hospice services.
- Define a pharmacotherapeutic pain management plan.
- Differentiate between palliative care and hospice care.
- Select or recommend medication options for managing nausea in a hospice setting.
- Define the roles of continued nutritional support and antibiotic therapy in a hospice setting.

PATIENT PRESENTATION

■ Chief Complaint

"I have been having fevers up to 102°F and chills for two days. I have also noticed that my skin is orange."

■ HPI

Jamie Park is a 48-year-old woman with a history of metastatic gastric adenocarcinoma originally diagnosed 3 years ago. At that time, she had a subtotal gastrectomy with 16 out of 16 positive lymph nodes, HER-2–negative disease. She received adjuvant chemoradiation with 6 months of 5-fluorouracil. Two years ago, she developed gastric outlet obstruction and underwent laparotomy with extensive lysis of adhesions and revision of the gastrojejunostomy. She had no evidence of malignancy after this surgery. Three months later, she presented with symptoms of obstruction and underwent a sigmoid colectomy with pathology, revealing metastatic gastric adenocarcinoma, mismatch repair deficient, and PDL-1 <1. She was then started on chemotherapy with fluoropyrimidine and cisplatin × 6 cycles. Her chemotherapy course was complicated by neutropenia requiring significant dose reduction. After completing six cycles, she had worsening small bowel obstruction and underwent surgery, where recurrent metastases to the small intestine were found. The metastases were resected, but several other malignant peritoneal nodules were seen during surgery. Four months after the surgery, she underwent colonoscopy due to further obstruction at the level of the colon. The procedure was complicated by cecal dilatation, requiring an urgent percutaneous cecostomy. A week later, she underwent a repeat exploratory laparotomy with jejunojunctional bypass and ileosigmoid bypass. After the last surgery, the patient did not recover any intestinal function and was started on chronic TPN therapy. Four months ago, the patient underwent elective percutaneous biliary drain placement for biliary obstruction due to tumor. She was recently enrolled in supportive hospice services but continues on TPN for treatment of chronic small bowel obstruction.

Mrs Park presents to her primary oncologist office with a 2-day history of fevers and chills, abdominal pain, and recurrent jaundice. She is directly admitted from the oncologist clinics to the hospital. She had been using Tylenol suppositories for the fevers at home without relief. Her abdominal pain has worsened over the past 2 days, and she currently rates the pain as 8 out of 10. This pain is not relieved by the use of as-needed oxycodone liquid.

■ PMH

Cholangitis
Gastric outlet obstruction and small bowel obstruction
Subtotal gastrectomy 5 years ago
Sigmoid colectomy 2 years ago

■ FH

Mother—Living, with cervical cancer
Maternal aunt—Deceased from laryngeal cancer
Maternal uncle—Deceased from liver cancer

■ SH

Mrs Park is from Korea and has lived in the United States for 10 years. She is married and has two children. She denies use of alcohol or tobacco.

■ Meds

Total parental nutrition
Fentanyl 200-mcg patch, change every 72 hours

Oxycodone concentrated liquid 20 mg/mL, 1 mL PO every 3 hours PRN pain
 Ondansetron 8 mg ODT, one tablet PO every 8 hours PRN nausea or vomiting
 Acetaminophen suppository 650 mg, one rectally every 6 hours PRN fever

■ All

NKDA

■ ROS

Ten organ systems were reviewed. The patient reports fever, chills, nausea, vomiting, headache, and abdominal pain rated 8 out of 10. She denies chest pain, sore throat, cough, increased urinary frequency, rash, hematuria, hemoptysis, hematemesis, or black stool.

■ Physical Examination

Gen

The patient is a 48-year-old woman in acute distress holding her abdomen.

VS

BP 77/50, P 90, RR 16, T 100.9°F (38.3°C); Wt 101 lb (45.8 kg), Ht 5'2" (157.5 cm); pain 8/10 sharp, and stabbing in nature

Skin

Warm; dry; jaundice is appreciated.

HEENT

PERRLA; EOMI; sclerae jaundiced, TMs intact; moist mucous membranes

Neck

No JVD; full range of motion; no masses

Resp

CTA; no crackles, rhonchi, or wheezes

CV

Normal S₁, S₂; RRR; no murmurs

Abd

Soft and distended; (+) BS; moderate RUQ pain with deep palpation and mild guarding; biliary drain is in place and noted to be draining appropriately but with a foul-smelling, greenish liquid.

Genit/Rect

Deferred

MS/Ext

Negative lower extremity edema; palpable pedal and radial pulsations

Neuro

CN II–XII intact, A&O × 3; no sensory or focal deficits apparent

■ Labs

Na 147 mEq/L	WBC $27.71 \times 10^3/\text{mm}^3$	T. Prot 8 g/dL
K 4.5 mEq/L	Neutros 65%	Alb 2.4 g/dL
Cl 115 mEq/L	Bands 12%	T. bili 13.5 mg/dL
CO ₂ 19 mEq/L	Lymphs 22%	D. bili 11.2 mg/dL
BUN 50 mg/dL	Eos 0%	AST 402 IU/L
SCr 1.7 mg/dL	Monos 1%	ALT 400 IU/L
Glu 101 mg/dL	Hgb 10 g/dL	Alk phos 321 IU/L
Ca 8.8 mg/dL	Hct 31.1%	Cortisol 39.8 mcg/dL
Phos 3.9 mg/dL	Plt $158 \times 10^3/\text{mm}^3$	Lactic acid 0.7 mmol/L
Mg 3.0 mg/dL		

■ Chest X-Ray

Mild increased interstitial lung markings; bilateral nonspecific changes that can be seen with pulmonary edema; no consolidation to suggest pneumonia

■ RUQ Ultrasound

Sonographically abnormal appearance of the gallbladder, which is ill defined on this examination; no intrahepatic or extrahepatic biliary ductal dilatation; however, cholangitis cannot be excluded based on these findings

■ Blood Cultures × 2 Sets

Pending

■ Urine Culture

Pending

■ Biliary Drainage Culture

Pending

■ Assessment

1. Acute-on-chronic abdominal pain due to peritoneal metastases from gastric cancer
2. Hypotension and probable cholangitis due to biliary obstruction
3. Chronic bowel obstruction requiring TPN for nutrition
4. Nausea due to pain medications and chronic small bowel obstruction

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of an acute-on-chronic pain syndrome?
- 1.b. What subjective and objective data support the diagnosis of cholangitis in this patient?
- 1.c. What additional information is needed to fully assess this patient's pain?

Assess the Information

- 2.a. Assess the severity of the patient's pain using an appropriate patient assessment tool.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. How does the role of hospice services affect the treatment plan for this patient's care?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. Compare the pharmacotherapeutic alternatives available for treating this patient's pain.
- 3.d. Create an individualized, patient-centered, team-based care plan to treat this patient's pain. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial therapy fails or cannot be used?
- 3.f. Compare the pharmacotherapeutic alternatives available for treatment of this patient's nausea and vomiting.
- 3.g. Create an individualized, patient-centered, team-based care plan to treat the patient's nausea.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate timeframes to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient was given IV fluids and started on empiric antibiotic therapy with meropenem 1 g IV Q 12 H, vancomycin 750 mg IV daily, and fluconazole 100 mg IV daily. The patient's blood pressure normalized to 105/75 mm Hg, and SCr improved to 1.5 mg/dL with NS at 150 mL/hr. The blood and urine cultures were negative, but the biliary drainage cultures were positive for *Enterococcus faecalis* sensitive to vancomycin and *Pseudomonas stutzeri* sensitive to cefepime, ciprofloxacin, piperacillin/tazobactam, and tigecycline. The empiric antibiotic therapy was continued due to appropriate sensitivities to the antibiotics. Interventional radiology was consulted to evaluate the biliary drain for possible obstruction due to poor output. The internal/external catheter was exchanged with an external drain. The patient's bilirubin did not improve after the new external biliary drain was placed and remained in the range of 8–10 mg/dL. The patient was started on a fentanyl PCA pump at a basal rate of 30 mcg/hr with on-demand dosing of 10 mcg every 8 minutes with an hourly lockout of 100 mcg/hr, which resulted in adequate pain control rated 2 out of 10. The patient's overall prognosis is poor due to chronic jaundice from biliary obstruction, worsening renal function, and infection. She has metastatic gastric adenocarcinoma of the colon and small bowel and is not a candidate for further chemotherapy or surgery. The patient and her husband discussed her overall prognosis and made the choice to transition to full hospice services. The patient chose to continue the 14-day course of IV antibiotic therapy. She was discharged home with home health services on IV meropenem 1 g IV Q 12 H, vancomycin 750 mg IV daily, and fluconazole 100 mg IV daily

× 14 days, fentanyl PCA basal rate 30 mcg/hr on demand 10 mcg Q 8 minutes, and TPN. After the patient completes the IV antibiotics, she will choose to stop the TPN and continue with comfort measures only and enroll in full hospice services.

FOLLOW-UP QUESTIONS

1. Based on this new information of the patient discontinuing TPN and being discharged to hospice, are there any other supportive medications that may benefit the patient?
2. If the patient reports her pain to be 7 out of 10 at the time of discharge, how would you alter your treatment plan?

SELF-STUDY ASSIGNMENTS

1. Prepare a list of opioids and their corresponding equianalgesic dosing.
2. Prepare a set of guidelines for managing chronic malignant cancer pain reflecting the recommendations in the NCCN guidelines.
3. Prepare a list of antiemetics and dosing regimens useful in palliative care.

CLINICAL PEARL

Hospice is a specific type of palliative care team dedicated to managing patients with advanced illness who have a life expectancy of less than 6 months. Hospice has various levels of service and covers different therapies/services depending on the area in which the patient lives. Some hospice services will allow palliative therapy (ie, chemotherapy), IV antibiotics, and IV nutrition, whereas other hospice agencies require the patient to stop all such therapies prior to enrolling in their services.

REFERENCES

1. Adult Cancer Pain. NCCN Clinical Practice Guidelines in Oncology. Available at: https://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed November 1, 2018.
2. Williamson A, Hoggart B. Pain: a review of three commonly used pain rating scales. *J Clin Nurs* 2005;14:798–804.
3. Cassileth B. Psychiatric benefits of integrative therapies in patients with cancer. *Int Rev Psychiatry* 2014;26:114–127.
4. World Health Organization. WHO definition of palliative care. Available at: <http://www.who.int/cancer/palliative/definition/en/>. Accessed November 1, 2018.
5. Hui D, Mori M, Parsons HA, et al. The lack of standard definitions in supportive and palliative oncology literature. *J Pain Symptom Manage* 2012;43:582–592.
6. McCarberg BH, Barkin RL. Long-acting opioids for chronic pain: pharmacotherapeutic opportunities to enhance compliance, quality of life, and analgesia. *Am J Ther* 2001;8:181–186.
7. Trescot AM, Datta S, Lee M, Hansen H. Opioid pharmacology. *Pain Physician* 2008;11(2 Suppl):S133–S153.
8. Kress H, Von der Laage D, Hoerauf K, et al. A randomized, open, parallel group, multicenter trial to investigate analgesic efficacy and safety of a new transdermal fentanyl patch compared to standard opioid treatment in cancer pain. *J Pain Symptom Manage* 2008;36:268–279.
9. Palliative Care NCCN Clinical Practice Guideline in Oncology. Available at: https://www.nccn.org/professionals/physician_gls/pdf/palliative.pdf. Accessed November 10, 2018.

9

CLINICAL TOXICOLOGY:
ACETAMINOPHEN TOXICITY

If One Is Good, More Is Better... Level II

Elizabeth J. Scharman, PharmD, DABAT, BCPS, FAAC

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine when a potentially toxic acetaminophen exposure exists.
- Monitor a patient for signs and symptoms associated with acetaminophen toxicity.
- Recommend appropriate antidotal therapy for acetaminophen poisoning, and monitor its use for effectiveness and adverse effects.
- Describe the appropriate management of adverse drug reactions related to *N*-acetylcysteine.

PATIENT PRESENTATION

■ Chief Complaint

The patient is uncooperative and states that he just wants to be left alone.

■ HPI

The poison center receives a telephone call at 1:40 AM from a physician in a local ED regarding a 54-year-old man named Steven Marks. Mr Marks was brought to the ED via ambulance accompanied by police because the patient had been belligerent and was refusing referral. According to his wife, he took a handful of pills following a heated argument she had with him earlier that evening. She estimates the time of the fight was about 6:00 PM. She left the house and came back 2 hours later. When she returned, she found him lying on the bed and saw two empty bottles in the bathroom wastepaper basket that were not there before. The wife thinks he was trying to kill himself. He states that he took a few extra pills because he had a backache and did not think one or two pills would work. The ambulance crew brings in the two empty bottles of medicine. The wife cannot remember how many pills, if any, were remaining in the bottles prior to today. According to the wife, all other medications in the house are accounted for. One of the bottles originally contained sixty 500-mg acetaminophen tablets, and the other bottle originally contained thirty 300-mg acetaminophen/5-mg hydrocodone tablets. The physician reports that Mr Marks vomited twice in the ambulance and an additional four times since his arrival in the ED. He has not received any antiemetics.

■ PMH

Patient states that he is healthy. He has not seen a physician “in years” according to his wife.

■ FH

Father died of a heart attack when the patient was 12 years old. Mother is living. He has no sisters. He has one younger brother with “a bad heart.”

■ SH

Smokes two packs of cigarettes a day. Drinks “about as much as anybody else” according to his wife.

■ Meds

No prescription medications

Often takes nonprescription diphenhydramine because of insomnia

All

None

■ Physical Examination

Gen

The patient appears drowsy. There are no external signs of trauma. The patient has vomited a total of six times. The vomitus has not been bloody. His estimated height is 5'10".

VS

BP 142/98, HR 72, RR 14, O₂ sat 98% on room air, T 37°C; Wt 98 kg.

Skin

Mucous membranes are moist.

HEENT

Pupil size is normal; pupils are equal and reactive to light; retinal exam is unremarkable.

Lungs/Thorax

Occasional cough is noted.

CV

No murmurs or gallops heard

Abd

Bowel sounds are present. No guarding or tenderness.

Neuro

The patient is noticeably drowsy and uncooperative but is oriented to time and place; no tremors noted. The patient states that his headache has resolved.

■ Labs (Drawn at 01:00)

Na 142 mEq/L	Glucose 225 mg/dL	T. bili 0.8 mg/dL
K 3.1 mEq/L	Urine: (+) PCP	INR 1.2
Cl 96 mEq/L	Hgb 15.7 g/dL	Salicylates (–)
CO ₂ 23 mEq/L	Hct 48.2%	Acetaminophen 124 mcg/mL
BUN 24 mg/dL	AST 38 IU/L	Ethanol (EtOH) 138 mg/dL
SCr 1.1 mg/dL	ALT 42 IU/L	

■ ECG

Normal sinus rhythm

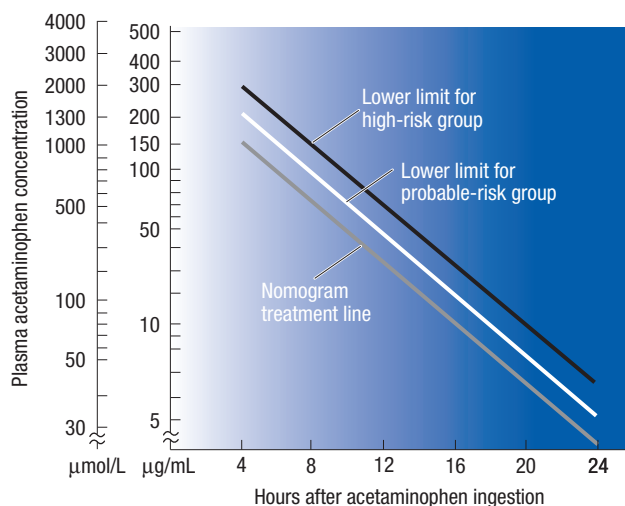


FIGURE 9-1. Nomogram for assessing hepatotoxic risk following acute ingestion of acetaminophen. (Reprinted with permission from DiPiro JT, Talbert RL, Yee GC, et al, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 9th ed. New York, NY: McGraw-Hill; 2014.)

■ Assessment

The physician asks the poison center if acetaminophen toxicity is present (Fig. 9-1).

QUESTIONS

Collect Information

- Is determining the amount of acetaminophen the patient ingested an important factor in determining whether acetaminophen toxicity is present? Why or why not?
- What subjective and objective information indicates that acetaminophen toxicity is present?
- What additional information is needed to fully assess this patient's acute overdose?

Assess the Information

- What are possible causes of vomiting in this patient?
- Does toxicity from any other drug(s)/toxin(s) need to be considered in this patient? If so, which one(s) and why?
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence. For the secondary problems, describe the rationale behind whether they need to be managed immediately or whether they can be addressed prior to discharge.

Develop a Care Plan

- What are the goals for managing acetaminophen toxicity in this case?
- What feasible pharmacotherapeutic alternatives are available for treating acetaminophen toxicity in this patient?
- Create an individualized, patient-centered, team-based care plan to treat acetaminophen toxicity for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

- If the physician asks the pharmacy to make an IV containing the exact dose of IV *N*-acetylcysteine (Acetadote) for this patient, instead of rounding to the nearest dose designated in the prescribing information dosing table, how many milliliters of *N*-acetylcysteine should this patient receive? Show all calculations, including how the total dose needed was obtained and how the amount of *N*-acetylcysteine in each milliliter of Acetadote was calculated.
- Will administration of *N*-acetylcysteine have any influence on the pharmacologic management of the patient's other problems as identified in his problem list? Why or why not?
- If this patient had been a female who was human chorionic gonadotropin (β -hCG) (+), would recommendations for *N*-acetylcysteine therapy change? Why or why not?

Implement the Care Plan

- What should the patient be told about the effectiveness of *N*-acetylcysteine therapy?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome for acetaminophen toxicity and to detect adverse effects?
- Develop a plan for follow-up that includes appropriate timeframes to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

At 02:20 the same day, the poison center gets a call from the patient's treating physician. He states that Mr Marks developed flushing and urticaria at the end of the loading dose; some faint wheezes were heard, and the baseline cough is unchanged. The physician thinks the patient may be having an anaphylactic reaction and has stopped the IV *N*-acetylcysteine. He wants poison center recommendations for an alternative antidote. The poison specialist determines that the correct mg/kg dosage was administered, although the loading dose was administered over 15 minutes. Vital signs are BP 138/99, HR 68, RR 14, and nonlabored. Blood chemistries are scheduled to be repeated at 08:00. Administration of ondansetron has controlled the vomiting.

■ FOLLOW-UP QUESTIONS

- Do you agree that this is an anaphylactic reaction? If not, what type of reaction is this and how is it different from an anaphylactic reaction?
- What are the appropriate management options for this reaction and for continued management of acetaminophen toxicity in this patient?
- The prescribing information for IV *N*-acetylcysteine lists one contraindication. Do you agree with this contraindication? Why or why not?
- If this patient is discharged from the hospital on medications to treat other medical problems, how will his history of an overdose affect the healthcare provider's decision on which medication(s) to select?

SELF-STUDY ASSIGNMENTS

1. Defend the argument that all patients with an intentional drug overdose, no matter what their stated history, should have an acetaminophen level drawn to rule out acetaminophen toxicity.
2. If this patient had been 104 kg instead of 98 kg, the dose given would have been the same as that of a person weighing 100 kg. Why do patients weighing over 100 kg not receive an IV *N*-acetylcysteine dose calculated on an mg/kg basis, and what is the rationale for this maximum dose being clinically effective?

CLINICAL PEARL

It is difficult to determine the best evidence-based practice for managing overdoses. It is unethical to withhold treatment or an antidote from a control group who has been poisoned. Therefore, there will never be a randomized control trial to determine an antidote's ideal dose or administration regimen. Use of historical cohort data from poisoning cases prior to antidote availability is the best available data; however, as with all retrospective studies, missing data are a limitation. For this reason, it is difficult to determine whether simplifying the FDA-approved three-bag IV *N*-acetylcysteine dosing regimen to a one- or two-bag total dose regimen has equal efficacy. Published case series using simplified regimens have only included acute acetaminophen exposures with early presentations in patients with unconfirmed exposure histories. Because the number of patients expected to progress to fulminant hepatotoxicity is so small (approximately 0.1–0.2%) if treatment is given within 10 and 16 hours, all published case series using simplified regimen have been underpowered to determine equal efficacy. Thousands of patients would be required to make a statistically valid conclusion. The use of more sensitive biomarkers of APAP hepatotoxicity (eg, microRNA rather than AST or ALT) may enable practitioners to better determine hepatotoxicity risk in the future and increase the ability to statistically compare dosing regimens.

REFERENCES

1. Dart RC, Erdman AR, Olson KR, et al. Acetaminophen poisoning: an evidence-based consensus guideline for out-of-hospital management. *Clin Toxicol (Phila)* 2006;44:1–18.
2. Payen C, Dachraoui A, Pulce C, et al. Prothrombin time prolongation in paracetamol poisoning: a relevant marker of hepatic failure? *Hum Exp Toxicol* 2003;22:617–621.
3. Rowden AK, Norvell J, Eldridge DL, et al. Acetaminophen poisoning. *Clin Lab Med* 2006;26:49–65.
4. Rumack BH, Bateman NS. Acetaminophen and acetylcysteine dose and duration: past, present and future. *Clin Toxicol* 2012;50:91–98.
5. Dribben WH, Porto SM, Jeffords BK. Stability and microbiology of inhalant *N*-acetylcysteine used as an intravenous solution for the treatment of acetaminophen poisoning. *Ann Emerg Med* 2003;42:9–13.
6. Acetadote Package Insert. Nashville, TN, Cumberland Pharmaceuticals Inc. December 2016.
7. Waring WS. Novel acetylcysteine regimens for treatment of paracetamol overdose. *Ther Adv Drug Saf* 2012;3:305–315.
8. Wilkes JM, Clark LE, Herrera JL. Acetaminophen overdose in pregnancy. *South Med J* 2005;98:1118–1122.
9. Curtis RM, Sivilotti ML. A descriptive analysis of aspartate and alanine aminotransferase rise and fall following acetaminophen overdose. *Clin Toxicol (Phila)* 2015;53:849–855.
10. Bateman DN, Dear JW, Thomas SH. New regimens for intravenous acetylcysteine, where are we now? *Clin Toxicol (Phila)* 2016;54(s):75–78.

10

CYANIDE EXPOSURE

Expect the Unexpected Level II

Elizabeth J. Scharman, PharmD, DABAT, BCPS, FAACT

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify which signs, symptoms, and laboratory data indicate a possible cyanide exposure.
- Compare and contrast the two different antidotes for cyanide exposure.
- Recommend specific dosing regimens for antidotes and supportive care for children and adults.
- State monitoring parameters and management of antidote side effects.
- Explain the factors involved in determining the amount of cyanide antidote a hospital should stock for immediate availability.

PRESENTATION OF PATIENTS

A 60-year-old laboratory worker with a history of major depressive disorder has stayed after normal laboratory hours on the pretense of completing a project. Once his coworkers have left, he ingests a bottle containing a toxic chemical. His biochemistry laboratory is on the fifth (top) floor of a university building containing eight other offices occupying the four floors below, all of which are faculty and staff offices for the biochemistry department. He loses consciousness. Meanwhile, the heating unit in the basement of the office building catches fire that quickly spreads through the first three floors of the building. At least 10 other individuals were in the other building's offices working late. They were not able to evacuate before being overcome by smoke.

HPI

Firefighters and emergency medical services (EMS) personnel are at the scene. Ambulances are bringing the 11 victims from the fire to your hospital's ED; some are comatose, and others present with a variety of signs/symptoms including confusion, coughing, wheezing, and minor burns. One of the victims brought in is a man who appears to be in his sixties. He has profound cyanosis and seizure activity. Unlike the other victims, he has no soot on his clothing. The ambulance worker reports that he was found on a floor receiving very little smoke damage and no fire damage. This victim has been tagged John Doe (JD).

PMH, PSH, FH, and SH

Not available. The hospital is initially overwhelmed because the ED was nearly full before the arrival of these patients.

ROS

Patients are presenting with a variety of symptoms and illness severity. ED nurses and doctors are only able to do brief physical exams. Ages and weights are being estimated as needed. JD is the most critically ill patient.

■ Physical Examination (Victims Excluding JD)

Gen

Four of the 10 patients appear weak and are breathing rapidly. Two additional victims are unconscious and required intubation to support breathing. All six of these patients have soot in their nares and around their mouths. The remaining four patients have mild coughing, wheezing, and burning eyes; soot is not present in their nares or inside their mouths, and systemic signs and symptoms are absent. Facial burns are not evident on any of these 10 individuals.

VS

BP: The six sickest patients are hypotensive.

HR: The six sickest patients have rates between 110 and 120 bpm.

RR: The six sickest patients have rates between 22 and 26.

T: All have normal temperatures.

Pain: Patients not intubated are anxious but are not in obvious pain.

O₂ sat: Normal for all.

Skin

No notable contusions, abrasions; second- and third-degree burns are absent. Two of the 10 have some mild blistering on their hands.

HEENT

Mydriasis observed in some patients

Neck/Lymph Nodes

No lymphadenopathy

Lungs/Thorax

Rapid respiratory rate; patients complain of some chest tightness and dyspnea

CV

Bradycardia for the six sickest patients, too noisy in ED to listen for heart sounds

Abd

Bowel sounds presents in all; the six sickest patients have nausea and some vomiting.

Genital/Rect

Deferred

MS/Ext

No abnormal movements noted

Neuro

Two of the six sickest victims are ventilated. No convulsions are observed. The six sickest patients are confused. The remaining four fire victims are neurologically intact.

■ Pertinent Physical Findings for JD

Gen

Unresponsive; generalized convulsions are present. Oxygen saturation via pulse oximetry was 98%. An almond smell was noted by one of the medical care providers after the patient vomited; this odor was not detected by others on the healthcare team. JD has been intubated.

VS: HR 22 bpm, RR 6, BP 60/35 mm Hg, T 37.0°C.

■ Lab

Ranges for the Six Sickest Fire Victims: HCO₃⁻ 13–15 mEq/L from the metabolic panel; CBC within normal limits; lactate 14 mmol/L; carboxyhemoglobin 12–15%

Reported for JD: HCO₃⁻ 8 mEq/L from the metabolic panel; CBC normal; lactate 22 mmol/L; carboxyhemoglobin 1%.

Four Remaining Fire Victims: Labs are within normal limits.

■ Other

Example initial blood gas for an intubated patient: pH 7.2, PaCO₂ 40 mm Hg, PaO₂ 110 mm Hg, HCO₃⁻ 13 mEq/L.

Blood gas for JD: pH 7.1, PaCO₂ 40 mm Hg, PaO₂ 240 mm Hg, HCO₃⁻ 9 mEq/L.

Blood gases were not obtained for the four fire victims without systemic symptoms.

Chest X-rays for JD and the six sickest fire victims are pending.

■ Follow-Up

The ED clinical pharmacist contacts the Poison Center after over-hearing one of the EMS workers mention that JD was found in his laboratory next to an opened and empty chemical bottle. The poison center will check with the on-scene Incident Commander (IC) and follow up with the clinical pharmacist as quickly as possible. Based on the presenting toxidrome, the most likely chemical ingested by JD is cyanide. There is agreement that products of combustion and toxic gases from smoke inhalation are causing toxicity in the six sickest patients.

QUESTIONS

Collect Information

- 1.a. JD and the six sickest fire victims share a similar toxidrome pattern. How is this possible when only JD ingested chemical from the bottle? Compare the signs and symptoms of severe cyanide poisoning with less severe intoxication.
- 1.b. List the laboratory tests that may be abnormal in patients exposed to cyanide. Explain the pathophysiology underlying these abnormalities.

Assess the Information

2. What are the potential short- and long-term sequelae from these cyanide exposures?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in these cases?
- 3.b. What nondrug measures are available to treat cyanide poisoning in these victims?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating cyanide poisoning (Fig. 10-1)? Include dose(s), route(s), and repeat dosing information (if any) for both adult and pediatric patients. Also describe use of administration devices or ancillary supplies.
- 3.d. Create an individualized, patient-centered, team-based care plan to treat cyanide poisoning in these patients. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What supportive care measures may be necessary for optimal management in these patients?



FIGURE 10-1. Nithiodote® (sodium nitrite injection and sodium thiosulfate injection for intravenous infusion). (Photo courtesy of Hope Pharmaceuticals.)

Implement the Care Plan

- 4.a. For patients who are alert and oriented, what information would you share with them about the possible immediate side effects of each of the antidotes?
- 4.b. Describe how care should be coordinated with other healthcare providers.
- 4.c. How long might it take for the patients to recover from potential long-term effects of acute cyanide exposure?

Follow-up: Monitor and Evaluate

- 5.a. Describe the clinical and laboratory parameters required to determine whether the treatment for these patients has been successful.
- 5.b. Develop a plan for follow-up that includes appropriate timeframes to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The bottle from the laboratory is confirmed to have contained cyanide. JD went into cardiac arrest shortly after being intubated. He was given the cyanide antidote during the resuscitation efforts. Catastrophic hypoxic brain injury became evident, and his family requested that life-support be withdrawn. Five of the six sickest patients survived; the sixth victim died of complications from cardiac arrest and acute respiratory distress syndrome. The four ambulatory patients were discharged to home from the ED. Legal charges were brought against the building's landlord because of the faulty heating unit and the fact that over one-quarter of the emergency exits were blocked.

FOLLOW-UP QUESTIONS

1. For how many patients should a hospital stock the cyanide antidotes? Consider the cost of the antidotes in your answer.
2. Suppose there are 100 patients in your hospital's ED requiring a cyanide antidote and you only have enough antidote to treat 4 patients. Who may be involved in making these ethical treatment decisions, and how would these decisions be made?

SELF-STUDY ASSIGNMENTS

1. Cyanide is usually obtained for suicidal exposures by persons who have access to it in a workplace setting. Other exposures to pure cyanide are the result of unintentional occupational exposures in industrial settings. The public might be exposed after a cyanide transportation accident that spills cyanide into sources of drinking water, leads to direct physical contact with the spilled cyanide, or results in the inhalation of cyanide fumes emanating from the spill. There is also the possibility that terrorists might obtain cyanide from manufacturing locations or transportation vehicles (chemical trucks, train cars). Describe which specific occupational settings utilize cyanide on a regular basis.
2. Describe why amyl nitrite is not required for the management of cyanide toxicity.

CLINICAL PEARL

Cyanide has an odor that has been described as that of “bitter almonds.” Unfortunately, only a small percentage of patients with cyanide poisoning present with this finding, and it is estimated that only 10% of the population is genetically able to detect cyanide's smell. Another classically reported finding is “cherry red skin” from increased venous oxygen saturation; however, this finding also occurs in only a small percentage of cyanide poisonings and is not a reliable indicator of cyanide toxicity.

REFERENCES

1. Thompson JP, Marrs TC. Hydroxocobalamin in cyanide poisoning. *Clin Toxicol (Phila)* 2012;50:875–885.
2. Leybell I, Borron SW, Roldan CJ, Rivers CM. Emedicine [Internet]. New York, Web MD Inc, © 1994–2013 [updated July 21, 2014]. Cyanide toxicity. Available at: <http://emedicine.medscape.com/article/814287-overview>. November 28, 2018.
3. Centers for Disease Control (CDC) Emergency Preparedness and Response [Internet]. Atlanta, GA. Facts about cyanide. Available at: <https://emergency.cdc.gov/agent/cyanide/basics/facts.asp>. October 10, 2019.
4. Baud FJ. Cyanide: critical issues in diagnosis and treatment. *Hum Exp Toxicol* 2007;26:191–201.
5. Borron SW, Baud FJ. Antidotes for acute cyanide poisoning. *Curr Pharm Biotechnol* 2012;13:1940–1948.
6. Baud FJ, Borron SW, Mégarbane B, et al. Value of lactic acidosis in the assessment of the severity of acute cyanide poisoning. *Crit Care Med* 2002;30:2044–2050.
7. Parker-Cote JL, Rizer J, Vakkalanka JP, Rege SV, Holstege CP. Challenges in the diagnosis of acute cyanide poisoning. *Clin Toxicol* 2018;56:609–617.
8. Nithiodote Package Insert. Scottsdale, AZ: Hope Pharmaceuticals, November 2017.
9. Cyanokit Package Insert. Columbia, MD: Meridian Medical Technologies™, Inc., June 2017.
10. Dal Ponte ST, Dornelles CF, Arquilla B, Bloem C, Roblin P. Mass-casualty response to the Kiss Nightclub in Santa Maria, Brazil. *Prehosp Disaster Med* 2015;30:93–96.

11

CHEMICAL THREAT AGENT EXPOSURE

Name That Poison Level II

Elizabeth J. Scharman, PharmD, BCPS, DABAT, FAACT

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify one of the toxidromes associated with a chemical threat agent attack.
- Determine the indications for antidotes and supportive care options based on patient signs and symptoms.
- State the difference between the utilization of a medical model and a mass care model during a public health emergency.
- Identify antidote and drug treatment stockpile sources and when state or national stockpiles options may be utilized.

PATIENT PRESENTATION

■ Patient Scenario

Via the disaster response radio in the emergency department (ED), hospital staff learn that attendees at an outdoor concert have suddenly become ill. A series of four loud popping sounds had been heard immediately prior. EMS personnel are on scene donning personal protective equipment (PPE) and setting up decontamination stations. Some concert attendees have been fleeing the scene despite orders from law enforcement to stay on site for decontamination. At least four backpacks have been observed in the area via binoculars but have not yet been examined. They are suspicious because backpacks were not allowed at the concert venue and attendees were checked for large bags prior to entry. Due to the large number of attendees, it is suspected that security measures were imperfect.

■ HPI

The on-scene incident commander ensures that the communication chief notifies all local EDs (total of four) to stand up their emergency operation centers (EOC). The concert venue held 1000, and seats had been sold out. Hospital 1 is the largest of the four and is also a Level I trauma center. Within 20 minutes of the notification, patients begin arriving at that hospital's outdoor staging and decontamination areas via car, by foot, and via ambulance. Hospital security personnel have donned full PPE and are working to ensure that those not arriving via ambulance (and therefore lacking prior decontamination) do not enter the ED until they have been through the hospital's decontamination stations, which are in the final stages of being set up. Security personnel are also directing friends and family members of the victims to a waiting area across the street so those needing care are not lost in the crowd.

An emergency triage center is established just outside ED entrance of Hospital 1. It is staffed by a lead physician, three nurses, two nursing aides, two medical residents, and the ED clinical pharmacist. Dozens of victims are in the staging area awaiting

decontamination, and they appear to be in various states of illness and anxiety levels. Victims arriving in the triage area via ambulance are unconscious.

In the triage area, the large number of victims and mass panic are creating chaos, making thorough individual assessment impossible. After ensuring that triage staff are properly gowned and double gloved, the ED lead physician at Hospital 1 instructs the nursing aides to obtain patient vital signs on those arriving via ambulance. Nurses are directed to establish an IV line in each comatose patient. The medical residents are assigned to triage patients into four groups based on need for immediate threats to life, focusing on prominent findings observed with a brief physical exam. The clinical pharmacist is instructed to call the poison center for information on what the chemical threat agent is likely to be based on the cluster of symptoms being observed and to obtain antidote information.

■ PMH, PSH, FH, and SH

Not obtained

■ ROS

At Hospital 1, at least 300 victims are waiting for care. In the triage area, patients are tagged with color-coded bracelets into one of four groups:

- *Red*—Unconscious and having immediate life-threatening symptoms.
- *Yellow*—Severe but not immediately life-threatening symptoms; awake but not ambulatory and not conversing well.
- *Green*—Distressing or mild symptoms, but ambulatory and conversing well. Care required but can be delayed.
- *White*—Ambulatory without symptoms, any minor injuries are amenable to self-care.

Because no deaths occurred, no victims were coded *Black*.

■ Physical Examination

Triage has been completed for an estimated 75% of those waiting for care at Hospital 1. Physical findings observed on each patient category are as follows:

- *Red*—45 patients, and all are unconscious; 11 are having multiple convulsions; 43 are having large- and small-muscle fasciculations. Breathing is labored, and rhonchi are present throughout the lung fields in all 45 victims; respiratory paralysis appears to be imminent in 28 cyanotic patients. CPR is being performed on one patient by an anesthesiologist who was called in for assistance. In the other victims, HRs are less than 40 bpm. Profuse diaphoresis is present, and bowel sounds are hyperactive; vomitus and fecal staining are present on the clothing of some of the victims. Miosis is present in approximately half of the patients.
- *Yellow*—36 patients; these victims have a decreased level of consciousness and severe muscle weakness but respond somewhat to stimuli. All are unable to communicate except for brief responses and sometimes not at all. Facial fasciculations are present in six, but none have experienced a witnessed convulsion. Wheezing is heard on auscultation, and patients complain of shortness of breath. None appear cyanotic. HRs are not less than 40 bpm, but it has been too chaotic to record individual rates consistently. Vomiting, hyperactive bowel sounds, and fecal incontinence are common. Moderate diaphoresis is noted. Miosis is present in 10 patients; communication difficulties make it impossible to assess if visual changes are present.

- **Green**—86 patients; victims are ambulating and conversing. Wheezing and rhonchi are absent and only four complain of chest tightness. Nausea is present in all, but no one has had more than one or two episodes of vomiting. Ten victims have miosis and are complaining of blurry vision. Tearing, runny noses, and mild-moderate diaphoresis are noted. Vital signs were not obtained at this time because nurses are overwhelmed.
- **White**—75 patients; victims are ambulating and conversing, although many are visibly distraught. Fifty-two patients are asymptomatic but are extremely concerned and demand to receive an antidote because they are sure they are going to die. Twenty-five victims complain of nausea, headache, and dizziness. Diaphoresis, tearing, and runny noses are absent. No vomiting or fecal incontinence has occurred in this group.

Next Steps

The clinical pharmacist at Hospital 1 contacted the poison center to report patient numbers and the signs and symptoms being observed. The poison center relates that victims from all four hospitals are showing a similar toxidrome pattern. The poison center has been in communication with the on-scene incident commander to review additional information from the concert venue. The category of chemical threat agent most likely involved and antidote and treatment recommendations are reviewed with the clinical pharmacist, who then reports this information to the lead physician. The poison center faxes information to the hospital ED and pharmacy to ensure that the antidote and dosing information are readily available.

The lead physician prioritized the Red group for entry into the ED for immediate care. He assigned the Yellow group to be managed in a medical tent set up near the ED entrance approximately 50 yards away from the triage area. The Green group was assigned to be managed as healthcare professionals become free. Those in the White group are moved to a location 200 yards from the triage area with a portable curtain erected to put them out of the line of sight of the other victims. The lead physician called for the behavioral health disaster response team to provide supportive mental health services to the White group. A clinical pharmacist will be there to answer questions about the incident. A nurse will be with the White group to observe for the onset of any new symptoms.

The ED clinical pharmacist contacted the clinical pharmacist in charge of the pharmacy's disaster plan to report the number of victims requiring antidotal and supportive therapies. The initial supply of pharmaceuticals is transported to the ED. Another cart of pharmaceuticals is on its way to the area serving the Yellow group. The pharmaceutical cart for the Green group will be ready in the next 5 minutes. Disaster plan of Hospital 1 has been activated and will be used to obtain additional antidotes, supportive therapies, and supplies. The ED clinical pharmacist and the clinical pharmacist in the pharmacy department will communicate with each other to coordinate antidote needs and availability.

Laboratory Findings

Immediate resuscitative measures on the 45 victims are taking precedence at this time. A team of phlebotomists has been called to the ED to begin drawing blood samples. Hand-printed labels are used to mark the vials to save time. Physicians use clinical judgment to monitor patient status.

Radiology Findings

Diffuse pulmonary edema is observed on plain film chest X-rays obtained on the victim who was receiving CPR and has now been intubated.

QUESTIONS

Collect Information

- What subjective and objective information about the event indicates exposure to a chemical agent?

Assess the Information

- Which category of chemical threat agent is most likely to be involved? Describe how you made this decision.
- To initiate antidotal therapies, is it important to know which specific chemical agent in this chemical agent category is involved? Why or why not?

Develop a Care Plan

- What are the goals of pharmacotherapy for each group (Red, Yellow, Green, and White)?
- How would your goals change if there were 5 victims instead of 300 victims presenting to your hospital with an exposure to a chemical threat agent?
- What nondrug measures are required and available to manage these patients?
- What feasible pharmacotherapeutic alternatives are available for treating these patients? (See Figs. 11-1 and 11-2.)
- Provide adult and pediatric doses by route for each chemical threat agent antidote required in this case scenario.
- If a patient's condition worsens and seizure activity occurs, what class of medications should be used for this chemical-induced seizure?
- Which clinical and/or laboratory findings determine whether or not an individual will require the antidote(s)?
- Suppose there are 100 patients in your hospital's emergency department meeting the criteria for the antidote(s), and you only have enough antidote(s) to treat 25 patients. How do you decide who receives the antidote?



FIGURE 11-1. (A) The Mark ITM autoinjector, consisting of two antidotes to be used after exposures to a nerve or organophosphate agent in a disaster situation. The kit contains an atropine autoinjector (2 mg/0.7 mL) and a pralidoxime chloride (2-PAM) autoinjector (600 mg/2 mL). (B) The DuoDoteTM autoinjector (replacing the Mark ITM autoinjector) contains 2.1 mg atropine and 600 mg of pralidoxime chloride in one syringe.

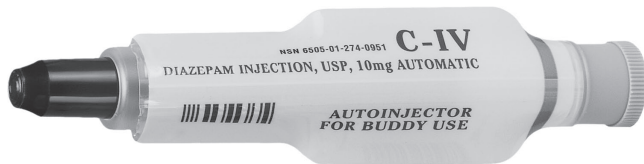


FIGURE 11-2. Diazepam provided as a 10-mg dose in a military designed autoinjector.

Implement the Care Plan

- 4.a. What information would you share with the patients about immediate side effects of each of the antidotes?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. Outline a monitoring plan to assess whether the pharmacotherapy treatment for these patients is successful.
- 5.b. Develop a plan for follow-up that includes appropriate timeframes to assess progress toward achievement of the goals of therapy.
- 5.c. How long might it take for patients to recover from the ocular effects of the chemical exposure? Incorporate this information into your educational efforts.

CLINICAL COURSE

At Hospital 1, 21 patients die from the exposure and 24 remain in critical condition. Critically ill patients are transferred to the ICUs, and half of the telemetry floor beds have been temporarily converted into additional ICU beds.

FOLLOW-UP QUESTION

1. What is the initial and ongoing source of antidotes for use after a chemical terrorist event at hospital pharmacies in the United States?

SELF-STUDY ASSIGNMENTS

1. Research information on the Strategic National Stockpile Program and the CHEMPACK program. Evaluate the difference in response times and focus for both programs.
2. Research information on your county and state threat preparedness plan. Review the expectations of healthcare professionals according to the plans. Identify gaps in the plan that

you may be able to assist in correcting by working with your local health department or state threat preparedness planning agency.

CLINICAL PEARL

Most chemical agents that could be used for a terrorist attack would likely be exploded or released as a gas or vapor in order to increase the extent of the exposure and allow for rapid systemic entry into victims. A general rule of thumb for chemical exposures is that the higher the concentration (or total dose), the faster the onset of symptoms; the lower the concentration (or total dose), the slower the onset of symptoms.

REFERENCES

1. US Army Medical Research Institute of Chemical Defense (USAMRICD). Field Management of Chemical Casualties Handbook, 2nd ed. [Internet]. Aberdeen Proving Ground, MD, Chemical Casualty Care Division, July 2000. Available at: <https://www.hsdl.org/?view&did=1021>. November 15, 2018.
2. Centers for Disease Control and Prevention. Emergency Preparedness and Response; Chemical Emergencies [Internet]. Atlanta, GA [updated November 25, 2014]. Available at: <http://emergency.cdc.gov/chemical/index.asp>. November 15, 2018.
3. Leikin JB, Thomas RG, Walter FG, Klein R, Meislin HW. A review of nerve agent exposure for the critical care physician. *Crit Care Med* 2002;30:2346–2354.
4. Bartlett JG, Sifton DW, Gwynned LK. PDR Guide to Biological and Chemical Warfare Response. 1st ed. Montvale, NJ: Thomson Healthcare; 2002:79–86, 101–102, 126–127.
5. Jones TF. Mass psychogenic illness: role of the individual physician. *Am Fam Physician* 2000;62:2649–2653.
6. Hick LH, Rubinson, L, O’Laughlin DT, Farmer JC. Clinical review: allocating ventilators during large-scale disasters—problems, planning, and process. *Crit Care* 2007;11(3):217.
7. Atropen Auto-Injector [package insert]. Columbia, MD, Meridian Technologies Inc, November 2005. Available at: https://www.meridianmeds.com/sites/default/files/atropen_uspi_2005.pdf. November 15, 2018.
8. Pralidoxime Chloride Injection Auto-Injector [package insert]. Columbia, MD, Meridian Technologies Inc, October 2003. Available at: https://www.meridianmeds.com/sites/default/files/pralidoxime_chloride_uspi_2016.pdf. November 15, 2018.
9. DuoDote [package insert]. Columbia, MD, Meridian Technologies Inc, April 2010. Available at: https://www.meridianmeds.com/sites/default/files/atnaa_uspi_2010.pdf. November 15, 2018.
10. Diazepam Autoinjector [package insert]. Columbia, MD, Meridian Technologies Inc, July 2005. Available at: https://www.meridianmeds.com/sites/default/files/pi/Diazepam_PI.pdf. November 15, 2018.

SECTION 2

CARDIOVASCULAR DISORDERS

12

HYPERTENSION

Pass the Salt, Please Level II

Julia M. Koehler, PharmD, FCCP

James E. Tisdale, PharmD, BCPS, FCCP, FAPhA, FNAP, FAHA, FACC

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Classify blood pressure according to current hypertension (HTN) guidelines and discuss the correlation between blood pressure (BP) and risk for cardiovascular morbidity and mortality.
- Identify medications that may cause or worsen HTN.
- Discuss complications (eg, target organ damage) that may occur as a result of uncontrolled and/or long-standing HTN.
- Establish goals for the treatment of HTN and choose appropriate lifestyle modifications and antihypertensive regimens based on patient-specific characteristics, comorbid disease states, and current HTN guidelines.
- Provide appropriate patient counseling for antihypertensive drug regimens.

PATIENT PRESENTATION

■ Chief Complaint

"I'm here to see my new doctor for a checkup. I'm just getting over a cold. Overall, I'm feeling fine, except for occasional headaches and some dizziness in the morning. My other doctor prescribed a low-salt diet for me, but I don't like it!"

■ HPI

James Frank is a 64-year-old black man who presents to his new family medicine physician for evaluation and follow-up of his medical problems. He generally has no complaints, except for occasional mild headaches and some dizziness after he takes his morning medications. He states that he is dissatisfied with being placed on a low-sodium diet by his former primary care physician.

■ PMH

HTN × 14 years

Type 2 diabetes mellitus (DM) × 16 years

COPD, GOLD 3/Group C

BPH

CKD

Gout

■ FH

Father died of acute MI at age 73. Mother died of lung cancer at age 65. Father had HTN and dyslipidemia. Mother had HTN and DM.

■ SH

Former smoker (quit 6 years ago; 35 pack-year history); reports moderate amount of alcohol intake (one to two drinks per day). He admits he has been nonadherent to his low-sodium diet (states, "I eat whatever I want"). He does not exercise regularly and is limited somewhat functionally by his COPD. He is retired and lives alone. He works at Wal-Mart and has healthcare insurance through his employer.

■ Meds

Hydrochlorothiazide/triamterene 25 mg/37.5 mg PO Q AM

Insulin glargine 36 units subcutaneously daily

Insulin lispro 12 units subcutaneously TID with meals

Doxazosin 2 mg PO Q AM

Carvedilol 12.5 mg PO BID

Albuterol HFA MDI, two inhalations Q 4–6 H PRN shortness of breath

Tiotropium DPI 18 mcg, one capsule inhaled daily

Fluticasone/salmeterol DPI 250/50, one inhalation BID

Mucinex D® two tablets Q 12 H PRN cough/congestion

Naproxen 220 mg PO Q 8 H PRN pain/HA

Allopurinol 200 mg PO daily

■ All

PCN—rash

■ ROS

Patient states that overall he is doing well and recovering from a cold. He has noticed no major weight changes over the past few years. He complains of occasional headaches, which are usually relieved by naproxen, and he denies blurred vision and chest pain. He states that shortness of breath is "usual" for him, and that his albuterol helps. He reports having had two COPD exacerbations within the past 12 months. He denies experiencing any hemoptysis or epistaxis; he also denies nausea, vomiting, abdominal pain, cramping, diarrhea, constipation, or blood in stool. He denies urinary frequency but states that he used to have more difficulty urinating until his physician started him on doxazosin a few months ago. He has no prior history of arthritic symptoms and states that his occasional gout pain is also relieved with naproxen.

■ Physical Examination

Gen

WDWN, black male; moderately overweight; in no acute distress

VS

BP 162/90 mm Hg (sitting; repeat 164/92 mm Hg), HR 76 bpm (regular), RR 16/min, T 37°C; Wt 95 kg, Ht 6'2"

HEENT

TMs clear; mild sinus drainage; AV nicking noted; no hemorrhages, exudates, or papilledema

Neck

Supple without masses or bruits, no thyroid enlargement or lymphadenopathy

Lungs

Lung fields CTA bilaterally. Few basilar crackles, mild expiratory wheezing.

Heart

RRR; normal S_1 and S_2 . No S_3 or S_4 .

Abd

Soft, NTND; no masses, bruits, or organomegaly. Normal BS.

Genit/Rect

Enlarged prostate

Ext

No CCE; no apparent joint swelling or signs of tophi

Neuro

No gross motor-sensory deficits present. CN II–XII intact. A & O $\times$ 3.

Labs

Na 138 mEq/L	Ca 9.7 mg/dL	<i>Fasting lipid panel</i>	<i>Spirometry</i>
K 4.7 mEq/L	Mg 2.3 mEq/L	Total Chol	(6 months ago)
Cl 99 mEq/L	A1C 6.1%	161 mg/dL	
CO ₂ 27 mEq/L	Alb 3.4 g/dL	LDL 79 mg/dL	FVC 2.38 L
BUN 22 mg/dL	Hgb 13 g/dL	HDL 53 mg/dL	(54% pred)
SCr 2.2 mg/dL	Hct 40%	TG 144 mg/dL	FEV ₁ 1.21 L
Glucose	WBC 9.0 $\times$		(38% pred)
110 mg/dL	10 ³ /mm ³		FEV ₁ /FVC 51%
Uric acid	Plts 189 $\times$		
6.7 mg/dL	10 ³ /mm ³		

UA

Yellow, clear, SG 1.007, pH 5.5, (+) protein, (–) glucose, (–) ketones, (–) bilirubin, (–) blood, (–) nitrite, RBC 0/hpf, WBC 1–2/hpf, neg bacteria, one to five epithelial cells.

ECG

Abnormal ECG: normal sinus rhythm; left atrial enlargement; left axis deviation; LVH

ECHO (6 Months Ago)

Mild LVH, estimated EF 45%

Assessment

HTN, uncontrolled
COPD, stable on current regimen
CKD, evidence of proteinuria
Type 2 DM, controlled on current insulin regimen
BPH, symptoms improved on doxazosin
Gout, controlled on current regimen

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of HTN in this patient?
- What evidence of target organ damage or clinical cardiovascular disease (CVD) does this patient have?
- What is this patient's 10-year atherosclerotic cardiovascular disease (ASCVD) risk?

Assess the Information

- How would you classify this patient's HTN, according to current HTN guidelines?
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating this patient's HTN?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's HTN and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect and prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

- Describe the major causes of secondary HTN and the methods by which those could be ruled out in this patient.
- Outline the changes, if any, that you would make to the pharmacotherapeutic regimen for this patient if he had a history of each of the following comorbidities or characteristics:
 - Severe persistent asthma
 - Major depression
 - Ischemic heart disease with a history of MI
 - Cerebrovascular accident
 - Peripheral arterial disease
 - Isolated systolic HTN
 - Migraine headache disorder
 - Liver disease



FIGURE 12-1. The LifeSource UA-767 Plus—One-Step Plus Memory digital home blood pressure monitor. (Photo courtesy of A&D Medical, Milpitas, California.)

- Renovascular disease (bilateral or unilateral renal artery stenosis)
 - Heart failure with reduced EF
3. Describe how you would explain to a patient how to use a digital home BP monitor such as the one shown in Fig. 12-1.

CLINICAL PEARLS

1. The risk of hemorrhagic stroke may be increased by the use of aspirin therapy in patients with uncontrolled HTN (eg, BP >150/90 mm Hg).
2. The majority of hypertensive patients will require two or more BP-lowering medications to achieve recommended BP goals.

REFERENCES

1. Welton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127–e248. doi: 10.1016/j.jacc.2017.11.006.
2. Salerno SM, Jackson JL, Berbano EP. Effect of oral pseudoephedrine on blood pressure and heart rate: a meta-analysis. *Arch Intern Med* 2005;165:1686–1694.
3. American Diabetes Association. Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019;42(1 Suppl):S1–S193.
4. KDIGO clinical practice guideline for the management of blood pressure in kidney disease. *Kidney Int Suppl* 2012;2:337–414. doi:10.1038/kisup.2012.46.
5. Douglas JG, Bakris GL, Epstein M, et al. Management of high blood pressure in African Americans: consensus statement of the Hypertension in African Americans Working Group of the International Society on Hypertension in Blacks. *Arch Intern Med* 2003;163:525–541.
6. Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting enzyme inhibitor, ramipril, on cardiovascular events in high-risk patients. *N Engl J Med* 2000;342:145–153.
7. Heart Outcomes Prevention Evaluation Study Investigators. Effects of ramipril on cardiovascular and microvascular outcomes in people with diabetes mellitus: results of the HOPE study and the MICRO-HOPE substudy. *Lancet* 2000;355:253–259.
8. The ALLHAT Officers and Coordinators for the ALLHAT Collaborative Research Group. Major cardiovascular events in hypertensive patients randomized to doxazosin vs chlorthalidone: the Antihypertensive and Lipid-Lowering Treatment to Prevent Heart Attack Trial (ALLHAT). *JAMA* 2000;283:1967–1975.

13

HYPERTENSIVE CRISIS

I Don't Really Need Those Pills Level I

James J. Nawarskas, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Distinguish a hypertensive urgency from a hypertensive emergency.
- Identify treatment goals for a patient with a hypertensive crisis.
- Develop an appropriate treatment plan for a patient with a hypertensive crisis.
- Describe how a pharmacist can help improve antihypertensive medication adherence and the importance of providing this education.

PATIENT PRESENTATION

■ Chief Complaint

“I’m having trouble breathing, and my chest feels tight.”

■ HPI

Jacqueline Santos is a 59-year-old Hispanic woman who was admitted to the emergency department with a chief complaint of difficulty breathing and chest tightness. She describes shortness of breath that she thinks started a few weeks ago but wasn’t really that noticeable at first. Over the last few weeks, she has noticed her ability to perform daily activities to be more and more limited due to shortness of breath. She is fine when she isn’t doing much, but simple activities such as walking her dog or going grocery shopping cause her to become short of breath rather quickly. Consequently, she moves around more slowly now when doing routine activities. She initially attributed this to just being “out of shape” but now is more concerned that it may be something else. The chest tightness started yesterday and was initially very mild, occurring when she would walk her dog outside and resolving readily with rest. However, it has since gotten more troublesome and is limiting her daily activities. While the chest discomfort still improves with rest, it no longer completely resolves. She tried to self-medicate by taking two doses (500 mg each) of acetaminophen last night and another dose this morning, but she says that didn’t help. She also states that this discomfort is very different from her gastroesophageal reflux pain. While seated in the emergency department she describes the chest discomfort as a 2 on a scale of 1–10 (highest). She has a past medical history significant for HTN and gastroesophageal reflux. She had been taking lisinopril and hydrochlorothiazide for several years with good blood pressure control, but about 6 months ago she stopped taking both medicines, because she had to make an urgent trip to visit her daughter out of state and ended up staying with her for a couple of months. Since her daughter lives in a rural area with no pharmacy nearby, she never got the medications refilled when she ran out. After several days, Ms Santos noticed that she felt just fine despite not taking the medicines. Consequently, she never resumed them and has not seen her provider since.

■ **PMH**

HTN × 9 years

Gastroesophageal reflux × 11 years

■ **FH**

Both parents had HTN. Father had a heart attack in his early 60s and died in his late 70s of a second heart attack; mother died a few years later from a stroke. Two brothers, 57 and 62 years old, are both alive; the elder has HTN and hypercholesterolemia and underwent CABG surgery 2 years ago; the younger has no chronic diseases. One sister who is 60 years old also has HTN.

■ **SH**

Married for 36 years with four children (two boys, two girls all older than 25 years with no notable medical problems); she works part time (2–3 days per week) as a cashier at a large department store. She smoked cigarettes rather heavily when she was younger, but cut back to one to two per day when she was raising her children. As her children got older, she gradually increased her cigarette use and is now smoking about one pack per day and has been doing so for about the past 10 years. She drinks alcohol infrequently (maybe once or twice a month), when she is at a social gathering. She denies ever using recreational drugs. She does not exercise and leads a rather sedentary lifestyle. In terms of diet, for breakfast she typically has a cup of coffee, toast with butter, and two eggs. For lunch, she usually eats a cold cut sandwich, although on days she works, she typically does not eat lunch at all and compensates by eating a large breakfast. She does munch on snack cakes and chips on breaks during her work shift, however. For dinner, she likes to eat baked chicken and prepares some canned vegetables as a side dish along with a dinner salad with Italian dressing. She admits to the liberal use of salt during breakfast and dinner. She has a high school education. Her husband is alive and well and works as an accountant. Her household income is average middle class. She has good health insurance through her husband's employer.

■ **Meds**

Ranitidine 75 mg PO once daily in the evening (over the counter).

Acetaminophen 500 mg as needed for headaches—she takes maybe two doses a month in addition to the doses mentioned in the HPI.

Lisinopril/hydrochlorothiazide 20/12.5 mg PO once daily—stopped approximately 6 months ago.

■ **All**

NKDA

■ **ROS**

Ms Santos complains of breathing trouble as mentioned above; no hearing problems. She complains of chest discomfort as mentioned above but denies palpitations and dizziness. She admits to feeling a lack of energy along with her dyspnea, although she never has been very active. She denies nausea, vomiting, or abdominal pain. She denies any swelling in her extremities or weight gain. She denies mental status changes.

■ **Physical Examination***Gen*

The patient is a middle-aged Hispanic woman appearing to be in moderate distress.

VS

BP 240/130 mm Hg right arm, 232/128 mm Hg left arm (automated readings performed in the emergency department). A manual measurement repeated in the right arm after several minutes yields a BP of 236/134 mm Hg.

P 74, RR 24, T 36.8°C; Wt 80 kg, Ht 5'5"

Skin

Normal tone and temperature, good turgor

HEENT

PERRLA; EOMI; funduscopic exam revealed arterial tortuosity and A/V nicking, but no papilledema

Neck/Lymph Nodes

Neck supple, no JVD, no bruits, no thyromegaly, or lymphadenopathy

Chest

Wheezing with faint crackles in both lung bases

CV

PMI shifted laterally, RRR, no murmurs or rubs appreciated; +S₄ heard at apex

Abd

Soft, NT/ND, no guarding, (+) BS, no abdominal bruits appreciated, liver span about 12 cm

Genit/Rect

Normal female genitalia, heme-negative stool

MS/Ext

Normal ROM, no CCE, pulses 2+ radial; 1+ to 2+ in the rest of her upper and lower extremities

Neuro

A & O × 3, CN II–XII intact, motor/sensory normal, DTRs 2+

■ **Labs**

Na 140 mEq/L	Hgb 13.2 g/dL	AST 27 IU/L
K 4.8 mEq/L	Hct 43%	ALT 45 IU/L
Cl 100 mEq/L	WBC $6.6 \times 10^3/\text{mm}^3$	Cholesterol 196 mg/dL
CO ₂ 28 mEq/L	Plt $222 \times 10^3/\text{mm}^3$	HDL 42 mg/dL
BUN 30 mg/dL		Triglycerides 142 mg/dL
SCr 2.3 mg/dL		LDL 126 mg/dL
Glu 122 mg/dL		Troponin-I normal

■ **UA**

Specific gravity 1.010; pH 5.8; negative for blood or protein; negative for recreational drugs

■ **Chest X-Ray**

Enlarged heart; cephalization of the pulmonary veins with indistinct vascular margins indicative of pulmonary edema

■ **ECG**

Normal sinus rhythm; LVH by voltage criteria. There are no ST-segment changes, although there does appear to be some T-wave flattening in the anterior leads. No old ECGs are available for comparison.

■ Chest CT

Negative for aortic dissection

■ Assessment

A 59-year-old woman with a long-standing history of HTN and gastroesophageal reflux presents with an extremely elevated blood pressure and signs and symptoms of target organ damage. She admits to not taking any antihypertensive drug therapy for 6 months, which was initially due to difficulty in getting her medications refilled, and then later due to feeling just fine despite not taking the medications.

QUESTIONS

Collect Information

- 1.a. Is this a hypertensive urgency or an emergency? What subjective and objective information helps distinguish a hypertensive urgency from an emergency in this patient?
- 1.b. What additional information, if any, is needed to help develop a treatment plan for this patient?

Assess the Information

- 2.a. Assess the severity of this patient's hypertensive crisis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating her hypertensive crisis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's hypertensive crisis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. How would the treatment goals differ if this patient presented with the same BP but was asymptomatic with normal laboratory findings and no acute changes on ECG or physical examination?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

Once Ms Santos blood pressure is lowered to an acceptable level, her inpatient provider consults with you regarding chronic antihypertensive therapy for Ms Santos.

■ FOLLOW-UP QUESTIONS

1. Do you recommend Ms Santos resume her lisinopril/HCTZ as prescribed, or would you recommend alternative drug therapy? Rationalize your answer. If you would recommend alternative drug therapy, which drug(s) would you recommend and why?
2. What nonpharmacologic measures can Ms Santos incorporate as part of an overall treatment plan for her chronic hypertension?

■ SELF-STUDY ASSIGNMENTS

1. You are a pharmacist working in a community pharmacy that has a designated patient care center equipped with a manual blood pressure cuff. Describe your approach in dealing with a patient who reports that the automated blood pressure monitor in the waiting area of the pharmacy provided him or her with extremely high blood pressure measurements.
2. Use an algorithm or flow diagram to illustrate your approach to dealing with a patient who is nonadherent to antihypertensive therapy. After you do so, read the article: Can drugs work in patients who do not take them? The problem of nonadherence in resistant hypertension (Curr Hypertens Rep 2015;17:69). Then redesign your approach if necessary.
3. Develop an evidence-based treatment algorithm for the use of various oral antihypertensive agents for the treatment of a hypertensive urgency.

CLINICAL PEARL

Of patients presenting to the emergency department with a hypertensive emergency, the vast majority of them have been diagnosed with hypertension and have been prescribed antihypertensive medication. Only 8% of hypertensive emergencies presenting to the emergency department involve patients unaware of having a diagnosis of hypertension.

REFERENCES

1. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71:e13–e115.
2. Rodriguez MA, Kumar SK, De Caro M. Hypertensive crisis. *Cardiol Rev* 2010;18:102–107.
3. Hebert CJ, Vidt DG. Hypertensive crises. *Prim Care Office Pract* 2008;35:475–487.
4. Ramos AP, Varon J. Current and newer agents for hypertensive emergencies. *Curr Hypertens Rep* 2014;16:450.
5. Mansoor GA, Frishman WH. Comprehensive management of hypertensive emergencies and urgencies. *Heart Dis* 2002;4:358–371.
6. Thach AM, Schultz PJ. Nonemergent hypertension: new perspectives for the emergency medicine physician. *Emerg Med Clin North Am* 1995;13:1009–1035.
7. Varounis C, Katsi V, Nihoyannopoulos P, Lekakis J, Tousoulis D. Cardiovascular hypertensive crisis: recent evidence and review of the literature. *Front Cardiovasc Med* 2017;3:51.
8. Varon J. Treatment of acute severe hypertension: current and newer agents. *Drugs* 2008;68:283–297.
9. Aggarwal M, Khan I. Hypertensive crisis: hypertensive emergencies and urgencies. *Cardiol Clin* 2006;24:135–146.
10. Gales MA. Oral antihypertensives for hypertensive urgencies. *Ann Pharmacother* 1994;28:274–284.

14

DYSLIPIDEMIA

Afraid of Another Attack Level II

Joel C. Marrs, PharmD, FAHA, FASHP, FCCP, FNLA, BCPS, BCACP, BCCP, CLS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify patients who require treatment for dyslipidemia.
- Stratify individual patients for risk of coronary heart disease (CHD) and stroke.
- Determine appropriate LDL and non-HDL goals and thresholds based on individual risk factors.
- Recommend a cholesterol management strategy that includes therapeutic lifestyle changes (TLC), drug therapy, patient education, and monitoring parameters.

PATIENT PRESENTATION

■ Chief Complaint

"I am here to see if I need additional meds."

■ HPI

Thomas Smith is a 52-year-old man who presents to pharmacotherapy for optimization of risk reduction therapy clinic by referral from his primary care provider following an ST-elevation myocardial infarction (STEMI) 6 months ago. He reports good adherence to his medications since having his heart attack.

■ PMH

Obesity (BMI 30.5 kg/m²)

Dyslipidemia × 6 years

HTN × 10 years

Chronic kidney disease (stage 3) × 5 years

CAD, s/p STEMI 6 months ago (drug-eluting stents placed in right circumflex and left anterior descending arteries)

GERD × 5 years

■ FH

Father: age 72 with MIs at age 50 and again at age 60

Mother: age 70 with no major medical conditions noted

Patient has one older brother age 55 with HTN and a history of one MI at the age of 48.

He has no children.

■ SH

Patient is married and lives with his wife.

College graduate, works as an accountant.

Admits to drinking one to two beers most days of the week and has never used tobacco.

Exercise regimen has increased since his MI; currently rides the bike at the gym for 30 minutes 2–3 days a week.

■ Meds (Per medication fill history)

Carvedilol 25 mg PO BID

Atorvastatin 80 mg PO once daily

Aspirin 81 mg PO once daily

Clopidogrel 75 mg PO once daily

Pantoprazole 40 mg PO once daily

Lisinopril 40 mg PO daily

Chlorthalidone 25 mg PO daily

Acetaminophen 500 mg, one to two tablets PO PRN every 6 hours for pain

Garlic capsules

■ All

No known drug allergies

■ ROS

Patient states that he had a heart attack about 6 months ago and was put on a number of medications after that happened. He saw his PCP last month who said he should be seen in the pharmacotherapy clinic for evaluation of his cardiovascular risk reduction medications. He reports he has been adherent to his medication regimen over the last 6 months. He went to cardiac rehab for the first 3 months after his MI but has just been going to the gym to ride the bike two to three times a week now. He denies unilateral weakness, numbness/tingling, or changes in vision. He denies CP and only has SOB if he really pedals hard on the bike for longer than 15 minutes. He denies changes in bowel or urinary habits. He denies any lower extremity edema.

■ Physical Examination

Gen

Obese, African-American man

VS

BP 136/84, P 64, RR 18, T 38.2°C; Wt 102.3 kg, Ht 6'0"

Skin

Warm and dry to touch, normal turgor, (–) for acanthosis nigricans

HEENT

PERRLA; EOMI; funduscopic exam deferred; TMs intact; oral mucosa clear

Neck/Lymph Nodes

Neck supple, no lymphadenopathy, thyroid smooth and firm without nodules

Chest

CTA bilaterally, no wheezes, crackles, or rhonchi

CV

RRR, no MRG, normal S₁ and S₂; no S₃ or S₄

Abd

(+) BS, no hepatosplenomegaly

Genit/Rect

Deferred

Ext

No pedal edema, pulses 2+ throughout

Neuro

No gross motor-sensory deficits present

■ Labs (Fasting)

Na 140 mEq/L	Ca 8.2 mg/dL	<i>Fasting lipid profile</i>
K 4.6 mEq/L	Mg 2.1 mEq/L	TC 190 mg/dL
Cl 103 mEq/L	AST 45 units/L	HDL 40 mg/dL
CO ₂ 23 mEq/L	ALT 40 units/L	LDL 121 mg/dL
BUN 19 mg/dL	T. bili 0.5 mg/dL	TG 145 mg/dL
SCr 1.6 mg/dL	T. prot 7.1 g/dL	
Glucose 119 mg/dL		
Hgb 12.0 mg/dL		
Hct 36%		

■ Assessment

Mr Smith is an obese African-American man who presents to pharmacotherapy clinic for follow-up about further optimization of this cardiovascular risk reduction therapy. He had a STEMI 6 months ago and has a significant family history of cardiovascular disease. He has uncontrolled dyslipidemia treated with atorvastatin and uncontrolled HTN treated with carvedilol, lisinopril, and chlorthalidone. He reports no drug allergies and rides the bike at the gym two to three days a week. He reports using acetaminophen, but no NSAIDs for occasional aches and pains. Patient is interested in what can be done to lower his risk of another heart attack as his dad has had two and his brother has had one. He consistently drinks one to two beers a day but has no history of tobacco use.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of dyslipidemia?
- What additional information is needed to fully assess this patient's dyslipidemia?

Assess the Information

- Assess the severity of dyslipidemia based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What economic, psychosocial, cultural, racial, and ethnic considerations are applicable to this patient?

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating dyslipidemia?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's dyslipidemia and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect and prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE: ALTERNATIVE THERAPY

Mr Smith is already taking garlic capsules, but he is not sure about the type or dose. Because you are making changes to his current prescription regimen, you need to investigate the advisability of continuing the garlic. Because Mr Smith is taking a statin drug as indicated, he should not take red yeast rice, a common supplement used for dyslipidemia, because it contains mevacolin K, a lovastatin analogue, and would be duplicative therapy. Would fish oil be a possible option for him? See Section 19 in this Casebook for questions about the use of garlic and fish oil for treatment of dyslipidemia.

■ SELF-STUDY ASSIGNMENTS

- Describe how this patient's other drug/disease interaction issues that are unrelated to dyslipidemia should be managed.
- What changes, if any, would you make to the pharmacotherapy regimen for this patient if he had presented at the initial visit with each of the following characteristics?
 - Cirrhosis of the liver
 - Stage 5 chronic kidney disease receiving hemodialysis
 - Significant alcohol use
 - Posttransplant
 - Human immunodeficiency virus

CLINICAL PEARL

Icosapent ethyl in a dose of 4 g per day added to statin therapy in patients with established ASCVD has demonstrated reduction in the composite outcome of cardiovascular death, nonfatal myocardial infarction, nonfatal stroke, coronary revascularization, or unstable angina in the REDUCE-IT trial. Addition of icosapent ethyl to statin therapy in patients with moderately elevated triglycerides (135–499 mg/dL) and established ASCVD may be warranted in addition to other lipid-lowering therapy (eg, ezetimibe, PCSK9 inhibitors) for secondary prevention.

REFERENCES

- Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA Guideline on the Management of Blood Cholesterol: a report of the

American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2019;73(24):3168–3209.

- Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults. *Hypertension* 2018 June;71(6):e13–e115.
- Eckel RH, Jakicic JM, Ard JD, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk: a report of the American College of Cardiology American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129:S76–S99.
- Jensen MD, Ryan DH, Apovian CM, et al. 2013 ACC/AHA/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines, and The Obesity Society. *J Am Coll Cardiol* 2014;63:2985–3023.
- Cannon CP, Blazing MA, Giugliano RP, et al. Ezetimibe added to statin therapy after acute coronary syndromes. *N Engl J Med* 2015;372:2387–2397.
- Sabatine MS, Giugliano RP, Keech AC, et al. Evolocumab and clinical outcomes in patients with cardiovascular Disease. *N Engl J Med* 2017;376:1713–1722.
- Schwartz GG, Steg PG, Szarek M, et al. Alirocumab and cardiovascular outcomes after acute coronary syndrome. *N Engl J Med* 2018;379:2097–2107.
- Bhatt DL, Steg PG, Miller M, et al. Cardiovascular risk reduction with icosapent ethyl for hypertriglyceridemia. *N Engl J Med* 2019;380:11–22.

15

STABLE ISCHEMIC HEART DISEASE

An Uphill Battle Level III

Alexander J. Ansara, PharmD, BCPS-AQ Cardiology

Regan M. Wade, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify modifiable risk factors for ischemic heart disease (IHD), and discuss the potential benefit to be gained by their modification in an individual patient.
- Optimize medical therapy in a patient with persistent angina considering response to current therapy and the presence of comorbidities.
- Assess clinical response to antianginal therapy by identifying relevant monitoring parameters for efficacy and adverse effects.
- Propose appropriate counseling points and follow-up recommendations for both stable and symptomatic patients with angina.

PATIENT PRESENTATION

■ Chief Complaint

“Doc, these drugs just aren’t working for my chest pain anymore.”

■ HPI

Jack Palmer is a 72-year-old man with coronary artery disease. He is an avid golfer and prefers to walk the course, but this is becoming progressively more difficult for him due to frequent angina. He has had two coronary artery bypass operations in the past. A coronary angiogram performed 1 month ago revealed significant disease in the RCA proximal to his graft, but this was considered high risk for angioplasty. His dose of isosorbide mononitrate was increased at that time from 60 to 120 mg once daily. This had no effect on his angina. He is still using about 30 nitroglycerin tablets a week, and these do relieve his chest pain. He reports that most often the chest discomfort comes on with activity, such as walking up slight inclines on the golf course. The discomfort is located in the center of his chest and rated 3–4/10 on average. He reports that the chest discomfort slowly fades as he slows his activity. He also complains of occasional lightheadedness with a pulse around 50 bpm and SBP near 100 mm Hg.

■ PMH

- Acute anterior wall MI with CABG surgery in 2009
- Posterior lateral MI in 1990 and PTCA to the circumflex at that time
- Dyslipidemia
- Chronic low back pain
- Depression

■ FH

Noncontributory for premature CAD

■ SH

Retired dairy farmer, lives with wife, drinks occasionally, previous smoker—quit in 1998

■ Meds

Carvedilol 6.25 mg PO twice daily
 Lisinopril 5 mg PO once daily
 Aspirin 325 mg PO once daily
 Isosorbide mononitrate, extended-release 120 mg PO once daily
 Diltiazem, extended-release 240 mg PO once daily
 St. John’s wort 300 mg PO three times daily
 Celecoxib 200 mg PO once daily
 Simvastatin 40 mg PO once daily
 Nitroglycerin 0.4 mg SL PRN

■ All

NKDA

■ ROS

No fever, chills, or night sweats. No recent viral illnesses. No shortness of breath; occasional cough with cold weather. No nausea, vomiting, diarrhea, constipation, melena, or hematochezia. No dysuria or hematuria. No myalgias or arthralgias.

■ Physical Examination

Gen

Pleasant, cooperative man in no acute distress

VS

BP 105/68, P 50, RR 22, T 36.4°C, Ht 5’11”, Wt 93 kg, waist circumference 43 in

Skin

Intact, no rashes or ulcers

HEENT

PERRL; EOMI; oropharynx is clear.

Neck

Supple, no masses; no JVD, lymphadenopathy, or thyromegaly

Lungs

Bilateral air entry is clear. No wheezes.

CV

RRR, S₁, S₂ normal; no murmurs or gallops; PMI palpated at left fifth ICS, MCL

Abd

Soft, NT/ND; bowel sounds normoactive

Genit/Rect

Heme (–) stool

Ext

No CCE; pulses 2+ throughout

Neuro

A&O × 3, CN II–XII intact; speech is fluent; no motor or sensory deficit; no facial asymmetry; tongue midline.

Labs

Na 137 mEq/L	Hgb 11.8 g/dL	<i>Fasting lipid profile</i>
K 4.8 mEq/L	Hct 35.1%	Chol 202 mg/dL
Cl 103 mEq/L	Plt $187 \times 10^3/\text{mm}^3$	LDL 121 mg/dL
CO ₂ 21 mEq/L	WBC $7.9 \times 10^3/\text{mm}^3$	HDL 38 mg/dL
BUN 24 mg/dL	MCV 77 μm^3	Trig 215 mg/dL
SCr 1.2 mg/dL	MCHC 29 g/dL	
Glu 98 mg/dL	Trop I 0.02 ng/mL × 2	

ECG

Sinus rhythm, first-degree AVB, 50 bpm, old AWMI, no ST–T wave changes noted, QT 406 milliseconds

Assessment

A 72-year-old man with poorly controlled angina on multiple medications, who is a poor candidate for angioplasty.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of chronic angina?
- What additional information is needed to fully assess this patient?

Assess the Information

- Assess the severity of the patient's chronic angina based on the subjective and objective information available.

- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating chronic angina?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's chronic angina and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Mr Palmer improved hemodynamically following a switch from diltiazem to amlodipine. However, due to continued frequent episodes of angina, his amlodipine was titrated to 10 mg once daily. He returned to cardiology clinic today, stating that his angina frequency has improved somewhat on the maximum dose of amlodipine but is still bothersome to him. His cardiologist decided to add ranolazine 500 mg twice daily to his regimen in an attempt to further decrease his angina frequency.

SELF-STUDY ASSIGNMENTS

- Summarize the potential role of L-arginine in the treatment of chronic angina.
- Describe the potential role of allopurinol in the treatment of chronic angina.

CLINICAL PEARL

The COURAGE trial made major headlines in 2007 by showing that coronary stenting with optimal medical therapy is no better at preventing future coronary events than optimal medical therapy alone in patients with stable coronary disease, potentially saving the US healthcare system \$5 billion a year.

REFERENCES

- Fihn SD, Gardin JM, Abrams J, et al. 2012 ACCF/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease. *J Am Coll Cardiol* 2012; 60:e44–e164.

2. Grundy S, Stone N, Bailey A et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. *J Am Coll Cardiol* 2019;73(24):3168–3209.
3. Antman E, Bennett J, Daugherty A, Furberg C, Roberts H, Taubert K. Use of nonsteroidal antiinflammatory drugs. *Circulation* 2007;115(12):1634–1642.
4. Smith SC, Benjamin EJ, Bonow RO, et al. AHA/ACCF secondary prevention and risk reduction therapy for patients with coronary and other atherosclerotic vascular disease: 2011 update. *J Am Coll Cardiol* 2011;58:2432–2446.
5. Boden WE, Finn AV, Patel D, et al. Nitrates as an integral part of optimal medical therapy and cardiac rehabilitation for stable angina: review of current concepts and therapeutics. *Clin Cardiol* 2012;35:263–271.
6. Bangalore S, Steg PG, Deedwania P, et al. β -Blocker use and clinical outcomes in stable outpatients with and without coronary artery disease. *JAMA* 2012;308:1340–1349.
7. Chaitman BR. Ranolazine for the treatment of chronic angina and potential use in other cardiovascular conditions. *Circulation* 2006;113:2462–2472.
8. Antithrombotic Trialists' Collaboration. Collaborative meta-analysis of randomised trials of antiplatelet therapy for prevention of death, myocardial infarction, and stroke in high risk patients. *BMJ* 2002;324:71–86.
9. CAPRIE Steering Committee. A randomised, blinded, trial of clopidogrel versus aspirin in patients at risk of ischaemic events (CAPRIE). *Lancet* 1996;348:1329–1339.
10. Heart Outcomes Prevention Evaluation Study Investigators. Effects of an angiotensin-converting-enzyme inhibitor, ramipril, on cardiovascular events in high risk patients. *N Engl J Med* 2000;342:145–153.

16

ACUTE CORONARY SYNDROME: ST-ELEVATION MYOCARDIAL INFARCTION

I Can't Handle the Pressure Level III

Kelly C. Rogers, PharmD, BCCP, FCCP, FACC

Robert B. Parker, PharmD, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine the goals of pharmacotherapy for patients with ST-segment elevation myocardial infarction (STEMI).
- Discuss interventional strategies for patients with STEMI, and understand the pharmacotherapeutic agents used with interventions.
- Design an optimal therapeutic plan for the management of STEMI, and describe how the selected drug therapy achieves the therapeutic goals.
- Identify appropriate parameters to assess the recommended drug therapy for both efficacy and adverse effects.
- Provide appropriate education to a patient who has suffered STEMI.

PATIENT PRESENTATION

Chief Complaint

"This is the worst pain I have ever felt in my life."

HPI

Gary Roberts is a 68-year-old man admitted to the ED complaining of chest pressure/pain lasting 20–30 minutes occurring at rest. He describes the pain as substernal, crushing, and pressure-like that radiates to his jaw and is accompanied by nausea and diaphoresis. The pain first started approximately 6 hours ago after he ate breakfast and was unrelieved by antacids or SL NTG $\times$ 3. He also states that he has been experiencing intermittent chest pain over the past 3–4 weeks with minimal exertion.

PMH

HTN
Type 2 DM
Dyslipidemia
CAD with PCI with a drug-eluting stent (DES) 3 years ago

FH

Father died from heart failure at age 75 and mother is alive at age 88 with HTN and type 2 DM.

SH

(+) Tobacco $\times$ 20 years but quit when he received his DES 3 years ago; drinks beer usually on weekends; denies illicit drug use

Meds

Aspirin 81 mg PO daily
Metoprolol tartrate 25 mg PO BID
Atorvastatin 40 mg PO QHS
Metformin 500 mg PO BID
SL NTG PRN CP

All

NKDA

ROS

Positive for some baseline CP on exertion for the past 3–4 weeks, now with CP at rest

Physical Examination

Gen

WDWN man, A&O $\times$ 3, still with ongoing chest pain, somewhat anxious

VS

BP 145/92, P 89, RR 18, T 37.1°C; Wt 95 kg, Ht 5'10"

HEENT

PERRLA, EOMI, fundi benign; TMs intact

Neck

No bruits; mild JVD; no thyromegaly

Lungs

Few dependent inspiratory crackles; bibasilar rales; no wheezes

CV

Normal S₁ and S₂, no MRG

Abd

Soft, nontender; liver span 10–12 cm; no bruits

Genit/Rect

Deferred

MS/Ext

Normal ROM; muscle strength on right 5/5 UE/LE; on left 4/5 UE/LE; pulses 2+; no femoral bruits or peripheral edema

Neuro

CNs II–XII intact; DTRs decreased on left; negative Babinski sign

Labs

Na 134 mEq/L	Ca 9.8 mg/dL	Hgb 14.0 g/dL	<i>Fasting lipid profile</i>
K 4.4 mEq/L	Mg 2.0 mg/dL	Hct 44%	T. chol 159 mg/dL
Cl 102 mEq/L	PO ₄ 2.4 mg/dL	WBC 5.0 × 10 ³ /mm ³	Trig 92 mg/dL
CO ₂ 23 mEq/L	AST 22 units/L	Plt 268 × 10 ³ /mm ³	LDL 105 mg/dL
BUN 15 mg/dL	ALT 30 units/L	PT 12.5 s	HDL 36 mg/dL
SCr 1.0 mg/dL	Alk Phos	aPTT 32.4 s	A1C 7.6%
Glu 140 mg/dL	75 units/L	INR 1.0	NT-pro-BNP
	Troponin I		400 pg/mL
	8.6 ng/mL		

ECG

ST-segment elevation of 2–3 mm in leads II, III, and aVF (Fig. 16-1)

Assessment

Acute inferior STEMI

QUESTIONS**Collect Information**

1. What subjective and objective findings in this patient are consistent with acute STEMI?

Assess the Information

- 2.a. What risk factors for the development of coronary artery disease are present in this patient?
- 2.b. Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What pharmacotherapeutic alternatives are available for reperfusion in STEMI?
- 3.c. What nonpharmacologic alternatives are available for reperfusion in STEMI?
- 3.d. What is the role of anticoagulant therapy during PCI, and how should these therapies be monitored?
- 3.e. What is the role of antiplatelet therapy before, during, and after PCI, and how should these therapies be monitored?
- 3.f. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for the initial (first 24–48 hours) management of this patient's STEMI. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

CLINICAL COURSE

The patient received aspirin, morphine, oxygen, IV unfractionated heparin (UFH), IV nitroglycerin, and oral metoprolol. An

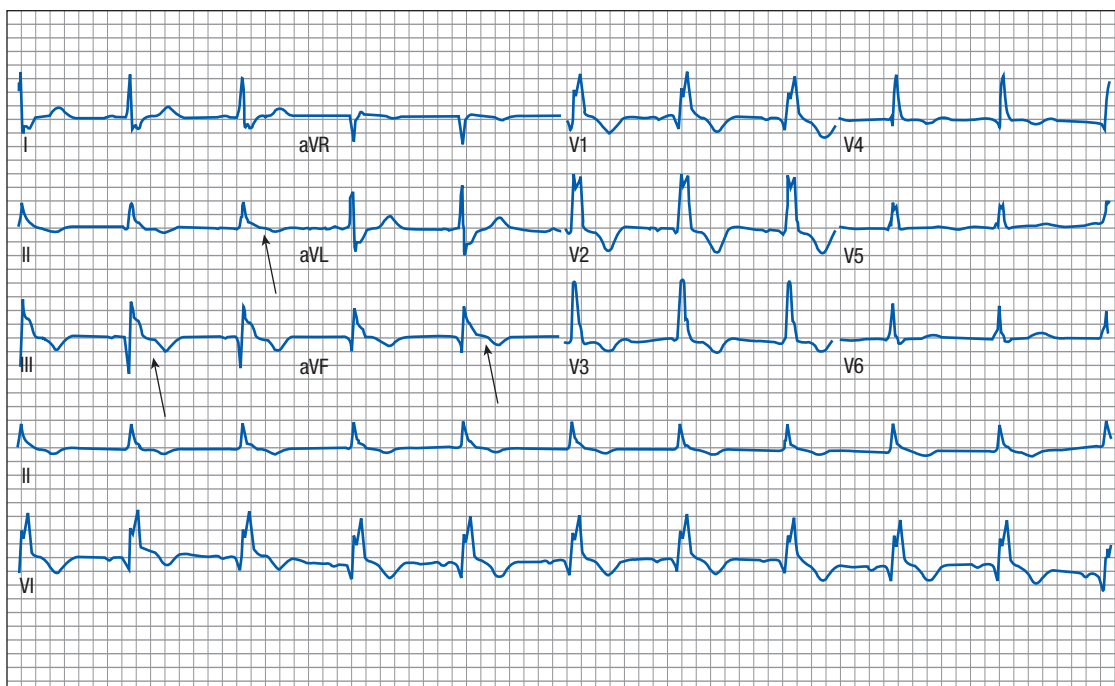


FIGURE 16-1. ECG taken on arrival in the emergency department showing ST-segment elevation (arrows) in leads II, III, and aVF, consistent with acute inferior myocardial infarction. Right bundle branch block is also present in leads V₁–V₃.

interventional cardiologist was consulted and discussed with the patient the need for primary PCI to restore blood flow to the heart. Within 1 hour of his arrival to the ED, the patient was transported to the cardiac catheterization lab. The catheterization revealed a 60–70% proximal stenosis in the RCA with thrombus. Additionally, there was a 40% mid-LAD obstruction and 20–30% distal circumflex disease, neither of which was amenable to PCI. In the catheterization lab, the patient was loaded with oral ticagrelor 180 mg, anticoagulation was continued with UFH, and an eptifibatide infusion was started. The following day, the echocardiogram reported an LVEF of 35%. The remainder of the patient's hospital stay was uncomplicated, and he was discharged 4 days post-MI.

- 3.g. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for the post-discharge management of this patient's CAD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. It is not uncommon for patients with coronary atherosclerotic disease to have concomitant comorbid conditions such as diabetes mellitus. Review recent clinical trials that demonstrate improvement in cardiovascular outcomes with sodium-glucose cotransporter 2 (SGLT2) inhibitors.
2. A patient comes into your pharmacy with a prescription for clopidogrel 75 mg daily and a bottle of aspirin. He tells you that he received a drug-eluting stent in one of his coronary arteries and asks you how long he is supposed to take the clopidogrel. Based on current guideline recommendations on duration of dual-antiplatelet therapy, how should you respond to this patient?
3. After an ACS episode, patients with increased LDL cholesterol levels despite high-intensity statin therapy are at increased risk for recurrent ischemic events. Review recent clinical trials that evaluate the role of proprotein convertase subtilisin-kexin type 9 (PCSK9) inhibitors in reducing cardiovascular events after ACS.

CLINICAL PEARL

Opioids such as morphine or fentanyl are frequently administered to patients with ACS undergoing PCI. Numerous small studies show that these agents delay the absorption of clopidogrel, ticagrelor,

and prasugrel resulting in decreased inhibition of platelet activity. Although the impact of this drug interaction on clinical outcomes remains to be determined, clinicians should be cautious about combining these opioids with P2Y₁₂ inhibitors.

REFERENCES

1. O'Gara PT, Kushner FG, Ascheim DD, et al. 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;127:e362–e425.
2. Levine GN, Bates ER, Blankenship JC, et al. 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines and the Society for Cardiovascular Angiography and Interventions. *Circulation* 2011;124:e574–e651.
3. Fleg JL, Forman DE, Berra K, et al. Secondary prevention of atherosclerotic cardiovascular disease in older adults: a scientific statement from the American Heart Association. *Circulation* 2013;128:2422–2473.
4. Guimarães PO, Tricoci P. Ticagrelor, prasugrel, or clopidogrel in ST-segment elevation myocardial infarction: which one to choose? *Expert Opin Pharmacother* 2015;16(13):1983–1995. doi: 10.1517/14656566.2015.1074180. Epub 2015 Jul 29.
5. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2011 ACCF/AHA/SCAI guideline for percutaneous coronary intervention, 2011 ACCF/AHA guideline for coronary artery bypass graft surgery, 2012 ACC/AHA/ACP/AATS/PCNA/SCAI/STS guideline for the diagnosis and management of patients with stable ischemic heart disease, 2013 ACCF/AHA guideline for the management of ST-elevation myocardial infarction, 2014 ACC/AHA guideline for the management of patients with non-ST-elevation acute coronary syndromes, and 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *J Am Coll Cardiol* 2016;68:1082–1115. <http://dx.doi.org/10.1016/j.jacc.2016.Febuary.19.2019>.
6. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. *J Am Coll Cardiol* 2019;73(24):3168–3209.
7. Lloyd-Jones DM, Morris PB, Ballantyne CM, et al. 2016 ACC expert consensus decision pathway on the role of non-statin therapies for LDL-cholesterol lowering in the management of atherosclerotic cardiovascular disease risk: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Documents. *J Am Coll Cardiol* 2016;68:92–125.
8. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127–248.
9. American Diabetes Association. Standards of medical care in diabetes-2019. *Diabetes Care* 2019; 42(Suppl. 1):S1–S193. Available at: https://care.diabetesjournals.org/content/diacare/suppl/2018/12/17/42.supplement_1.DC1/DC_42_S1_2019_UPDATED.pdf. October 15, 2019.
10. FDA Drug Safety Communication: FDA strengthens warning that non-aspirin nonsteroidal anti-inflammatory drugs (NSAIDs) can cause heart attacks or strokes. Available at: <http://www.fda.gov/Drugs/DrugSafety/ucm451800.htm>. Accessed December 10, 2015.

17

PERIPHERAL ARTERIAL DISEASE

Cold Feet? Level III

Tracy J. Costello, PharmD, BCPS

Tracy L. Sprunger, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify risk factors for peripheral arterial disease (PAD).
- Describe the symptoms and diagnosis of PAD.
- Recommend appropriate nonpharmacologic treatment strategies for PAD, including risk factor modification, exercise, and revascularization.
- Design an appropriate pharmacologic treatment plan for a patient with PAD.
- Provide appropriate education to a patient with PAD.

PATIENT PRESENTATION

■ Chief Complaint

"I am having pain in both legs and in my left foot."

■ HPI

Angie Belden is a 56-year-old woman with hypertension, diabetes, hypothyroidism, dyslipidemia, and a history of bilateral leg weakness for the previous year. She reports to her primary care provider today with increased numbness and weakness when she walks. She reports that it is painful to walk even for 4–5 minutes and that her legs are often weak and "give out." She is concerned because she lives alone and is responsible for walking her beloved Labrador retriever, Jules. Her symptoms tend to get better when she is able to rest and prop her feet up. She would also like a "checkup" on her other chronic conditions as well.

■ PMH

HTN
Diabetes
Hypothyroidism
Dyslipidemia

■ FH

Mother died of a stroke at the age of 67; father died of pneumonia at the age of 62.

■ SH

Works as a biller in a dentist's office; has one child; lives alone; smokes 1 ppd × 25 years; denies ETOH and illicit drug use; has one dog at home

■ Meds

Aspirin 81 mg PO daily
Atenolol 50 mg PO daily
Gabapentin 600 mg PO TID
Hydrocodone/acetaminophen 7.5/500 mg q 6 hours PRN pain
Levothyroxine 75 mcg PO daily
Metformin 1000 mg PO BID
Simvastatin 20 mg PO daily
Hydrochlorothiazide 25 mg PO daily

■ All

NKDA

■ ROS

The patient complains of dyspnea on exertion, lower extremity muscle aches, and muscle weakness. Denies chest pains, palpitations, syncope, and orthopnea. Denies nausea, vomiting, diarrhea, constipation, change in bowel habits, abdominal pain, or melena. Denies transient paralysis, seizures, syncope, and tremors.

■ Physical Examination

Gen

The patient is a Caucasian woman in NAD. She appears older than her stated age.

VS

BP 149/87, P 73, RR 17, T 98.2°F; Wt 85 kg, Ht 5'4"

Skin

Distal to midshin with shiny-appearing skin, skin atrophy, and lack of hair growth. No evidence of skin breakdown or ulceration.

HEENT

PERRLA; conjunctivae and lids normal; TM intact; normal dentition, no gingival inflammation, no labial lesions; tongue normal, posterior pharynx without erythema or exudate

Neck/Lymph Nodes

Supple, no masses, trachea midline; no carotid bruit; no lymphadenopathy or thyromegaly

Lungs/Thorax

No rales, rhonchi, or wheezes; no intercostal retractions or use of accessory muscles

CV

RRR, S₁, S₂ normal; no murmurs, rubs, or gallops; no thrill or palpable murmurs, no displacement of PMI

Abd

Soft, nontender, no masses, bowel sounds normal; no enlargement or nodularity of liver or spleen

Genit/Rect

Deferred

MS/Ext

Normal gait; no clubbing, cyanosis, petechiae, or nodes; normal ROM and strength, good stability, and no joint enlargement or tenderness; pedal pulses 1+, symmetric

Neuro

CN II–XII grossly intact; DTRs 2+, no pathologic reflexes; sensory and motor levels intact

Labs

Na 137 mEq/L	Hgb 12.7 g/dL	WBC $6.3 \times 10^3/\text{mm}^3$
K 3.9 mEq/L	Hct 34.4%	CPK 71 IU/L
Cl 97 mEq/L	Plt $313 \times 10^3/\text{mm}^3$	AST 22 IU/L
CO ₂ 24 mEq/L	TSH 1.12 mIU/L	ALT 30 IU/L
BUN 12 mg/dL	TC 224 mg/dL	
SCr 1.0 mg/dL	TG 220 mg/dL	
Glu 99 mg/dL	LDL 140 mg/dL	
A1C 6.3%	HDL 40 mg/dL	

Lower Extremity Arterial Doppler

Ankle–brachial index (ABI)—right: 0.53; left: 0.62

Assessment

A 56-year-old woman with a significant smoking history presents with uncontrolled hypertension, dyslipidemia, and new symptoms of intermittent claudication (IC).

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of peripheral arterial disease?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of peripheral arterial disease based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating peripheral arterial disease?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's peripheral arterial disease and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Review the recommendations for dual antiplatelet therapy for the treatment of PAD. Would a patient benefit from combination therapy?
2. Perform a literature search to determine the role of warfarin and non–vitamin K oral anticoagulant agents for the management of PAD.

CLINICAL PEARL

Although cilostazol has antiplatelet effects, it is currently not recommended for the prevention of atherosclerotic events or the treatment of atherosclerotic disease.

REFERENCES

1. Gerhard-Herman MD, Gornik HL, Barrett C, et al. 2016 ACCF/AHA guideline on the management of patients with lower extremity peripheral artery disease. *Circulation* 2017;135:e726–e779.
2. ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127–e248.
3. American Diabetes Association. Standards of medical care in diabetes—2019. *Diabetes Care* 2018;42 (Suppl 1):S1–S194.
4. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol. *J Am Coll Cardiol* 2019;73(24):3168–3209.
5. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an endocrine society clinical practice guideline. *J Clin Endocrinol Metab* 2015;100:342–362.
6. Bonaca MP, Scirica BM, Creager MA, et al. Vorapaxar in patients with peripheral artery disease: results from TRA2D P-TIMI 50. *Circulation* 2013;127:1522–1529.
7. Eikelboom JW, Connolly SJ, Bosch J, et al; for the COMPASS Investigators. Rivaroxaban with or without aspirin in chronic cardiovascular disease. *N Engl J Med* 2017;377(14):1319–1330.

18

HEART FAILURE WITH REDUCED EJECTION FRACTION

Cross My Heart and Hope to Live Level III

Julia M. Koehler, PharmD, FCCP

Alison M. Walton, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of heart failure.
- Develop a pharmacotherapeutic plan for treatment of heart failure with reduced ejection fraction (HF/rEF).
- Outline a monitoring plan for heart failure that includes both clinical and laboratory parameters.

PATIENT PRESENTATION

■ Chief Complaint

"I've been more short of breath lately. I can't seem to walk as far as I used to, and either my feet are growing or my shoes are shrinking!"

■ HPI

Rosemary Quincy is a 68-year-old African-American woman who presents to her family medicine physician for evaluation of her shortness of breath and increased swelling in her lower extremities. She reports that her shortness of breath has been gradually increasing over the past 4 days. She has noticed that her shortness of breath is particularly worse when she is lying in bed at night, and she has to prop her head up with three pillows in order to sleep. She also reports exertional dyspnea that is usual for her, but especially worse over the past couple of days.

■ PMH

Hypertension × 20 years
CHD with history of MI in 2005 (PCI performed and bare metal stents placed in LAD and RCA)
Heart failure (NYHA FC III)
Type 2 DM × 25 years
Atrial fibrillation
COPD (GOLD 3, group D)
CKD (stage 4)

■ FH

Father died of lung cancer at age 71, mother died of MI at age 73.

■ SH

Reports occasional alcohol intake. States she has been trying to follow her low-cholesterol and low-sodium diet. Former smoker (35 pack-year history; quit approximately 10 years ago).

■ Meds

Valsartan 160 mg PO BID
Furosemide 40 mg PO BID
Warfarin 2.5 mg PO once daily
Carvedilol 3.125 mg PO BID
Pioglitazone 30 mg PO once daily
Glimepiride 2 mg PO once daily
Potassium chloride 20 mEq PO once daily
Atorvastatin 40 mg PO once daily
Aspirin 81 mg PO once daily
Albuterol MDI, two inhalations by mouth q 4–6 hours PRN shortness of breath
Tiotropium DPI 18 mcg, one inhalation by mouth daily
Fluticasone/salmeterol DPI 250 mcg/50 mcg, one inhalation by mouth BID

■ All

Lisinopril (cough)

■ ROS

Approximate 7-kg weight gain over the past week. No fever or chills. Denies any recent chest pain, palpitations, or dizziness. Reports worsening shortness of breath with exertion and three-pillow orthopnea. Describes a chronic, dry (nonproductive), hacking cough, which she describes as usual without recent worsening. No abdominal pain, nausea, constipation, or change in bowel habits. Denies joint pain or weakness.

■ Physical Examination

Gen

African-American woman in moderate respiratory distress

VS

BP 134/76 (sitting; repeat 138/78), HR 65 (irreg irreg), RR 24, T 37°C, O₂ sat 90% RA, Ht 5'5", Wt 79 kg (Wt 1 week ago: 72 kg)

Skin

Color pale and diaphoretic; no unusual lesions noted

HEENT

PERRLA; lips mildly cyanotic; dentures

Neck

(+) JVD at 30° (7 cm); no lymphadenopathy or thyromegaly

Lungs/Thorax

Crackles bilaterally, 2/3 of the way up; no expiratory wheezing

Heart

Irregularly irregular; (+) S₃; displaced PMI

Abd

Soft, mildly tender, nondistended; (+) HJR; no masses, mild hepatosplenomegaly; normal BS

Genit/Rect

Guaiac (–), genital examination not performed

MS/Ext

3+ pitting pedal edema bilaterally; radial and pedal pulses are of poor intensity bilaterally

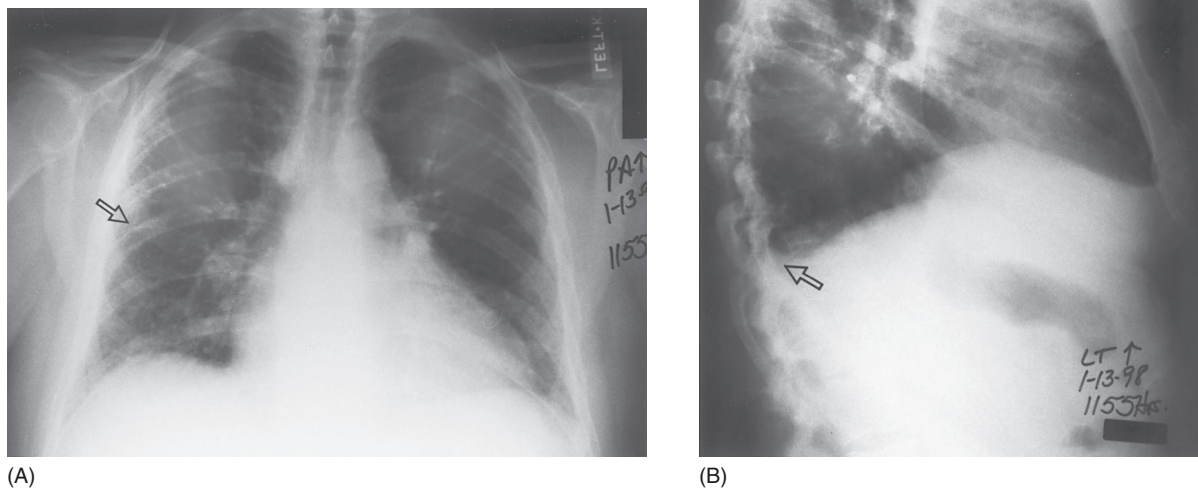


FIGURE 18-1. A. PA CXR demonstrates increased vascular markings representative of interstitial edema, with some early alveolar edema. The arrow points out fluid lying in the fissure of the right lung. Note the presence of cardiomegaly. B. Lateral view of CXR. Arrow points out the presence of pulmonary effusion.

Neuro

A & O $\times$ 3, CNs intact. No motor deficits.

Labs

Na 131 mEq/L	Hgb 13 g/dL	Mg 1.9 mEq/L	INR 2.3
K 3.5 mEq/L	Hct 40%	Ca 9.3 mg/dL	A1C 6.1%
Cl 99 mEq/L	Plt $192 \times 10^3/\text{mm}^3$	Phos 4.3 mg/dL	
CO ₂ 28 mEq/L	WBC $9.1 \times 10^3/\text{mm}^3$	AST 34 IU/L	
BUN 32 mg/dL		ALT 27 IU/L	
SCr 2.3 mg/dL (baseline SCr 2.1 mg/dL)			
eGFR 20 mL/minute/1.73 m ²			
Glucose 124 mg/dL			
BNP 776 pg/mL (BNP drawn 2 months prior: 474 pg/mL)			

ECG

Atrial fibrillation, LVH

Chest X-Ray

PA and lateral views (Fig. 18-1) show evidence of congestive failure with cardiomegaly, interstitial edema, and some early alveolar edema. There is a small right pleural effusion.

No evidence of infiltrates; evidence of pulmonary edema suggestive of congestive heart failure; enlarged cardiac silhouette.

Echocardiogram

LVH, reduced global left ventricular systolic function, estimated EF 20%; evidence of impaired ventricular relaxation, stage 1 diastolic dysfunction

Assessment

Admit to hospital for acute exacerbation of heart failure

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of heart failure?
- What additional information is needed to fully assess this patient's heart failure?

Assess the Information

- Assess the type and severity of heart failure based on the subjective and objective information available.
- Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating an acute exacerbation of heart failure and for chronic management of heart failure with reduced ejection fraction?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's heart failure and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect and prevent adverse events?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Develop a table illustrating the recommended target doses for ACE inhibitors, angiotensin II receptor blockers, an angiotensin receptor-neprilysin inhibitor, and β -blockers in patients with heart failure with reduced EF.
2. Research the topic of diuretic resistance, and write a report describing the phenomenon and methods used to overcome it.
3. Review the guidelines and evidence describing the role of routine BNP monitoring in patients with heart failure.

CLINICAL PEARL

The presence of pitting edema is associated with a substantial increase in body weight; it typically takes a weight gain of 10 lb to result in the development of pitting edema.

REFERENCES

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2013;62:e147–e239. doi: 10.1016/j.jacc.2013.05.019.
2. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation* 2017;136:e137–e161.
3. McMurray JV, Packer M, Desai AS, et al. Angiotensin-neprilysin inhibition versus enalapril in heart failure. *N Engl J Med* 2014;371:993–1004.
4. Yancy CW, Januzzi JL Jr, Allen LA, et al. 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Decision Pathways. *J Am Coll Cardiol* 2018;71(2):201–230.
5. Mentz RJ, Wojdyla D, Fiuzat M, Chiswell K, Fonarow GC, O'Connor CM. Association of beta-blocker use and selectivity with outcomes in patients with heart failure and chronic obstructive pulmonary disease (from OPTIMIZE-HF). *Am J Cardiol* 2013;111:582–587.
6. Swedberg K, Komajda M, Bohm M, et al. Ivabradine and outcomes in chronic heart failure (SHIFT): a randomised placebo-controlled study. *Lancet* 2010;367:875–885.
7. Page RL, O'Bryant CL, Cheng D, et al. Drugs that may cause or exacerbate heart failure: a scientific statement from the American Heart Association. *Circulation* 2016;134:e32–e69.
8. American Diabetes Association. Cardiovascular disease and risk management: standards of medical care in diabetes—2019. *Diabetes Care* 2019;42(1):S103–S123.
9. Jackevicius CA, Page RL, Buckley LF, Jennings DL, Nappi JM, Smith AJ. Key articles and guidelines in the management of heart failure: 2018 update. *J Pharm Pract* 2019;32(1):77–92.

19

HEART FAILURE WITH PRESERVED EJECTION FRACTION

A Balancing Act Level II

Joel C. Marrs, PharmD, FAHA, FASHP, FCCP, FNLA, BCPS, BCACP, BCCP, CLS

Sarah L. Anderson, PharmD, FCCP, BCPS, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of heart failure with preserved ejection fraction (HFpEF).
- Develop a pharmacotherapeutic plan for treatment of HFpEF.
- Outline a monitoring plan for HFpEF that includes both clinical and laboratory parameters.
- Initiate, titrate, and monitor guideline-directed medical therapy (GDMT) in HFpEF when indicated.

PATIENT PRESENTATION

Chief Complaint

“Why can’t we get my weight stabilized?”

HPI

Lawrence Smith is a 67-year-old man who presents to the ED with shortness of breath and bilateral lower extremity edema. He reports his symptoms started approximately 3 weeks ago. He noted that he was gaining about 1–2 lb daily and gained approximately 25 lb of weight over the month prior to admission. He attempted to use his albuterol/ipratropium MDI for relief of his shortness of breath symptoms at home without improvement. As his symptoms of edema and shortness of breath worsened, he called his primary care physician, who increased his furosemide dose over the phone to 80 mg twice daily more than 1 week ago. In the ED he was noted to be hypoxic with an increased oxygen need from 2 to 4 L by nasal cannula. He was given one dose of IV furosemide 80 mg with minimal improvement in his symptoms and then admitted to the medicine service for further evaluation and management.

PMH

CAD (s/p STEMI 10 years ago)
COPD $\times$ 5 years
HFpEF $\times$ 6 years (last hospitalization 4 months ago)
Dyslipidemia $\times$ 15 years
HTN $\times$ 25 years
Type 2 DM $\times$ 5 years

FH

Father is alive at age 88 with type 2 DM; mother is alive at age 87 and has HTN and dyslipidemia; two brothers (age 60 and 64) are alive and both have type 2 DM and HTN.

■ SH

History of tobacco use (40 pack-year history), but quit 5 years ago. Denies any alcohol or substance abuse. Lives alone.

■ Meds

Albuterol/ipratropium MDI, two puffs inhaled Q 6 H PRN
 Aspirin 81 mg PO daily
 Clopidogrel 75 mg PO daily
 Lisinopril 40 mg PO daily
 Carvedilol 12.5 mg PO BID
 Furosemide 80 mg PO BID (previously 40 mg PO BID)
 Amlodipine 5 mg PO daily
 Metformin 1000 mg PO BID
 Nitroglycerin 0.4 mg SL q 5 minutes PRN chest pain
 Potassium chloride 20 mEq PO daily
 Rosuvastatin 20 mg PO daily
 Seasonal influenza vaccine (previous year)

■ All

NKDA

■ ROS**Gen**

Patient reports a recent 25-lb weight gain over the past month

CV

No complaints of chest pain

Resp

Reports an increase in shortness of breath from baseline over the last month and dyspnea on exertion

GI

No recent changes noted in bowel habits

GU

No complaints

MS

No complaints of MS pain or weakness

Neuro

No complaints

■ Physical Examination**Gen**

Patient with 25-lb weight gain over past month with increased shortness of breath

VS

BP 150/82, P 64 (regular), RR 26, T 36.9°C; Wt 102 kg (usual weight 90 kg), Ht 5'10", oxygen saturation of 95% on 4-L nasal cannula

Skin

Chronic venous stasis changes on bilateral lower extremities and 3+ edema to the knees bilaterally

HEENT

PERLLA, EOMI, fundi were not examined. Normocephalic, atraumatic. Nasal cannula in place.

Neck

(+) JVD at 30° (6 cm). No carotid bruit is appreciated. No lymphadenopathy or thyromegaly.

Lungs/Thorax

Respirations are even. Crackles noted in the bilateral lung bases.

Heart

RRR. No murmurs, rubs, or gallops.

Abd

Obese with a nontender, nondistended abdomen; hypoactive bowel sounds

Genit/Rect

Guaic (-), genital examination not performed

MS/Ext

3+ pitting pedal edema bilaterally; radial and pedal pulses are of poor intensity bilaterally; grip strength even.

Neuro

A&O × 3; CNs intact; DTR intact

■ Labs

Na 138 mEq/L	Hgb 15.3 g/dL	Mg 1.7 mEq/L	CK 20 IU/L
K 4.0 mEq/L	Hct 47.2%	Ca 9.1 mg/dL	CK-MB 0.8 IU/L
Cl 103 mEq/L	Plt 298 × 10 ³ /mm ³	AST 60 IU/L	PT 12.6 s
CO ₂ 26 mEq/L	WBC 6.4 × 10 ³ /mm ³	ALT 60 IU/L	INR 1.1
BUN 30 mg/dL	Troponin I 0.5 ng/mL	Alk phos 80 IU/L	TSH 1.12 mIU/L
SCr 1.2 mg/dL		GGT 24 IU/L	A1C 7.5%
Glucose		T. bili 0.2 mg/dL	
108 mg/dL			
BNP			
2000 pg/mL			

■ ECG

Sinus rate of 66; QRS 0.08; no ST-T wave changes; low voltage

■ CXR

PA and lateral views show evidence of interstitial edema and some early alveolar edema.

■ Assessment

Decompensated heart failure with pulmonary and lower extremity edema

■ CLINICAL COURSE

The patient was admitted to a telemetry unit. The patient has a known history of HFpEF (EF 52%) per an echocardiogram from 6 months ago. A 2D echocardiogram was obtained today to evaluate the patient's current LV and valvular function. Results revealed evidence of impaired ventricular relaxation and elevated left atrial filling pressures consistent with grade III diastolic dysfunction. EF was estimated at 53%; there was no evidence of mitral stenosis or pericardial disease. A dilated inferior vena cava suggests increased right atrial pressure. Moderate pulmonary HTN is evident.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of HFpEF?
- 1.b. What additional information is needed to fully assess this patient's HFpEF?

Assess the Information

- 2.a. Assess the severity of HFpEF based on subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethnic considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating HFpEF?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's HFpEF and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect and prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Describe the common causes of HFpEF.
2. Describe how you would evaluate and monitor this patient's quality of life.
3. Evaluate whether evidence exists to support the role of eplerenone in HFpEF.

CLINICAL PEARL

Patients with heart failure who require chronic diuretic therapy with furosemide and are unable to maintain fluid balance (eg, multiple hospitalizations for fluid overload despite maximized furosemide as an outpatient) may need their diuretic therapy optimized by switching to another loop diuretic with better oral bioavailability (eg, torsemide or bumetanide).

REFERENCES

1. Tang WH, Francis GS, Morrow DA, et al. National Academy of Clinical Biochemistry Laboratory Medicine Practice Guidelines: clinical utilization of cardiac biomarker testing in heart failure. *Circulation* 2007;116:e99–e109.
2. Yancy C, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;128:eh240–e327.
3. Yancy CW, Jessup M, Bozkurt B et al. 2016 ACC/AHA/HFSA focused update on new pharmacological therapy for heart failure: an update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *J Am Coll Cardiol* 2016;68:1476–1488.
4. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation* 2017 August 8;136(6):e137–e161.
5. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018 November 8. pii: S0735–1097(18)39034–X.
6. Basaraba JE, Barry AR. Pharmacotherapy of heart failure with preserved ejection fraction. *Pharmacotherapy* 2015;35:351–360.
7. Hernandez AF, Hammill BG, O'Connor CM, Schulman KA, Curtis LH, Fonarow GC. Clinical effectiveness of beta-blockers in heart failure: findings from the OPTIMIZE-HF (organized program to initiate lifesaving treatment in hospitalized patients with heart failure) registry. *J Am Coll Cardiol* 2009;53:184–192.
8. Nichols GA, Reynolds K, Kimes TM, Rosales AG, Chan WW. Comparison of risk of re-hospitalization, all-cause mortality, and medical care resource utilization in patients with heart failure and preserved versus reduced ejection fraction. *Am J Cardiol* 2015;116:1088–1092.
9. Pitt B, Pfeffer MA, Assmann SF, et al. Spironolactone for heart failure with preserved ejection fraction. *N Engl J Med* 2014;370:1383–1392.
10. Mentz RJ, Wojdyla D, Fiuzat M, et al. Association of beta-blocker use and selectivity with outcomes in patients with heart failure and chronic obstructive pulmonary disease (from OPTIMIZE-HF). *Am J Cardiol* 2013;111:582–587.

20

ACUTE DECOMPENSATED HEART FAILURE

Don't Be Such a Busy Body Level II

Kena J. Lanham, PharmD, BCPS, BCGP, BCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs and symptoms of acute decompensated heart failure (ADHF).
- Classify a patient into the appropriate hemodynamic subset based on symptoms and clinical presentation.

- List goals of therapy for treating ADHF.
- Develop a pharmacotherapeutic plan for treating a patient with ADHF in the hemodynamic subset presented.
- Outline a monitoring plan for treating a patient with ADHF in the hospital.

PATIENT PRESENTATION

■ Chief Complaint

“I can no longer lie down flat because I can’t breathe and I’ve gained 5 pounds in 3 days.”

■ HPI

Bizzy Fuller is a 64-year-old woman with a history of ischemic cardiomyopathy with last known EF 25% (ECHO 1.5 years ago). She presents to the emergency department with approximately 2–3 days of increasing shortness of breath, and she reports having gained approximately 5 lb over the past 3 days. She also notes that she has had increasing leg swelling over the same time period. Over the past week, the patient has noted increasing bloating in her abdomen and has felt slightly nauseated. She has had problems with diarrhea and constipation since her cholecystectomy several months ago. She has been on a fiber supplement, from which she has derived some benefit. She states that she had been on torsemide many years ago but for an unknown reason was switched to furosemide.

■ PMH

CAD (status postmyocardial infarction $\times$ 2 in early 2000s; CABG in 2000, PCI in May 2002)
 Paroxysmal ventricular tachycardia (status post-ICD placement in 2011)
 Obstructive sleep apnea
 Diabetes mellitus type 2
 Depression
 Dyslipidemia
 Mild osteoarthritis
 GERD
 Seasonal allergies

■ FH

Both her mother and father died of MI in their 60s.

■ SH

Patient is a happily married, retired school teacher and is fully functional with ADLs. She is an occasional alcohol drinker (two to three drinks per week) and has a 30 pack-year history, but quit smoking approximately 12 years ago.

■ Meds

Fexofenadine 60 mg orally BID
 Insulin detemir 40 units subcutaneously at bedtime
 Insulin aspart 7 units subcutaneously before each meal
 Aspirin 81 mg orally once daily
 Carvedilol 12.5 mg orally BID
 Duloxetine 30 mg orally once daily
 Fluticasone nasal spray 50 mcg one spray BID
 Lasix 80 mg orally BID
 Valsartan 80 mg orally twice daily

Meloxicam 15 mg orally daily PRN joint pain
 Nitroglycerin 0.4 mg sublingually PRN chest pain
 Atorvastatin 40 mg orally QHS
 Ranitidine 150 mg orally BID

■ All

NKDA

■ ROS

She denies any fevers, chills, sweats, or coughs. She states that her diet has not changed recently, and she tries to watch her salt intake, but she states that she has been nonadherent to her medication regimen for the past 2 days, stating, “I have been too busy to take my medicine.” She denies any significant chest pain and also denies any history of additional coronary intervention procedures since 2002. All others negative.

■ Physical Examination

Gen

A 64-year-old obese, Caucasian woman in mild respiratory distress

VS

BP 186/92 mm Hg, P 68 bpm, RR 32 on admission (16 currently), oxygen saturation 86–92%; T 97.5°F; Ht 5’3”; Wt 87.4 kg

Skin

Warm and diaphoretic

HEENT

NC/AT with trachea midline

Neck/Lymph Nodes

Neck supple, (+) JVD, no bruits, no thyromegaly

Lungs/Thorax

Crackles in the bases bilaterally

Breasts

Normal

CV

Regular rate and rhythm without any murmurs, gallops, or rubs

Abd

Soft, nondistended, nontender

Genit/Rect

Deferred

MS/Ext

Extremities reveal 2+ pitting edema; all pulses palpable

Neuro

A&O $\times$ 3, CNs intact, history of depression but no apparent symptoms at present

■ Labs

Na 131 mEq/L
K 3.7 mEq/L
Cl 101 mEq/L
CO₂ 20 mEq/L
BUN 24 mg/dL
SCr 1.7 mg/dL
Glu 96 mg/dL
Ca 9.6 mg/dL

BNP 2867 pg/mL
Troponin 0.03 ng/mL
WBC $8.7 \times 10^3/\text{mm}^3$
Hgb 14.1 g/dL
Hct 42.3%
Plt $226 \times 10^3/\text{mm}^3$
A1C 6.5%

■ Chest X-Ray

Interstitial infiltrates throughout, tiny pleural effusions bilaterally; mild cardiomegaly; implanted defibrillator leads are at the right atrial appendage and right ventricular apex. No focal pneumonia, pneumothorax, or evidence of frank pulmonary edema.

■ ECG

Sinus rhythm with occasional premature ventricular complexes; no acute ischemia indicated

■ Assessment

Congestive heart failure exacerbation due to medication non-adherence; poorly controlled hypertension. Admit for medical management.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of ADHF?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of ADHF based on the subjective and objective information available.
- 2.b. Create a list of BF's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy regarding treatment of ADHF?
- 3.b. What nondrug therapies might be useful for alleviating this patient's symptoms and preventing a recurrence of ADHF?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treatment of this patient's ADHF?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's heart failure and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Review the current heart failure treatment guidelines, and create a table highlighting the patient characteristics that necessitate hospital admission versus those that are conducive to treatment in the outpatient setting.
2. List all Heart Failure National Hospital Inpatient Quality Measures (core measures) that must be fulfilled prior to BF's discharge.
3. Review the available literature on prognostic indicators in heart failure, and create a list of prognostic indicators for readmission or mortality in patients with heart failure.
4. Contrast the pharmacotherapeutic plan developed in this case with that of a pharmacotherapeutic plan for a patient presenting with heart failure with preserved EF.

CLINICAL PEARL

Patients with heart failure are at a high risk of mortality and morbidity and thus have increasingly high costs of care. Due to our aging population, among other factors, total costs for heart failure are estimated to reach almost \$70 billion by 2030, with 80% of these costs directed at treatment of the hospitalized patient with ADHF.

REFERENCES

1. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;128:e-240–e327.
2. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation* 2017;136:e137–e161.
3. Bumetanide Package Insert. Deerfield, IL, Baxter Healthcare, 2009.
4. Furosemide Package Insert. Lake Forest, IL, Hospira Incorporated, 2004.
5. Torsemide Package Insert. Somerset, NJ, Meda Pharmaceuticals, 2009.
6. Felker GM, Lee KL, Bull DA, et al. Diuretic strategies in patients with acute decompensated heart failure. *N Engl J Med* 2011;364:797–805.
7. Lindenfeld JA, Albert NM, Boehmer JP, et al. HFSA 2010 comprehensive heart failure practice guidelines. *J Card Fail* 2010;16:e1–e194.
8. O'Connor CM, Startling RC, Hernandez AF, et al. Effect of nesiritide in patient with acute decompensated heart failure. *N Engl J Med* 2011;365:32–43.

21

DEEP VEIN THROMBOSIS

Trouble From Deep Within Level II

Sally A. Arif, PharmD, BCPS-AQ Cardiology

Tran Tran, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Define acute deep vein thrombosis (DVT), and discuss its pathophysiology.
- Discuss the clinical presentation of patients with a DVT.
- Develop a pharmacotherapeutic care plan for the management of a patient with a DVT.
- Educate a patient receiving anticoagulation therapy for the treatment of a DVT.

PATIENT PRESENTATION

■ Chief Complaint

“I’m having pain in my leg.”

■ HPI

Rodney Cross is a 51-year-old Caucasian man who presents to his primary care physician because of pain in his right leg. He states that he awoke with the pain 3 days ago and that it has been continuous, although it hurts more when he walks. The pain is located behind his right knee and extends down into his calf. He rates the pain intensity as 3/10 at this time. The patient denies CP and SOB. He denies recent travel, immobility, and leg injury. The patient started atorvastatin 40 mg daily for treatment of dyslipidemia approximately 3 months prior to this visit. He stopped the atorvastatin 3 days ago because he thought it might be causing his leg pain, but the pain has continued.

■ PMH

Hypertension

Dyslipidemia

Graves disease with thyroid ablation

Gout

Left ankle fracture 9 years ago that required a cast but no surgery

Remote history of depression

■ PSH

Left herniorrhaphy about 10 years ago. Pilonidal cyst excision in remote past.

■ FH

Father died at age 81 of liver failure. Mother, one brother, and son all alive and well. No family history of venous thromboembolism or clotting disorders.

■ SH

Married, one adult child. Drinks one to two alcoholic beverages daily. Smokes ½ pack per day of cigarettes but trying to quit. Denies illicit drug use.

■ Meds

Allopurinol 300 mg PO once daily

Lisinopril 10 mg PO once daily

Levothyroxine 150 mcg PO once daily

Aspirin 81 mg PO daily

Atorvastatin 40 mg PO once daily (discontinued 3 days ago)

■ All

NKDA

■ ROS

Constitutional: No chills, no fatigue.

Eyes: No eye pain or changes in vision.

ENT: No sore throat.

Skin: No pigmentation changes, no nail changes.

Cardiovascular: No CP, palpitations, or syncope.

Respiratory: No cough, SOB, wheezing, or stridor.

GI: No abdominal pain, nausea, diarrhea, or vomiting.

Musculoskeletal: No neck pain, back pain, or injury.

Neurologic: No dizziness, headache, or focal weakness.

Psychiatric/behavioral: Remote history of depression. Not a current problem.

■ Physical Examination

Gen

Somewhat overweight, Caucasian man who appears comfortable. Cooperative, A&O × 3, normal affect.

VS

BP 132/76, P 75 regular, RR 16, T 98.3°F, O₂ sat 97%/RA; Wt 194 lb, Ht 6’0”

Skin

Warm, dry, normal color. No rash or induration.

HEENT

Pupils equal and reactive to light. EOM intact. Mucous membranes moist and pink.

Neck

Normal range of motion with no meningeal signs

Lungs/Thorax

Breath sounds normal, no respiratory distress

CV

RRR, no rubs, murmurs, or gallops

Abd

Nontender, no masses, no distension, no peritoneal signs

MS/Ext

Upper extremities: Normal by inspection, no CCE, normal ROM.
 Lower extremities: Right calf tight, warm to touch, and tender with 1+ pretibial pitting edema. LLE without redness, warmth, and swelling. Lower extremity pulses and sensation are normal bilaterally. Normal ROM.

Neuro

Glasgow coma scale of 15, no focal motor deficits, no focal sensory deficits

■ Labs

Na 140 mEq/L	WBC $5.9 \times 10^3/\mu\text{L}$	AST 16 IU/L
K 3.9 mEq/L	RBC $4.28 \times 10^6/\mu\text{L}$	ALT 20 IU/L
Cl 103 mEq/L	Hgb 13.5 g/dL	Alk phos 67 IU/L
CO ₂ 27 mEq/L	Hct 39.3%	GGT 20 IU/L
BUN 10 mg/dL	Platelets $175 \times 10^3/\mu\text{L}$	Lipid panel (fasting)
SCr 0.84 mg/dL	CK 117 IU/L	TC 180 mg/dL
Glucose 88 mg/dL	INR 1.0	HDL 30 mg/dL
Uric acid 5.0 mg/dL	PT 11.4 seconds	Trig 250 mg/dL
	aPTT 34.8 seconds	LDL 100 mg/dL

Lower extremity venous duplex ultrasonography: Acute DVT of right distal superficial femoral, popliteal, and peroneal veins. No compression or flow in these vessels.

(Note to reader: The “superficial femoral vein” is actually a deep vein, in spite of its name. Use of the name “femoral vein” is preferred because it is less confusing. However, the name “superficial femoral vein” is still encountered, as it is in this patient’s venous duplex report.)

■ Assessment

Acute DVT in right distal femoral, popliteal, and peroneal veins

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of DVT?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of an acute DVT based on the subjective and objective information available.
- 2.b. Create a list of the patient’s drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient’s DVT?
- 3.d. To keep medication costs low, the clinician and patient agree to start warfarin therapy to manage the patient’s DVT. Design a treatment plan for the initial management of this patient’s DVT and other drug therapy problems. Be sure to include dosage

form, dose, schedule, and durations of therapy for each drug that is part of the plan.

Implement the Care Plan

- 4.a. What information should be provided for this patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE (PART 1)

Mr Cross presents to his PCP 3 days after his first visit. He has been administering his injections and taking warfarin 5 mg daily, as instructed. He continues to experience RLE pain and swelling, but these symptoms are somewhat improved. He denies new CP or SOB. He reports no missed warfarin doses, no changes in his other medications, a diet with consistent vitamin K intake, no change in his alcohol intake, and no acute health problems. He denies bruising and bleeding, other than minor bruising related to his injections. His INR is 1.7.

■ FOLLOW-UP QUESTION

- 1.a. Identify the patient’s anticoagulation therapy-related problem(s), and design treatment and monitoring plans for managing each problem you identify.

■ CLINICAL COURSE (PART 2)

Mr Cross presents to his PCP’s office approximately 2 months after his acute DVT episode. He reports that he experienced an episode of very dark brown, “cola”-colored urine 2 days before this visit. He has had no recurrences. The patient denies dysuria, back or groin pain, and blood in his bowel movements. His current dose of warfarin is 2.5 mg on Monday, Wednesday, Friday, and Saturday, and 5 mg on Tuesday, Thursday, and Sunday. Physical examination reveals no CVA tenderness. His INR is 2.3.

■ FOLLOW-UP QUESTION

- 1.b. Identify the patient’s anticoagulation therapy-related problem(s), and design treatment and monitoring plans for managing each problem you identify.

■ CLINICAL COURSE (PART 3)

Three months after his initial presentation, you see Mr Cross in the new anticoagulation clinic at his primary care physician’s office. He is currently taking warfarin 2.5 mg on Monday, Wednesday, Friday, and Saturday, and 5 mg on Tuesday, Thursday, and Sunday. His INR is 4.3. The patient’s INR 4 weeks ago was 2.3 on the same warfarin dose. Mr Cross has not experienced any symptoms suggesting DVT recurrence or PE occurrence. He states that he has not had any problem with bleeding, has not missed doses or taken extra doses of warfarin in the last month, and has not changed his diet or alcohol intake. His medications have been unchanged, except for

TABLE 21-1 Thrombophilia Test Results

Test	Result	Reference interval
Antithrombin III (% activity)	101	85–118
Protein C (% activity)	122	72–220
Protein S (% activity)	111	50–168
Factor V Leiden mutation	Negative	Normal: negative
Prothrombin G-20210-A mutation	Negative	Normal: negative
Anticardiolipin antibodies IgG (GPL units)	5.0	0.0–15.0
Anticardiolipin antibodies IgM (MPL units)	<4.7	0.0–12.5
Thrombin time (s)	15.5	13.0–20.0
DRVVT (s)	63.2	35.0–47.0
DRVVT confirm (s)	36.3	—
DRVVT ratio	1.74	1.10–1.41
StaClot LA	Positive	Normal: negative
Homocysteine, plasma (μmol/L)	10.0	3.7–13.9

a switch from atorvastatin 40 mg daily to rosuvastatin 20 mg daily for the treatment of his dyslipidemia approximately 2–3 weeks ago. You note that the thrombophilia tests given in Table 21-1 were completed prior to the initiation of anticoagulation therapy.

The laboratory summarizes the results in Table 21-1 as consistent with the presence of lupus anticoagulants.

■ FOLLOW-UP QUESTION

- 1.c. Identify this patient's anticoagulation therapy-related problem(s), and design a treatment and monitoring plan for each problem that you identify. Be sure to specify the anticipated duration of his anticoagulation therapy.

■ SELF-STUDY ASSIGNMENTS

1. Create a summary of antiphospholipid syndrome, including its definition, clinical presentation, and management.
2. Summarize the existing literature regarding the effects of various statins on response to warfarin. Does warfarin alter the effect of statins?

CLINICAL PEARL

Current guidelines propose long-term anticoagulation (up to 3 months) over anticoagulation for a shorter period of time. Longer treatment courses (eg, 6, 12, or 24 months) or extended therapy (no scheduled stop date) are recommended for patients with a proximal DVT, isolated distal DVT, or PE provoked by surgery/nonsurgical transient risk factors. Extended therapy is recommended in patients with an unprovoked proximal DVT of the leg or PE, or second unprovoked VTE with a low or moderate risk of bleed. Use of anticoagulation should be reassessed annually in all patients who receive extended anticoagulation therapy.

REFERENCES

1. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST Guideline and Expert Panel Report. *Chest* 2016; 149(2):315–352.
2. Robertson L, Kesteven P, McCaslin JE. Oral direct thrombin inhibitors or oral factor Xa inhibitors for the treatment of deep vein thrombosis. *Cochrane Database Syst Rev* 2015;6:CD010956.
3. Schulman S, Kearon C, Kakkar AK, for the RE-COVER Study Group. Dabigatran versus warfarin in the treatment of acute venous thromboembolism. *N Engl J Med* 2009;361(24):2342–2352.
4. Schulman S, Kakkar AK, Goldhaber SZ, for the RE-COVER II Trial Investigators. Treatment of acute venous thromboembolism with dabigatran or warfarin and pooled analysis. *Circulation* 2014; 129(7):764–772.
5. Garcia DA, Baglin TP, Weitz JI, Samama MM. Parenteral anticoagulants: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(Suppl):e24S–e43S.
6. Van Dongen CJ, MacGillavry MR, Prins MH. Once versus twice daily LMWH for the initial treatment of venous thromboembolism. *Cochrane Database Syst Rev* 2005;3:CD003074.
7. Stern A, Abel R, Gibson GL, et al. Atorvastatin does not alter the anticoagulant activity of warfarin. *J Clin Pharmacol* 1997;37:1062–1064.
8. Simonson SG, Martin PD, Mitchell PD, et al. Effect of rosuvastatin on warfarin pharmacodynamics and pharmacokinetics. *J Clin Pharmacol* 2005;45(8):927–934.
9. Tripodi A, de Groot PG, Pengo V. Antiphospholipid syndrome: laboratory detection, mechanisms of action and treatment. *J Intern Med* 2011;270(2):110–122.

22

PULMONARY EMBOLISM

HIT Can Happen Level II

Kristen L. Longstreth, PharmD, BCPS

Mary E. Fredrickson, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs, symptoms, and risk factors associated with pulmonary embolism (PE).
- Evaluate a patient for heparin-induced thrombocytopenia (HIT).
- Select an appropriate anticoagulant for the treatment of PE complicated by HIT.
- Monitor anticoagulation therapy for the treatment of PE complicated by HIT.
- Educate a patient on anticoagulation therapy.

PATIENT PRESENTATION

■ Chief Complaint

“I’m having chest pain, and I can’t catch my breath.”

■ HPI

Mary Anton is a 70-year-old woman who arrives at the hospital’s emergency department by ambulance transfer from her home. The patient is S/P right TKR (postoperative day 10) for severe osteoarthritis. She was discharged from the hospital’s orthopedic nursing

unit 4 days ago with a prescription for enoxaparin for DVT prophylaxis. The patient was scheduled to receive physical therapy at a local rehabilitation center; however, she canceled therapy due to pain. She has been inactive at home with the exception of completing her activities of daily living with the assistance of her husband. This morning, the patient developed sharp chest pain and shortness of breath while watching television. She denies nausea, vomiting, and diaphoresis. The patient has a nonproductive cough. She is anxious and complains of pain in her right knee and right lower extremity.

■ PMH

HTN × 30 years
Dyslipidemia × 25 years
Chronic stable angina × 2 years (negative regadenoson stress test 2 months ago)
CKD secondary to previously uncontrolled HTN, stage 4 (baseline creatinine 1.8–2.0 mg/dL)
Osteoarthritis
Obesity
S/P TKR right leg (postoperative day 10)

■ FH

Father died at age 74 (lung CA)
Mother died at age 89 (MI)
No siblings

■ SH

The patient is retired. She lives at home with her husband. Prior to surgery, she avoided most physical activity due to severe osteoarthritis. Negative for tobacco abuse. Denies alcohol use.

■ Meds

Home medications:

Aspirin 81 mg PO once daily
Metoprolol succinate 100 mg PO daily
Amlodipine 10 mg PO once daily
Hydralazine 50 mg PO TID
Atorvastatin 20 mg PO once daily
Nitroglycerin 0.4 mg sublingually PRN chest pain
Sevelamer carbonate 1600 mg PO TID with meals
Enoxaparin 30 mg subcutaneously Q 24 hours
Oxycodone sustained release 20 mg PO Q 12 hours
Oxycodone immediate release 5 mg PO Q 6 hours PRN pain
Docusate 100 mg PO QHS
Sennosides 17.2 mg PO QHS

■ All

Lisinopril (angioedema)

■ ROS

Positive for shortness of breath and nonproductive cough. Positive for sharp chest pain at rest. The pain does not radiate and is not reproducible by touch. No palpitations, diaphoresis, nausea, vomiting, or diarrhea. The patient denies headache, fever, and chills. Pain rated by patient as 9/10 in chest and 7/10 in right knee and lower extremity.

■ PE

Gen

Moderate respiratory distress

VS

BP 128/68, P 101, RR 21, T 36.9°C; Wt 85 kg, Ht 5'4", O₂ sat 88% on RA

Skin

Warm and dry; no rashes

HEENT

Head: atraumatic; PERRLA; EOMI

Neck/Lymph Nodes

No carotid bruits; no lymphadenopathy; no thyromegaly

Lungs/Thorax

CTA; no wheezing or crackles

CV

Tachycardia with regular rhythm; normal heart sounds; no MRG

Abd

Obese, soft; NT/ND; +BS; no organomegaly

Genit/Rect

WNL

MS/Ext

S/P TKR right leg; right lower extremity ROM limited with slight redness, warmth, and edema; pain in right knee and right lower extremity

Neuro

A&O × 3; no focal deficits noted; cranial nerves intact

■ Labs (Nonfasting)

Na 140 mEq/L	Mg 2.1 mEq/L	T. chol 165 mg/dL	D-dimer 975 ng/mL
K 4.5 mEq/L	Phos 4.4 mg/dL	LDL 97 mg/dL	Cardiac enzymes,
Cl 105 mEq/L	Ca 8.9 mg/dL	HDL 42 mg/dL	time 1245
CO ₂ 26 mEq/L	Alb 3.5 g/dL	TG 130 mg/dL	CK 67 IU/L
BUN 35 mg/dL	AST 18 IU/L	Hgb 12.1 g/dL	CK-MB 1.1 IU/L
SCr 1.8 mg/dL	ALT 12 IU/L	Hct 36.5%	Troponin I
Glu 106 mg/dL	Alk Phos	Plt 72 × 10 ³ /mm ³	0.03 ng/mL
A1C 5.5%	57 IU/L	WBC 6 × 10 ³ /mm ³	

■ ECG

Sinus tachycardia. No T wave or ST changes present.

■ Venous Doppler Ultrasound of Right Lower Extremity

Occlusive DVT from the right popliteal vein to the right common femoral vein

■ Chest X-Ray

No evidence of acute cardiopulmonary disease

■ Assessment

1. Chest pain, SOB—history of chronic stable angina; R/O ACS, R/O PE
2. Right lower extremity DVT
3. Thrombocytopenia—R/O HIT
4. S/P TKR right leg for severe osteoarthritis (postoperative day 10)—not infected, pain not controlled

TABLE 22-1 Cardiac Enzymes (Second Set; Time: 1905)

CK 45 IU/L
CK-MB 0.7 IU/L
Troponin I 0.02 ng/mL

5. CKD—stage 4, creatinine at patient's baseline
6. HTN—stable on current regimen
7. Dyslipidemia—stable on current regimen

QUESTIONS

Collect Information

- 1.a. What subjective and objective information is consistent with a diagnosis of PE for this patient?
- 1.b. What risk factors for PE are present for this patient?
- 1.c. What additional information is needed to fully assess this patient?

CLINICAL COURSE (PART 1)

The patient is admitted to a telemetry nursing unit within the hospital for treatment of the DVT and further workup for chest pain and shortness of breath (Table 22-1). A V/Q scan is ordered. The patient's medical chart from the previous admission is reviewed to obtain a more complete medication and laboratory history (Table 22-2).

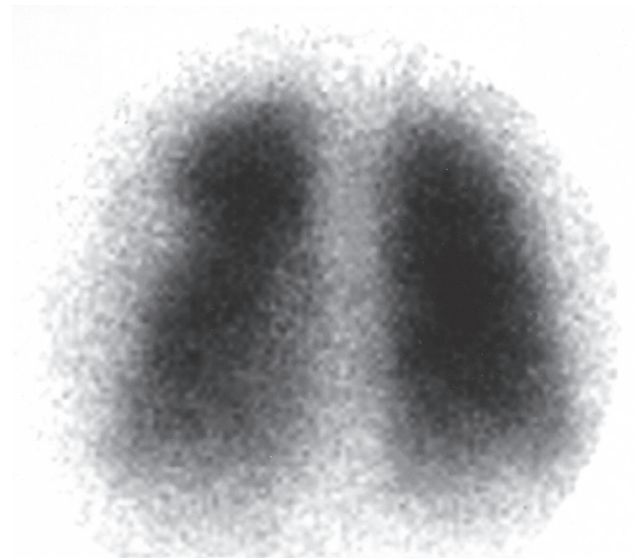
While completing the admission medication reconciliation, an internal medicine resident physician discontinues enoxaparin and restarts the patient's other home medications. The resident physician also orders the following: consult clinical pharmacist to dose and monitor fondaparinux and warfarin; morphine 2 mg IV or IM Q 4 hours PRN severe pain (pain score of 7–10); ibuprofen 600 mg PO Q 8 hours PRN mild to moderate pain (pain score of 1–6).

V/Q SCAN

Multiple segmental perfusion defects, indicating a ventilation-perfusion mismatch and high probability of PE (Fig. 22-1).

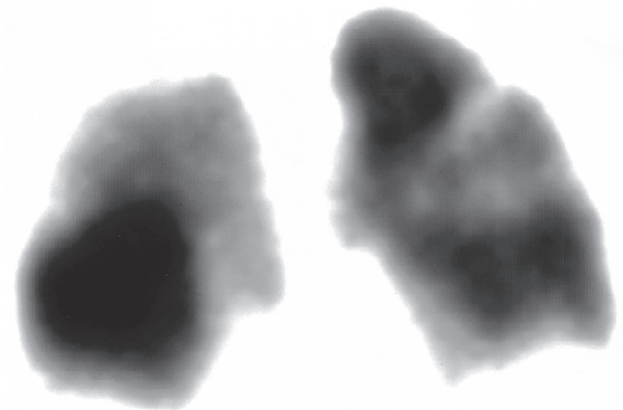
TABLE 22-2 Pertinent Medication and Laboratory History From the Previous Admission

TKR	Plt 239 × 10 ³ /mm ³	Hgb 12.2 g/dL	
Postoperative day 1	Plt 233 × 10 ³ /mm ³	Hgb 11.9 g/dL	Enoxaparin 30 mg subcutaneously Q 24 hours started
Postoperative day 2	Plt 227 × 10 ³ /mm ³		
Postoperative day 3	Plt 229 × 10 ³ /mm ³		
Postoperative day 4	Plt 221 × 10 ³ /mm ³	Hgb 12.0 g/dL	
Postoperative day 5	Plt 234 × 10 ³ /mm ³		
Postoperative day 6	Plt 141 × 10 ³ /mm ³	Hgb 12.0 g/dL	Discharged from hospital on enoxaparin 30 mg subcutaneously Q 24 hours



(A)

1st Breath



(B)

FIGURE 22-1. Ventilation-perfusion lung scan. (A) Normal ventilation; (B) multiple segmental perfusion defects, indicating a ventilation-perfusion mismatch and high probability of PE. (Reproduced with permission from Rao RK. Pulmonary embolic disease. In: Crawford MH, ed. *Current Diagnosis and Treatment in Cardiology*. 5th ed. New York, NY: McGraw-Hill Education, 2017:389.)

Assess the Information

- 2.a. Assess the severity of the patient's pulmonary embolism based on the subjective and objective information available.
- 2.b. Develop a list of the drug therapy problems for this patient and prioritize them. Include an assessment of medication appropriateness, effectiveness, and safety.
- 2.c. Discuss the process to confirm or rule out a suspected diagnosis of HIT.

CLINICAL COURSE (PART 2)

A heparin-induced platelet antibody ELISA is drawn and sent to an outside laboratory. An order is written to avoid all heparin (including heparin catheter flushes). Prior to initiating anticoagulation, a baseline aPTT (32.7 seconds; hospital laboratory's normal range is 25–40 seconds), PT (10.8 seconds), and INR (1.0) are obtained to assist with anticoagulation dosing. The nursing unit notifies the clinical pharmacist of the consultation order to dose and monitor fondaparinux and warfarin.

Develop a Care Plan

- 3.a. What are the pharmacotherapy goals for the treatment of PE?
- 3.b. What additional pharmacotherapy goals exist for a patient with HIT?
- 3.c. Which agents are available to initiate anticoagulation for the treatment of PE in this patient?
- 3.d. What non-anticoagulant therapies (pharmacologic and nonpharmacologic) are available for the treatment of PE? Is this patient an appropriate candidate for any of these therapeutic options?
- 3.e. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's anticoagulation and other drug therapy problems. For the patient's anticoagulation therapy, select an appropriate parenteral anticoagulant to begin therapy. Calculate the initial dose and therapeutic range for this patient.

Implement the Care Plan

- 4.a. Coordinate a pharmacotherapeutic plan to transition the patient to warfarin and discontinue the parenteral anticoagulant.
- 4.b. Collaborate with other healthcare providers to determine the appropriate length of warfarin therapy for this patient.
- 4.c. Prior to discharge, what information should be provided to this patient about warfarin therapy to enhance compliance and ensure efficacy and safety?

Follow-up: Monitor and Evaluate

- 5.a. In addition to the parenteral anticoagulant therapeutic monitoring parameter, what clinical and laboratory parameters will you use to monitor the efficacy and safety of anticoagulation in this patient during hospitalization and post-discharge?
- 5.b. If a diagnosis of HIT is confirmed, document a plan regarding the future use of heparin and low-molecular-weight heparin therapy in this patient.

CLINICAL COURSE (PART 3)

The results of the heparin-induced platelet antibody ELISA were reported as positive with an optical density (OD) of 1.20 (the hospital's laboratory reports OD values greater than 0.40 as positive for heparin-induced antibodies). The patient's INR has been therapeutic for 72 hours on warfarin. The parenteral anticoagulant was discontinued yesterday, and the patient will be discharged home today.

SELF-STUDY ASSIGNMENTS

1. Determine the appropriate frequency of platelet count monitoring when therapeutic or prophylactic unfractionated heparin, low-molecular-weight heparin, or fondaparinux is used in medical or postoperative patients.
2. Investigate the sensitivity and specificity of the various activation and antigen assays available to confirm the diagnosis of HIT.
3. Compare the effects of bivalirudin and argatroban on INR measurement and warfarin monitoring.
4. Describe the role of platelet transfusion in the management of HIT.

CLINICAL PEARL

The optimal duration of anticoagulation in a patient with HIT who does not have evidence of thrombosis (isolated HIT) is unknown. Anticoagulation with a direct thrombin inhibitor should be continued

until the platelet count has recovered to at least $150 \times 10^3/\text{mm}^3$ and stabilized. Evidence-based guidelines also suggest initiating warfarin therapy for 4 weeks to prevent HIT-related thrombosis.²

REFERENCES

1. Witt DM, Clark NP, Vazquez SR. Venous thromboembolism. In: DiPiro JT, Talbert RL, Yee GC, et al., eds. *Pharmacotherapy: A Pathophysiologic Approach*, 10th ed. New York, NY: McGraw-Hill, 2017:231–260.
2. Linkins LA, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(2 Suppl):e495S–e530S.
3. Kearon C, Akl EA, Ornelas J, et al. Antithrombotic therapy for VTE disease: CHEST Guideline and Expert Panel Report. *Chest* 2016;149(2):315–352.
4. Tritschler T, Kraaijpoel N, Le Gal G, Wells PS. Venous Thromboembolism: advances in diagnosis and treatment. *JAMA* 2018;320(15):1583–1594.
5. Lexicomp Online, Lexi-Drugs Online, Hudson, Ohio: Wolters Kluwer Clinical Drug Information, Inc. <https://wolterskluwercli.com/lexicomp-online/>. Published 2018. Accessed February 23, 2019.
6. Salter BS, Weiner MM, Trinh MA, et al. Heparin-induced thrombocytopenia: a comprehensive clinical review. *J Am Coll Cardiol* 2016;67:2519–2532.
7. Kang M, Alahmadi M, Sawh S, Kovacs MJ, Lazo-Langner A. Fondaparinux for the treatment of suspected heparin-induced thrombocytopenia: a propensity score-matched study. *Blood* 2015;125(6):924–929.
8. Warkentin TE, Pai M, Linkins LA. Direct oral anticoagulants for treatment of HIT: update of Hamilton experience and literature review. *Blood* 2017;130(9):1104–1113.
9. Garcia DA, Baglin TP, Weitz JI, Samama MM. Parenteral anticoagulants: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(2 Suppl):e24S–e43S.
10. Bristol-Myers Squibb. Coumadin medication guide. Food and Drug Administration. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/009218s118lbl.pdf#page=30. Published 2017. Accessed November 14, 2018.

23

CHRONIC ANTICOAGULATION

Crossing the “Bridge” Level II

Mikayla L. Spangler, PharmD, BCPS

Beth Bryles Phillips, PharmD, FCCP, FASHP, BCPS, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- List the goals of anticoagulant therapy for periprocedural management of anticoagulation.
- Appropriately assess a patient's response to chronic warfarin therapy.
- Evaluate thromboembolic risk for patients receiving warfarin therapy and determine the need for bridging therapy.

- Develop a patient-specific pharmacotherapeutic plan for warfarin therapy and periprocedural management of anticoagulation.
- Educate patients appropriately about administration of low-molecular-weight heparins (LMWH) and chronic warfarin therapy.

PATIENT PRESENTATION

■ Chief Complaint

"I am scheduled to have a colonoscopy and my physician said to talk to you about what to do with my warfarin."

■ HPI

Elizabeth Heartly is a 53-year-old woman with a past medical history of severe mitral regurgitation status post (S/P) mitral valve replacement (MVR) 5 years ago who is receiving chronic anticoagulation. Today, she presents to the anticoagulation clinic for a follow-up appointment. She also reports that she is scheduled for a colonoscopy with possible polypectomy 2 weeks from today. She states her physician has been recommending the colonoscopy for routine screening since she turned 50. However, she has been reluctant to schedule it. She realized the need for the procedure after a friend was diagnosed with colon cancer. Although no biopsy is planned, her physician explained that she should be off warfarin in case a biopsy is needed. Ms Heartly reports taking one-half of a peach-colored warfarin tablet every Tuesday and Saturday, and one whole peach-colored tablet on the other days of the week. She states she uses a medication box and has not missed any of her warfarin doses during the last month. She denies any bleeding, excessive bruising, severe headaches, abdominal pain, numbness, tingling, or inability to move one side of her body. Her diet with respect to green, leafy vegetables has been consistent. She states that her arthritis has been really flaring up and therefore has been taking ibuprofen 800 mg TID for the last 2.5 weeks. She has one glass of red wine with dinner each evening. She confirms taking all other medications on her medication list and has not started any other new prescription, over-the-counter or alternative therapies.

■ PMH

Mitral regurgitation S/P MVR with St. Jude's mechanical cardiac valve 5 years ago
Hypothyroidism
Osteoarthritis of the knee

■ FH

Father—colon polyps removed when he was in his 50s but is currently alive and well in his 80s.
Mother—hypertension and is 79 years of age.
Brother—healthy.
She has two children who are alive and well.

■ SH

(+) ETOH—one glass of red wine each evening with supper;
(-) smoking

■ Meds

Ibuprofen 200 mg one to two tablets PO TID PRN for osteoarthritis pain
Calcium carbonate 600 mg PO BID with meals
Aspirin 81 mg PO daily

Levothyroxine 125 mcg PO once daily
Warfarin 2.5 mg PO Tuesday, Saturday; 5 mg 5 days per week

■ All

Penicillin—bumps, rash/hives

■ ROS

(-) For severe headaches, abdominal pain, numbness, tingling or inability to use one side of her body, bruises, or change in color of stool or urine

■ Physical Examination

Gen

Pleasant obese woman in NAD

VS

BP 116/78, HR 76, RR 14, T 36.5°C; Wt 96.3 kg, Ht 5'6"

Skin

Normal turgor and color; warm

HEENT

PERRLA, EOMI; disks flat; fundi with no hemorrhages or exudates

Neck/Lymph Nodes

No lymphadenopathy, thyromegaly, or carotid bruits

Lungs

CTA bilaterally

CV

RRR; normal S₁ and S₂; no S₃ or S₄; no M/R/G

Abd

Obese, soft, nontender, nondistended, (+) BS

Genit/Rect

Deferred

Ext

Warm with no clubbing, cyanosis, or edema

Neuro

A&O × 3; CN II–XII intact; DTR 2+; Babinski negative

■ Labs

Date	INR	Warfarin dose
Today	2.8	2.5 mg Tuesday, Saturday; 5 mg 5 days per week
1 month ago	2.7	2.5 mg Tuesday, Saturday; 5 mg 5 days per week
2 months ago	3.2	2.5 mg Tuesday, Saturday; 5 mg 5 days per week
3 months ago	2.6	2.5 mg Tuesday, Saturday; 5 mg 5 days per week

One month ago TSH 1.93 mIU/L

Six months ago 25(OH)D 45 ng/mL

■ Assessment

S/P MVR requiring chronic anticoagulation with target INR 3.0 (range, 2.5–3.5)

Therapeutic INR (target 3.0; range, 2.5–3.5)

Periprocedural management of anticoagulation needed
 Euthyroid with current dose of levothyroxine
 High-dose ibuprofen use for recent osteoarthritis flare

QUESTIONS

Collect Information

- 1.a. What subjective and objective information is relevant for a patient with a mechanical cardiac valve requiring chronic anticoagulation?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Provide an assessment of her anticoagulation therapy based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What are the most important non-pharmacologic considerations for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for periprocedural management of anticoagulation?
- 3.d. Create an individualized, patient-centered, team-based care plan for this patient's anticoagulation therapy and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

On return to clinic 1 week after the colonoscopy, Ms Heartly reports that the procedure went well, and she has taken her usual weekly dose of warfarin therapy and continues on her bridging therapy. Her INR is 2.5, and she is in need of further instructions regarding her warfarin and bridging therapy.

FOLLOW-UP QUESTION

1. Based on this information, what are your recommendations for her warfarin and LMWH therapy?

ADDITIONAL CASE QUESTION

1. Ms Heartly has been diagnosed with hypothyroidism. Although her TSH is within normal range at this time, how would untreated hypothyroidism affect the INR?

SELF-STUDY ASSIGNMENTS

1. Research the options for bridging in patients with a history of heparin-induced thrombocytopenia, and create a table highlighting the various management options.
2. Research the data on LMWH dosing in morbidly obese patients, and write a one-page paper summarizing how LMWH should be dosed in such patients.

CLINICAL PEARL

Dosing LMWH in obese patients can present challenges due to product availability of dosage strengths. Doses may need to be rounded up or down to the nearest available syringe. The availability of dosage forms may also determine whether enoxaparin may be administered once or twice daily.

REFERENCES

1. Douketis JD, Spyropoulos AC, Spencer FA, et al. Perioperative management of antithrombotic therapy. *Chest* 2012;141:e326S–e350S.
2. Nishimura RA, Otto CM, Bonow RO, et al. 2017 AHA/ACC focused update of the 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2017;135:e1159–e1195.
3. Whitlock RP, Sun JC, Freme SE, Rubens FD, Teoh KH. Antithrombotic and thrombolytic therapy for valvular disease: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e576S–e600S.
4. Holbrook A, Schulman S, Witt DM, et al. Evidence-based management of anticoagulant therapy. *Chest* 2012;141:e152S–e184S.
5. Ageno W, Gallus AS, Wittkowsky A, et al. Oral anticoagulant therapy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141:e44S–e88S.
6. Nishimura RA, Otto CM, Bonow RO, et al. 2014 AHA/ACC guideline for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129:e521–e643.
7. Baron TH, Kamath PS, McBane RD. Management of antithrombotic therapy in patients undergoing invasive procedures. *N Engl J Med* 2013;368:2113–2124.
8. Linkins L, Dans AL, Moores LK, et al. Treatment and prevention of heparin-induced thrombocytopenia. *Chest* 2012;141:e495S–e530S.
9. Garcia DA, Baglin TP, Weitz JI, Samama MM. Parenteral anticoagulants. *Chest* 2012;141:e24S–e43S.
10. Garwood CL, Gortney JS, Corbett TL. Is there a role for fondaparinux in perioperative bridging? *Am J Health Syst Pharm* 2011;68:36–42.

24

STROKE

One Stroke Off Par Level II

Alexander J. Ansara, PharmD, BCPS AQ-Cardiology

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify risk factors for ischemic stroke.
- Discuss the role of thrombolytics in the management of acute ischemic stroke.
- Formulate an appropriate patient-specific drug regimen for the treatment of an acute ischemic stroke.
- Discuss the approach to multidisease state management for the secondary prevention of ischemic stroke, including the management of hypertension, dyslipidemia, and the use of antiplatelet agents.
- Educate a patient regarding secondary stroke prevention strategies.

PATIENT PRESENTATION

■ Chief Complaint

“My dad is having trouble talking and seems to be losing feeling in his left arm and leg.”

■ HPI

Marvin Palmer is a 57-year-old man who was brought to the ED by his son at 10 AM after experiencing left arm numbness, slurred speech, and dizziness. His son states that the two of them were enjoying their typical Saturday morning golf outing at the country club when Mr Palmer, upon teeing off on hole 6 at 9:30 AM, dropped his golf club and went down on one knee. Mr Palmer's words were “slow and deliberate” according to his son who immediately called 9-1-1. While in the ED, Mr Palmer began to have a left-sided facial droop. He admitted noticing minor dizziness and slight tingling in his left hand at 8 AM, both of which resolved soon thereafter. He assumed these were symptoms due to low blood pressure and therefore opted not to take his blood pressure medications this morning.

■ PMH

HTN, diagnosed 10 years ago
Dyslipidemia

■ FH

Both parents alive and relatively healthy. Sister, age 62, also has HTN. Son, age 31, has type 1 DM.

■ SH

Married, lives with wife and three children. Occasional recreational beer or wine consumption. Denies tobacco use.

■ Meds

Amlodipine 2.5 mg PO daily
Simvastatin 10 mg PO daily
Chlorthalidone 25 mg PO daily

■ All

Shellfish (hives)

■ ROS

Mild blurry vision, but no double vision, loss of vision, or oscillopsia

■ Physical Examination

Gen

Slender Caucasian man lying in bed in no acute distress, responsive with occasionally slurred speech

VS

BP 192/98, P 70, RR 19, T 98.6°F, O₂ sat 97% on RA; Wt 80 kg, Ht 6'0"

Skin

Warm, dry

HEENT

PERRLA, EOMI; no nystagmus, exudates, hemorrhages, or papilledema; mild left-sided facial droop. Normal hearing acuity bilaterally.

Neck

(-) Carotid bruits, (-) lymphadenopathy

Chest

Lungs clear to auscultation bilaterally

CV

RRR, S₁ and S₂ normal, no S₃ or S₄

Abd

Soft, nontender, nondistended, (+) BS

GU

Deferred

MS/Ext

RUE: 5/5; RLE 4/5; LUE: 2/5; LLE: 3/5. No abnormal or involuntary movements. Strong peripheral pulses and brisk capillary refill; no CCE; DTR: 2+ throughout, normal Babinski reflex.

Neuro

Awake, A&O × 3. No aphasia, agnosia, or apraxia. Attention, concentration, and vocabulary are all excellent. No impairment of facial sensation noted with light touch bilaterally. Moderate left facial weakness, as noted by the presence of left-sided facial droop. Mild dysarthria. Shoulder shrug is symmetrical, and tongue is midline on protrusion. Can easily touch chin to chest, and there are no other signs of meningismus.

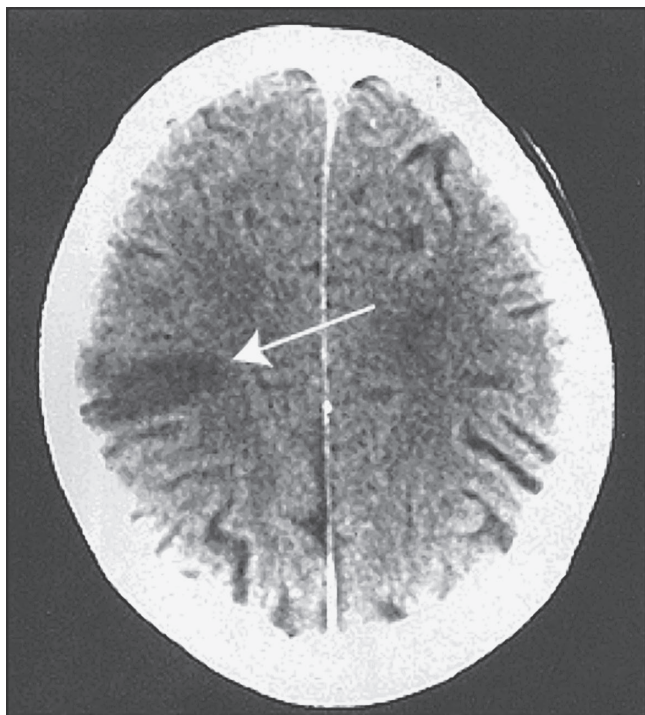


FIGURE 24-1. Head CT scan without contrast negative for hemorrhage and showing right-sided middle cerebral artery infarct.

Labs

Na 140 mEq/L	WBC $5.9 \times 10^3/\text{mm}^3$	<i>Fasting lipid profile</i>
K 4.2 mEq/L	Hgb 16.4 g/dL	Total cholesterol 200 mg/dL
Cl 103 mEq/L	Hct 49.6%	LDL-C 118 mg/dL
CO ₂ 28 mEq/L	Plt $310 \times 10^3/\text{mm}^3$	Triglycerides 160 mg/dL
BUN 10 mg/dL	aPTT 25.3 s	HDL-C 50 mg/dL
SCr 0.6 mg/dL	Trop I 0.01 ng/mL	
Glu 98 mg/dL		

Head CT scan: right-sided middle cerebral artery infarct; no evidence of hemorrhage (Fig. 24-1)

Carotid Dopplers: normal blood flow bilaterally, no appreciable ischemia or stenosis

Angiogram: not performed

Echocardiogram: no evidence of LV thrombus, ejection fraction 55–60%; overall unremarkable

EKG: normal sinus rhythm (Fig. 24-2)

Assessment

Acute ischemic stroke secondary to atherosclerosis and ischemic disease in a patient with HTN, dyslipidemia, and no prior history of stroke or transient ischemic attack

CLINICAL COURSE

It is now 11:00 AM, and you are seeing the patient with the rest of the neurology team.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of an acute ischemic stroke?
- What additional information is needed to fully assess this patient and to determine a treatment approach?

Assess the Information

- Assess the severity of this patient's stroke, using the National Institute of Health Stroke Severity Scale, based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for the treatment of acute ischemic stroke?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's acute stroke and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome(s) and to detect or prevent adverse effects?

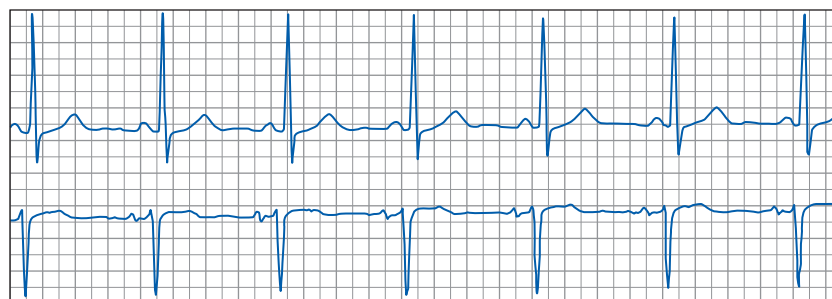


FIGURE 24-2. ECG showing normal sinus rhythm.

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Explain which patients are candidates to receive aspirin instead of warfarin or direct oral anticoagulants for the prevention of stroke in the setting of atrial fibrillation.
2. Read the CHANCE trial and explain when, and for how long, treatment with combination aspirin and clopidogrel is indicated post-stroke or transient ischemic attack.
3. Write a one-page report summarizing the findings of clinical trials utilizing tenecteplase for the treatment of acute ischemic stroke.

CLINICAL PEARL

Initially elevated blood pressures often decrease, without the use of antihypertensive therapy, within the first few days after an ischemic stroke. When initiating antihypertensive therapy after an acute ischemic stroke, caution should be used to not reduce blood pressures too aggressively unless clinically indicated. This approach to blood pressure management in the acute stroke setting is referred to as “permissive hypertension.”

REFERENCES

1. AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol*. 2019;73(24):3168–3209.
2. Powers WJ, Rabinstein AA, Ackerson T, et al; American Heart Association Stroke Council. 2018 guidelines for the early management of patients with acute ischemic stroke: a guideline for healthcare professionals from the American Heart Association/American Stroke Association. *Stroke* 2018;49:e46–e99.
3. Nogueira RG, Jadhav AP, Haussen DC, et al; DAWN Trial Investigators. Thrombectomy 6 to 24 hours after stroke with a mismatch between deficit and infarct. *N Eng J Med* 2018;378:11–21.
4. Ricotta JJ, AbuRahma A, Ascher E, et al. Updated society for vascular surgery guidelines for the management of extracranial carotid disease: executive summary. *J Vasc Surg* 2011;54:832–836.
5. National Institute of Neurological Disorders and Stroke r-tPA Stroke Study Group. Tissue plasminogen activator for acute ischemic stroke. *N Engl J Med* 1995;333:1581–1587.
6. Hacke W, Kaste M, Bluhmki E, et al. Thrombolysis with alteplase 3 to 4.5 hours after acute ischemic stroke. *N Eng J Med* 2008;359:1317–1329.
7. Logallo N, Novotny V, Assmus J, et al. Tenecteplase versus alteplase for management of acute ischaemic stroke (NOR-TEST): a phase 3, randomised, open-label, blinded endpoint trial. *Lancet Neurol* 2017;16:781–788. doi: 10.1016/S1474-4422(17)30253-3.
8. Chinese Acute Stroke Trial Collaborative Group (CAST). Randomized placebo-controlled trial of early aspirin use in 20,000 patients with acute ischemic stroke. *Lancet* 1997;349:1641–1649.
9. International Stroke Trial Collaborative Group (IST). A randomized trial of aspirin, subcutaneous heparin, both, or neither among 19435 patients with acute ischaemic stroke. *Lancet* 1997;349:1569–1581.
10. Wang Y, Wang Y, Zhao X, et al; CHANCE Investigators. Clopidogrel with aspirin in acute minor stroke or transient ischemic attack. *N Engl J Med* 2013;369:11–19.

25

VENTRICULAR ARRHYTHMIA

Nyagon's Parking Lot Accident Level III

Kwadwo Amankwa, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe risk factors for the development of drug-induced torsades de pointes (TdP).
- Differentiate TdP from other cardiac arrhythmias.
- Select appropriate first-line therapy for acute treatment of TdP.
- Recommend appropriate dosing, common adverse effects, and monitoring parameters for pharmacologic agents used to treat TdP.
- Discuss long-term approaches for the prevention of drug-induced TdP.

PATIENT PRESENTATION

■ Chief Complaint

“I was not feeling well, and I think I passed out.”

■ HPI

Nyagon Doellefeld is a 55-year-old woman who experienced syncope while parking her car in the parking lot of the neighborhood grocery store. There were no injuries from the accident, and she was brought to the ED for evaluation. She reports being in her usual state of relatively good health until she developed a “cold” approximately 4 days before admission. She called her primary care physician complaining of her upper respiratory tract symptoms, and the physician called in a prescription for erythromycin 500 mg QID for 10 days to her pharmacy. She took the first dose on the morning of admission. She started feeling that something was wrong on her way to the grocery store approximately 1 hour after taking the second dose of erythromycin. She reports symptoms of lightheadedness, shortness of breath, as well as palpitations while driving. She passed out while parking, and her car collided with another car with minimal impact, damage, or injury. On medic arrival, she was awake and alert but looked shaken. She was transported to the ED without further events. While being evaluated in the ED, she had another syncopal episode. ACLS protocol was initiated, and a rhythm strip showed TdP.

■ PMH

CAD S/P PCI 3 years prior to present admission
Heart failure (EF 30%)
Dyslipidemia
Paroxysmal atrial fibrillation
GERD

■ SH

She lives with her husband and does not smoke or drink alcohol.

■ Meds

Carvedilol 3.125 mg PO BID
 Atorvastatin 80 mg PO at bedtime
 Furosemide 40 mg PO BID (recently increased from 40 mg PO once a day due to increased edema)
 Warfarin 4 mg PO once daily
 Amiodarone 200 mg PO BID
 Centrum silver PO once daily
 Ranitidine 150 mg PO once daily
 Candesartan 8 mg PO once daily
 Aspirin 81 mg PO once daily
 Erythromycin 500 mg PO QID (taken the day of admission)

■ All

NKDA

■ ROS

The patient has no complaints other than those mentioned in the HPI.

■ Physical Examination

Gen

The patient is awake on an ED bed in moderate distress.

VS

BP 104/50, P 98 (200 during syncope), RR 30, T 36.3°C; Ht 5'7", Wt 90 kg.

Skin

Warm and dry; no rashes seen

HEENT

NC/AT. PERRLA. EOMI. Oropharynx is clear.

Neck/Lymph Nodes

Supple; no JVD or bruits; no lymph nodes palpated

Lungs/Thorax

CTA bilaterally

Breasts

Deferred

CV

RRR with no murmurs or gallops

Abd

NTND; no rebound or guarding; (+) bowel sounds

Genit/Rect

Deferred

MS/Ext

Trace edema in the lower extremities; pulses intact

Neuro

A&O × 3

■ Labs

Na 140 mEq/L	Hgb 12.1 g/dL	WBC $12 \times 10^3/\text{mm}^3$
K 2.8 mEq/L	Hct 35%	
Cl 100 mEq/L	RBC $3.88 \times 10^6/\text{mm}^3$	
CO ₂ 29 mEq/L	Plt $200 \times 10^3/\text{mm}^3$	
BUN 36 mg/dL	MCV 90.5 μm^3	
SCr 1.4 mg/dL	MCHC 34.4 g/dL	
Glu 110 mg/dL	INR 2.3	
Mg 1.2 mg/dL		

■ ECG

NSR, QTc 605 milliseconds; rhythm strip from oscilloscope during syncope: TdP (Fig. 25-1)

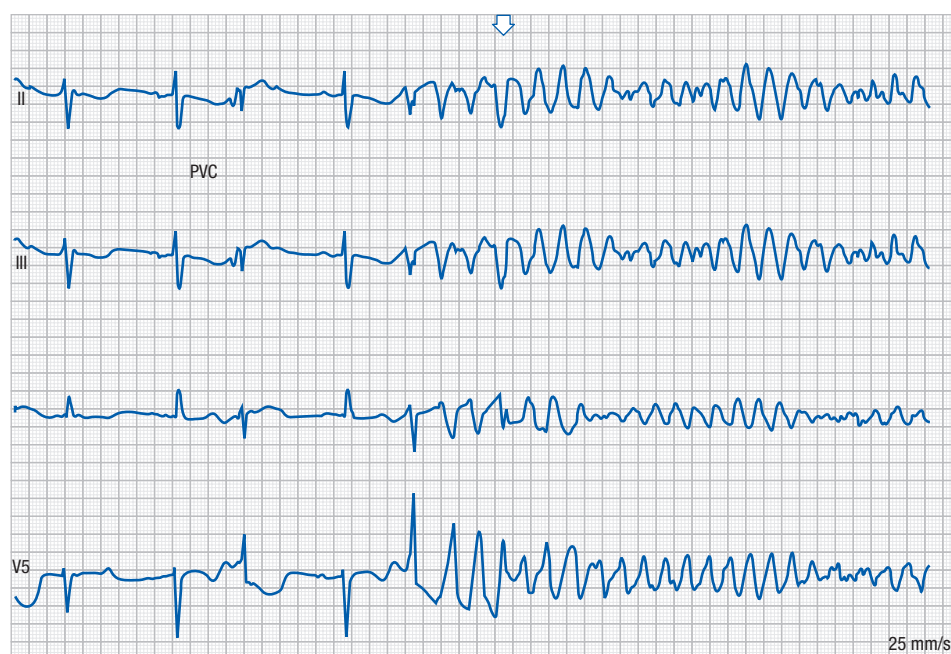


FIGURE 25-1. Electrocardiogram showing torsades de pointes.

■ Assessment

A 55-year-old white woman S/P syncopal episodes from drug-induced TdP; upper respiratory tract symptoms; drug-induced electrolyte imbalance.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of TdP?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. What risk factors predisposed this patient to TdP?
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the short-term goals of pharmacotherapy for this patient?
- 3.b. What nondrug therapies may be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for the acute treatment of TdP?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's TdP and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and prevent recurrence of TdP?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect and prevent adverse events?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The patient was treated with a magnesium infusion, and she converted to normal sinus rhythm. The erythromycin was stopped. Potassium and magnesium were replaced, and the patient was admitted for further electrophysiology workup.

■ SELF-STUDY ASSIGNMENTS

1. List the most common drug classes associated with TdP.
2. List 10 commonly used medications that have a potential to cause TdP.

CLINICAL PEARL

There is a need for increased pharmacovigilance regarding drug-induced arrhythmias in the outpatient setting because many pharmacologic agents and/or conditions that cause QT prolongation and TdP are present in the outpatient population.

REFERENCES

1. Schwartz PJ, Woosley RL. Predicting the unpredictable. *J Am Coll Cardiol* 2016;67:1639–1650.
2. Woosley RL, Heise CW, Gallo T, Tate J, Woosley D, Romero KA. QT drugs list, AZCERT, AZ. Available at: www.CredibleMeds.org. Accessed December 11, 2018.
3. Niedrig D, Maechler S, Hoppe L, et al. Drug safety of macrolide and quinolone antibiotics in a tertiary care hospital: administration of interacting co-medication and QT prolongation. *Eur J Clin Pharmacol* 2016;72:859–867.
4. Owens RC, Nolin TD. Antimicrobial-associated QT interval prolongation: point of interest. *Clin Infect Dis* 2006;43:1603–1611.
5. Tisdale JE. Ventricular arrhythmias. In: Tisdale JE, Miller DA, eds. *Drug-Induced Diseases: Prevention, Detection and Management*. 3rd ed. Bethesda, MD: American Society of Health-Systems Pharmacists, 2018:523–568.
6. Al-Khatib SM, Stevenson WG, Ackerman MJ, et al. 2017 AHA/ACC/HRS guideline for management of patients with ventricular arrhythmias and the prevention of sudden cardiac death: executive summary. *Circulation* 2018;138:e210–e271.
7. Berul CI. Acquired QT syndrome. In: Asirvatham S, Zimetbaum PJ, eds. *UpToDate*. Available at: <http://www.uptodateonline.com>. Accessed December 13, 2018.
8. Roden DM. Predicting drug-induced QT prolongation and torsades de pointes. *J Physiol* 2016;594:2459–2468.
9. Sanoski CA, Bauman JL. The Arrhythmias. In: DiPiro JT, Talbert RL, Yee GC, Matzke GR, Wells BG, Posey L, eds. *Pharmacotherapy: A Pathophysiologic Approach*. 10th ed. New York, NY: McGraw-Hill. Available at: <http://accesspharmacy.mhmedical.com.suscorp.idm.oclc.org/content.aspx?bookid=1861&sectionid=146057036>. Accessed February 11, 2019.

26

ATRIAL FIBRILLATION

Go Easy on My Beating Heart Level III

Virginia H. Fleming, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the cornerstones of atrial fibrillation (AF) treatment.
- Determine therapeutic goals for managing AF in patients with heart failure.
- Recommend an optimal agent for anticoagulation in AF patients with heart failure.

PATIENT PRESENTATION

■ Chief Complaint

"Lately, I feel like my heart has been racing a bit. It really doesn't bother me that much, but I wanted to have it checked out to be sure."

■ HPI

Cooper Riley is a 64-year-old man with heart failure and a history of persistent AF who presents to his primary care physician complaining of palpitations that he first noticed 7 days ago. He reports that he is aware of the palpitations but that he has remained relatively asymptomatic. There has not been a noticeable change in his level of fatigue or exercise capacity during his normal daily activities. Mr Riley was diagnosed with heart failure 6 years ago. For the past few years, his baseline exercise capacity would be described as slight limitation of physical activity with some symptoms during normal daily activities but asymptomatic at rest. He has a history of AF that was cardioverted to NSR, and he has been on amiodarone to maintain NSR for the past 8 months. In the office today, Mr Riley's ECG shows that he is in AF (Fig. 26-1).

■ PMH

Hypertension

Persistent AF (previously in NSR with amiodarone therapy)

Heart failure with reduced ejection fraction (LVEF 35%)

Obstructive sleep apnea (AHI 28 events/hr), alleviated with CPAP therapy

■ FH

Both parents are deceased. Father died of an AMI at age 64. Mother died of breast cancer at age 70 years.

■ SH

Mr Riley works as an accountant. He is married with two healthy children. He does not smoke but occasionally "drinks a few beers on the weekend."

■ Medications

Carvedilol 6.25 mg PO BID

Digoxin 0.0625 mg PO once daily

Amiodarone 400 mg PO once daily

Furosemide 40 mg PO once daily

KCl 20 mEq PO once daily

Lisinopril 10 mg PO once daily

Warfarin 5 mg PO once daily

CPAP therapy (8 cm H₂O) at night

■ Allergies

NKDA

■ ROS

Reports no change in level of fatigue, some exercise intolerance; no headache, lightheadedness, chest pain, angina, or fainting spells; 2+ pitting edema

■ Physical Examination

Gen

Cooperative overweight man in no apparent distress

VS

BP 158/92, P 110 (irregular), RR 20, T 36.3°C, Wt 108.3 kg, Ht 5'11"

Skin

Cool to touch, normal turgor and color

HEENT

PEERLA, EOMI; fundoscopic exam reveals mild arteriolar narrowing but no hemorrhages, exudates, or papilledema.

Neck

Large and supple, no carotid bruits; no lymphadenopathy or thyromegaly, (–) JVD

Lungs/Thorax

Inspiratory and expiratory rales bilaterally, no rhonchi

CV

Pulse 110 bpm and irregular; normal S₁, S₂, (+) S₃, no S₄

Abd

NT/ND, (+) BS; no organomegaly, (–) HJR

Genit/Rect

Normal male anatomy; stool heme (–)

MS/Ext

Pulses 1+ weak, full ROM, no clubbing or cyanosis; mild edema (2+)

Neuro

A&O × 3; CN II–XII intact; DTR 2+, negative Babinski

■ Labs

Na 140 mEq/L

K 4.0 mEq/L

Cl 105 mEq/L

CO₂ 24 mEq/L

BUN 22 mg/dL

SCr 1.1 mg/dL

Glu 109 mg/dL

INR 2.3

Hgb 12.0 g/dL

Hct 35.8%

Plt 212 × 10³/mm³

WBC 9.5 × 10³/mm³

Polys 65%

Bands 2%

Lymphs 30%

Mono 3%

Ca 8.5 mg/dL

Mg 2.1 mEq/L

Dig 0.8 ng/mL

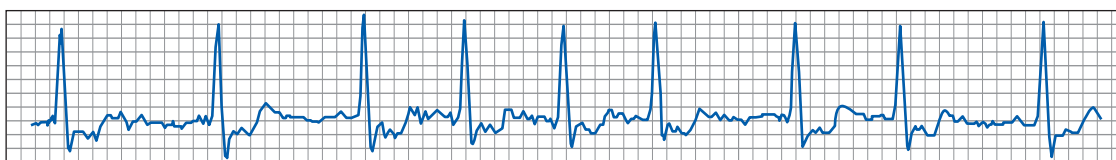


FIGURE 26-1. Rhythm recorded in Mr Riley's physician's office that depicts AF with a ventricular response rate of 110 bpm. AF is characterized by the absence of atrial "p" waves with varying distances between QRS complexes. AF is sometimes referred to as an irregularly irregular rhythm: irregular because it is not NSR; irregular because it produces an irregular ventricular response rate or peripheral pulse.

■ ECG

Persistent AF, ventricular rate 110 bpm (see Fig. 26-1).

■ Echo

Evidence of systolic dysfunction (LVEF 35%) and moderate left atrial enlargement (5.2 cm). No thrombus seen.

■ Chest X-Ray

Enlarged cardiac silhouette; no evidence of acute pulmonary infection or edema

■ Assessment

Persistent AF, previously in NSR on amiodarone therapy: mildly symptomatic, appropriately anticoagulated with warfarin therapy. Ventricular response rate not controlled.

HF: mildly symptomatic, standard meds not at target doses.

HTN: not controlled; optimize therapy for blood pressure control.

OSA: controlled on CPAP therapy.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of persistent atrial fibrillation with HFrEF?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of Mr Riley's AF based on the subjective and objective information available. How would you evaluate the effectiveness of his current medication regimen?
- 2.b. Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals for pharmacotherapy in patients with AF?
- 3.b. What are the goals for pharmacotherapy for this patient's comorbid disease states or conditions?
- 3.c. What nondrug therapies might be useful for Mr Riley?
- 3.d. What feasible pharmacotherapeutic alternatives are available for rhythm control in AF? What feasible pharmacotherapeutic alternatives are available for rate control in AF?
- 3.e. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's AF and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTIONS

1. How effective is amiodarone therapy in maintaining NSR long-term in patients with AF?
2. What factors may hinder preservation of NSR in Mr Riley?
3. Mr Riley has persistent AF. How is this different than permanent AF?

■ SELF-STUDY ASSIGNMENTS

1. Recommend a management strategy/plan for Mr Riley if he returned in 2 weeks with a therapeutic INR, a heart rate of 95 bpm, and no symptoms of tachycardia but with 2+ pitting edema and a 1.2-kg gain in body weight.
2. List the drugs that have been demonstrated to improve mortality in the setting of heart failure and AF.

CLINICAL PEARL

In treating AF with concomitant systolic heart failure, lenient ventricular rate control (<110 bpm) plus anticoagulation is a viable treatment option over maintaining NSR with antiarrhythmic therapy.

REFERENCES

1. January CT, Wann LS, Alpert JS, et al. 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: executive summary. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and the Heart Rhythm Society. *JACC* 2014;64(21):2246–2280.
2. Fuster V, Ryden LE, Cannom DS, et al. 2011 ACCF/AHA/HRS focused update incorporated into the ACC/AHA/EHC 2006 guidelines for management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/American Heart Association Task Force on practice guidelines. *Circulation* 2011;123:e269–e367.
3. Shelton RJ, Clark AL, Goode K, et al. A randomized, controlled study of rate versus rhythm control in patients with chronic atrial fibrillation and heart failure: (CAFE-II Study). *Heart* 2009;95(11):924–930.
4. Roy D, Talajic M, Nattel S, et al. Rhythm control versus rate control for atrial fibrillation and heart failure. *N Engl J Med* 2008;358:2667–2677.
5. Hunt SA, Abraham WT, Chin MH, et al. 2009 focused update incorporated into the ACC/AHA 2005 guidelines for the diagnosis and management of heart failure in adults: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines: developed in collaboration with the International Society for Heart and Lung Transplantation. *Circulation* 2009; 119:e391–e479.
6. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;128:e240–e327.
7. Yancy CW, Jessup M, Bozkurt B, et al. 2017 ACC/AHA/HFSA focused update of the 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Failure Society of America. *Circulation* 2017;136:e137–e161.

8. Van Gelder IC, Groenveld HF, Crijns HJ, et al; RACE II Investigators. Lenient versus strict rate control in patients with atrial fibrillation. *N Engl J Med*. 2010;362(15):1363–1373.
9. Lip GYH, Banerjee A, Boriani G, et al. Antithrombotic therapy for atrial fibrillation. *Chest*. 2018;154(5):1121–1201.
10. Ruff, CT, Giugliana RP, Braunwald E, et al. Comparison of the efficacy and safety of new oral anticoagulants with warfarin in patients with atrial fibrillation: meta-analysis of randomized trials. *Lancet*. 2014;383(9921):955–962.

27

CARDIAC ARREST

Staying Alive Level II

Jennifer McCann, PharmD, BCCCP

Sarah Hittle, PharmD, BCCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Discuss possible causes for cardiac arrest.
- Analyze medications used to treat cardiac arrest.
- List the pharmacologic actions of medications used in cardioversion.
- Outline the Advanced Cardiac Life Support (ACLS) guidelines.
- Identify appropriate parameters to monitor a patient who has had circulation restored after cardiac arrest.

PATIENT PRESENTATION

■ Chief Complaint

“I feel like I can’t breathe.”

■ HPI

Beatrice (“Bee”) A. Hart is a 68-year-old woman who presented to the emergency department Monday morning with shortness of breath and weakness. She reports these symptoms along with a decreased oral intake beginning Thursday last week, which ultimately led to her missing her scheduled dialysis session prior to the weekend.

■ PMH

ESRD requiring hemodialysis Monday, Wednesday, and Friday
Endometriosis
HTN
Dyslipidemia
Type 2 DM

■ PSH

Hysterectomy in 1985

■ FH

Mother had HTN and died of an AMI at age 69; no information available for father; one brother is alive with HTN and DM at age 73.

■ SH

Former smoker; quit 8 years ago; previously 1.5 ppd

■ Meds PTA

Atorvastatin 20 mg PO daily
Metoprolol 50 mg PO twice daily
Sevelamer 800 mg PO TID with meals
Lisinopril 20 mg PO daily
Epoetin alfa 10,000 units subcutaneously three times a week
Insulin glargine 40 units subcutaneously daily
Insulin lispro 5 units subcutaneously with meals

■ All

Sulfa

■ ROS

Difficulty breathing

■ Physical Examination

Gen

White woman

VS

BP 98/60, P 112, RR 24, O₂ saturation 81% on 4L NC; T 37.9°C; dry weight 90 kg; height 162.5 cm

Skin

Cold

HEENT

PERRLA; EOMI; arteriolar narrowing on fundoscopic exam; no hemorrhages, exudates, or papilledema; oral mucosa clear

Neck/Lymph Nodes

Supple with no JVD or bruits; no lymphadenopathy or thyromegaly

Chest

Mild bibasilar rales with decreased breath sounds

CV

Tachycardic; S₁, S₂ normal; no S₃ or S₄; no murmurs or rubs

Abd

Obese, soft, nontender; (+) BS

Genit/Rect

Stool heme (–)

MS/Ext

3+ pitting edema, age-appropriate strength, and ROM

Neuro

A&O × 3, GCS 15

■ Labs

Na 130 mEq/L	Mg 4 mg/dL	Hgb 8.3 g/dL
K 6.3 mEq/L	Phos 6.5 mg/dL	Hct 28%
Cl 106 mEq/L	Alb 1.8 g/dL	Plt $229 \times 103/\text{mm}^3$
CO ₂ 20 mEq/L		WBC $9.9 \times 103/\text{mm}^3$
BUN 55 mg/dL		PMNs 79%
SCr 4.6 mg/dL		Bands 1%
Glu 55 mg/dL		Lymphs 17%
Ca 6.7 mg/dL		Monos 3%

■ ECG

Sinus tachycardia at a rate of 112 bpm

■ Clinical Course

The patient's clinical condition deteriorated shortly after presentation to the ED, at which time she was subsequently intubated for respiratory failure. The patient was noted to have multifocal PVCs with a disorganized rhythm on the monitor and no pulse was detected. A code was called.

■ Assessment

68-Year-old patient with a complex medical history presents to the ED and develops cardiac arrest after missing a hemodialysis session.

QUESTIONS

Collect Information

1. Discuss possible causes for the development of PEA, and identify which potential causes are present in this patient.

Assess the Information

2. Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, and safety.

■ CLINICAL COURSE

See Table 27-1 for a record of cardiopulmonary resuscitation (CPR) events and orders.

- 2.b. Assess the appropriateness of the treatment used to resuscitate this patient (see Table 27-1).

Develop a Care Plan

- 3.a. What are the short-term goals of pharmacotherapy for this patient?
- 3.b. What nonpharmacologic maneuvers should be taken immediately in a patient with PEA?
- 3.c. What pharmacotherapeutic alternatives are available for the acute treatment of PEA?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy, maintain the patient's stability, and optimize neurological function following the return of spontaneous circulation (ROSC).

Implement the Care Plan

4. Describe how care should be coordinated with other healthcare professionals.

Follow-up: Monitor and Evaluate

5. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired outcome and to detect and prevent adverse effects?

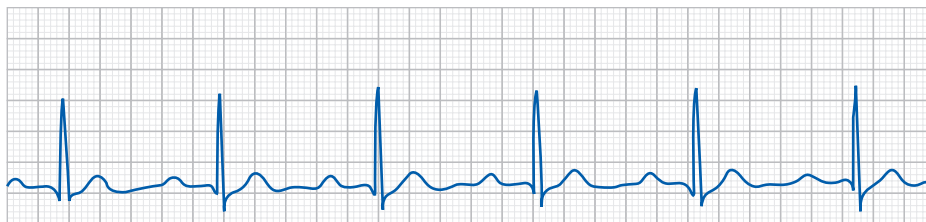
■ SELF-STUDY ASSIGNMENTS

1. Search the Internet for commercially available automated external defibrillator (AED) devices. Explain how such a device would be used by a layperson during a cardiac arrest that occurred in the home or workplace.
2. Perform a literature search to determine the odds of surviving a cardiac arrest while hospitalized.
3. List medications that can be administered via the intraosseous route in an emergent situation.
4. Investigate the effects of induced hypothermia following cardiac arrest on patient outcomes.

TABLE 27-1 Cardiopulmonary Resuscitation Record of Events and Orders

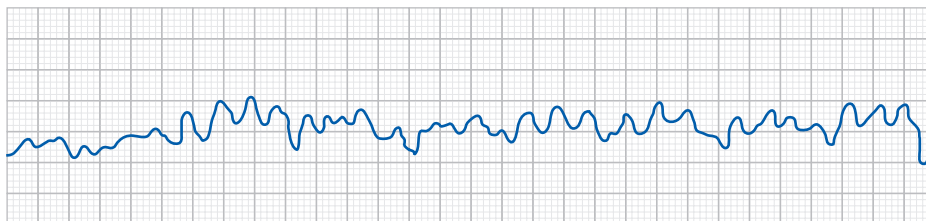
Time	BP	Rhythm	Pulse	Defib. (J)	Treatment Given
0220	56/?	PEA	No pulse Chest compressions	None	Epi 1 mg IVP IO placement Labs ordered: Potassium, ABG, Lactate
0221	46/?	PEA	No pulse	None	Resume compressions Regular insulin 10 units IVP Sodium bicarbonate 50 mEq IVP Calcium chloride 1 gram IVP
0223	73/?	Bradycardia (Fig. 27-1)	Pulse detected HR 50	None	Epi 1 mg IVP D50 1 amp
0225	88/?	VF (Fig. 27-2)	No pulse Chest compressions	360	Vasopressin 40 units IVP
0227	?/133	SVT (Fig. 27-3)	No pulse Chest compressions	360	Chest compressions resumed
0229	160/84	Sinus tach	Pulse detected HR 180	None	

Key: ?, not recorded; ABG, arterial blood gas; BP, blood pressure; Defib., defibrillation; D50, dextrose 50%; Epi, epinephrine; HR, heart rate; IO, intraosseous; IVP, intravenous push; PEA, pulseless electrical activity; Sinus tach, sinus tachycardia; SVT, supraventricular tachycardia; VF, ventricular fibrillation.



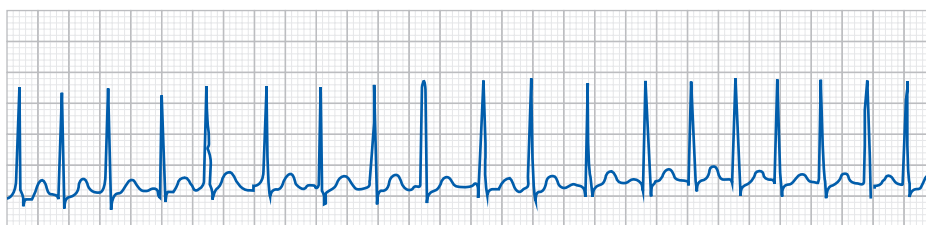
Bradycardia

FIGURE 27-1. Electrocardiogram showing bradycardia. (Reproduced with permission from acls-algorithms.com, Jeffery Media Productions, LLC.)



Ventricular fibrillation

FIGURE 27-2. Electrocardiogram showing ventricular fibrillation. (Reproduced with permission from acls-algorithms.com, Jeffery Media Productions, LLC.)



Supraventricular tachycardia (SVT)

FIGURE 27-3. Electrocardiogram showing supraventricular tachycardia. (Reproduced with permission from acls-algorithms.com, Jeffery Media Productions, LLC.)

CLINICAL PEARL

During a cardiac arrest, it is important to identify the underlying cause of the arrest through a rapid assessment of the H's (hypoglycemia, hypovolemia, hypoxia, hydrogen ion, hyper-/hypokalemia, hypothermia) and T's (toxins, tamponade, tension pneumothorax, thrombosis).

REFERENCES

1. Link MS, Berkow LC, Kudenchuk PJ, et al. 2015 American Heart Association update for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2015;132(Suppl 2):S444–S464.
2. Vanden Hoek TL, Morrison LJ, Shuster M, et al. Part 12: cardiac arrest in special situations: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010;122:S829–S861.
3. Neumar RW, Otto CW, Link MS, et al. Part 8: Advanced Life Support: 2010 American Heart Association guidelines for cardiopulmonary resuscitation and emergency cardiovascular care. *Circulation* 2010;122:S729–S767.
4. Ong ME, Tiah L, Leong BS, et al. A randomized, double-blind, multicentre trial comparing vasopressin and adrenaline in patients with cardiac arrest presenting to or in the emergency department. *Resuscitation* 2012;83:953–960.
5. Gueugniaud PY, David JS, Chanzy E, et al. Vasopressin and epinephrine vs. epinephrine alone in cardiopulmonary resuscitation. *N Engl J Med* 2008;359:21–30.
6. Mukoyama T, Kinoshita K, Nagao K, et al. Reduced effectiveness of vasopressin in repeated doses for patients undergoing prolonged cardiopulmonary resuscitation. *Resuscitation* 2009;80:755–761.

7. Mentzelopoulos SD, Malachias S, Chamos C, et al. Vasopressin, steroids, and epinephrine and neurologically favorable survival after in-hospital cardiac arrest: a randomized clinical trial. *JAMA* 2013;310:270–279.
8. Devlin JW, Skrobik Y, Celine G, et al. Clinical practice guidelines for the management of pain, agitation/sedation, delirium, immobility, and sleep disruption in adult patients in the ICU. *Crit Care Med* 2018;46:e825–e873.

28

HYPOVOLEMIC SHOCK

A Glass Half Full Level II

Brian L. Erstad, PharmD, FCCP, MCCM, FASHP

Brian J. Kopp, PharmD, BCPS, FCCM

Yvonne C. Huckleberry, PharmD, BCPS, FCCM

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Develop a plan for implementing fluid or medication therapies for treating a patient in the initial stages of shock.

- Outline the major parameters used to monitor hypovolemic shock and its treatment.
- List the major disadvantages of using only isolated hemodynamic recordings, such as blood pressure measurements, for monitoring the progression of shock.
- Compare and contrast fluids and medications used for treating hypovolemic shock.

PATIENT PRESENTATION

■ Chief Complaint

"I'm beat. I have vomited four times in the last 24 hours and had diarrhea last evening. Now is not a great time to get sick since I'm in college and have finals next week."

■ HPI

Four days PTA, Mr Hobbs, a 20-year-old college student, had abdominal pain that he attributed to a flare-up in his Crohn disease due to the stress of final examinations. He has an infliximab infusion scheduled for next week; he has them every 8 weeks and does not miss these infusions. However, he admits that he forgets to take his oral medications now that he lives away from his family. When he has Crohn disease pain, he does not feel like eating since this worsens his stomach pain. Furthermore, he has vomiting and diarrhea, which is aggravated by food intake. Per the recommendation of his community pharmacist, Mr Hobbs purchased a commercially available rehydration solution and attempted to drink the small but frequent volumes recommended by his pharmacist, but he could not keep up with fluid losses. His primary care physician referred him to the local hospital for rehydration and further evaluation.

■ PMH

Crohn disease, diagnosed 4 years ago

Ankylosing spondylitis, diagnosed 3 years ago

Pulmonary coccidioidomycosis (small ill-defined mass in the lungs with positive cocci titers), diagnosed 1 year ago

■ FH

Noncontributory

■ SH

Does not smoke or use illicit drugs; admits to occasional ETOH use at parties

■ Meds

Infliximab 300 mg by IV infusion over 3 hours every 8 weeks

Azathioprine 100 mg PO daily

Fluconazole 400 mg PO daily

Fish oil (unknown strength) one capsule PO BID

Multivitamin one tablet PO daily

Whey shakes for protein supplementation, one shake PO daily

■ All

NKDA

■ ROS

The patient has had a recent increase in weight over the past month (6 kg), although this has decreased by 2 kg in the past few days.

Hearing is intact with no vertigo. No dizziness or fainting episodes. No chest pain or dyspnea, but heart has been "racing." Has had one episode of diarrhea and four episodes of vomiting with abdominal pain in the past 24 hours. No musculoskeletal pain or cramping.

■ Physical Examination

Gen

Thin, somewhat anxious man in mild distress

VS

BP 84/58 (baseline 122/78), but possible orthostatic changes not determined, HR 132 (baseline 80), RR 16, T 38.2°C; admission Wt 60 kg, Ht 5'10"

Skin

Pale color (including nail beds) and dry, but not cyanotic; no lesions

HEENT

Normal scalp/skull; conjunctivae pale and dry with clear sclerae; PERRLA, dry oral mucosa; remainder of ophthalmologic exam not performed

Neck/Lymph Nodes

Supple, no lymphadenopathy or thyromegaly

Lungs/Thorax

Clear by palpation and auscultation

CV

RRR; S₁ and S₂ normal; apical pulse difficult to palpate; no MRG

Abd

Perigastric pain on light palpation, no hepatosplenomegaly or masses; bowel sounds present

Genit/Rect

Normal male genitalia; no hemorrhoids or fistulas noted; stool heme (–)

MS/Ext

No deformities with normal ROM of joints except for hips and knees (somewhat limited ROM); no edema, ulcers, or tenderness

Neuro

Mild muscular atrophy with weak grip strength; CN II–XII intact; 2+ reflexes throughout; Babinski downgoing

■ Labs

Na 149 mEq/L	Hgb 11.9 g/dL	Phos 2.9 mg/dL
K 3.3 mEq/L	Hct 34.3%	AST 35 IU/L
Cl 112 mEq/L	Plt 151 × 10 ³ /mm ³	ALT 23 IU/L
CO ₂ 30 mEq/L	WBC 13 × 10 ³ /mm ³	T. bili 1.1 mg/dL
BUN 32 mg/dL	PT 12.1 s	Alk phos 83 IU/L
SCr 1.4 mg/dL ^a	aPTT 33 s	CRP 16 mg/dL
Glu 105 mg/dL	Albumin 3.3 g/dL	ESR 48 mm/hr

^aBaseline SCr 1.1 mg/dL.

■ Other Test Results

CXR negative. I/O 1200/150 (urinary catheter) for first 6 hours of hospitalization. Results pending for ABG with lactate level, blood and urine cultures, gastroenteric pathogens on stool culture, O & P, and *Clostridium difficile* titer.

■ Assessment

Volume depletion, acute kidney injury, Crohn disease exacerbation, possible acid–base disorder, possible infectious process in setting of immunosuppression, medication noncompliance, malnutrition, anemia.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of hypovolemic shock and acute kidney injury?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of hypovolemic shock and acute kidney injury based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug-related problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating hypovolemic shock and the associated laboratory alterations?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's hypovolemic shock and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse events?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

No evidence of infection was found. All cultures were negative, and the elevated temperature abated within 12 hours of admission. However, the patient had a complicated clinical course since he received treatment with hypotonic fluids early in his hospital course, which provided inadequate intravascular expansion to correct his hypovolemic shock. After approximately 24 hours, the patient had to be admitted to the ICU for hypotension and acute kidney injury.

■ FOLLOW-UP QUESTION

1. Explain why hypotonic IV fluids such as 5% dextrose are not indicated in a patient with overt hypovolemia, who is going into shock.

■ SELF-STUDY ASSIGNMENTS

1. Search the literature and discuss the results of comparative trials involving crystalloids and colloids for plasma expansion.
2. Write a two-page report that compares the advantages and limitations of each type of fluid for the plasma expansion indication.

CLINICAL PEARL

Isotonic or near-isotonic IV crystalloid solutions are indicated in patients with extracellular fluid depletion, who cannot receive oral rehydration solutions due to the severity of presentation or inability to absorb adequate volumes. Isotonic solutions replenish the extracellular space and have minimal intracellular distribution.

REFERENCES

1. Kidney Disease. Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. Clinical Practice Guideline for Acute Injury. *Kidney Int Suppl* 2012;2:1–138.
2. Rhodes A, Evans LE, Alhazzani W, et al. Surviving Sepsis Campaign: international guidelines for management of sepsis and septic shock 2016. *Crit Care Med* 2017;45:486–552.
3. Yunos NM, Bellomo R, Hegarty C, et al. Association between chloride-liberal vs chloride-restrictive intravenous fluid administration strategy and kidney injury in critically ill adults. *JAMA* 2012;308:1566–1572.
4. Krajewski ML, Raghunathan K, Paluszkiwicz SM, et al. Meta-analysis of high- versus low-chloride content in perioperative and critical care fluid resuscitation. *Br J Surg* 2015;102:24–36.
5. Semler MW, Self WH, Wanderer JP, et al. Balanced crystalloids versus saline in critically ill adults. *N Engl J Med* 2018;378:829–839.
6. Self WH, Semler MW, Wanderer JP, et al. Balanced crystalloids versus saline in noncritically ill adults. *N Engl J Med* 2018;378:819–828.
7. Finfer S, Bellomo R, Boyce N, et al; SAFE Study Investigators. A comparison of albumin and saline for fluid resuscitation in the intensive care unit. *N Engl J Med* 2004;350:2247–2256.
8. Brunkhorst FM, Engel C, Bloos F, et al. Intensive insulin therapy and pentastarch resuscitation in severe sepsis. *N Engl J Med* 2008;358:125–139.
9. Myburgh JA, Finfer S, Bellomo R, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med* 2012;367:1901–1911.
10. Perner A, Haase N, Guttormsen AB, et al. Hydroxyethyl starch 130/0.42 versus Ringer's acetate in severe sepsis. *N Engl J Med* 2012;367:124–134.

This page intentionally left blank

SECTION 3

RESPIRATORY DISORDERS

29

ACUTE ASTHMA

A Little Influenza, a Big Asthma Attack Level I

Rebecca S. Pettit, PharmD, MBA, BCPS, BCPPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of an acute asthma exacerbation.
- Formulate therapeutic endpoints based on the initiation of a pharmacotherapy plan used to treat the acute asthma symptoms.
- Identify appropriate dosage form selection based on the patient's age, ability to take medication, or adherence to technique.
- Determine an appropriate home pharmacotherapy plan, including discharge counseling, as the patient nears discharge from a hospital setting.

PATIENT PRESENTATION

■ Chief Complaint

"My daughter has had a bad fever, and now she is having trouble breathing, and albuterol doesn't help."

■ HPI

Terri Collins is an 8-year-old African-American girl who presents to the ED with a 2-day history of fevers, malaise, and nonproductive cough. The mother gave acetaminophen and ibuprofen to help control the fever. Mother stated that "a lot of other kids in her class have been sick this fall, too." Terri started having trouble breathing the morning of admission, and the mother gave her albuterol, 2.5 mg via nebulization twice within an hour. Terri still sounded wheezy to the mother after the albuterol, and Terri stated it was "hard to breathe." Terri was previously well controlled regarding asthma symptoms. Previous clinic notes reported symptoms during the day only with active play at school or at home and rare nighttime symptoms. She uses PRN albuterol to help with symptoms after playing. Her assessment in the emergency department revealed Terri to have labored breathing, such that she could only complete four- to five-word sentences. She had subcostal retractions, tracheal tugging with tachypnea at 54 breaths/min. Her other vital signs were a heart rate of 160 bpm, blood pressure of 115/59, temperature of 38.8°C, and a weight of 22.7 kg. The initial oxygen saturation was 88%, and she was started on oxygen at 1 L/min via nasal

cannula. Bilateral expiratory and inspiratory wheezes were noted on examination. A chest x-ray revealed a right lower lobe consolidation consistent with pneumonia and possible effusion. After receiving three albuterol/ipratropium nebulizations, her breath sounds and oxygenation did not improve, so she was started on albuterol via continuous nebulization at 10 mg/hr and her oxygen was titrated to 3 L/min. She was also given a dose of 25 mg IV methylprednisolone and a dose of 600 mg IV magnesium sulfate. Terri was then transferred to the PICU for further treatment and monitoring.

■ PMH

Asthma; last hospitalization 4 years ago, and has had two courses of oral corticosteroids in the past year

■ FH

Asthma on father's side of the family

■ SH

Lives with mother, father, and two siblings, both of whom have asthma. There are two cats and a dog in the home. Father is a smoker but states that he tries to smoke outside and not around the kids. She is in the second grade and is very active on the playground.

■ Meds

Albuterol 2.5 mg nebulized Q 4–6 H PRN wheezing
Fluticasone propionate 44 mcg MDI two puffs BID
Acetaminophen 160 mg/5 mL—10 mL Q 4 H PRN fever
Ibuprofen 100 mg/5 mL—10 mL Q 6 H PRN fever

■ All

NKA

■ ROS

(+) Fever, cough, increased work of breathing

■ Physical Examination

Gen

Alert and oriented but in mild distress with difficulty breathing

VS

BP 125/69, P 120, T 37.9°C, RR 40, O₂ sat 94% on 3 L/min nasal cannula

Skin

No rashes, no bruises

HEENT

NC/AT, PERRLA

Neck/LN

Soft, supple, no cervical lymphadenopathy

Chest

Wheezes throughout all lung fields, still with subcostal retractions

CV

RRR, no m/r/g

Abd

Soft, NT/ND

Ext

No clubbing or cyanosis

Neuro

A&O, no focal deficits

■ Labs

Na 141 mEq/L	WBC $34.2 \times 10^3/\text{mm}^3$
K 3.1 mEq/L	Neut 91%
Cl 104 mEq/L	Lymph 5%
CO ₂ 29 mEq/L	Mono 4%
BUN 16 mg/dL	RBC $5.07 \times 10^6/\text{mm}^3$
SCr 0.52 mg/dL	Hgb 13 g/dL
Glu 154 mg/dL	Hct 41%
	Plt $310 \times 10^3/\text{mm}^3$

Respiratory viral panel nasal swab: positive for influenza A

■ Chest X-Ray

RLL consolidation

■ Assessment

Asthma exacerbation with viral pneumonia

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of an asthma exacerbation?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of the asthma exacerbation based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's asthma exacerbation?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's asthma exacerbation and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

Within 48 hours of initiation of the treatment plan for management of the acute exacerbation, Terri was stable enough to transfer to the general pediatric floor. Her vital signs were BP 103/70, P 82, RR 35, T 37.2°C, and O₂ sat 99% on 1 L/min nasal cannula. Mother states that she is able to speak in full sentences now and no longer seems to have trouble breathing.

■ FOLLOW-UP QUESTIONS

1. Should any cough and cold products be used for asthma symptoms? Why or why not?
2. What information should be given to patients/families regarding influenza?
3. What information can be given to families who are concerned about giving their child "steroids" for asthma treatment (either in an acute asthma exacerbation or for controller therapy)?

■ SELF-STUDY ASSIGNMENTS

1. Research the efficacy of systemic corticosteroids for treatment of acute asthma exacerbation when given intravenously versus orally (enterally).
2. Discuss the differences in acute asthma exacerbation symptoms in an adult patient versus a pediatric patient, and describe when you would refer a patient (or family) to the physician or emergency department based on an individualized asthma action plan.
3. Discuss the appropriate use of IV magnesium in an acute asthma exacerbation.

CLINICAL PEARL

For proper treatment of an acute asthma exacerbation, the patient (or family) needs to be aware of the first symptoms of an exacerbation and possible triggers. At this point, the patient (family) should initiate her asthma action plan to minimize the symptoms, duration of drug therapy, and severity of the exacerbation. This, in turn, should decrease the number of severe exacerbations and hospital admissions.

ACKNOWLEDGMENT

Special thanks to Jennifer Donaldson, PharmD, BCPPS for her contribution in the initial development of this case.

REFERENCES

1. Basnet S, Mander G, Andoh J, et al. Safety, efficacy, and tolerability of early initiation of noninvasive positive pressure ventilation in pediatric patients admitted with status asthmaticus: a pilot study. *Pediatr Crit Care Med* 2012;13:393–398.
2. National Asthma Education and Prevention Program Expert Panel report 3: guidelines for the diagnosis and management of asthma. Bethesda, MD, National Institutes of Health, 2007. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm>. Accessed March 16, 2010.
3. Aldington S, Beasley R. Asthma exacerbations. 5: assessment and management of severe asthma in adults in hospital. *Thorax* 2007;62:447–458.
4. Andrew T, McGintee E, Mittal MK, et al. High-dose continuous nebulized levalbuterol for pediatric status asthmaticus: a randomized trial. *J Pediatr* 2009;155:205–210.
5. Vezina K, Chauhan BF, Ducharme FM. Inhaled anticholinergics and short-acting beta(2)-agonists versus short-acting beta2-agonists alone for children with acute asthma in hospital. *Cochrane Database Syst Rev* 2014;7:1–55.
6. Rowe BH, Camargo CA. The role of magnesium sulfate in the acute and chronic management of asthma. *Curr Opin Pulm Med* 2008;15:70–76.
7. Kokotajlo S, Degnan L, Meyers R, et al. Use of intravenous magnesium sulfate for the treatment of an acute asthma exacerbation in pediatric patients. *J Pediatr Pharmacol Ther* 2014;19(2):91–97.
8. Link HW. Pediatric asthma in a nutshell. *Pediatr Rev* 2014;35(7):287–298.
9. Rank MA, Li JT. Clinical pearls for preventing, diagnosing, and treating seasonal and 2009 H1N1 influenza infections in patients with asthma. *J Allergy Clin Immunol* 2009;124:1123–1126.
10. Global Initiative for Asthma (GINA). 2018. Global strategy for asthma management and preventions. Available at: www.ginasthma.org/. Accessed November 15, 2018.

30

CHRONIC ASTHMA

Dust in the Wind Level II

Julia M. Koehler, PharmD, FCCP

Meghan M. Bodenbergh, PharmD, BCPS

Jennifer R. Guthrie, MPAS, PA-C

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize signs and symptoms of uncontrolled asthma.
- Identify potential causes of uncontrolled asthma, and recommend preventive measures.
- Formulate a patient-specific therapeutic plan (including drugs, route of administration, and appropriate monitoring parameters) for management of a patient with chronic asthma.
- Develop a self-management action plan for improving control of asthma.

PATIENT PRESENTATION

■ Chief Complaint

“I think the dust is getting to me!”

■ HPI

Lilly Madison is a 17-year-old Caucasian girl who presents to her primary care provider for follow-up and evaluation regarding her asthma. During her visit, she reports having had to use her albuterol MDI approximately 3–4 days per week over the past 2 months, but over the past week she admits to using albuterol once daily. She reports being awakened by a cough at night once a week during the past month. She states she especially becomes short of breath when she visits her father’s workshop (“Madison Custom Cabinetry”) and when she exercises (although she admits that her shortness of breath is not always brought on by exercise and sometimes occurs when she is not actively exercising). In addition to her albuterol MDI, which she uses PRN, and she also has a fluticasone MDI, which she uses “most days of the week.” She indicates that her morning peak flows have been running around 300 L/min (personal best = 400 L/min) over the past several weeks.

■ PMH

Asthma (previously documented as “mild persistent”) diagnosed at age 7; no prior history of intubations; hospitalized once in the past year for asthma exacerbation; one visit to the ED in the past 6 months; treated with oral systemic corticosteroids during last hospitalization and at ED visit.

Migraine headache disorder (without aura; diagnosed at age 15); currently taking prophylactic medication; has had only one migraine attack in the last year.

■ FH

Mother 49 years old with HTN, migraine HA disorder, and asthma; (nonsmoker); father 50 years old (smoker) with HTN and type 2 DM; brother, age 21, healthy (smoker); twin sister, age 17, healthy (nonsmoker)

■ SH

No alcohol or tobacco use. Single, not sexually active. Lives at home with parents (father is a cabinet maker), twin sister, and two cats. Brother is currently away at college.

■ Meds

Flovent HFA 44 mcg, two puffs BID

Proventil HFA two puffs Q 4–6 H PRN shortness of breath, cough, wheezing

Propranolol 80 mg PO BID

Maxalt-MLT 5 mg PO PRN acute migraine

■ All

PCN (rash)

■ ROS

Denies fever, chills, headache, eye discharge or redness, rhinorrhea, sneezing, sputum production, chest pain, palpitations, dizziness, or confusion

■ Physical Examination

Gen

Well-developed, well-nourished white female appearing stated age in NAD

VS

BP 110/68, HR 78, RR 16, T 37°C; Wt 58 kg, Ht 5'5"

HEENT

PERRLA; mild oral thrush present on tongue and buccal mucosa

Neck/Lymph Nodes

Supple; no lymphadenopathy or thyromegaly

Lungs/Thorax

No intercostal retractions or accessory muscle use with respirations; good air movement; mild expiratory wheezes bilaterally

CV

RRR; no MRG

Abd

Soft, NTND; (+) BS

Ext

Normal ROM; peripheral pulses 3+; no CCE

Neuro

A&O × 3. Cranial nerves II–XII grossly intact. No focal weakness or loss of sensation.

■ Labs

Na 136 mEq/L	Hgb 14 g/dL	WBC $6.0 \times 10^3/\text{mm}^3$
K 3.6 mEq/L	Hct 42%	PMNs 56%
Cl 99 mEq/L	RBC $5.0 \times 10^6/\text{mm}^3$	Bands 1%
CO ₂ 27 mEq/L	Plts $192 \times 10^3/\text{mm}^3$	Eosinophils 3%
BUN 18 mg/dL		Basophils 2%
SCr 0.6 mg/dL		Lymphocytes 33%
Glu 98 mg/dL		Monocytes 5%
Ca 9.3 mg/dL		

■ Assessment

A 17-year-old girl with uncontrolled chronic asthma and mild oral thrush

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's chronic asthma?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's asthma and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Review the GINA guidelines on the management of asthma during pregnancy, and develop a pharmacotherapeutic treatment plan for this patient's asthma if she were to become pregnant.
2. Review the literature on the impact of chronic inhaled corticosteroid use on the risk for development of osteoporosis, and write a two-page paper summarizing the available published literature on this topic.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of uncontrolled chronic asthma?
- 1.b. What additional information do you need to assess this patient? (Consider factors that may have contributed to this patient's uncontrolled asthma.)

Assess the Information

- 2.a. Assess this patient's level of asthma control based on the subjective and objective information available.

CLINICAL PEARL

Patients with asthma who report that taking aspirin makes their asthma symptoms worse may respond well to leukotriene modifiers. Aspirin inhibits prostaglandin synthesis from arachidonic acid through inhibition of cyclooxygenase. The leukotriene pathway may play a role in the development of asthma symptoms in such patients, as inhibition of cyclooxygenase by aspirin may shunt the arachidonic acid pathway away from prostaglandin synthesis and toward leukotriene production. Although inhaled corticosteroids are still the preferred anti-inflammatory medications for patients with asthma and known aspirin sensitivity, leukotriene modifiers may also be useful in such patients based on this theoretical mechanism.

REFERENCES

1. National Asthma Education and Prevention Program. Executive Summary of the NAEPP Expert Panel Report 3: Guidelines for the Diagnosis and Management of Asthma. Bethesda, MD, U.S. Department of Health and Human Services, Public Health Service, National Institutes of Health, National Heart, Lung, and Blood Institute, 2007. Full report. Available at: <http://www.nhlbi.nih.gov/guidelines/asthma/index.htm>. Accessed April 19, 2019.
2. Global Initiative for Asthma (GINA). Global strategy for asthma management and prevention (updated 2018). Available at: <http://www.ginasthma.com>; 2018. Accessed April 19, 2019.
3. Lemanske RF, Mauger DT, Sorkness CA, et al. Step-up therapy for children with uncontrolled asthma while receiving inhaled corticosteroids. *N Engl J Med* 2010;362:975–985.
4. Busse W, Raphael GD, Galant S, et al. Fluticasone Propionate Clinical Research Study Group. Low-dose fluticasone propionate compared with montelukast for first-line treatment of persistent asthma: a randomized clinical trial. *J Allergy Clin Immunol* 2001;107:461–468.
5. Busse W, Nelson H, Wolfe J, Kalberg C, Yancey SW, Rickard KA. Comparison of inhaled salmeterol and oral zafirlukast in patients with asthma. *J Allergy Clin Immunol* 1999;103:1075–1080.
6. Humbert M, Beasley R, Ayres J, et al. Benefits of omalizumab as add-on therapy in patients with severe persistent asthma who are inadequately controlled despite best available therapy (GINA 2002 step 4 treatment): INNOVATE. *Allergy* 2005;60:309–316.
7. Ortega HG, Liu MC, Pavord ID, et al. Mepolizumab treatment in patients with severe eosinophilic asthma. *N Engl J Med* 2014;371:1198–1207.
8. Bleecker ER, FitzGerald JM, Chanez P, et al. Efficacy and safety of benralizumab for patients with severe asthma uncontrolled with high-dosage inhaled corticosteroids and long-acting β -agonists (SIROCCO): a randomized, multicentre, placebo-controlled phase 3 trial. *Lancet* 2016;388:2115–2127.
9. FitzGerald JM, Bleecker ER, Nair P, et al. Benralizumab, an anti-interleukin-5 receptor monoclonal antibody, as add-on treatment for patients with uncontrolled, eosinophilic asthma (CALIMA): a randomized, double-blind, placebo-controlled phase 3 trial. *Lancet* 2016;388:2128–2141.
10. Rabe KF, Nair P, Brusselle G, et al. Efficacy and safety of dupilumab in glucocorticoid-dependent severe asthma. *N Engl J Med* 2018;378:2475–2485.

- Identify the importance of nonpharmacologic therapy in patients with COPD.
- Develop an appropriate medication regimen for a patient with COPD based on disease classification.

PATIENT PRESENTATION

■ Chief Complaint

“My wife says I need to get my lungs checked. Ever since we moved, I’m having a hard time breathing.”

■ HPI

Dwayne Morrison is a 59-year-old man who is presenting to a new provider at the family medicine clinic today with complaints of increasing shortness of breath. He points out that he first noticed some difficulty catching his breath at his job 3 years ago. He had been able to carry heavy loads up and down a flight of stairs daily for the past 35 years without any problem. However, his shortness of breath began to make this very difficult. Coincidentally at that time, he accepted a managerial position at his company that significantly reduced his activity level. After taking this position, he no longer noticed any problems, but he admits that he avoids activities that cause him to physically exert himself. He noticed significant shortness of breath again after he moved to Colorado from a lower elevation 2 months ago to be closer to his grandchildren. His shortness of breath is worst when he is outside playing with his grandchildren. He maintained his same managerial position with the move and does not physically exert himself at work. His previous physician had placed him on budesonide/formoterol (Symbicort) two inhalations twice daily 2 years ago. He thinks his physician initiated the medication for the shortness of breath, but he is not entirely sure. He is hoping to get a good medication that will help relieve his shortness of breath because the gardening season is right around the corner, and he enjoys this hobby.

■ PMH

Coronary artery disease (CAD; MI 7 years ago, resulting in a drug-eluting stent [DES] placement at that time; additional DES placed 2 years ago; normal echocardiogram and stress test 3 months ago) Chronic bronchitis $\times$ 8 years (has had one exacerbation in the past 12 months; received oral antibiotic treatment but was not hospitalized) Cervical radiculopathy

■ FH

Father (alive) with COPD (smoked a pipe for 40 years). Mother (alive) with CAD and cerebrovascular disease.

■ SH

He lives with his wife, who is a nurse. He has a 40 pack-year history of smoking. When he had an MI at age 52, he quit smoking temporarily. At present, he continues to smoke five to six cigarettes per day. He drinks two beers most nights of the workweek and two to three glasses of wine on the weekends.

■ Meds

Aspirin 81 mg PO once daily
Bupropion SR 150 mg PO twice daily
Clopidogrel 75 mg PO once daily
Budesonide/formoterol 80 mcg/4.5 mcg, two inhalations twice daily

31

CHRONIC OBSTRUCTIVE PULMONARY DISEASE

Treading on Thin Air Level II

Sarah L. Anderson, PharmD, FCCP, BCPS, BCACP

Joel C. Marrs, PharmD, FAHA, FASHP, FCCP, FNLA, BCPS, BCACP, BCCP, CLS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize modifiable risk factors for the development of chronic obstructive pulmonary disease (COPD).
- Interpret spirometry readings and patient-specific factors to evaluate and appropriately classify an individual patient's COPD.

OTC naproxen 220 mg PO every 12 hours PRN neck pain
 Rosuvastatin 20 mg PO once daily
 Metoprolol succinate 50 mg PO once daily
 Seasonal influenza vaccine (previous year)

■ All

NKDA

■ ROS

(+) Chronic cough with sputum production; (+) exercise intolerance

■ Physical Examination

Gen

WDWN man in NAD

VS

BP 110/68, P 60, RR 16, T 37°C; Wt 82 kg, Ht 5'9"; pulse ox 93% on RA

Skin

Warm, dry; no rashes

HEENT

Normocephalic; PERRLA, EOMI; normal sclerae; mucous membranes are moist; TMs intact; oropharynx clear.

Neck/Lymph Nodes

Supple without lymphadenopathy

Lungs

Decreased breath sounds; no rales, rhonchi, or crackles

CV

RRR without murmur; normal S₁ and S₂

Abd

Soft, NT/ND; (+) bowel sounds; no organomegaly

Genit/Rect

No back or flank tenderness; normal male genitalia

MS/Ext

No CCE; pulses 2+ throughout

Neuro

A&O × 3; CN II–XII intact; DTRs 2+; normal mood and affect

■ Labs

Na 135 mEq/L	Hgb 13.5 g/dL	AST 40 IU/L	Ca 9.6 mg/L
K 4.2 mEq/L	Hct 41.2%	ALT 19 IU/L	Mg 3.6 mg/L
Cl 108 mEq/L	Plt 195 × 10 ³ /mm ³	T. bili 1.1 mg/dL	Phos 2.9 mg/dL
CO ₂ 26 mEq/L	WBC 5.4 × 10 ³ /mm ³	Alb 3.8 g/dL	
BUN 19 mg/dL			
SCr 1.1 mg/dL			
Glu 89 mg/dL			
NT pro-BNP			
0 pg/mL			
Troponin			
0 ng/mL			

■ Pulmonary Function Tests (During Clinic Visit Today)

Prebronchodilator FEV₁ = 2.98 L (predicted is 4.02 L)

FVC = 4.5 L

Postbronchodilator FEV₁ = 2.75 L

■ Assessment

This is a normal-appearing 59-year-old man presenting to the clinic with complaints of shortness of breath that is limiting his activity and affecting his quality of life. Given the results of spirometry and patient history, patient has COPD in addition to a history of CAD, daily pain from cervical radiculopathy, and chronic cough. Cardiac pathology as a cause of current symptoms is unlikely, given lack of chest pain and recent normal cardiovascular stress test. The patient states that he is adherent to his current medication regimen.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of COPD?
- What additional information is needed to fully assess this patient's COPD?

Assess the Information

- Assess the severity of COPD based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What economic and psychosocial considerations are applicable to this patient?

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating COPD?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's COPD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect and prevent adverse effects?

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Describe and compare the expectations for deterioration in pulmonary function in patients with COPD who have quit smoking with those who continue smoking. In particular, emphasis should be placed on expected patterns of change in FEV₁, FVC, and general health over time in years.
2. Research and describe the appropriate use of inhaled corticosteroids for the management of stable COPD. Be able to compare and contrast the benefits and risks of this therapy.
3. Analyze the safety surrounding the use of β -blockers in patients with COPD versus those with asthma.

CLINICAL PEARL

COPD can lead to exercise deconditioning, mood disorders such as depression, progressive muscle loss, and weight loss. A pulmonary rehabilitation program including mandatory exercise training of the muscles used in respiration is recommended for patients with COPD because of the established benefit related to improvements seen in dyspnea symptoms, health-related quality of life, reduced anxiety and depression, reduced number of hospital days secondary to exacerbations, and improved response to bronchodilators.

REFERENCES

1. Global Initiative for Chronic Obstructive Lung Disease (GOLD). Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: 2019 Report. Available at: <http://www.goldcopd.org>. Accessed December 27, 2018.
2. Qaseem A, Wilt TJ, Weinberger SE, et al. Diagnosis and management of stable chronic obstructive pulmonary disease: a clinical practice guideline update from the American College of Physicians, American College of Chest Physicians, American Thoracic Society, and European Respiratory Society. *Ann Intern Med* 2011;155:179–191.
3. Reynolds NA, Perry CM, Keating GM. Budesonide/formoterol: in chronic obstructive pulmonary disease. *Drugs* 2004;64(4):431–41.
4. Szafranski W, Cukier A, Ramirez A, et al. Efficacy and safety of budesonide/formoterol in the management of chronic obstructive pulmonary disease. *Eur Respir J* 2003;21:74–81.
5. Jones PW, Willits LR, Burge PS, Calverley P. Disease severity and the effect of fluticasone propionate on chronic obstructive pulmonary disease exacerbations. *Eur Respir J* 2003;21:68–73.
6. Kew KM, Mavergames C, Walters JA. Long-acting beta2-agonists for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2013;10:CD010177.
7. Tashkin DP, Pearle J, Iezzoni D, Varghese ST. Formoterol and tiotropium compared with tiotropium alone for treatment of COPD. *COPD* 2009;6:17–25.
8. van Noord JA, Aumann JL, Janssens E, et al. Comparison of tiotropium once daily, formoterol twice daily, and both combined once daily in patients with COPD. *Eur Respir J* 2005;26:214–222.
9. Karner C, Cates CJ. Long-acting beta(2)-agonist in addition to tiotropium versus either tiotropium or long-acting beta(2)-agonist alone for chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2012;4:CD008989.
10. Recommended Immunization Schedule for Adults Aged 19 Years of Older, United States, 2018. Available at: <https://www.cdc.gov/vaccines/schedules/hcp/imz/adult.html>. Accessed April 14, 2019.

32

PULMONARY ARTERY HYPERTENSION

Windy Cindy Level II

Marta A. Miyares, PharmD, BCPS, BCCP, CACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine risk factors for developing pulmonary artery hypertension (PAH).
- Discuss common signs and symptoms associated with PAH.
- List the pharmacologic agents used to treat PAH.
- List the nonpharmacologic agents used to treat PAH.
- Recommend appropriate pharmacologic and nonpharmacologic education for a patient with PAH.

PATIENT PRESENTATION

Chief Complaint

“I felt really dizzy and short of breath, and I suddenly passed out on the bathroom floor.”

HPI

Cindy Jackson is a 32-year-old woman who presents to the ED complaining of episodes of dyspnea and dizziness. While stepping out of the shower this morning, she became very weak and experienced a syncopal episode. She remembers falling to the floor and hitting her head but remembers nothing after that. She was brought to the ED this morning by her sister.

PMH

Hypertension $\times$ 4 years
Diabetes mellitus $\times$ 2 years
Asthma (intermittent)

FH

Father died of heart failure at the age of 62. Mother is 57 and was diagnosed with PAH 4 years ago. Cindy is single and lives with her sister (her only sibling).

SH

Denies tobacco or alcohol use. Admits to heavy cocaine use in her late 20s. Has tried various fad diets (including prescription amphetamines) since she was in college.

Meds

Hydrochlorothiazide 12.5 mg PO Q AM
Glyburide 5 mg PO daily with breakfast
Albuterol MDI one to two puffs Q 6 H PRN SOB

■ All

NKDA

■ ROS

Today, Cindy says she is comfortable at rest but complains of having experienced increased dyspnea, fatigue, and dizziness with her everyday activities for the past 6 months. She says that these symptoms only mildly limit her physical activity and denies experiencing these symptoms at rest. Over the past 2–3 months, she has developed palpitations and noticeable swelling in her ankles. She denies episodes of syncope before this acute incident. Approximately 9 months ago, Cindy was seen by her family physician for increasing shortness of breath. Her physician believed that her increasing dyspnea was attributed to asthma, so he prescribed an albuterol inhaler for her to use. The patient says that the albuterol inhaler did not improve her shortness of breath.

■ Physical Examination

Gen

Patient is lying in ED bed and appears to be in moderate distress.

VS

BP 128/78, P 120, RR 26, T 37°C; Wt 128 kg, Ht 5'6", O₂ sat 88% on room air

Skin

Cool to touch; no diaphoresis

HEENT

PERRLA; EOMI; dry mucous membranes; TMs intact

Neck/Lymph Nodes

(+) JVD; no lymphadenopathy; no thyromegaly; no bruits

Lungs/Thorax

Clear without wheezes, rhonchi, or rales

Breasts

Deferred

CV

Split S₂, loud P₂, S₃ gallop

Abd

Soft; (+) HJR; liver slightly enlarged; normal bowel sounds; no guarding

Genit/Rect

Deferred

MS/Ext

Full range of motion; 2+ edema to both lower extremities; no clubbing or cyanosis; pulses palpable

Neuro

A&O × 3; normal DTRs bilaterally

■ Labs

Na 138 mEq/L	Hgb 14 g/dL	WBC $8.8 \times 10^3/\text{mm}^3$	Mg 2.1 mg/dL
K 3.8 mEq/L	Hct 40%	Neutros 62%	Ca 8.4 mg/dL
Cl 98 mEq/L	RBC $5.1 \times 10^6/\text{mm}^3$	Bands 2%	BNP 60 pg/mL
CO ₂ 28 mEq/L	Plt $311 \times 10^3/\text{mm}^3$	Eos 1%	
BUN 12 mg/dL	MCV 84 μm^3	Lymphs 32%	
SCr 0.9 mg/dL	MCHC 34 g/dL	Monos 3%	
Glu 88 mg/dL			

■ ECG

Sinus tachycardia (rate 120 bpm); right-axis deviation; ST-segment depression in right precordial leads; tall P waves in leads 2, 3, and aVF

■ Chest X-Ray

Cardiomegaly; prominent main pulmonary artery; no apparent pulmonary edema

■ Two-Dimensional Echocardiography

Right ventricular and atrial hypertrophy; tricuspid regurgitation; estimated mean pulmonary arterial pressure (mPAP) 55 mm Hg

■ Ventilation/Perfusion Scan

Negative for pulmonary embolism

■ Pulmonary Function Tests

FEV₁ = 1.87 L (61% of predicted)
FVC = 2.10 L (57% of predicted)
FEV₁/FVC = 0.89

■ Assessment

A 32-year-old woman presents with signs/symptoms of PAH (likely familial).

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of PAH?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of PAH based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating PAH?

■ CLINICAL COURSE (PART 1)

After admission into the ED, the patient underwent a right heart catheterization for vasoreactivity testing. The results indicated that

after receiving the short-acting vasodilator epoprostenol, the patient did not have significant reductions in mPAP and therefore was deemed a nonresponder. The patient's pulmonologist wants to start the patient on bosentan and asks for your recommendation.

- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's PAH and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

CLINICAL COURSE (PART 2)

After 3 months of bosentan therapy, the patient's liver function tests (LFTs) are elevated, so the patient's pulmonologist tells the patient to stop the bosentan for 1 month. It has now been 1 month and the patient returns with normal LFTs.

- 3.e. What alternatives to bosentan would be appropriate to try next?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

- Perform a literature search to determine which medications used for the treatment of PAH have been shown to be safe in pregnancy. Identify the risks associated with pregnancy in female patients with PAH.
- Use primary and tertiary literature to identify the potential visual side effects associated with oral phosphodiesterase inhibitors. Identify the visual side effect that is a medical emergency.
- Review primary and tertiary literature to compare the advantages and disadvantages of using the vasodilators epoprostenol, treprostinil, and iloprost for PAH.
- Use two different drug information sources to develop a recommendation for transitioning a patient from intravenous epoprostenol to subcutaneous treprostinil.

CLINICAL PEARL

Calcium channel blockers should only be used in patients with PAH who respond favorably to short-acting vasodilators during right heart catheterization.

REFERENCES

- McLaughlin VV, Archer SL, Badesch DB, et al. ACCF/AHA 2009 expert consensus document on pulmonary hypertension: a report of the American College of Cardiology Foundation Task Force on Expert Consensus Documents and the American Heart Association developed in collaboration with the American College of Chest Physicians;

American Thoracic Society, Inc.; and the Pulmonary Hypertension Association. *J Am Coll Cardiol* 2009;53(17):1573–1619.

- Galiè N, Humbert M, Vachiery JL, et al. 2015 ESC/ERS guidelines for the diagnosis and treatment of pulmonary hypertension: the Joint Task Force for the Diagnosis and Treatment of Pulmonary Hypertension of the European Society of Cardiology (ESC) and the European Respiratory Society (ERS): endorsed by Association for European Paediatric and Congenital Cardiology (AEPC), International Society for Heart and Lung Transplantation (ISHLT). *Eur Heart J* 2016 Jan 1;37(1):67–119.
- Taichman DB, Ornelas J, Chung L, et al. Pharmacologic therapy for pulmonary arterial hypertension in adults: CHEST guideline and expert panel report. *Chest* 2014 Aug;146(2):449–475.
- McLaughlin VV, Shah SJ, Souza R, Humbert M. Management of pulmonary arterial hypertension. *J Am Coll Cardiol* 2015 May 12; 65(18):1976–1997.
- Običan SG, Cleary KL. Pulmonary arterial hypertension in pregnancy. *Semin Perinatol* 2014 Aug;38(5):289–294.
- Xu QX, Yang YH, Geng J, et al. Clinical study of acute vasoreactivity testing in patients with chronic thromboembolic pulmonary hypertension. *Chin Med J (Engl)* 2017 Feb 20;130(4):382–391.
- Bishop BM, Mauro VF, Khouri SJ. Practical considerations for the pharmacotherapy of pulmonary arterial hypertension. *Pharmacotherapy* 2012;32(9):838–855.
- Montani D, Chaumais MC, Guignabert C, et al. Targeted therapies in pulmonary arterial hypertension. *Pharmacol Ther* 2014 Feb;141(2):172–191.
- McLaughlin VV, McGoon M. Pulmonary arterial hypertension. *Circulation* 2006;114:1417–1431.

33

CYSTIC FIBROSIS*

Blood, Sweat, Lungs, and Gut Level III

Kimberly J. Novak, PharmD, BCPS, BCPPS, FPPAG

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify signs and symptoms of common problems in patients with cystic fibrosis (CF).
- Develop an antimicrobial therapy plan and appropriate monitoring strategy for treatment of an acute pulmonary exacerbation in CF.
- Devise treatment strategies for common complications of drug therapy in patients with CF.
- Provide education on aerosolized medications to patients with CF, including appropriate instructions for dornase alfa and inhaled tobramycin.

PATIENT PRESENTATION

Chief Complaint

As reported by patient's father: "My daughter's experiencing shortness of breath, fast breathing, increasing cough and sputum production, and decreased energy, and she has a poor appetite."

*Additional cystic fibrosis guidelines and clinical information can be found at www.cff.org.

HPI

Jenna O'Mally is a 7-year-old girl with a lifetime history of CF; she was diagnosed with CF at birth after presenting with meconium ileus. She had been doing well until 4 weeks ago, when she developed cold-like symptoms, with a runny nose, dry cough, sore throat, and subjective fever. She was seen at her local pediatrician's office and prescribed a 5-day course of azithromycin suspension 200 mg/5 mL, 160 mg (10 mg/kg) PO on day 1 and 80 mg (5 mg/kg) PO daily on days 2–5 for possible pneumonia. After completing the antibiotic course, Jenna was not feeling any better. Father called the pulmonary clinic regarding her symptoms, and Jenna's pulmonologist called in a prescription to a local pharmacy for ciprofloxacin suspension 250 mg/5 mL, 325 mg PO BID (~40 mg/kg per day), and prednisolone syrup 15 mg/5 mL, one teaspoonful PO twice daily. Father was also instructed to perform three chest physiotherapy sessions (vest treatments) per day and increase her hypertonic saline schedule from once per day to twice daily with her vest treatments. The patient now presents to the pulmonary clinic for a follow-up to her outpatient treatment course. She describes worsening shortness of breath and chest pain, lung and sinus congestion, poor appetite, and severe fatigue. Father reports increasing cough productive of very dark green sputum but no fever. The patient has lost 2 lb since her last clinic visit and has missed 7 days of school. Her oxygen saturation is 88% in clinic on room air, and she was immediately placed on 1 L of O₂ by nasal cannula.

PMH

CF (Phe508del/G551D)

Significant for seven hospitalizations for acute pulmonary exacerbations of CF and two hospitalizations for distal intestinal obstruction syndrome (DIOS) since her initial NICU stay at birth; last hospitalization was 4 months ago

Sinus surgery × 2, last 1 year ago

Pancreatic insufficiency

Poor nutritional status

Recurrent constipation/DIOS

Pulmonary changes c/w long-standing CF with mild bronchiectasis

Seasonal allergies

Asthma

Broken clavicle previous summer after falling from a tree

ADHD

FH

Both parents are alive and generally well (father has hypercholesterolemia). Jenna has an older half-brother (age 15) without CF who had a recent bout of gastroenteritis and a younger sister (age 2) with CF who was recently diagnosed with RSV bronchiolitis. Two maternal uncles died at ages 13 and 17 from CF.

SH

Jenna is in first grade and is enrolled in the gifted program at her school. Family is considering home schooling due to frequent absences in the past school year. Lives with her mother, father, and younger sister approximately 100 miles from the nearest CF center. Her older half-brother visits every other weekend. They have well water and a small mixed-breed family dog; father smokes but only outside of the home. Family is experiencing financial difficulties due to a job layoff and recently lost health insurance. Family is in the process of applying for state Medicaid assistance.

Meds

Ciprofloxacin suspension 250 mg/5 mL, 325 mg PO BID
Prednisolone syrup 15 mg/5 mL, one teaspoonful PO BID

Aerosolized tobramycin 300 mg BID via nebulizer (every other month, currently "on")
Albuterol 0.083% 3 mL (one vial) BID via nebulizer with vest therapy (currently using TID)
Dornase alfa (Pulmozyme) 2.5 mg via nebulizer once daily with morning vest therapy
Sodium chloride 7% aerosol (Hyper-Sal) 4 mL via nebulizer once daily with evening vest therapy (currently using BID)
Fluticasone propionate (Flovent HFA) 44 mcg, one puff once daily
Budesonide (Rhinocort AQ) one spray each nostril once daily
Saline nasal rinse (neti pot) daily
Loratadine 5 mg PO once daily
Creon 12,000 two caps with meals (1500 units of lipase/kg/meal) and one cap with snacks and supplement shakes (750 units of lipase/kg/snack)
Omeprazole 20 mg PO once daily
Ferrous sulfate 324 mg PO BID
AquADEKs one chewable tablet PO once daily
Children's multivitamin with iron one chewable tablet PO once daily
Polyethylene glycol 17 g PO once daily
Atomoxetine 25 mg PO once daily
Ibuprofen 200 mg PO three to four times daily as needed for chest pain
PediaSure two cans per day

All

Codeine (itching), bacitracin cream (rash), strawberries (anaphylaxis)

ROS

Patient complains of chest pain when coughing and large amounts of expectorated green sputum. Reduced ability to perform usual daily activities and play because of SOB. No current hemoptysis, constipation, vomiting, or abdominal pain. Reports having three to four loose or partially formed stools each day. Patient usually has a large appetite but has not been able to finish a meal for the past week.

Physical Examination**Gen**

A shy, thin, cooperative, 7-year-old girl who has shortness of breath with her oxygen cannula removed during the examination

VS

BP 100/65, P 144, RR 45, T 37.8°C; Wt 16 kg, Ht 3'10"; oxygen saturation 95% on 1 L of oxygen; 88% on room air

Skin

Normal tone and color, some eczematous lesions at the elbows

HEENT

EOMI, PERRLA; nares with dried mucus in both nostrils; sinuses tender to palpation; no oral lesions, but secretions noted in the posterior pharynx

Neck/Lymph Nodes

Supple; no lymphadenopathy or thyromegaly

Lungs

Crackles heard bilaterally in the upper lobes greater than in the lower lobes; mild scattered wheezes; chest pain not reproducible with palpation

Breasts

Tanner stage I

CV

Tachycardic, regular rate without murmurs

Abd

Ticklish during examination; (+) bowel sounds; abdomen soft and supple; mild bloating noted, with palpable stool

Genit/Rect

Tanner stage I, deferred internal exam

MS/Ext

Clubbing noted, with no cyanosis; capillary refill <2 seconds

Neuro

Jenna is alert and awake though reserved; CNs intact; somewhat uncooperative with the full neurologic examination.

Labs

Na 149 mEq/L	Hgb 15.4 g/dL	WBC $16.5 \times 10^3/\text{mm}^3$	AST 30 IU/L
K 4.5 mEq/L	Hct 45.2%	Segs 72%	ALT 20 IU/L
Cl 108 mEq/L	MCV 78 μm^3	Bands 10%	LDH 330 IU/L
CO ₂ 34 mEq/L	MCH 31.1 pg	Lymphs 10%	GGT 75 IU/L
BUN 18 mg/dL	MCHC 34 g/dL	Monos 2%	T. Prot 7.3 g/dL
SCr 0.45 mg/dL	Ca, 4.6 mEq/L ^a	Eos 6%	Alb 3.1 g/dL
Glu 195 mg/dL	Phos 4.6 mEq/L	Mg 2.1 mg/dL	IgE 85 IU/mL
	^a Ca _i , ionized calcium.		

Virology/Serology Results

Respiratory viral antigen panel: negative

Influenza A/B PCRs: negative

Bordetella pertussis PCR: negative

Sputum Culture Results

Organism A: *Pseudomonas aeruginosa*

Sensitive: piperacillin/tazobactam, cefepime, ceftazidime, meropenem, aztreonam, tobramycin, amikacin

Intermediate: ciprofloxacin, levofloxacin

Resistant: gentamicin

Organism B: *Stenotrophomonas maltophilia*

Sensitive: trimethoprim-sulfamethoxazole, minocycline, moxifloxacin

Resistant: ceftazidime, meropenem, levofloxacin, all aminoglycosides

Organism C: *P. aeruginosa*, mucoid strain

Sensitive: piperacillin/tazobactam, cefepime, ceftazidime, meropenem, aztreonam, tobramycin

Resistant: ciprofloxacin, levofloxacin, gentamicin, amikacin

Organism D: *Staphylococcus aureus*

Sensitive: vancomycin, linezolid, trimethoprim-sulfamethoxazole, minocycline

Resistant: nafcillin, cefazolin, clindamycin, erythromycin

Organism E: *Achromobacter xylosoxidans*

Sensitive: piperacillin/tazobactam, ceftazidime, trimethoprim-sulfamethoxazole, minocycline

Resistant: meropenem, cefepime, ciprofloxacin, all aminoglycosides

PFTs

FEV₁ 65% of predicted (baseline 90%); FVC 82% of predicted (baseline 95%)

Chest X-Ray

Bronchiectatic and interstitial fibrotic changes consistent with CF

High-Resolution Chest CT (HRCT)

Interval worsening of bronchiectasis in all lobes; increased mucus plugging in left lower lobe

Sinus CT

Panopacification of ethmoid and maxillary sinuses, possible polyp extending into right nasal passage

Assessment

A 7-year-old CF patient with failed outpatient management of acute pulmonary exacerbation and sinusitis, also with nutritional failure

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of an acute pulmonary exacerbation of cystic fibrosis?
- What additional information is needed to fully assess this patient's cystic fibrosis?

Assess the Information

- Assess the severity of this patient's acute pulmonary exacerbation of cystic fibrosis based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating the patient's cystic fibrosis?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's cystic fibrosis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress towards achievement of the goals of therapy.

5.c. During the clinical course, serum tobramycin concentrations were drawn after the second dose of tobramycin, 160 mg (10 mg/kg/dose) IV Q 24 H. Levels are reported as follows:

- Random level: 7.4 mcg/mL collected 4 hours after the end of the 30-minute infusion
- Random level: 1.4 mcg/mL collected 10 hours after end of the 30-minute infusion

Based on this new information, evaluate her drug therapy. Calculate the maximum concentration at end of infusion (C_{max}), true trough, AUC, elimination rate, half-life, volume of distribution, and clearance (standardized for body surface area [BSA]) of her tobramycin therapy. If necessary, suggest modifications. Assume that the previous doses were administered on time.

■ SELF-STUDY ASSIGNMENTS

1. Investigate aztreonam lysine for inhalation (Cayston) and the unique drug delivery device required for administration (Altera Nebulizer System). How are these products prescribed and dispensed to patients?
2. Analyze the role of azithromycin in the chronic medical management of CF. What is/are the proposed mechanism(s) of action of azithromycin in CF management?
3. Review the recommendations for use of fluoroquinolones in children. What data support these recommendations?
4. Investigate CFTR potentiators and modulators used in chronic CF management: ivacaftor (Kalydeco), lumacaftor–ivacaftor (Orkambi), and tezacaftor–ivacaftor (Symdeko). What other research is being conducted in the new drug class of CFTR potentiators and modulators?

CLINICAL PEARL

Chronic gastric acid suppression (proton pump inhibitor or histamine-2 receptor antagonist) is often used in CF patients to improve efficacy of pancreatic enzyme replacement therapy

regardless of the presence of gastroesophageal reflux symptoms. Due to defective bicarbonate transport in the small intestine and subnormal pH, enteric coating may not dissolve consistently in CF patients. Suppression of gastric acid can subsequently raise small intestine pH through mixing of gastrointestinal fluids.

REFERENCES

1. Moran A, Pillay K, Becker DJ, Acerini CL. ISPAD Clinical Practice Consensus Guidelines 2014. Management of cystic fibrosis-related diabetes in children and adolescents. *Pediatr Diabetes* 2014;15(Suppl 20): 65–76.
2. Solomon M, Bozic M, Mascarenhas M. Nutritional issues in cystic fibrosis. *Clin Chest Med* 2016;37:97–107.
3. Mogayzel PJ, Naureckas ET, Robinson KA, et al. Cystic fibrosis pulmonary guidelines. Chronic medications for maintenance of lung health. *Am J Respir Crit Care Med* 2013;187(7):680–689.
4. Elborn JS. Cystic fibrosis. *Lancet* 2016;388(10059):2519–2531.
5. Chmiel JF, Aksamit TR, Chotirmall SH, et al. Antibiotic management of lung infections in cystic fibrosis. I. The microbiome, methicillin-resistant *Staphylococcus aureus*, gram-negative bacteria, and multiple infections. *Ann Am Thorac Soc* 2014;11(7):1120–1129.
6. Patel K, Goldman JL. Safety concerns surrounding quinolone use in children. *J Clin Pharmacol* 2016;56(9):1060–1075.
7. Zobel JT, Young DC, Waters CD, et al. Optimization of anti-pseudomonal antibiotics for cystic fibrosis pulmonary exacerbations: VI. Executive summary. *Pediatr Pulmonol* 2013;48(6):525–537.
8. Fusco NM, Toussaint KA, Prescott WA, Jr. Antibiotic management of methicillin-resistant *Staphylococcus aureus*-associated acute pulmonary exacerbations in cystic fibrosis. *Ann Pharmacother* 2015;49(4):458–468.
9. Paranjape SM, Mogayzel PJ, Jr. Cystic fibrosis in the era of precision medicine. *Paediatr Respir Rev* 2018;25:64–72.

SECTION 4

GASTROINTESTINAL DISORDERS

34

GASTROESOPHAGEAL REFLUX DISEASE

A Burning Question Level II

Brian A. Hemstreet, PharmD, FCCP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the clinical presentation of gastroesophageal reflux disease (GERD), including typical, atypical, and alarm symptoms.
- Discuss appropriate diagnostic approaches for GERD, including when patients should be referred for further diagnostic evaluation.
- Recommend appropriate nonpharmacologic and pharmacologic measures for treating GERD.
- Develop a treatment plan for a patient with GERD, including both nonpharmacologic and pharmacologic measures and monitoring for efficacy and toxicity of selected drug regimens.
- Outline a patient education plan for proper use of drug therapy for GERD.

PATIENT PRESENTATION

■ Chief Complaint

"I'm having a lot of heartburn. These pills I have been using have helped a little but it's still keeping me up at night."

■ HPI

Janet Swigel is a 68-year-old woman who presents to the GI clinic with complaints of heartburn four to five times a week over the past 5 months. She also reports some regurgitation after meals that is often accompanied by an acidic taste in her mouth. She states that her symptoms are worse at night, particularly when she goes to bed. She finds that her heartburn worsens and she coughs a lot at night, which keeps her awake. She has had difficulty sleeping over this time period and feels fatigued during the day. She reports no difficulty swallowing food or liquids. She has tried OTC Prevacid 24HR as needed for the past 3 weeks. This has reduced the frequency of her symptoms to 3–4 days per week, but they are still bothering her.

■ PMH

Asthma × 10 years
Type 2 DM × 5 years
HTN × 10 years

■ FH

Father died of pneumonia at age 75; mother died of gastric cancer at age 68.

■ SH

Patient is married with three children. She is a retired school bus driver. She drinks one to two glasses of wine 4–5 days per week. She does not use tobacco. She has commercial prescription drug insurance.

■ MEDS

Amlodipine 5 mg PO once daily
Hydrochlorothiazide 25 mg PO once daily
Metformin 500 mg PO twice daily
Aspirin 81 mg PO daily
Fluticasone/salmeterol DPI 100 mcg/50 mcg one inhalation twice daily

■ All

Peanuts (hives)

■ ROS

Reports being tired all the time, (–) SOB or hoarseness; (+) cough at night, (+) frequent episodes of heartburn, sometimes after meals, but is worse at night; (–) N/V; (–) BRBPR or dark/tarry stools; (–) dysuria, nocturia, or frequency

■ Physical Examination

Gen

Well-developed African-American woman in NAD

VS

BP 148/85, P 90, RR 17, T 36°C; Wt 220 lb (100 kg), Ht 5'7" (170 cm)

Skin

No lesions or rashes

HEENT

PERRLA; EOMI; moist mucous membranes; intact dentition; oropharynx clear

Neck/Lymph Nodes

Trachea midline; (–) thyromegaly; (–) lymphadenopathy; (–) JVD

Lungs/Thorax

Mostly CTA bilaterally, some intermittent wheezes

CV

Tachycardia with irregularly irregular rhythm; no MRG

Abd

Obese; NT/ND; (+) BS; (–) HSM

Genit/Rect

Gyn exam deferred; heme (–) brown stool

MS/Ext

No CVA tenderness

Neuro

A&O × 3, CN II–XII intact, 5/5 upper- and lower-extremity strength bilaterally

Labs

Na 138 mEq/L	Hgb 13 g/dL	WBC 8.7 ×	AST 21 IU/L
K 3.8 mEq/L	Hct 39%	10 ³ /mm ³	ALT 24 IU/L
Cl 108 mEq/L	RBC 4.6 ×	Neutros 60%	Alk Phos 55 IU/L
CO ₂ 21 mEq/L	10 ⁶ /mm ³	Bands 1%	Fasting lipid panel
BUN 18 mg/dL	Plt 400 ×	Eos 2%	TC 230 mg/dL
SCr 1.1 mg/dL	10 ³ /mm ³	Lymphs 32%	LDL 130 mg/dL
Fasting Glu		Monos 5%	TG 170 mg/dL
220 mg/dL		A1C 9.0%	HDL 42 mg/dL
Ca 8.9 mg/dL			
Phos 4.1 mg/dL			

EGD

Grade B esophagitis; normal gastric and duodenal mucosa. Biopsy results of esophagus and stomach are negative for atypical cells and *Helicobacter pylori*.

Assessment

A 68-year-old woman presenting with uncontrolled GERD symptoms despite self-treatment with intermittent OTC PPI therapy. EGD reveals erosive esophagitis.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of GERD in this patient?
- What additional information is needed to fully assess this patient's GERD?

Assess the Information

- Assess the severity of the GERD symptoms this patient is experiencing based on the subjective and objective information available. Are the symptoms typical or atypical in nature? Are any alarm symptoms or features present?
- Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What patient or lifestyle factors could be contributing to the development of GERD symptoms in this patient?
- What are other potential complications of long-standing untreated GERD?

Develop a Care Plan

- What are the goals of pharmacotherapy for this patient?
- What lifestyle modifications or nonpharmacologic therapies may improve this patient's GERD symptoms?

- What feasible pharmacotherapeutic alternatives are available to treat this patient's GERD symptoms?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's GERD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Four weeks later, Mrs Swigel returns to the clinic for follow-up. Her symptoms have greatly improved, but she is considering stopping therapy because she heard that "all sorts of bad side effects" can happen to her. She saw on television that she could get osteoporosis and that she should be taking calcium. Someone told her that she may also develop some "nasty infections." She does not think it is worth staying on the medication. She also states that she sometimes has brief episodes of heartburn after meals and wishes to know if she should take more of her medication to manage these symptoms.

FOLLOW-UP QUESTIONS

- Should the patient be placed on calcium and vitamin D supplementation because of her acid-suppressive therapy?
- How would you address her concerns regarding the potential for developing infections due to acid-suppressive therapy?
- What recommendations could you give her regarding management of the breakthrough symptoms after meals?

SELF-STUDY ASSIGNMENTS

- H. pylori* is a common cause of peptic ulcer disease and is often tested for in patients presenting with upper GI complaints. Perform a literature search on the relationship between GERD symptoms and *H. pylori*. What conclusions can you draw from the results of these articles? Should *H. pylori* be tested for and treated in patients with GERD?
- Clinical practice involves providing care to diverse patient populations. Identify and review tertiary drug references and Internet websites that provide educational materials about GERD or its treatment in languages other than English.

CLINICAL PEARL

PPIs may cause false-negative results in patients undergoing urease-based *H. pylori* testing, such as with the urea breath test or rapid urease test, or stool antigen tests. Ideally, these drugs should be discontinued 2 weeks before performing these diagnostic tests.

REFERENCES

1. American Gastroenterological Association Institute. Guideline for the diagnosis and management and diagnosis of gastroesophageal reflux disease. *Gastroenterology* 2013;108:308–328.
2. Richter JE, Rubenstein JH. Presentation and epidemiology of gastroesophageal reflux disease. *Gastroenterology* 2018;154:267–276.
3. Vaezi MF, Pandolfino JE, Vela MF, et al. White paper AGA: Optimal strategies to define and diagnose gastroesophageal reflux disease. *Gastroenterology* 2017;15:1162–1172.
4. Pandit S, Boktor M, Alexander JS, et al. Gastroesophageal reflux disease: a clinical overview for primary care physicians. *Pathophysiology* 2018;25(1):1–11.
5. Nadaletto BF, Herbella FAM, Patti MG. Gastroesophageal reflux disease in the obese: Pathophysiology and treatment. *Surgery* 2016;159:475–486.
6. Shaheen NJ, Falk GW, Iyer PG, et al. ACG Clinical Guideline: Diagnosis and management of Barrett's esophagus. *Am J Gastroenterol* 2016;111:30–50.
7. Sandhu DS, Fass R. Current trends in the management of gastroesophageal reflux disease. *Gut Liv* 2018;12:7–16.
8. Gyawali CP, Fass R. Management of gastroesophageal reflux disease. *Gastroenterology* 2018;154:302–318.
9. Savarino E, Zentilin P, Marabotto E, et al. A review of pharmacotherapy for treating gastroesophageal reflux disease (GERD). *Expert Opin Pharmacother* 2017;18:1333–1343.
10. Gyawali CP. Proton pump inhibitors in gastroesophageal reflux disease: friend or foe. *Curr Gastroenterol Rep* 2017;(19)46: doi: 10.1007/s11894-017-0586-5.

35

PEPTIC ULCER DISEASE

Feel the Burn Level II

Ashley H. Meredith, PharmD, FCCP, BCACP, BCPS, CDE

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- List the options for the evaluation and treatment of a patient with symptoms suggestive of peptic ulcer disease (PUD).
- Identify the desired therapeutic outcomes for patients with PUD.
- Identify the factors that guide selection of a *Helicobacter pylori* eradication regimen and improve adherence with the regimen.
- Compare the efficacy of three- and four-drug *H. pylori* treatment regimens and regimens lasting 7, 10, and 14 days or provided in sequential order.
- Create a treatment and monitoring plan for a patient diagnosed with PUD, given patient-specific information.

PATIENT PRESENTATION

■ Chief Complaint

“My stomach has been hurting really badly for the past month or so. It seems to get worse at night.”

■ HPI

Justine Ward is a 67-year-old woman who presents to her primary care physician with complaints of episodic epigastric pain for the past 6 weeks. Her pain is nonradiating. It is sometimes worse with meals, but sometimes eating helps improve the pain. She has been experiencing occasional nausea, bloating, and heartburn. She denies any change in color or frequency of bowel movements. She does not have a history of PUD or GI bleeding. She mentions that she has been having frequent headaches for the past month and has been taking naproxen sodium one to two times daily.

■ PMH

CAD with drug-eluting stent placement × 3 months
Hypothyroidism × 22 years
Hyperlipidemia × 10 years
Lactose intolerance × 47 years
Postmenopausal; LMP ~13 years ago

■ FH

Her mother died at the age of 75 from lymphoma. Her father is alive and has a history of glaucoma, prostate cancer, and AMI at age 70. She has five siblings who are alive. All siblings have a history of hypertension and hyperlipidemia.

■ SH

She is married and has raised three children; she is not employed outside the home. She has never smoked and drinks one to two glasses of wine most days of the week.

■ Meds

Plavix 75 mg PO daily
Lisinopril 5 mg PO daily
Metoprolol tartrate 25 mg PO twice daily
Aspirin 325 mg PO daily
Synthroid 125 mcg PO daily
Atorvastatin 80 mg PO daily
MVI tablet PO daily
Tums 500 mg PO PRN stomach pain
Naproxen sodium 220 mg PO PRN headache (one to two times daily for the past month)
Lactaid one tablet PO PRN dairy product consumption

■ All

NKDA

■ ROS

Unremarkable except for complaints noted above

■ Physical Examination

Gen

Slightly overweight woman in moderate distress

VS

BP 110/72 left arm (seated), P 99, RR 16 reg, T 37.2°C; Wt 149.6 lb (68 kg), Ht 5'3" (160 cm)

Skin

Warm and dry

HEENT

Normocephalic; PERRLA; EOMI

Chest

CTA

CV

RRR; S₁ and S₂ normal; no MRG

Abd

Soft; mild epigastric tenderness; (+) BS; no splenomegaly or masses; liver size normal

Rect

Nontender; stool heme (+)

Ext

Normal ROM; no cyanosis, clubbing, or edema

Neuro

CN II–XII intact; A&O × 3

Labs

Na 142 mEq/L	Hgb 10.1 g/dL	Ca 9.5 mg/dL
K 4.7 mEq/L	Hct 30%	Mg 2.2 mEq/L
Cl 98 mEq/L	Plt 320 × 10 ³ /mm ³	Phos 3.8 mg/dL
CO ₂ 30 mEq/L	WBC 7.6 × 10 ³ /mm ³	Albumin 5.0 g/dL
BUN 8 mg/dL	MCV 72 μm ³	TSH 2.4 μU/mL
SCr 0.7 mg/dL	Retic 0.4%	TC 142 mg/dL
FBG 92 mg/dL	Fe 48 mcg/dL	LDL 64 mg/dL
		HDL 53 mg/dL
		TG 127 mg/dL

EGD

Justine's PCP referred her for a nonemergent EGD, which revealed a 5.5-mm superficial ulcer in the superior duodenum. The ulcer base was clear and without evidence of active bleeding (Fig. 35-1). In addition, inflammation of the duodenum was detected and biopsied.

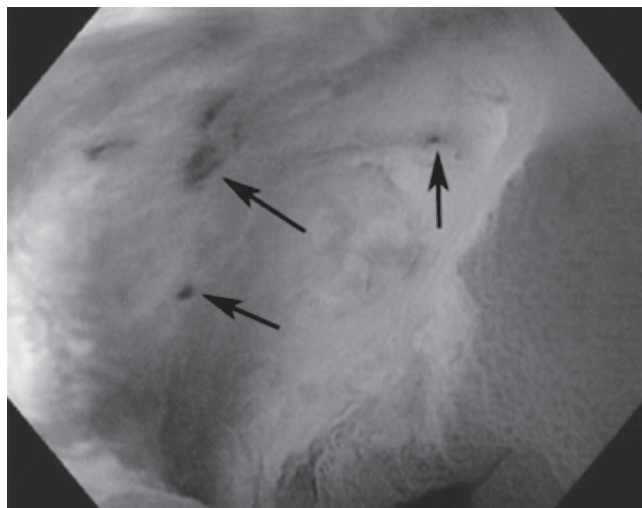


FIGURE 35-1. Endoscopy depicting duodenal ulcer with flat pigmented spots as noted by arrows. (Reprinted with permission from Jameson JL, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York, NY: McGraw-Hill Education, 2018.)

Assessment

PUD with duodenal ulcer and anemia

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of PUD?
- What additional information is needed to fully assess this patient's PUD?

Assess the Information

- Assess the severity of PUD based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy for this case?
- What nondrug recommendations might be useful for this patient?
- In the absence of information about the presence of *H. pylori*, what pharmacologic alternatives are available to treat PUD?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's PUD and other drug therapy problems. Include specific drugs, doses, dosage forms, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

At the time of the EGD, a biopsy of the duodenal mucosa was taken and indicated the presence of inflammation and abundant *H. pylori*-like organisms.

FOLLOW-UP QUESTIONS

- What is the significance of finding *H. pylori* in the duodenal biopsy?
- Based on this new information, how would you modify your goals for treating this patient's PUD?

3. What pharmacotherapeutic alternatives are available to achieve the new goals?
4. Design a pharmacotherapeutic regimen for this patient's ulcer that will accomplish the new treatment goals.
5. How should the PUD therapy you recommended be monitored for efficacy and adverse effects?
6. What information should be provided to the patient about her therapy?
7. How should her frequent headaches now be treated?

SELF-STUDY ASSIGNMENTS

1. Describe the advantages and limitations of both endoscopic and nonendoscopic diagnostic tests to detect *H. pylori*.
2. After performing a literature search on *H. pylori* eradication therapy, compare the efficacy of three- and four-drug regimens.
3. Based on the literature search on *H. pylori* eradication therapy, determine whether therapy should be continued for 7–14 days or provided in a sequential order.

CLINICAL PEARL

Rapid urease breath tests for diagnosis of *H. pylori* should not be used for patients who have received bismuth-containing medications, proton pump inhibitors, or antimicrobials within the previous 4 weeks due to the increased risk of a false-negative result.

REFERENCES

1. Kennigott S, Olze R, Kollmer M, et al. Clopidogrel and proton pump inhibitor (PPI) interaction: separate intake and a non-omeprazole PPI the solution? *Eur J Med Res* 2010;15:220–224.
2. Bouziana SD, Tziomalos K. Clinical relevance of clopidogrel-proton pump inhibitors interaction. *World J Gastrointest Pharmacol Ther* 2015;6:17–21.
3. Frelinger AL, Lee RD, Mulford DJ, et al. A randomized, 2-period, cross-over design study to assess the effects of dexlansoprazole, lansoprazole, esomeprazole and omeprazole on the steady-state pharmacokinetics and pharmacodynamics of clopidogrel in healthy volunteers. *J Am Coll Cardiol* 2012;59:1304–1311.
4. Melloni C, Washam JB, Jones WS, et al. Conflicting results between randomized trials and observational studies on the impact of proton pump inhibitors on cardiovascular events when coadministered with dual antiplatelet therapy. *Circ Cardiovasc Qual Outcomes* 2015;8:47–55.
5. Bhatt DL, Cryer BL, Contant CF, et al. Clopidogrel with or without omeprazole in coronary artery disease. *N Engl J Med* 2010;363:1909–1917.
6. Drepper MD, Spahr L, Frossard JL. Clopidogrel and proton pump inhibitors—where do we stand in 2012? *World J Gastroenterol* 2012;18:2161–2171.
7. McColl KE. *Helicobacter pylori* infection. *N Engl J Med* 2010;362:1597–1604.
8. Chey WD, Leontiadis GI, Howden CW, Moss SF. Treatment of *Helicobacter pylori* infection. *Am J Gastroenterol* 2017;112:212–238.
9. Yang JC, Lu CW, Lin CJ. Treatment of *Helicobacter pylori* infection: current status and future concepts. *World J Gastroenterol* 2014;20:5283–5293.
10. Lanza FL, Chan FKL, Quigley EMM, et al. Guidelines for the prevention of NSAID-related ulcer complications. *Am J Gastroenterol* 2009;104:728–238.

36

NSAID-INDUCED ULCER DISEASE

To Protect and Serve Level II

Carmen B. Smith, PharmD, BCPS

Jay L. Martello, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine whether patients with diabetes who have risk factors for NSAID-induced ulcer disease should remain on aspirin and at what dose.
- Identify the hallmark signs and symptoms of NSAID-induced PUD.
- Recommend appropriate therapy for the treatment of NSAID-induced PUD while taking into account *Helicobacter pylori* infection and its appropriate diagnosis and follow-up.
- Recommend alternative therapies besides traditional NSAIDs for treatment of pain and inflammation in patients with PUD.
- Educate patients effectively on treatment options for NSAID-induced PUD.

PATIENT PRESENTATION

Chief Complaint

“I have had constant stomach pain, nausea, and bloating in the last 2 weeks.”

HPI

Shirley Jackson is a 72-year-old woman who presents to the emergency department for epigastric pain, early satiety, and nausea for 2 weeks. She normally takes OTC Zantac for her symptoms, which she states is usually sufficient; however, this time the symptoms persisted. When asked about any recent medication changes, she admits to frequent naproxen use the past 2 weeks for increased osteoarthritis pain.

PMH

GERD
OA primarily in right wrist/hand and knees
HTN
Type 2 DM
S/P appendectomy after appendicitis in the 1980s

FH

Father died of MI at age 65; mother died of cervical CA in her eighties.

SH

Retired school teacher; smoked one pack per day for 15 years, quit 6 years ago; drinks one alcoholic drink per day but admits to occasionally having more

■ Meds

ASA 325 mg PO once daily
 Lisinopril 20 mg PO once daily
 Amlodipine 10 mg PO once daily
 Metformin 1000 mg PO twice daily
 Atorvastatin 40 mg PO nightly
 OTC naproxen 200 mg, two tablets PO one to four times daily for OA pain
 OTC ranitidine 75 mg, one tablet two to three times daily for heartburn

■ All

Codeine (rash); penicillin (rash/hives)

■ ROS

Denies headache or chest pain. Occasional SOB. Positive heartburn. No weakness, polyphagia, polydipsia, or polyuria. Gait slow but steady. Complains of some chronic pain in left knee, which she has been told is from OA.

■ Physical Examination**Gen**

The patient is a pleasant woman in mild distress.

VS

BP 130/60, P 80, RR 12, T 36.3°C; Wt 141 lb (64.1 kg), Ht 5'5" (157 cm)

HEENT

PERRLA; fundoscopic exam without hemorrhages, exudates, or papilledema; mild cataracts bilaterally

Neck/Lymph Nodes

Supple; no JVD or thyromegaly; no carotid bruits

Lungs

CTA

CV

RRR, normal S₁, S₂

Abd

Normal BS, moderate epigastric pain on palpation

Genit/Rect

Fecal occult blood test positive × 3

MS/Ext

No skin breakdown or ulcers; mild weakness of RUE; mild deformity of right first finger at MCP joint and swelling of DIP joints on first and second fingers

Neuro

A&O × 3; CN II–XII intact; negative Babinski. Normal sensation in hands bilaterally, decreased pain and vibratory sensation in right foot, normal in left.

■ Labs

Na 136 mEq/L	Hgb 8.5 g/dL	<i>Fasting lipid profile</i>
K 3.8 mEq/L	Hct 26%	T. Chol 171 mg/dL
Cl 107 mEq/L	Plt 290 × 10 ³ /mm ³	LDL-C 95 mg/dL
CO ₂ 22 mEq/L	WBC 7.0 × 10 ³ /mm ³	HDL-C 42 mg/dL
BUN 21 mEq/L	Retic 1.8%	TG 170 mg/dL
SCr 1.3 mg/dL	A1C 6.9%	TSH 2.93 µIU/mL
Glu 119 mg/dL		

■ H. pylori Testing

Rapid urease test of gastric biopsy and serology positive

■ EGD

Two small gastric ulcers approximately 6 mm in diameter, trace blood seen but no obvious active bleeding

■ Assessment

The 72-year-old black woman presenting with peptic ulcer disease secondary to NSAID use and *H. pylori* infection

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of PUD in this patient?
- 1.b. What additional diagnostic tests could be ordered to assess the patient's PUD?

Assess the Information

- 2.a. Assess the severity of PUD based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating PUD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's PUD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTIONS

1. What are the strengths and weaknesses of the different methods available for *H. pylori* diagnosis?
2. What feasible pharmacotherapeutic options are available for preventing future GUs in this patient?

■ SELF-STUDY ASSIGNMENTS

1. Perform a literature search and assess current information on the efficacy of various agents for secondary prevention of NSAID-induced ulcers. Review expert opinion on the data specific to prevention of aspirin-induced PUD.
2. Review the ASPREE and ASCEND trials examining the cardiac benefits and bleeding risk of low-dose aspirin for primary prevention in elderly and persons with diabetes, respectively.
3. Perform a literature search and assess the cost-effectiveness of *H. pylori* screening in patients on chronic NSAID therapy.

CLINICAL PEARL

Documented or undocumented use of NSAIDs plays a role in 60% of peptic ulcers that occur in patients who are *H. pylori* negative. Risk factors for developing NSAID-induced ulcer disease include (1) prior history of PUD; (2) age >65 years; (3) high-dose NSAID therapy; and (4) concomitant use of anticoagulants, antiplatelet agents, and/or corticosteroids.

REFERENCES

1. Chey WD, Leontiadis GI, Howden CW, Moss SF. ACG clinical guideline: treatment of *Helicobacter pylori* infection. *Am J Gastroenterol* 2017;112:212–238.
2. Hochberg MC, Altman RD, April KT. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoporosis of the hand, hip, and knee. *Arthritis Care Res* 2012;62:465–474.
3. Lanza FL, Chan FKL, Quigley EMM. Prevention of NSAID-related ulcer complications. *Am J Gastroenterol* 2009;104:728–738.
4. Katz PO, Gerson LB, Vela MF. Guidelines for the diagnosis and management of gastroesophageal reflux disease. *Am J Gastroenterol* 2013;108:308–328.
5. U.S. Preventive Services Task Force. Aspirin use for the primary prevention of cardiovascular disease and colorectal cancer: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2016;164(12):836–845.
6. McNeil JJ, Wolfe R, Woods RL, et al. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. *N Engl J Med* 2018;379:1509–1518.
7. The ASCEND Study Collaborative Group. Effects of aspirin for primary prevention in persons with diabetes mellitus. *N Engl J Med* 2018;379:1529–1539.

37

STRESS ULCER PROPHYLAXIS/UPPER GI HEMORRHAGE

A Bloody Good Time Level I

Jay L. Martello, PharmD, BCPS

Lena M. Maynor, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify risk factors associated with stress ulcer formation and determine which critically ill patients should receive pharmacologic prophylaxis.
- Recommend appropriate pharmacologic alternatives, including agent, route of administration, and dose for the prevention of stress-induced ulcers.
- Identify and implement monitoring parameters for the recommended stress ulcer prophylaxis regimens.
- Discuss the pharmacologic approaches to the management of stress ulcer-induced bleeding.

PATIENT PRESENTATION

■ Chief Complaint

No complaint—patient is unresponsive.

■ HPI

Penny Robinson is a 26-year-old woman who presents to the ED with traumatic injuries following a motor vehicle accident (MVA). She was the restrained driver of a car who was hit on the driver's side by a tractor-trailer that ran a red light. When EMS arrived in the field, the patient was unresponsive with labored breathing. She was given fentanyl 50 mcg, succinylcholine 40 mg, midazolam 5 mg, and was intubated prior to transfer to the hospital. The EMS report indicates that the intubation was very difficult. The extraction time from the vehicle to the ED was 25 minutes.

■ PMH (Provided by Patient's Mother)

PE × 1 about 2 months ago

IBS-C × 10 years

S/P cholecystectomy 8 years ago

Contact dermatitis from recent poison ivy exposure

■ FH

Both mother and father are still alive and in “good health.”

■ SH

Patient is a graduate student at a local university. She smoked cigarettes 1 ppd × 6 years until she was hospitalized for a PE and has since quit. She does not drink alcohol or use illicit drugs.

■ **ROS**

Patient is unresponsive after an MVA.

■ **Meds**

Lubiprostone 24 mcg PO Q 12 H
Apixaban 10 mg PO BID
Prednisone 40 mg daily

■ **Allergies**

No known drug allergies

■ **Review of Systems**

Unable to be provided

■ **Physical Examination****Gen**

Young, unresponsive woman; no obvious bleeding on exam

VS

BP 96/64, P 106, RR 24, T 37.3°C; Wt 112 lb (51 kg), Ht 5'11" (180 cm)

Skin

Warm, dry; small lacerations across forehead and chest; ecchymoses present on both legs and arms

Neck/Lymph Nodes

Supple, no palpable areas of deformity or masses

HEENT

No blood visible in the nose or ears; no obvious damage to the ears, eyes, or nose

Lungs

Patient is intubated.

CV

S₁, S₂ normal; sinus tachycardia with no S₃, S₄

Abd

Firm; decreased bowel sounds

Genit/Rect

No obvious damage to the genital area; otherwise deferred

MS/Ext

(-) CCE, pulses intact

Neuro

Glasgow coma score = 7; negative Babinski; 2+ deep tendon reflexes

■ **Labs (upon ED presentation)**

Na 135 mEq/L	Hgb 8.5 g/dL	PO ₄ 3.0 mg/dL
K 3.6 mEq/L	Hct 25.2%	Ca 10.2 mg/dL
Cl 101 mEq/L	WBC 8.0 × 10 ³ /mm ³	AST 29 IU/L
CO ₂ 22 mEq/L	Plt 112 × 10 ³ /mm ³	ALT 22 IU/L
BUN 40 mg/dL		Alk phos 66 IU/L
SCr 1.0 mg/dL		T. bili 0.4 mg/dL
Glu 91 mg/dL		Alb 3.8 g/dL
		INR 1.1

■ **ABG**

pH 7.43, PaCO₂ 48 mm Hg, PaO₂ 74 mm Hg, HCO₃⁻ 23 mEq/L, pulse ox 92%

■ **AP Chest X-Ray**

Multiple left and right rib fractures. There is evidence of a right hemopneumothorax with protrusion to the right lung.

■ **Focused Assessment With Sonography in Trauma (FAST) Exam**

No evidence of fluid in the perihepatic, hepatorenal, perisplenic, pericardial, or pelvic spaces

■ **CT Abdomen/Pelvis With IV Contrast**

There is no evidence for bowel obstruction. The common bile duct does not appear to be dilated. No free fluid present in the abdominal cavity.

■ **CT Head With IV Contrast**

No midline shift. No evidence for intracranial hemorrhage.

■ **Urinalysis**

Yellow color, specific gravity 1.026, pH 4.6, ketones negative, protein negative, nitrite negative, bilirubin negative, glucose negative, bacteria 0, WBC 0, RBC 3+, hCG negative

■ **Fecal Occult Blood**

Positive, with dark red blood

■ **Trauma Surgeon Postoperative Note**

Prior to transfer to the OR for repair of her rib fractures and hemo-pneumothorax, the patient is given 1 L NS, increasing her BP to 122/76. A central line is placed intraoperatively. She is given cefazolin 1 g every 8 hours for antimicrobial prophylaxis. Her fractures are repaired without significant incident and a chest tube is placed to drain fluid. During the surgery, the patient was given 2 L of LR and 2 units of PRBC to correct for blood and fluid loss. The patient's vitals on exiting surgery and arriving in the surgical ICU are BP 106/62 and P 92. She is currently on assist/control mechanical ventilation. The patient's urine output has been 40 mL/hr for the past 2 hours. The repeat Hgb is 9.6 g/dL, K 3.2 mEq/L, and pulse ox 94%. She is started on NS at 125 mL/hr, enoxaparin 30 mg SQ Q 12 H, a fentanyl drip, and a midazolam drip. An NG tube is also placed.

■ **Assessment**

This is a 26-year old presenting with rib fractures secondary to an MVA s/p operative repair with a high suspicion for a preexisting GI bleed.

QUESTIONS

Collect Information

- What subjective and objective information indicates the need for stress ulcer prophylaxis?
- What additional information is needed to fully assess this patient's GI risk and presence of a current bleed?

Assess the Information

- Assess the patient's risk for a possible upper GI bleed based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in management of the GI bleed?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for managing the GI bleed?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's GI bleed and other drug-related problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Identify commercially available GI protective products that may be administered via nasogastric or orogastric tube.
2. Identify potential drug interactions and adverse effects with antacids, sucralfate, H₂-receptor antagonists, and proton pump inhibitors.
3. Identify methods of reversing direct-acting oral anticoagulants in the acute setting.
4. Describe the advantages and disadvantages of different reversal methods for direct-acting oral anticoagulants.

CLINICAL PEARL

When performing medication reconciliation, always be on the lookout for ulcer prophylaxis agents on the patient's profile. They are often relics from a previous problem that has resolved and are no longer indicated. Patients on ulcer prophylaxis agents without an indication incur increased healthcare costs and are at increased risk for drug interactions and side effects, including a greater risk of pneumonia and *Clostridium difficile* infection, as well as hypomagnesemia and hypocalcemia.

REFERENCES

1. Guillaumondegui OD, Gunter OL, Bonadies JA, et al. Practice Management Guidelines for Stress Ulcer Prophylaxis. Eastern Association for the Surgery of Trauma (EAST). 2008. Available at: <https://www.east.org/education/practice-management-guidelines/stress-ulcer-prophylaxis>. Accessed February 11, 2019.

2. Barkun AN, Bardou M, Pham CQ, Martel M. Proton pump inhibitors vs. histamine 2 receptor antagonists for stress-related mucosal bleeding prophylaxis in critically ill patients: a meta-analysis. *Am J Gastroenterol* 2012;107:507–520.
3. Marik PE, Vasu T, Hirani A, Pachinburavan M. Stress ulcer prophylaxis in the new millennium: a systematic review and meta-analysis. *Crit Care Med* 2010;38:2222–2228.
4. Barkun AN, Bardou M, Kuipers EJ, et al. International consensus recommendations on the management of patients with nonvariceal upper gastrointestinal bleeding. *Ann Intern Med* 2010;152:101–113.

38

CROHN DISEASE

A Sense of Urgency Level II

Brian A. Hemstreet, PharmD, FCCP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the typical clinical presentation of active Crohn disease (CD), including signs, symptoms, and disease distribution and severity.
- Identify exacerbating factors and potential complications of CD.
- Recommend appropriate pharmacologic treatment for active CD.
- Review major toxicities of drugs commonly used for managing CD.
- Educate a patient on the proper use of medications used to treat CD.

PATIENT PRESENTATION

Chief Complaint

"I'm having occasional diarrhea, sometimes with blood. I occasionally have mild abdominal pain. I feel run down lately and have lost a few pounds."

HPI

John Jensen is a 32-year-old man who presents to the clinic with a 3-month history of intermittent episodes of diarrhea. He states that he has been having one to two loose bowel movements a day over this time. This is different from his typical bowel pattern. Over the past 4 weeks, he has also noticed blood in some of his stools. The episodes of diarrhea are frequently accompanied by brief periods of mild abdominal pain. These symptoms have caused significant problems with his job, as he is a sales representative for a pharmaceutical company and spends a lot of time driving to appointments. He reports a 5-lb unintentional weight loss over this time period that he attributes to "not having a great appetite and not wanting to make his abdominal pain worse." He has tried OTC naproxen for the abdominal pain and Pepto-Bismol for the diarrhea, both of which have provided little relief. He does not recall any exposure

to sick contacts. He reports no recent international travel. His PCP referred him to a gastroenterologist.

■ PMH

GERD

Sinusitis (last treated with antibiotics 8 months ago)

Seasonal allergic rhinitis

Exercise-induced bronchoconstriction

ACL repair of the right knee 2 years ago due to a skiing accident

■ FH

Father with DM, mother with HTN. Older sister with CD.

■ SH

Single. Works as a sales representative for a pharmaceutical company. Occasional alcohol use on the weekends. Smokes 0.5 ppd × 10 years.

■ Meds

Loratadine 10 mg PO once daily

Fluticasone two sprays each nostril PRN

Naproxen sodium 220 mg PO Q 8–12 H PRN pain

Albuterol HFA MDI PRN prior to exercise

■ All

Hydrocodone (GI upset)

Sulfa drugs (severe rash)

■ ROS

No sick contacts. Heartburn one to two times a week and rhinorrhea one to two times a week in the summer. No cough, SOB, HA, or mental status changes. No knee or joint pain. No jaundice or rashes. No mouth sores.

■ Physical Examination

Gen

Well-developed Caucasian man in no apparent distress

VS

Sitting: BP 139/89, P 82; standing: BP 136/70, P 85; RR 17, T 37.9°C; Wt 215 lb (97.7 kg), Ht 5'9" (175 cm)

Skin

No lesions or rashes

HEENT

PERRLA, EOMI, pale conjunctivae, moist mucous membranes, intact dentition, oropharynx clear

Neck/Lymph Nodes

Trachea midline, (–) thyromegaly, (–) lymphadenopathy, (–) JVD

Lungs/Thorax

CTA bilaterally

CV

Regular rate and rhythm, no MRG

Abd

Nontender, nondistended, no rebound or guarding; (+) BS, (–) HSM

Genit/Rect

Prostate size WNL, (–) tenderness, heme (+) stool, no evidence of hemorrhoids

MS/Ext

No CVA tenderness

Neuro

A&O × 3, CN II–XII intact, 5/5 upper and lower extremity strength bilaterally

■ Labs

Na 139 mEq/L	Hgb 12 g/dL	AST 25 IU/L
K 3.0 mEq/L	Hct 37%	ALT 28 IU/L
Cl 100 mEq/L	RBC $2.86 \times 10^6/\text{mm}^3$	Alk phos 50 IU/L
CO ₂ 26 mEq/L	Plt $400 \times 10^3/\text{mm}^3$	Total bili 1.2 mg/dL
BUN 15 mg/dL	MCV 80 μm^3	Direct bili 0.6 mg/dL
SCr 1.1 mg/dL	WBC $12.7 \times 10^3/\text{mm}^3$	Albumin 4.1 g/L
Glu 104 mg/dL	Neutros 67%	CRP 20 mg/dL
Ca 8.7 mg/dL	Bands 1%	Lipase 15 units/L
Phos 3.9 mg/dL	Eos 2%	ESR 105 mm/hour
	Lymphs 26%	Stool O & P (–)
	Monos 4%	Stool <i>C. diff</i> toxin (–)

■ Radiology

An abdominal x-ray reveals no evidence of obstruction, dilation, or free air.

■ Other

Colonoscopy: reveals a patchy “cobblestone” pattern of inflammation in the terminal ileum. The inflammatory process extends below the intestinal mucosa, and there is evidence of mucosal friability and recent bleeding. A biopsy of the intestinal mucosa reveals leukocyte infiltration and submucosal granulomas consistent with active CD.

■ Assessment

A 32-year-old man presenting with new-onset active CD involving the terminal ileum requiring treatment

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of CD in this patient?
- What additional information is needed to assess whether this patient has any extraintestinal manifestations of CD?

Assess the Information

- Assess the severity and risk for disease progression and complications of CD in this patient based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and adherence.
- What factors could lead to the development or exacerbation of CD in this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient's CD?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's CD symptoms?
- 3.d. Create an individualized, patient-centered, team based care plan to optimize medication therapy for this patient's CD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

It is now 12 months after treatment was started. Mr Jensen achieved remission after 3 months of initial treatment. Following remission, he continued therapy for an additional 12-week period, after which he was withdrawn from drug treatment. He has had only a few intermittent episodes of diarrhea and abdominal pain over the next 6 months. However, over the past week he has had an increase in the frequency of bowel movements to three to four times per day with intermittent blood. He has developed significant abdominal pain, malaise, fever, and dehydration requiring hospitalization. He is admitted to the general medicine floor of the hospital with a recurrence of active moderate to severe CD.

FOLLOW-UP QUESTIONS

1. Given this new information, how would you modify the patient's drug therapy?
2. What baseline testing would be required if infliximab, adalimumab, or certolizumab were to be used in this patient?

SELF-STUDY ASSIGNMENTS

1. Search for websites containing information about local support groups in your area to which you may refer patients with CD for help and support.
2. Construct a table outlining the major differences between CD and ulcerative colitis.
3. Review the FDA recommendations for use of the major drug classes for treatment of both active CD and maintenance of remission in pregnant patients.

CLINICAL PEARL

Hospitalized patients with active CD are at high risk for venous thromboembolism due to the inflammatory nature of the disease and should be placed on prophylactic therapy for deep vein thrombosis.

REFERENCES

1. Lichtenstein GR, Loftus EV, Isaacs KL, et al. American College of Gastroenterology Clinical Guideline: management of Crohn's disease in adults. *Am J Gastroenterol* 2018;113:481–517.
2. American Gastroenterological Association Institute Guidelines for the Identification, Assessment and Initial Medical Treatment in Crohn's Disease Clinical Decision Support Tool. Available at: <https://s3.amazonaws.com/agaassets/pdf/guidelines/IBDCarePathway.pdf>. Accessed November 8, 2018.
3. Gajendran M, Loganathan P, Catinella AP, Hashash JG. A comprehensive review and update on Crohn's disease. *Dis Mon* 2018;64(2):20–57.
4. Torres J, Mehandru J, Colombel JF, Peyrin-Biroulet L. Crohn's disease. *Lancet* 2017;389:1741–1755.
5. Harbord M, Annese V, Vavricka SR, et al. The first European evidence-based consensus on extra-intestinal manifestations in inflammatory bowel disease. *J Crohns Colitis* 2016;10(3):239–254.
6. Moja L, Danese S, Fiorino C, et al. Systematic review with network meta-analysis: comparative efficacy and safety of budesonide and mesalazine (mesalamine) for Crohn's disease. *Aliment Pharmacol Ther* 2015;41:1055–1065.
7. Coward S, Kuenzig ME, Hazlewood G, et al. Comparative effectiveness of mesalamine, sulfasalazine, corticosteroids, and budesonide for the induction of remission in Crohn's disease: a Bayesian Network Meta-analysis. *Inflamm Bowel Dis* 2017;23:461–472.
8. Ford AC, Bernstein CN, Khan KJ, et al. Glucocorticosteroid therapy in inflammatory bowel disease: systematic review and meta-analysis. *Am J Gastroenterol* 2011;106:590–599.
9. Farraye FA, Melmed GY, Lichtenstein GR, Kane SV. American College of Gastroenterology Clinical Guideline: preventive care in inflammatory bowel disease. *Am J Gastroenterol* 2017;112:241–258.

39

ULCERATIVE COLITIS

Seriously? Four Times a Day? Level I

Nancy S. Yunker, PharmD, FCCP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the common signs and symptoms of ulcerative colitis (UC).
- Evaluate treatment options for an acute episode of UC and recommend a specific treatment plan that includes the medication, dosing regimen, potential side effects, and monitoring parameters.
- Develop a pharmacotherapeutic plan for a patient with UC whose disease is in remission.
- Discuss recent advances in the pharmacotherapy of UC.

PATIENT PRESENTATION

Chief Complaint

"I can't take the pain and diarrhea anymore. I thought I could make it until I got home to see my doctor but today I realized I needed to see someone."

HPI

Bonnie Smith is a 32-year-old woman who presents to the ED with the chief complaint of a 1.5-week history of abdominal pain associated with cramping, bloody diarrhea, and mucus that she states is typical of her UC flares. She states that she has been having about four bloody bowel movements a day for most of the time that she has been in our city on vacation, but today she was dizzy when she stood up; she did not have any symptoms while sitting or lying down. She has been here on vacation for almost 2 weeks and is scheduled to return home in 3 days. She has not traveled outside the country, been hospitalized, or received antibiotics recently. She was diagnosed with UC approximately 3 years ago and has had approximately one exacerbation a year that her physician has treated with Pentasa capsules four times a day during each exacerbation. Each time her symptoms have resolved with 4–6 weeks of therapy. She has refused maintenance therapy because she does not want to take a medication four times a day; it is not conducive to her work and social life and she has refused rectal medications for the same reason. Her last exacerbation was approximately 10 months ago.

PMH

UC, diagnosed 3 years ago
Type 1 DM

FH

Mother has a history of CAD and lung CA; father has a history of UC, S/P colectomy 18 years ago.

SH

Works as an office manager; lives with her fiancée; no children; denies tobacco use; drinks one to two glasses of wine every few weeks; acknowledges marijuana use from 2005 to 2008 but states none in the past 10 years

Meds

Insulin aspart via insulin pump; settings per endocrinology.
Vaccination history is unavailable.

All

NKDA

ROS

Negative for chest pain, SOB, dysuria, fever, chills, N/V, myalgias, arthralgias, polyuria, or recent allergic reaction. Positive for mild abdominal soreness, cramping, and intermittent bloody diarrhea with occasional urgency.

Physical Examination**Gen**

A&O, pleasant, healthy-appearing Caucasian woman in NAD

VS

At 8 AM:
BP (lying down) 100/58 mm Hg, P 60 bpm
BP (standing) 80/40 mm Hg, P 75 bpm
RR 18/min, T 37.0°C
Wt 145 lb (66 kg), usual weight 150 lb (68 kg); Ht 5'7" (170 cm);
BMI 23.5 kg/m²

Skin

No lesions; warm, adequate turgor

HEENT

PERRLA; EOMI; mucous membranes without lesions or exudates; TMs intact

Lungs

CTA, no rales or rhonchi

CV

RRR, normal S₁ and S₂; no S₃, S₄

Abd

Normal active BS, soft, nondistended; tender to deep palpation but no palpable mass; no liver or spleen enlargement; no rebound tenderness or guarding

Rect

Somewhat tender; no hemorrhoids, fissures, or lesions by anoscopy; heme (+) stool

MS/Ext

No CCE; pulses 2+; normal ROM; strength 5/5 bilaterally

Neuro

A&O × 3; CN II–XII intact; DTRs 2+

Labs

At 10:00 AM:

Na 137 mEq/L	Hgb 13 g/dL	WBC $5.5 \times 10^3/\text{mm}^3$	AST 22 IU/L
K 3.4 mEq/L	Hct 38%	PMNs 52%	ALT 20 IU/L
Cl 105 mEq/L	Plt $242 \times 10^3/\text{mm}^3$	Bands 5%	Alk phos 36 IU/L
CO ₂ 27 mEq/L	MCV 85.3 μm^3	Lymphs 36%	T. Bili 0.5 mg/dL
BUN 26 mg/dL	MCH 29.1 pg	Basos 1%	PT 12.0 s
SCr 1.0 mg/dL	MCHC 34.1 g/dL	Monos 6%	INR 1.0
Glu 113 mg/dL			Ca 8.9 mg/dL
			Mg 1.9 mEq/L
			PO ₄ 4.2 mg/dL
			Alb 3.9 g/dL
			A1C 6.2%

Fecal calprotectin: 160 mcg/g

Urinalysis

Color yellow; transparency clear; negative for protein, leukocyte esterase, nitrite, blood, ketones, RBCs, WBCs, and bilirubin; pH 7.0; specific gravity 1.019

Assessment

Lower GI bleeding with a history of UC in a patient who has declined maintenance therapy in the past
D/C with instructions to return to ED if symptoms worsen and to contact PCP on return home

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of active UC?
- What additional information is needed to fully assess the patient's UC?

Assess the Information

- 2.a. Assess the severity of the UC based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating UC?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's UC and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient presents to her local PCP for follow-up 1 month after her initial presentation to the ED. She states that her bowel movements are "completely normal," and she no longer has pain. She states that the symptoms started to resolve about 2 weeks after she started treatment. She has had no further complaints of weakness or dizziness. The repeat Hgb today is 12.9 g/dL.

FOLLOW-UP QUESTIONS

1. Considering this new information, what therapeutic intervention(s) do you recommend at this time?
2. What additional information should be provided to the patient regarding this therapeutic intervention?
3. What other healthcare maintenance issues should now be addressed in this patient with UC?

SELF-STUDY ASSIGNMENTS

1. Review the literature comparing mesalamine, olsalazine, balsalazide, and sulfasalazine preparations regarding efficacy, adverse effects, and cost; include all currently available mesalamine dosage forms.
2. Perform a literature search to determine what new therapies are being evaluated for UC, including biologics and biosimilars.
3. Review the literature supporting use of cyclosporine, tacrolimus, anti-TNF- α agents in patients with severe, extensive disease poorly responsive to initial corticosteroid treatment.

4. Conduct a literature search to determine how pharmacogenomics is affecting therapy of UC patients.

CLINICAL PEARL

Similar secondary loss of response rates to TNF- α antagonists and vedolizumab have been reported. Vedolizumab dose intensification has been reported to restore response to approximately 50% of patients who lose response to vedolizumab.

REFERENCES

1. Rubin DT, Ananthakrishnan AN, Siegel CA, Sauer BG, Long MD. ACG clinical guideline: ulcerative colitis in adults. *Am J Gastroenterol* 2019;114:384–413.
2. Harbord M, Eliakim R, Bettenworth D, et al. For the European Crohn's and Colitis Organisation (ECCO). Third European evidence-based consensus on the management of ulcerative colitis Part 2: current management. *J Crohn's Colitis* 2017;11:769–784.
3. Jeon SR, Chai J, Kim C, Lee CH. Current evidence for the management of inflammatory bowel diseases using fecal microbiota transplantation. *Curr Infect Dis Rep* 2018;20:21.
4. Ye B, van Langenberg DR. Mesalazine preparations for the treatment of ulcerative colitis: are all created equal? *World J Gastrointest Pharmacol Ther* 2015;6:137–144.
5. Bressler B, Marshall JK, Bernstein CN, et al. On behalf of the Toronto Ulcerative Colitis Consensus Group. Clinical practice guidelines for the medical management of nonhospitalized ulcerative colitis: The Toronto Consensus. *Gastroenterology* 2015;148:1035–1058.
6. Dassopoulos T, Cohen RD, Scherl EJ, Schwartz RM, Kosinski L, Regueiro MD. Ulcerative colitis care pathway. *Gastroenterology* 2015;149:238–245.
7. Chang S, Hanauer S. Optimizing pharmacologic management of inflammatory bowel disease. *Expert Rev Clin Pharmacol* 2017;6:595–607.
8. Aggarwal A, Sabol T, Vaziri H. Update on the use of biologic therapy in ulcerative colitis. *Curr Treat Options Gastroenterol* 2017;15:155–167.
9. Iskandar HN, Dhere T, Farraye FA. Ulcerative colitis Update on medical management. *Curr Gastroenterol Rep* 2015;17:44.
10. Ungaro R, Mehandru S, Allen PB, Peyrin-Biroulet L, Colombel JF. Ulcerative colitis. *Lancet* 2017;389:1756–1770.

40

NAUSEA AND VOMITING

In for a Tune-Up Level II

Kelly K. Nystrom, PharmD, BCOP

Amy M. Pick, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Develop a prophylactic antiemetic regimen based on the chemotherapeutic agents' emetic risk that optimizes the management of nausea and vomiting.
- Design an appropriate treatment regimen for anticipatory and breakthrough nausea and vomiting.

- Design a monitoring plan to assess the effectiveness of an antiemetic regimen.
- Discuss with patients and caregivers the reason for antiemetics, their appropriate use, and the management of side effects.
- Recommend appropriate alternative antiemetic strategies based on patient-specific conditions, such as previous response to chemotherapy and side effects.

PATIENT PRESENTATION

■ Chief Complaint

"I have difficulty swallowing."

■ HPI

Mr Wilson is a 57-year-old man who presents to his primary care provider with complaints of pain in the back of his throat and difficulty swallowing. He has had a 14-lb weight loss over the previous 2 months because it has been difficult to eat. Upon physical exam, a mass is felt in his neck. His primary care provider orders a biopsy, and the histopathology reveals squamous cell carcinoma. A PET-CT scan reveals a 3-cm mass in the oropharynx with disease found in multiple cervical lymph nodes. A diagnosis of advanced stage oropharyngeal cancer is made with the plan to begin systemic chemotherapy and radiation in the outpatient setting.

■ PMH

BPH

Cancer of the oropharynx (p16 negative)

GERD

■ FH

Father died at age 82 of heart and renal failure; mother died at age 68 with emphysema, obesity, MI, hypertension; two sisters, one with diabetes; three adult children, alive and healthy.

■ SH

Single and works as a salesman at a car dealership. He has smoked 1–1.5 packs of cigarettes a day starting at the age of 14. He still smokes but has cut back because his employer has a campus-wide no smoking policy. He routinely consumes alcohol, averaging four to five alcoholic drinks per week.

■ ROS

Complaints include difficulty swallowing, pain in throat, and weight loss over the past 2 months.

■ Home Meds

Tamsulosin 0.4 mg PO daily

Esomeprazole 40 mg PO daily

Oxycodone ER 10 mg PO Q 12 H

Oxycodone 5 mg PO Q 3 H PRN

■ All

NKDA

■ Physical Examination

Gen

This is a pleasant thin Caucasian man who appears to be in acute distress due to throat pain.

VS

BP 160/82, P 91, RR 20, T 36.6°C; Wt 149.6 lb (68 kg), Ht 6'0" (183 cm)

Skin

Warm and dry to touch

HEENT

No discharge noted in the external ear canals. Mouth is pink and dry. An abnormal mass is present in the oropharynx.

Neck/Lymph Nodes

Enlarged cervical lymph nodes that are tender to the touch. No JVD or thyromegaly noted.

Lungs/Thorax

Good air movement. No wheezes or rhonchi noted. No spinal abnormalities appreciated.

CV

RRR. No rubs, murmurs, or gallops

Abd

Positive bowel sounds, no hepatosplenomegaly

Genit/Rect

Deferred

MS/Ext

Normal range of motion and equal strength in upper and lower extremities. Positive for 2+ pitting edema in the feet and ankles.

Neuro

Patient is awake, alert, and oriented. Cranial nerves intact. Gait was not assessed. Patient is very anxious about his diagnosis and treatment.

■ Labs

Na 141 mEq/L	Hgb 12.4 g/dL	T. bili 0.8 mg/dL
K 4.3 mEq/L	Hct 36.3%	Albumin 2.4 g/dL
Cl 106 mEq/L	Plt $148 \times 10^3/\text{mm}^3$	AST 18 IU/L
CO ₂ 21 mEq/L	WBC $18.4 \times 10^3/\text{mm}^3$	ALT 12 IU/L
BUN 21 mg/dL	Neutros 72%	Alk Phos 65 IU/L
SCr 0.7 mg/dL	Bands 8%	GGT 40 IU/L
Glu 97 mg/dL	Lymphs 11%	
	Monos 4%	
	Eos 1%	
	Basos 1%	
	Promyelo 1%	
	Meta 2%	

■ Assessment

Mr Wilson has very advanced oropharyngeal cancer and is not a candidate for surgical intervention. He would like to proceed with concurrent chemotherapy and radiation, which is planned at the outpatient cancer clinic. He continues to have pain and is anxious about his diagnosis and the chemotherapy he is about to receive. The selected regimen is high-dose cisplatin with concurrent external beam radiation. Orders include

Ondansetron 32 mg IV 30 minutes prior to chemotherapy

Dexamethasone 20 mg IV 30 minutes prior to chemotherapy

Fosaprepitant 150 mg IV 30 minutes prior to chemotherapy on day 1, and then aprepitant 80 mg PO daily on days 2 and 3
 Cisplatin 100 mg/m² IV once every 3 weeks administered on days 1, 22, and 43
 Radiation therapy 2 Gy/day for a total of 70 Gy over 7 weeks
 Ondansetron 4 mg PO Q 8 H PRN nausea and vomiting

QUESTIONS

Collect Information

- 1.a. What subjective and objective information may influence this patient's risk for chemotherapy-induced nausea and vomiting?
- 1.b. What additional information is needed to fully assess this patient's risk of nausea and vomiting?

Assess the Information

- 2.a. Assess the emetic risk of this patient's treatment regimen.
- 2.b. Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies may be useful to prevent nausea and vomiting?
- 3.c. What feasible pharmacotherapeutic alternatives are available for the prophylaxis of acute and delayed nausea and vomiting and for the treatment of breakthrough nausea and vomiting?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical parameters should be used to determine whether the antiemetic regimen the patient received was effective for preventing acute and delayed nausea and vomiting?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE (PART 1)

You review Mr Wilson's antiemetics prior to administering the high-dose cisplatin, and the provider makes changes based on your recommendations. Mr Wilson does well for the first 24 hours, but around hour 30, he develops nausea and vomiting. He follows the instructions provided and takes the ondansetron he has at home. He calls his pharmacy on day 3 for advice, as he is still experiencing vomiting despite taking the antiemetics. The pharmacist asks

about hydration status and learns he has had limited fluid intake over the past 3 days and cannot recall the last time he urinated. He is tired but assumes this is due to the cisplatin therapy. The pharmacist considers an over-the-counter recommendations but recognizes they may offer little relief.

FOLLOW-UP QUESTIONS

1. What pharmacologic alternatives may be helpful for treatment of breakthrough nausea and vomiting in this patient?
2. Design a plan to address this patient's dehydration and need for fluid and electrolyte replacement.

CLINICAL COURSE (PART 2)

Five days later, Mr Wilson's nausea and vomiting have resolved. He continues to receive concurrent radiation and will return to the clinic on day 22 to receive cycle 2 of his chemotherapy.

FOLLOW-UP QUESTIONS (CONTINUED)

3. What changes can be made to prevent delayed nausea and vomiting for subsequent chemotherapy cycles?
4. Design a plan to prevent anticipatory nausea and vomiting in this patient for subsequent chemotherapy cycles.

CLINICAL COURSE: ALTERNATIVE THERAPY

While discussing Mr Wilson's antiemetic regimen, he says, "I remember that my sister used to take ginger to prevent sea sickness when she went on a cruise, and my cousin used ginger when he was having chemotherapy a few years ago. Would that be good for me to try?" See Section 19 in this Casebook for questions about the use of ginger for treatment of nausea and vomiting.

SELF-STUDY ASSIGNMENTS

1. Compare the indications, doses, and costs of the 5-HT₃ antagonists: dolasetron, ondansetron, granisetron, palonosetron, and the combination product netupitant/palonosetron.
2. Discern in which patients it would be appropriate to use palonosetron and/or one of the NK₁ receptor antagonists: aprepitant, fosaprepitant, rolapitant, or netupitant; discern the advantages and limitations of each drug.
3. Review the antiemetic regimens that incorporate olanzapine for the prevention of nausea and vomiting.
4. Review various guidelines for antiemetic options for the treatment of refractory nausea and vomiting.

CLINICAL PEARL

Appropriate use of antiemetics is essential. The combination of a 5-HT₃ antagonist, dexamethasone and an NK₁ receptor antagonist is the regimen of choice for preventing acute nausea and vomiting with highly emetic and some moderately emetic chemotherapy regimens. The NK₁ receptor antagonists, dexamethasone and palonosetron, or combination netupitant/palonosetron are also useful for preventing delayed nausea and vomiting. For those patients who fail the above three-drug regimen, olanzapine is a nice alternative either with palonosetron and dexamethasone or in addition to the three-drug regimen. Antiemetic therapy decisions should be based on efficacy, patient-specific factors, and cost.

REFERENCES

1. Ettinger DS, Berger MJ, Aston J, et al. NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) Guideline Antiemesis 3.2018. © 2018 National Comprehensive Cancer Network, Inc. Available at: www.NCCN.org. Accessed September 28, 2018.
2. Navari RM. Managing nausea and vomiting in patients with cancer: what works. *Oncology* 2018;32:121–125, 131, 136.
3. Warr D. Prognostic factors for chemotherapy induced nausea and vomiting. *Eur J Pharmacol* 2014;722:192–196.
4. Jordan K, Jahn F, Aapro M. Recent developments in the prevention of chemotherapy-induced nausea and vomiting (CINV): a comprehensive review. *Ann Oncol* 2015;26:1081–1090.
5. Herrstedt J, Roila F, Warr D, et al. Updated MASCC/ESMO consensus recommendations: prevention of nausea and vomiting following high emetic risk chemotherapy. *Support Care Cancer* 2017;25:277–288.
6. Roila F, Warr D, Hesketh PJ, et al. 2016 updated MASCC/ESMO consensus recommendations: prevention of nausea and vomiting following moderately emetogenic chemotherapy. *Support Care Cancer* 2017;25:289–294.
7. Clinical Pharmacology powered by ClinicalKey. Tampa (FL): Elsevier. C2018. Available at: <http://www.clinicalkey.com>. Accessed October 27, 2018.

41

DIARRHEA

Diner's Diarrhea Level I

Marie A. Abate, BS, PharmD

Charles D. Ponte, BS, PharmD, BC-ADM, BCPS, CDE, CPE FADE, FAPhA, FASHP, FCCP, FNAP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the most likely causes of acute diarrhea.
- Establish primary goals for the treatment of acute diarrhea based on signs, symptoms, and patient background.
- Recommend appropriate nonpharmacologic therapy for patients experiencing acute diarrhea.
- Explain the place of drug therapy in the treatment of acute diarrhea and recommend appropriate products.

PATIENT PRESENTATION

■ Chief Complaint

"I've had the runs for a couple of days, along with vomiting. I haven't been able keep anything down and I feel awful."

■ HPI

Mindy Reynolds is a 25-year-old woman who comes to the Family Medicine Clinic with a complaint of nausea, vomiting, and diarrhea.

She had been well until 1.5 days ago, when she began to experience severe nausea that occurred about 6 hours after eating out at a large chain buffet restaurant. She had granola and yogurt for breakfast and a chicken pesto and avocado sandwich for lunch the day her symptoms began. Her boyfriend ate an assortment of seafood and beef dishes for dinner while she had salads, chicken stir fry, and shrimp. He has felt fine with no symptoms.

She had eaten several plates of food for dinner along with two glasses of iced tea. She had a few sips of her boyfriend's soda, but did not have any milk or other dairy products. She woke up from sleep with severe nausea and took two tablespoonfuls of Maalox Plus at that time. The nausea persisted, and she began to vomit "several times" with some relief. As the night progressed, she still felt "queasy" and took two extra Prilosec OTC tablets to settle her stomach. She began to feel dizzy, achy, and warm, and her temperature at the time was 100°F. These complaints continued to persist, and she vomited a few more times. She has not tolerated any solid foods, but she has been able to keep down small amounts of fluid. Since yesterday, she has had four to six liquid stools along with crampy abdominal pain. She has not noticed any blood or mucus in the bowel movements. Her boyfriend brought her to the clinic because she was becoming weak and lightheaded when she tried to stand up. She denies antibiotic use, laxative use, or excessive caffeine intake. She usually drinks bottled water and has not been traveling outside the country. She often experiences stress-related constipation and occasionally (once every 2 months) has some loose stools alternating with constipation. These are usually accompanied by abdominal discomfort that is relieved by a bowel movement. She states that this episode is different.

■ PMH

IBS × 2 years

Migraine headaches × 10 years

GERD × 5 years

Depression × 3 years

UTI—6 months ago (treated successfully with ciprofloxacin × 10 days)

■ FH

Noncontributory

■ SH

No current tobacco use, uses marijuana occasionally; drinks wine or a mixed drink socially, usually not more than one glass per week; has about two cups of caffeinated coffee daily. She works as an administrative associate for a local bank. Single, sexually active (one partner, monogamous relationship).

■ ROS

Dizzy on standing but no complaints of vertigo; denies headache, sore throat, ear pain, or nasal discharge. Denies coughing or congestion. Frequent bouts of nausea. Frequent loose stools associated with significant cramping. Decreased urination; no dysuria or frequency. Complains of generalized lassitude, mild aching; feels like her heart is skipping beats.

■ Meds

Valproic acid 500 mg PO BID × 6 years

Triphasil oral contraceptive 1 PO at bedtime × 3 years (last taken the evening after the dinner out)

Prilosec 20–40 mg PO daily as needed

One A Day Women's Formula Multivitamin 1 PO daily

Metamucil one tablespoonful daily
St John's wort two 900 mg tablets daily

All

Penicillin → itching, rash on legs, 10 years ago; dust → nasal congestion, watery eyes

PE

Gen

White female, appears ill, in moderate distress

VS

BP 125/82, P 80 (supine), BP 90/60, P 90 (standing), RR 16, T 38°C; Wt 165 lb (75 kg), Ht 5'4" (162.5 cm)

Skin

Slightly warm to touch, fair skin turgor (mild tenting noted)

HEENT

Dry mucous membranes, nonerythematous TMs, PERRLA, fundi benign, slight erythema in throat

Neck/Lymph Nodes

Without masses, lymphadenopathy, or thyromegaly

Chest

Clear to A&P

CV

RRR without MRG

Abd

Diffuse tenderness, no guarding or rebound, without organomegaly, nondistended, hyperactive bowel sounds

Genit/Rect

Heme (–) stool in the rectal vault; no gross blood

MS/Ext

Normal muscle strength, no CCE

Neuro

A&O × 3; CN II–XII intact; normal reflexes, normal sensory and motor function

Labs

Na 135 mEq/L	Hgb 12.0 g/dL	AST 35 IU/L
K 3.2 mEq/L	Hct 35%	ALT 30 IU/L
Cl 97 mEq/L	Plt $350 \times 10^3/\text{mm}^3$	T. bili 1.5 mg/dL
CO ₂ 25 mEq/L	WBC $12.0 \times 10^3/\text{mm}^3$	
BUN 25 mg/dL	PMNs 62%	
SCr 1.2 mg/dL	Lymphs 36%	
Glu 90 mg/dL	Monos 2%	

Serum pregnancy test—negative

Stool sample obtained for ova and parasites

UA

Clear, dark amber; SG 1.030; pH 6.0; protein (–); glucose (–); acetone (–), bilirubin (–), blood (–); microscopic: 0–2 WBC/hpf, 0–2 RBC/hpf, several hyaline casts

Assessment

Probable acute gastroenteritis; R/O other causes
Depression
Migraine headaches
GERD
Irritable bowel syndrome

Plan

Admit to observation unit for acute therapy

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of diarrhea?
- What additional information is needed to fully assess this patient's diarrhea?

Assess the Information

- Assess the severity of the diarrhea based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What are other possible causes of this patient's diarrhea?

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating diarrhea?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's diarrhea and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The treatment and monitoring plan you recommended was initiated on admission. The patient's diarrhea slowed by the evening of day 1. The patient had no further episodes of diarrhea or vomiting after

midnight. On the morning of day 2, her orthostasis had resolved, her temperature was normal, the IV fluids were stopped, and she received clear liquids by mouth for breakfast and lunch. The patient was discharged during the late afternoon.

■ FOLLOW-UP QUESTIONS

1. How should this patient's contraception be managed after she is rehydrated and returns home?
2. Does the patient need any changes in her prophylactic migraine headache therapy?
3. How should her IBS be managed?

■ SELF-STUDY ASSIGNMENTS

1. Identify the infectious causes of diarrhea. Design an effective pharmacotherapy treatment regimen for each cause.
2. Provide recommendations for the prevention and treatment of traveler's diarrhea.
3. Describe whether or not antidiarrheal drug products can be safely recommended for use in very young children (<3 years old) or in patients with bloody diarrhea and, if so, the specific products that could be used.
4. Describe when oral rehydration products should be used, and recommend a specific product and dosage for young or older patients who present with mild to moderate diarrhea and minimal dehydration.
5. Investigate the relationship between the development of IBS and bacterial gastroenteritis.

CLINICAL PEARL

Broad-spectrum antibiotics (especially clindamycin and the fluoroquinolones) are a common cause of *Clostridium difficile* colitis. Diarrhea is a common sign of the disease and may begin 3 days after initiating an antibiotic or up to 3 months after a course of antibiotics (the Rule of 3's).

REFERENCES

1. Riddle MS, DuPont HL, Connor BA. ACG clinical guideline: diagnosis, treatment, and prevention of acute diarrheal infections in adults. *Am J Gastroenterol* 2016;111:602–622.
2. Acree M, Davis AM. Acute diarrheal infections in adults. *JAMA* 2017;318:957–958.
3. DuPont HL. Acute infectious diarrhea in immunocompetent adults. *N Engl J Med* 2014;370:1532–1540.
4. Barr W, Smith A. Acute diarrhea. *Am Fam Physician* 2014;89:180–189.
5. Hatchette TF, Farina D. Infectious diarrhea: when to test and when to treat. *CMAJ* 2011;183:339–344.
6. Pulling M, Surawicz CM. Loperamide use for acute infectious diarrhea in children: safe and sound? *Gastroenterology* 2008;134:1260–1262.
7. Sarowska J, Choroszy-Król I, Regulska-Ilow B, Frej-Mądrzak M, Jama-Kmiecik A. The therapeutic effect of probiotic bacteria on gastrointestinal diseases. *Adv Clin Exp Med* 2013;22:759–766.
8. Sayuk GS, Gyawali CP. Irritable bowel syndrome: modern concepts and management options. *Am J Med* 2015;128:817–827.
9. Wilkins T, Sequoia J. Probiotics for gastrointestinal conditions: a summary of the evidence. *Am Fam Physician* 2017;96:170–178.
10. Ford AC, Talley NJ. Irritable bowel syndrome *BMJ* 2012;345:e5836.

42

CONSTIPATION

All Bound Up Level II

Michelle Fravel, PharmD, BCPS

Beth Bryles Phillips, PharmD, FASHP, FCCP, BCPS, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify medications that can exacerbate constipation.
- Describe the advantages and disadvantages of each class of laxatives and discuss the appropriate use of each class.
- Recommend an appropriate plan for the treatment of constipation, including lifestyle modifications and drug therapy.
- Educate patients regarding laxative therapy.

PATIENT PRESENTATION

■ Chief Complaint

"I feel just awful ever since starting these pain pills—I think I'd rather be in pain!"

■ HPI

Kerry Reynolds is a 64-year-old black woman who presents to the emergency treatment center (ETC) complaining of increasing abdominal cramping and nausea for several days and now vomiting for the past several hours. She says this all started when she began Percocet therapy 2 weeks ago for postprocedural pain in association with right TKA. Her last bowel movement was 6 days ago. She began "not feeling well" 4 days ago, with bloating, decreased appetite, decreased thirst, and fatigue. She reports that yesterday, when her cramping was at its worst, she even used a couple of doses of Metamucil, but it did not help. She says she was almost to the point where she thought about trying some powerful laxatives, but she has heard about the addiction they can cause and the last thing she wants is to be addicted to a laxative. She has also tried to just quit taking the pain meds altogether, but she only makes it about halfway through the morning before the pain becomes unbearable. She reports that she has cut back on the pain pills and is only taking one pill four times a day now, compared with a week ago when she was taking two pills four times a day. On a scale of 1–10, with 1 being no pain and 10 being the worst pain ever experienced, she rates her pain at a 5 today. She does say the pain is improving every day. Her plan is to take one less pain pill every 3 days so that she can successfully taper the meds in about 2 weeks. She reports no fever, CP, or SOB. She states that she typically has daily bowel movements, with no straining, and spends less than 10 minutes, with little effort, having a bowel movement. Her last colonoscopy, performed 2 years ago, was unremarkable.

■ PMH

Hypothyroidism
Type 2 diabetes mellitus

Hypertension
Dyslipidemia
Osteoarthritis status post right TKA 2 weeks ago

■ FH

Her mother is in her 80s and is healthy. Her father died in his 60s from heart disease. She has three brothers and three sisters; one brother has type 2 diabetes. She has two sons who are healthy.

■ SH

She is married and works as a social worker. She quit smoking more than 20 years ago. She does not drink alcohol and does not use illicit drugs.

■ ROS

(+) For constipation, lower abdominal fullness, N/V, right knee pain, (–) for SOB, CP, or fever/chills

■ Meds

Apixaban 2.5 mg BID
Levothyroxine 50 mcg PO daily
Lisinopril 20 mg daily
Metformin 1000 mg PO twice daily
Multivitamin one tablet PO daily
Oxycodone/acetaminophen 5 mg/325 mg one to two tablets Q 4–6 H PRN
Simvastatin 10 mg PO at bedtime
Verapamil SR 360 mg daily

■ All

NKDA

■ Physical Examination

Gen

Pleasant woman in distress because of abdominal discomfort; is visibly uncomfortable and holding her stomach during the visit; appears tired

VS

BP 122/60, P 57, RR 16, T 36.2°C; Wt 247 lb (112.4 kg), Ht 5'5" (165 cm); waist circumference 37 in (94 cm); pain rated 5 on scale of 1–10

Skin

Normal skin turgor and color

HEENT

PERRLA and EOM full without nystagmus; no scleral icterus; oral mucosa moist; no ulcerations noted

Neck/Lymph Nodes

Supple, no lymphadenopathy or JVD; no thyromegaly or bruits

CV

Regular, S₁ and S₂ without murmur

Lungs

Normal breath sounds; no crackles or wheezes

Abd

Soft, obese, tender; decreased bowel sounds; stool palpable on left side

Rectal

Stool present in rectal vault; no masses felt; tone fair; push strength fair; nontender

MS/Ext

S/P right TKA; surgical wound healing appropriately; no redness, swelling, exudation; range of motion within normal limits

Neuro

A&O × 3; CNs II–XII symmetric and intact; DTRs 2+

■ Labs

Na 138 mEq/L	Glu 133 mg/dL (fasting)	RBC $6.05 \times 10^6/\text{mm}^3$
K 4.3 mEq/L	A1C 6.4%	Hgb 15.5 g/dL
Cl 101 mEq/L	Ca 9.3 mg/dL	Hct 48%
CO ₂ 30 mEq/L	TSH 2.70 mIU/mL	MCV 79 μm^3
BUN 14 mg/dL		MCH 26 pg
SCr 0.8 mg/dL		MCHC 33%
ACR 227 mg/g		RDW 15.4%

■ Radiology

X-ray: A plain x-ray of the abdomen showed gas-dilated loops in the colon.
Abdominal CT: scan demonstrated a large amount of stool in the colon and rectal vault.

■ Assessment

Constipation with fecal impaction; secondary symptoms of abdominal discomfort, nausea, and vomiting; etiology likely drug-induced. Disimpaction was successfully performed with no complications. A follow-up PEG-based bowel preparation was successful in clearing bowel and relieving the patient's abdominal pain.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of constipation?
- What additional information is needed to fully assess this patient's constipation?

Assess the Information

- Assess the severity of constipation based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What are some of the possible nonpharmacologic contributors to her constipation?
- What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in treating constipation?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What are the pharmacologic options for the treatment of constipation?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's constipation and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The recommendations you made were implemented, and Ms Reynolds returns to your clinic 1 month later. She reports that the drug therapy you recommended resulted in regular bowel function throughout the last 2 weeks of her opioid therapy but expresses she is concerned she'll be "hooked on the laxatives." She does report, however, that her orthopedic physicians have now recommended TKA on the opposite knee. She says that after the last episode with constipation, she just does not think she wants to go through with it.

FOLLOW-UP QUESTIONS

1. What regimen would you recommend for preventing opioid-induced constipation in this patient if she chooses to go through with the second TKA procedure?
2. What education would you provide to this patient who has concerns about recurrence of drug-induced constipation?
3. What education would you provide to this patient regarding her concerns about laxative addiction?

SELF-STUDY ASSIGNMENTS

1. Suggest pharmacotherapeutic options for the treatment of opioid-induced constipation in a pediatric patient. How does this approach compare with that used in treatment of adults?
2. Perform a literature search to find medications under investigation for the treatment of constipation. What different types of constipation will these new entities be used to treat? What place in therapy will these medications have?

CLINICAL PEARL

When a patient presents with constipation, obtain a detailed medication history because medications commonly cause constipation. Management of medication-related constipation may include

discontinuation of the offending agent with initiation of an appropriate alternative or initiation of a medication designed to address medication-related constipation. Failure to recognize medications as contributors to constipation may lead to inappropriate treatment and inadequate relief of constipation symptoms.

REFERENCES

1. Kumar L, Barker C, Emmanuel A. Opioid-induced constipation: pathophysiology, clinical consequences, and management. *Gastroenterol Res Pract* 2014; Article ID 141737, 6 pages.
2. American Diabetes Association. Standards of medical care in diabetes—2019. *Diabetes Care* 2019;42:S1–S193.
3. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127–248.
4. Shah BJ, Rughwani N, Rose S. Constipation. *Ann Intern Med* 2015;162:ITC1. doi:10.7326/AITC201504070.
5. Murphy J, Sheridan E. Evidence based review of pharmacotherapy for opioid-induced constipation in noncancer pain. *Ann Pharmacother* 2018;52:370–379.
6. Mozaffari S, Nikfar S, Abdollahi M. Methylnaltrexone bromide for the treatment of opioid-induced constipation. *Expert Opin Pharmacother* 2018;19:1127–1135.
7. Baker D. Formulary drug review: Naldemedine. *Hospital Pharmacy* 2017;52:464–468.
8. Martin K, Beyer-Westendorf J, Davidson BL, Huisman M, Sandset PM, Moll S. Use of the direct oral anticoagulants in obese patients: guidance from the SSC of the ISTH. *J Thromb Haemost* 2016;14:1308–1313.
9. Tarumi Y, Wilson MP, Szafran O, et al. Randomized, double-blind, placebo-controlled trial of oral docusate in the management of constipation in hospice patients. *J Pain Symptom Manage* 2013;45:2–13.

43

IRRITABLE BOWEL SYNDROME

Life in the Slow Lane Level II

Nancy S. Yunker, PharmD, FCCP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine the signs and symptoms of irritable bowel syndrome associated with constipation (IBS-C).
- Devise patient management strategies for patients with IBS, including pharmacologic and nonpharmacologic options.
- Recommend parameters for monitoring the safety and efficacy of therapy used in patients with IBS-C.
- Discuss treatment options for IBS with diarrhea (IBS-D).
- Evaluate the efficacy of treatment options for patients with IBS.

PATIENT PRESENTATION

■ Chief Complaint

“My IBS is acting up again. I feel all bloated and I really have to strain to have a bowel movement. I have been really uncomfortable for the past 4 weeks. Most recently, I added Metamucil capsules to the docusate I was already taking because someone in the past told me that I would probably be able to tolerate the capsules better than Metamucil powder. I haven’t seen much improvement in the 8 weeks that I have been using them, plus it is hard to remember to take them three times a day. I have tried to live with this but I really think I need to try something else. Is there anything you can give me?”

■ HPI

Jane Hoffman is a 28-year-old woman who presents to her PCP with the chief complaint of a 7-month history of hard pellet-like stools and difficulty passing stools. She was diagnosed with IBS her freshman year in college. She has been able to tolerate the minimal symptoms until about 8 months ago when she began to notice some bloating and a decrease in the number of bowel movements per week. She states that she now constantly feels bloated and has taken to wearing loose-fitting clothing because she cannot tolerate anything tight around her abdomen. She attributes the worsening symptoms to the stress associated with trying to complete classes for a graduate degree and serving as a teaching assistant (TA) for two courses. In addition to the 20 hours a week that she serves as a TA, she also works at least two weekends a month in a department store as a sales assistant. She also states the symptoms worsened since she went back to school, especially during midterms, finals, or when she needs to complete a major writing assignment. Other than stress, she cannot think of anything else that has changed in her life. She does not remember having any gastroenteritis symptoms in the last year, and she dislikes eating yogurt.

Prior to 8 months ago, she states that she averaged about six stools a week. She estimates that she has had one or two bowel movements a week for the past 6 weeks. She complains of straining to pass her stools and states that she is getting up 60 minutes early in the morning to allow for an attempt to pass a stool and uses the additional time exercising in order to “stimulate her bowels.” She also tried eating more bran products but felt like that made the pain and bloating worse, so she stopped. She states that the abdominal pain is not limited to when she passes a stool. She complains of abdominal pain and bloating almost continuously throughout the day for the past 2 months, although her symptoms are somewhat alleviated by passing a “good stool.” She resumed taking docusate 8 months ago. She briefly took senna in addition to the docusate but found that she sometimes had to go to the bathroom at inopportune times and felt that it caused additional cramping. She tried psyllium powder several years ago but hated the taste. She thought about MiraLAX, but her mother took that prior to a GI procedure and said that it caused diarrhea, so the patient is hesitant to try it with all her responsibilities.

■ PMH

Seasonal allergies
Headaches
Anxiety
UTIs

■ PSH

Cholecystectomy 2 years ago

■ FH

Lives alone. She separated from her boyfriend 2 months ago due to school and other job commitments. She became solely responsible for the apartment rent when he left. He has been “hassling” her recently, and there is a question of verbal and physical abuse. Her mother is alive with HTN and recently had an MI, and her father is alive with hypercholesterolemia. No siblings.

■ SH

No alcohol use or smoking. No history of military service. No travel outside the United States.

■ Meds

Diphenhydramine 25 mg orally Q 6 H allergy symptoms
Ibuprofen 200 mg, two tablets orally Q 4–6 H PRN headaches, menstrual cramps
Metamucil 0.52 g, four capsules orally three times a day
Docusate 100 mg orally twice daily
Ortho-Novum 1/35 (discontinued 2 months ago)

■ All

NKDA

■ ROS

Occasional headaches, usually associated with stress or allergy symptoms; occasional nausea, no vomiting; (–) blood in the stool or tarry stools; (+) flatulence and bloating. States that the abdominal symptoms may improve at night before bedtime especially if she uses a heating pad; she is not awakened at night with abdominal pain.

■ Physical Examination

Gen

A&O, WDNW pleasant Caucasian woman appearing slightly anxious

VS

BP 116/78, P 68, RR 18, T 37.0°C; Wt 134 lb (61 kg), Ht 5’6” (168 cm)

Skin

Dry skin on lower extremities, no rashes noted

HEENT

PERRLA, EOMI, moist mucus membranes, TMs intact

Neck/Lymph Nodes

No thyromegaly, lymphadenopathy, or JVD

Lungs

CTA; no rales or rhonchi

Breasts

Symmetric; no lumps or masses detected; nipples without discharge

CV

RRR, normal S₁ and S₂; no S₃ or S₄

Abd

(+) BS, slightly tender in LLQ, no HSM

Genit/Rect

Vulva normal; no palpable rectal masses; brown stool with no occult blood; no hemorrhoids

MS/Ext

No CCE, pulses 2+, normal ROM, normal strength bilaterally

Labs

Na 142 mEq/L	WBC $5.2 \times 10^3/\text{mm}^3$
K 4.0 mEq/L	Hgb 14.1 g/dL
Cl 106 mEq/L	Hct 42.4%
CO ₂ 27 mEq/L	Platelets $210 \times 10^3/\mu\text{L}$
BUN 9 mg/dL	
SCr 0.8 mg/dL	
Glu 88 mg/dL	

Serum pregnancy test: Negative

Other

FBDISI score: 66

IBS-SSS score: 300

Assessment

IBS associated with abdominal discomfort, bloating, and constipation

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of IBS or other problems associated with IBS?
- 1.b. What additional information is needed to fully assess the patient's IBS?

Assess the Information

- 2.a. Assess the severity of and classify this patient's IBS based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating IBS-C?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's IBS and other drug-related problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient returns to the physician 6 weeks later and reports that her symptoms are much improved and that the abdominal pain has resolved. She is happy with her medication regimen, but her friends have suggested that herbal medications may be just as effective. She would like more information about the use of these products for IBS. She also mentions that a friend was recently diagnosed with IBS-D and she wants to know if her friend's treatment will be similar.

FOLLOW-UP QUESTIONS

1. What information would you provide regarding the addition or substitution of alternative medications (eg, herbal medications) to this patient's regimen?
2. What therapeutic alternatives are available for the treatment of IBS-D?

SELF-STUDY ASSIGNMENTS

1. Conduct a literature search to determine what types of alternative therapies, including probiotics, have been evaluated in IBS. Include a discussion of the scientific rigor of these studies.
2. Conduct an informal survey among friends, family members, coworkers, and fellow students about the incidence of IBS and what therapeutic options they would recommend to a person suffering from IBS.
3. Conduct a search of IBS drug treatment studies on www.clinicaltrials.gov and conduct a literature search to identify new and emerging therapies for IBS. Determine the commercial availability of these agents or potential research trial referral centers.
4. Discuss the hypothesized pathogenesis of IBS including the disorder of the brain-gut axis, disturbed motility, impaired gut barrier function, visceral hypersensitivity, immunologic and infectious causation, genetic factors, psychosocial factors, and dietary alterations.

CLINICAL PEARL

Increasing evidence suggests that alterations in gut bacteria are seen in IBS which has led to the investigation of fecal microbiota transplant (FMT) to restore healthy bacteria to the gastrointestinal tract. A randomized, double-blind placebo-controlled trial in patients with moderate to severe IBS-D and IBS-M found the severity of symptoms improved at 3 months but not 12 months after FMT. While encouraging, further trials are needed.

REFERENCES

1. Ford AC, Moayyedi P, Chey WD, et al. for the Task Force on the Management of Irritable Bowel Syndrome. American College of Gastroenterology monograph on the management of irritable bowel syndrome. *Am J Gastroenterol* 2018;113:1-18.

2. Ford AC, Lacy BE, Talley NJ. Irritable bowel syndrome. *N Engl J Med* 2017;376:2566–2578.
3. Moayyedi P, Mearin F, Azpiroz F, et al. Irritable bowel syndrome diagnosis and management: a simplified algorithm for clinical practice. *United European Gastroenterol J* 2017;5:773–788.
4. Drossman DA. Functional gastrointestinal disorders: history, pathophysiology, clinical features and Rome IV. *Gastroenterology* 2016;150:1262–1279.
5. Sultan S, Malhotra A. Irritable bowel syndrome. *Ann Intern Med* 2017;166:ITC81–ITC96. doi: 10.7326/AITC201706060.
6. Defrees DN, Bailey J. Irritable bowel syndrome: epidemiology, pathophysiology, diagnosis, and treatment. *Prim Care Clin Office Pract* 2017;44:655–671.
7. National Institute for Health and Care Excellence (2008, updated 2017) Irritable bowel syndrome in adults: diagnosis and management. (NICE Guideline CG61) Available at: <https://www.nice.org.uk/guidance/cg61>. Accessed January 14, 2019.
8. Thomas RH, Luthin DR. Current and emerging treatments for irritable bowel syndrome with constipation and chronic idiopathic constipation: focus on prosecretory agents. *Pharmacotherapy* 2015;35:613–630.
9. Chang L, Lembo A, Sultan S. American Gastroenterological Association Institute technical review on the pharmacological management of irritable bowel syndrome. *Gastroenterology* 2014;147:1149–1172.
10. Shah ED, Kim HM, Schoenfeld P. Efficacy and tolerability of guanylate cyclase-C agonists for irritable bowel syndrome with constipation and chronic idiopathic constipation: a systematic review and meta-analysis. *Am J Gastroenterol* 2018;113:329–338.
11. Kulak-Bejda A, Bejda G, Waszkiewicz N. Antidepressants for irritable bowel syndrome—a systematic review. *Pharmacol Rep* 2017;69:1366–1379.

44

PEDIATRIC GASTROENTERITIS

One Thing You *Should* Try at Home Level II

Willia McGhee, PharmD

Laura M. Panko, MD, FAAP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of diarrhea with dehydration and be able to assess the severity of the problem.
- Describe the available rotavirus vaccines in the United States, contrast their dosage and product availability, compare their safety and efficacy with the previously available RotaShield® vaccine, and explain their worldwide impact on rotavirus-induced diarrhea.
- Recommend appropriate oral rehydration therapy (ORT) products and treatment regimens for varying degrees of dehydration severity and assess the effectiveness of ORT using clinical parameters.
- Outline education for parents about the limited usefulness of all antidiarrheal products and the role of ondansetron and probiotics in the treatment of acute diarrhea in children.
- Identify the signs and symptoms of severe dehydration that require referral to an ED for immediate IV volume replacement.

PATIENT PRESENTATION

■ Chief Complaint

Lydia Mason is a 9-month-old girl who presents to the ED with a three day history of fever, vomiting, and diarrhea. Her mother states, “I am worried that Lydia may be dehydrated.”

■ HPI

Lydia is an otherwise healthy child, last evaluated by her primary care provider at a scheduled well-child checkup 2 weeks ago, with no concerns identified during the appointment. Three days before presentation, she developed a tactile fever, confirmed at 100.4°F (38.0°C) rectally, and seemed more tired than usual. Two days before presentation, she awoke from sleep due to an episode of nonbloody, nonbilious emesis. Throughout that day, she had five more episodes of vomiting after attempts at oral intake. She continued to have fatigue and low-grade fevers.

One day before presentation to the ED, she had only two episodes of emesis but developed diarrhea. The stools were initially described as slightly formed, but as the day progressed, the stools became watery and voluminous. Her mother estimates that Lydia had five to eight episodes of diarrhea. Lydia's appetite continued to be poor, with refusal of solid foods. On her primary care provider's recommendation, Lydia's parents offered her liquids including formula and Pedialyte, but she refused these, preferring to drink small amounts of water and dilute apple juice.

On the morning of presentation to the ED, the patient had another large, watery stool and was more fussy than usual. Her diaper was dry, with no urine output since the night prior to presentation. The family could not accurately assess the number of wet diapers she had in the last 24 hours due to her stooling frequency and consistency. They also noted this morning that her lips appeared dry and she was not producing tears when crying.

On further history, no sick contacts were noted until the day Lydia presented to the ED, when her mother developed abdominal discomfort and loose stools. In addition, multiple infants at the day-care Lydia attends are experiencing similar symptoms. Her diet normally consists of 24–32 oz of cow's milk-based infant formula per day and a wide variety of solid foods. There has been no exposure to undercooked chicken, beef, or fish.

■ PMH

Lydia was born at 38 weeks via spontaneous vaginal delivery without complications. Her birth weight was 7 lb 10 oz. She required 1 day of phototherapy for hyperbilirubinemia. She was discharged from the newborn nursery on day 3 of life. She has had monthly viral upper respiratory tract infections and two episodes of otitis media since starting daycare at 3 months of age.

Lydia has no prior hospitalizations or ED visits for illness.

Immunizations are up-to-date.

Development is normal: she is cruising on furniture, speaks three words, and can drink from a sippy cup.

■ FH

Lydia's mother has a history of mild intermittent asthma. Her father is healthy. She has two older siblings (6 years and 3 years of age), who have no chronic medical conditions.

■ SH

Lydia lives with her parents and siblings. There are two pet fish in the home but no reptile or other animal exposures. The patient attends daycare 3 days a week. The family uses city water and has not traveled out of state recently.

■ Meds

Multivitamin. No prescriptions or over-the-counter medications.

■ All

NKDA, no food allergies

■ ROS

Negative for cough, congestion, drooling, noisy breathing, constipation, abdominal pain, easy bruising, or bleeding. Positive for rash in diaper area and as otherwise noted in the HPI.

■ Physical Examination**Gen**

Patient is ill but nontoxic appearing sitting in her mother's arms quietly. She is very fussy during the examination though could be consoled by her mother.

VS

BP 92/50, P 145, RR 32, T 38.4°C (R), Wt. 18 lb (8.2 kg; 50–75%), Ht 27 in (68 cm, 25%ile) OFC 17 in (43 cm; 50%ile), *Wt. at recent well-child check 20 lb (9 kg)*

Skin

Pink, no tenting noted, capillary refill 2–3 seconds

HEENT

Anterior fontanelle sunken, eyes moderately sunken, scant tears, nose with clear rhinorrhea, lips and tongue dry, TMs gray and translucent

Neck/Lymph Nodes

Supple, no lymphadenopathy

Lungs/Thorax

Clear, equal breath sounds bilaterally, no increased work of breathing, no wheezes, rales, rhonchi, retractions, or grunting

CV

Tachycardia, 1/6 flow murmur heard in the mid-left sternal border, 2+ radial and femoral pulses bilaterally

Abd

Mildly distended, hyperactive bowel sounds, soft, nontender, no masses, or hepatosplenomegaly

Genit/Rect

Normal female genitalia, mild diaper dermatitis

MS/Ext

Normal muscle bulk, full range of motion of extremities, no peripheral edema

Neuro

Sleepy but arousable, fussy when awake, cranial nerves grossly intact bilaterally, normal strength and tone for age, no focal deficits

■ Labs

Na 137 mEq/L	Hgb 12.8 g/dL	WBC $14.0 \times 10^3/\text{mm}^3$
K 4.4 mEq/L	Hct 41%	Polys 52%
Cl 113 mEq/L	Plt $300 \times 10^3/\text{mm}^3$	Bands 5%
CO ₂ 14 mEq/L		Eos 0%
BUN 23 mg/dL		Basos 3%
SCr 0.4 mg/dL		Lymphs 24%
Glu 80 mg/dL		Monos 16%

Urinalysis: Specific gravity 1.029, 2+ ketones, 1 WBC, 0 RBC, negative for protein

■ Assessment

1. Acute viral gastroenteritis
2. Dehydration with metabolic acidosis

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of gastroenteritis and dehydration?
- 1.b. Is additional information needed to fully assess the patient's gastroenteritis and dehydration? If so, what additional information is needed?

Assess the Information

- 2.a. Assess the severity of dehydration based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problem(s) and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. Assess the possible viral causes of this patient's gastroenteritis.
- 2.d. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this case?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's gastroenteritis and dehydration?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's gastroenteritis. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient's caregiver to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

A few months later, Lydia returns to her pediatrician for a 1-year well checkup. Her mother inquires about vaccines to possibly prevent the illness that required the emergency department visit. She asks why the rotavirus vaccine that Lydia received did not prevent her diarrheal illness.

FOLLOW-UP QUESTIONS

1. Outline the incidence of rotavirus-related diarrhea and the worldwide effect of the rotavirus vaccines on diarrhea-related morbidity and mortality.
2. Describe the vaccine products available in the United States, including safety and efficacy against rotavirus and the potential for resistance.
3. What information should be provided to the patient's caregiver to explain why the patient experienced AGE in spite of being fully vaccinated with rotavirus vaccine?

SELF-STUDY ASSIGNMENTS

1. Explain the limitations of using probiotics for treating pediatric gastroenteritis, including lack of FDA oversight, purity and standardization of products, lack of recognized treatment regimens, and safety concerns. Write a brief educational document explaining to parents when the use of probiotics should be considered in acute viral gastroenteritis.
2. What role does zinc supplementation have in the treatment of diarrhea in developing countries? Describe the rationale for its use and the most efficient way to administer it.
3. What barriers exist to the widespread implementation of ORT by parents and medical providers? How can these barriers be overcome? (*Hint:* Explore the advantages of ORT vs IV rehydration therapy, including ease of care at home vs hospitalization, insurance issues, and physician reluctance.)
4. Write a two-page essay describing the role of the community-based practitioner in the care of patients with pediatric gastroenteritis and dehydration. Emphasize how you would monitor patient safety and outcome and what you would tell the parents to optimize treatment at home.

CLINICAL PEARL

ORT is the standard of care in the treatment of children with gastroenteritis and diarrhea with mild to moderate dehydration and usually is successful when administered at home. Liquids, including water as well as full-strength and diluted juice and soda, are inadequate ORS and have the potential to contribute to diarrhea and the development of electrolyte disturbances.

REFERENCES

1. Troeger C, Khalil I, Rao P, et al. Rotavirus vaccination and the global burden of rotavirus diarrhea among children younger than 5 years. *JAMA Pediatr* 2018;172:958–965. doi:10.1001/jamapediatrics.2018.1960
2. Banyai K, Estes M, Martella V, Parashar U. Viral gastroenteritis. *Lancet* 2018;392:175–186. doi:10.1016/S0140-6736(18)31128-0.

3. Centers for Disease Control and Prevention. Updated norovirus outbreak management and disease prevention guidelines. *MMWR Morb Mortal Wkly Rep* 2011;60(3):1–15.
4. Guarino A, Ashkenazi S, Gendrel D, Lo Vecchio A, Shamir R, Szajewska H. European Society for Pediatric Gastroenterology, Hepatology, and Nutrition/European Society for Pediatric Infectious Diseases Evidence-Based Guidelines for the Management of Acute Gastroenteritis in Children in Europe: update 2014. *J Pediatr Gastroenterol Nutr* 2014;59:132–152.
5. Schnadower D, Tarr P, Casper T, et al. *Lactobacillus rhamnosus* GG versus placebo for acute gastroenteritis in children. *N Engl J Med* 2018;379:2015–2016.
6. Marchetti F, Bonati M, Maestro A, et al. Oral ondansetron versus domperidone for acute gastroenteritis in pediatric emergency departments: multicenter double blind randomized controlled trial. *PLoS One* 2016;11:e0165441.
7. Freedman S, Hall M, Shah S, et al. Impact of increasing ondansetron use on clinical outcomes in children with gastroenteritis. *JAMA Pediatr* 2014;168:321–329.
8. Nunez J, Liu D, Nager A. Dehydration treatment practices among pediatrics-trained and non-pediatrics trained emergency physicians. *Pediatr Emerg Care* 2012;28:322–328.
9. Riddle M, Chen W, Kirkwood C, et al. Update on vaccines for enteric pathogens. *Clin Microbiol Infection* 2018;24:1039–1045.
10. American Academy of Pediatrics. Rotavirus infections. In: Kimberlin DW, Brady MT, Jackson MA, Long SS, eds. *Red Book: 2018 Report of the Committee on Infectious Diseases*. 31st ed. Itasca, IL: American Academy of Pediatrics, 2018:700–704.

45

ASCITES MANAGEMENT IN PORTAL HYPERTENSION AND CIRRHOSIS

Back to Drinking Level II

Laurel A. Sampognaro, PharmD

Jeffery D. Evans, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify signs and symptoms of cirrhosis and associated complications.
- Provide pharmacotherapeutic and lifestyle recommendations for managing ascites due to portal hypertension and cirrhosis.
- Develop a patient-specific regimen and monitoring parameters to meet the needs of a patient with ascites, esophageal varices, and hepatic encephalopathy.
- Interpret laboratory values associated with ascites.
- Provide appropriate patient education for the recommended pharmacologic and nonpharmacologic therapy to control complications of cirrhosis, as well as to prevent further complications.

PATIENT PRESENTATION

■ Chief Complaint

"I look like I'm pregnant and it's getting worse."

■ HPI

Robert Smith is a 38-year-old man with a history of alcoholic cirrhosis who has been admitted to the hospital due to an unexplained 8-kg weight gain over the past 6 days, abdominal swelling and pain, shortness of breath, and mild confusion.

■ PMH

Alcoholic cirrhosis diagnosed 2 years ago, Child–Pugh grade A on diagnosis.

EGD performed at time of cirrhosis diagnosis showed no esophageal varices.

Allergic rhinitis.

Hypertension.

■ FH

Father is alive and well at the age of 70 without significant disease. Mother died at age 47 due to complications of type 1 DM.

■ SH

Recently separated from wife of 10 years and lives alone. Works as a plumber. History of extreme alcohol abuse but had quit drinking on cirrhosis diagnosis. Admits to heavy alcohol use over the past 2 months since separating from his wife and went on a drinking binge about 1 week ago.

■ Meds

Fluticasone furoate two sprays per nostril once daily

Levocetirizine 5 mg once daily

Lisinopril 10 mg once daily

■ All

NKDA

■ ROS

Abdominal discomfort described as occurring throughout the abdomen, shortness of breath, and mild confusion. Patient denies chills or fevers.

■ Physical Examination

Gen

Pleasant, chronically ill black man appearing to be in mild distress and fatigued

VS

BP 118/76, P 78, RR 27, T 37.2°C; Wt 94.2 kg, Ht 6'2"

Skin

(+) Palmar erythema, (+) spider angiomas, otherwise normal color

HEENT

PERRL, EOMI, clear sclerae, TMs normal, mucous membranes moist

Neck/Lymph Nodes

Supple, no thyroid nodules

Lung/Thorax

Mild bilateral crackles, decreased breath sounds in right lower lobe likely due to enlarged liver and ascites

Breasts

Nontender without masses

CV

RRR, S₁ and S₂ are normal, no MRG

Abd

Bulging, tender abdomen; hepatomegaly; (+) fluid wave; bowel sounds normal

Genit/Rect

Guaiac negative

MS/Ext

1+ pitting edema in both LE, palmar erythema; no clubbing or cyanosis

Neuro

Mildly confused, forgetful, A&O × 2 (oriented to person and time but does not know at which hospital he is)

■ Labs

Na 135 mEq/L	Hgb 16 g/dL	AST 88 IU/L	Ca 8.5 mg/dL
K 4.1 mEq/L	Hct 47%	ALT 116 IU/L	Mg 1.9 mEq/L
Cl 98 mEq/L	Plt 81 × 10 ³ /mm ³	LDH 167 IU/L	Phos 3.5 mg/dL
CO ₂ 30 mEq/L	WBC 6.2 × 10 ³ /mm ³	T. bili 2.2 mg/dL	TSH 3.6 mIU/L
BUN 19 mg/dL	PT 14.3 seconds	D. bili 0.7 mg/dL	NH ₃ 94 mcg/dL
SCr 0.7 mg/dL	PTT 47 seconds	T. prot 7.3 g/dL	HIV (–)
Glu 97 mg/dL	INR 1.33	Alb 2.8 g/dL	

■ Paracentesis

Five liters of fluid removed by paracentesis with an analysis of the fluid performed. The analysis reported a protein level of 1.4 g/dL, PMN 140 cells/mm³, and SAAG 1.4 g/dL. Fluid was sent for culture.

■ EGD

Once stabilized, an EGD was performed, which showed small esophageal varices.

■ Assessment

Worsening cirrhosis; now presenting with ascites and acute encephalopathy

R/O spontaneous bacterial peritonitis (SBP)

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of ascites and cirrhosis?
- What additional information is needed to fully assess this patient's ascites and cirrhosis?

Assess the Information

- Assess the severity of the ascites and cirrhosis based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the ascites, portal hypertension, and cirrhosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's liver disease and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The culture results for the paracentesis fluid were negative after 3 days.

The patient's mental status began to improve after paracentesis and the administration of lactulose.

ADDITIONAL CASE QUESTIONS

1. What vaccinations should he receive on discharge, assuming that he has not had any vaccinations for over 20 years?

SELF-STUDY ASSIGNMENTS

1. Identify which pain medications may be used safely in patients with cirrhosis and ascites.
2. Based on this patient's history, what 1-, 2-, and 5-year survival rates would be expected if the patient does not receive a liver transplant?

CLINICAL PEARL

Lactulose is considered by many and mentioned in the guidelines as a first-line agent in the prevention of recurrent hepatic encephalopathy secondary to cirrhosis. However, there is a limited amount of data justifying its use in these patients.

REFERENCES

1. Runyon B. Management of adult patients with ascites due to cirrhosis: update 2012. American Association for the Study of Liver Diseases Practice Guidelines. Available at: http://www.aasld.org/sites/default/files/guideline_documents/adultascitesenhanced.pdf. Accessed January 14, 2019.
2. Jafri S, Gordon S. Care of the cirrhotic patient. *Infect Dis Clin N Am* 2012;26:979–994.
3. Vilstrup H1, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by the American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *Hepatology* 2014;60:715–735.
4. Garcia-Tsao G, Abraldes J, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology* 2017;65:310–335.
5. Cordon J, Torres C, García A, Rodríguez F, Suárez de Parga JM. Endoscopic management of esophageal varices. *World J Gastrointest Endosc* 2012;4(7):312–322.
6. O'Shea RS, Dasarthy S, McCullough AJ, et al. Alcoholic liver disease. *Hepatology* 2010;51:307–328.
7. Pedersen J, Bendtsen F, Moller, S. Management of cirrhotic ascites. *Ther Adv Chronic Dis* 2015;6(3):124–137.
8. Bernardi M, Maggioli C, Zaccherini G. Human albumin in the management of complications of liver cirrhosis. *Crit Care* 2012;16(2):211–217.
9. Ge P, Runyon B. The changing role of beta-blocker therapy in patients with cirrhosis. *J Hepatol* 2014;60:643–653.

46

ESOPHAGEAL VARICES

Banding the Bleeding Level II

Vanessa T. Kline, PharmD, BCPS

Jonathan M. Kline, PharmD, CACP, BCPS, CDE

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- List nonpharmacologic options for managing patients with bleeding esophageal varices.
- Recommend appropriate pharmacologic therapy for controlling bleeding esophageal varices and adjunctive therapy in the setting of acute variceal bleeding.
- Provide appropriate education for patients receiving therapy for portal hypertension.

PATIENT PRESENTATION

Chief Complaint

"I've been throwing up blood, enough to fill my bathroom sink!"

HPI

Ethyl Johnson is a 55-year-old woman who presents to the ED with complaint of vomiting blood and bright red blood per rectum.

She was in her usual state of health, until shortly after taking a dose of lactulose when she began to feel sick and subsequently vomited a large amount of blood into the bathroom sink. She also reports a 2-day history of BRBPR.

■ PMH

Cirrhosis secondary to alcohol abuse
History of hepatic encephalopathy
Ascites with history of paracentesis
Peptic ulcer disease
Hypertension
Cellulitis (two admissions in the past 3 years)

■ FH

Father with CAD and CABG; no other history known

■ SH

The patient lives alone and has been able to function independently. Quit drinking 5 years ago. Previously drank 6 beers per weekday and 750 mL of liquor on weekends. Quit smoking 3 years ago (35 pack-year history). She works as an accountant.

■ Meds

Sucralfate 1 g PO BID
Omeprazole 20 mg PO BID
Bumetanide 1 mg PO BID
Spironolactone 50 mg PO once daily
Propranolol 40 mg PO BID (may not be taking)
Bupropion XL 300 mg daily
Lactulose 20 g PO Q6H

■ All

NKDA

■ ROS

Negative except for complaints noted in HPI

■ Physical Examination

Gen

Obese woman looking older than stated age, looks somnolent but occasionally moves head

VS

BP 108/60, P 120, RR 14, T 37.8°C

Skin

Some spider angiomas on abdomen, thick skin, chronic venous stasis changes with lichenification

HEENT

PERRLA; icteric sclerae

Neck/Lymph Nodes

Neck supple; no masses

Lungs/Thorax

Clear to auscultation bilaterally

Breasts

No lumps or masses

CV

Tachycardia, RRR, no M/R/G

Abd

Obese, mildly distended, distant bowel sounds present, difficult to assess for hepatosplenomegaly; dull percussion noted

Rect

Frank blood

Ext

Bilateral 1+ pedal edema

Neuro

Sleepy, moves head occasionally; is arousable and oriented $\times 3$; no asterixis

■ Labs (on Admission)

Na 127 mEq/L	Hgb 7.8 g/dL	AST 104 IU/L
K 4.3 mEq/L	Hct 24.4%	ALT 49 IU/L
Cl 101 mEq/L	WBC $26.4 \times 10^3/\text{mm}^3$	Alk phos 114 IU/L
CO ₂ 22 mEq/L	Neutrophils 59%	T. bili 4.3 mg/dL
BUN 57 mg/dL	Bands 17%	D. bili 3.3 mg/dL
SCr 1.9 mg/dL	Lymphs 23%	Protein 5.5 g/dL
Glu 155 mg/dL	Monos 1%	Alb 2.5 g/dL
	Plt $68 \times 10^3/\text{mm}^3$	Ca 8.4 mg/dL
	aPTT 42.1 seconds	Phos 4.4 mg/dL
	PT 16.5 seconds	Ammonia 117 mcg/dL
	INR 1.8	

■ EGD

There is a large esophageal varix, with one large red spot and bulge that began spurting blood during the procedure. Two bands were applied to varices (Fig. 46-1).

■ Assessment

This is a 55-year-old woman with a history of alcoholic cirrhosis who presents to the ED acutely ill after hematemesis secondary to bleeding esophageal varices. Labs show severe anemia, leukocytosis with

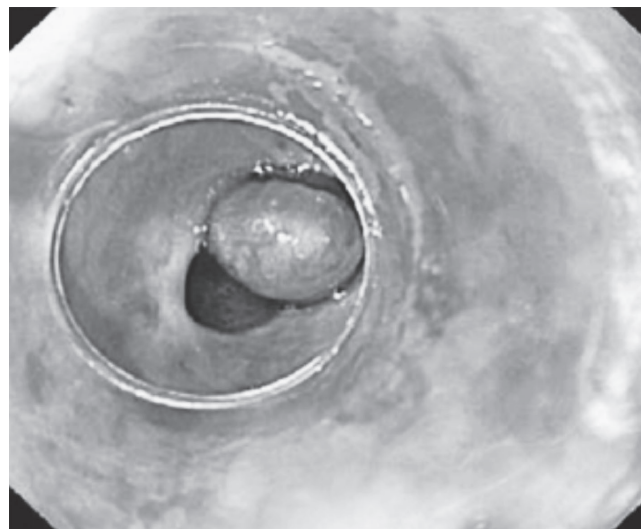


FIGURE 46-1. Endoscopic band ligation of esophageal varices. (Reprinted with permission from Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York, NY: McGraw-Hill Education, 2018.)

left shift, hyponatremia, renal dysfunction, hepatic encephalopathy, hypoalbuminemia, increased serum aminotransferases, and coagulopathy. The patient presents with Child–Pugh class C severity of disease. Will admit to an intensive care unit for further management.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of acute cirrhosis complications including bleeding esophageal varices?
- 1.b. What additional information is needed to fully assess the patient's acute cirrhosis complications including bleeding esophageal varices?

Assess the Information

- 2.a. Assess the severity of esophageal variceal bleeding based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the esophageal varices and other complications of cirrhosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's esophageal varices and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Examine the relative effectiveness of nonpharmacologic therapies versus available pharmacologic treatments for the acute management of variceal bleeding.
2. Describe the effect of fluoroquinolone resistance on use of antibiotics in patients presenting with variceal hemorrhage.
3. Describe the dose-related side effects in patients receiving combination β -blocker and isosorbide mononitrate therapy.

CLINICAL PEARL

While medication dosing and adjustments in hepatic disease is usually based on the Child–Pugh score, mortality prediction and assessment for hepatic transplantation is done using the Model of End-Stage Liver Disease (MELD) scoring system.

REFERENCES

1. United States Department of Health and Human Services. MELD Calculator—OPTN. Available at: <https://optn.transplant.hrsa.gov/resources/allocation-calculators/meld-calculator/>. Accessed October 28, 2018.
2. Garcia-Tsao G, Abraldes JG, Berzigotti A, Bosch J. Portal hypertensive bleeding in cirrhosis: risk stratification, diagnosis, and management: 2016 practice guidance by the American Association for the Study of Liver Diseases. *Hepatology* 2017;65:310–335.
3. Seo YS, Park SY, Kim MY, et al. Lack of difference among terlipressin, somatostatin, and octreotide in the control of acute gastroesophageal variceal hemorrhage. *Hepatology* 2014;60:954–963.
4. Satapathy SK, Sanyal AJ. Nonendoscopic management strategies for acute esophagogastric variceal bleeding. *Gastroenterol Clin N Am* 2014;43:819–833.
5. Marti-Carvajal AJ, Karakitsiou DE, Salanti G. Human recombinant activated factor VII for upper gastrointestinal bleeding in patients with liver diseases. *Cochrane Database Syst Rev* 2012;3:CD004887.
6. Alaniz C, Mohammad RA, Welage LS. Continuous infusion of pantoprazole with octreotide does not improve management of variceal hemorrhage. *Pharmacotherapy* 2009;29:248–254.
7. Lo GH, Perng DS, Chang CY, Tai CM, Wang HM, Lin HC. A controlled trial of ligation plus vasoconstrictor versus proton pump inhibitor in the control of acute esophageal variceal bleeding. *J Gastroenterol Hepatol* 2013;28:684–689.
8. Deshpande A, Pasupuleti V, Thota P, et al. Acid-suppressive therapy is associated with spontaneous bacterial peritonitis in cirrhotic patients: a meta-analysis. *J Gastroenterol Hepatol* 2013;28:235–242.
9. Shah HA, Azam Z, Rauf J, et al. Carvedilol vs. esophageal band ligation in the primary prophylaxis of variceal hemorrhage: a multicenter randomized controlled trial. *J Hepatol* 2014;60:757–764.
10. Lo GH, Chen WC, Wang HM, Yu HC. Randomized controlled trial of carvedilol versus nadolol plus isosorbide mononitrate for the prevention of variceal rebleeding. *J Gastroenterol Hepatol* 2012;27:1681–1687.

47

HEPATIC ENCEPHALOPATHY

State of Confusion Level I

Jeffrey T. Wiecekiewicz, PharmD, BCPS

Carrie A. Sincak, PharmD, BCPS, FASHP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify and correct the precipitating factors associated with the development of hepatic encephalopathy (HE) in a cirrhotic patient.
- Recommend appropriate nonpharmacologic and pharmacologic intervention for a cirrhotic patient who develops HE.

- Design a plan for monitoring the efficacy and adverse effects of recommended treatments for HE.
- Provide patient education for those receiving treatment for HE.

PATIENT PRESENTATION

■ Chief Complaint (From Son)

“My mother says she is dizzy and has felt a little off over the last couple of days.”

■ HPI

Charlene McInerney is a 65-year-old woman who was brought to the ED by her son because of dizziness and confusion. The patient became increasingly confused over the past 2 days and on admission was alert to person only. The son states she is normally able to converse without difficulty but does require some assistance with ambulation. Over the past 2 days, she has had increasing difficulty with answering questions in conversations. He mentioned that his mother had forgotten to refill her prescription for lactulose when she ran out 1 week ago. His mother had a scheduled endoscopy 2 days ago and did not take any of her medications the day prior to and the day of the test. She had also “retained a lot of water” and told her family that she was feeling bad.

■ PMH

ESLD secondary to NASH cirrhosis diagnosed 5 years ago; complicated by ascites
Grade 2 esophageal varices
Hypothyroidism
Colon cancer s/p resection (15 years ago)

■ FH

Not obtainable at this time

■ SH

Retired; lives with her husband; they have one son and two daughters
No history of alcohol use

■ Meds

Folic acid 1 mg PO daily
Furosemide 40 mg PO daily
Lactulose 10 g/15 mL, one tablespoonful PO TID
Levothyroxine 100 mcg PO daily
Multivitamin one tablet PO daily
Pantoprazole 40 mg PO daily
Rifaximin 550 mg PO BID
Thiamine 100 mg PO daily

■ All

No known allergies

■ ROS

Confusion with no loss of consciousness reported. Abdominal pain reported. No change in bowel habits, dysphagia, or odynophagia. Weight gain noted per son.

■ Physical Examination

Gen

Elderly woman in NAD who is disoriented to time and place

VS

BP 134/55, P 82, RR 20, T 36.7°C; Wt 174.7 lb (79.4 kg), Ht 5'0" (152.4 cm)

Skin

Normal skin turgor

HEENT

PERRLA; dry mucous membranes; TMs intact; EOMI; fundi benign; anicteric sclerae; no sinus tenderness

Neck/Lymph Nodes

No masses, thyromegaly or lymphadenopathy

Lungs

Chest symmetric; lungs CTA bilaterally; no wheezes or crackles

CV

S₁ and S₂ normal; RRR with no murmurs

Abd

Nontender; distended abdomen; no splenomegaly; liver edge not identifiable below the costal margin; hypoactive bowel sounds

Rect

Heme (–) stool; no masses

Ext

(+) LE edema; no clubbing or cyanosis

Neuro

Confused; oriented only to person; CNs II–XII intact; DTRs 2+; (+) asterixis

■ Labs

Na 138 mEq/L	Hgb 9.1 g/dL	WBC 6.4 × 10 ³ /mm ³	AST 68 IU/L
K 3.3 mEq/L	Hct 29%	PMNs 67%	ALT 25 IU/L
Cl 102 mEq/L	MCV 95 μm ³	Bands 3%	Alk Phos 127 IU/L
CO ₂ 24 mEq/L	MCHC 34 g/dL	Eos 3%	T. bili 1.1 mg/dL
BUN 14 mg/dL	Retic 1.1%	Lymphs 25%	D. bili 0.3 mg/dL
SCr 1.4 mg/dL	Plt 122 × 10 ³ /mm ³	Monos 2%	Alb 3.2 g/dL
Glu 118 mg/dL			NH ₃ 84 mcg/dL
			Ca 9.1 mg/dL
			Mg 2.7 mg/dL
			Phos 3.3 mg/dL
			PT 14.8 seconds
			aPTT 39.2 seconds
			INR 1.4
			TSH 0.42 μIU/mL

■ Assessment

HE, type C, grade III, episodic, precipitated (by brief noncompliance with maintenance lactulose and rifaximin therapy)

Glasgow coma scale		
Eye opening	Spontaneous	4
	To verbal command	3
	To pain	2
	None	1
Verbal responsiveness	Oriented	5
	Confused	4
	Inappropriate words	3
	Incomprehensible sounds	2
	None	1
Motor response	Obeys	6
	Localizes	5
	Withdraws (pain)	4
	Flexion (pain)	3
	Extension (pain)	2
	None	1
Total: _____		

FIGURE 47-1. Glasgow coma scale (GSC) is a clinical evaluation tool measuring the severity of hepatic encephalopathy. The scale includes an assessment of three separate areas of response: eyes, verbal, and motor. The scores of the individual sections are then added together to reveal the overall severity score. The lowest score (3) indicates the highest level of severity and the highest score (15) indicates the lowest level of severity. (Reprinted with permission from Stone CK, Humphries RL, eds. *Current Diagnosis & Treatment: Emergency Medicine*. 8th ed. New York, NY: McGraw-Hill Education, 2017.)

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of HE in this patient?
- What additional information is needed to fully assess this patient's HE? (See Fig. 47-1.)

Assess the Information

- Assess the severity of HE based on the subjective and objective information available and classify this patient's HE.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What precipitating factors in this patient could potentially cause an episode of HE?

Develop a Care Plan

- What are the goals for the management of HE in this case?
- Which nondrug therapies might be useful in this patient?
- What feasible pharmacotherapeutic alternatives are available for the treatment of HE?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's HE and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Two days after beginning treatment with the regimen you recommended, the patient is responding positively, and the dose has been titrated appropriately. The dizziness and confusion have subsided, and she is now oriented to time, place, and person, and no asterixis is detected. The plan is to discharge the patient home tomorrow.

SELF-STUDY ASSIGNMENTS

- Perform a literature search to assess the efficacy and role of rifaximin in the treatment of HE.
- List the potential advantages and disadvantages of using antibiotics for the treatment of HE.
- Perform a literature search to determine if protein restriction is appropriate in patients with liver disease, particularly patients with cirrhosis.

CLINICAL PEARL

Medication noncompliance, sedative-hypnotics, other CNS depressants, and narcotics may precipitate HE. A careful medication history is important in patients presenting with the disorder to identify and eliminate reversible causes.

REFERENCES

- Suraweera D, Sundaram V, Saab S. Evaluation and management of hepatic encephalopathy: current status and future directions. *Gut Liver* 2016;10(4):509–519.
- Weissenborn K. Hepatic encephalopathy: definition, clinical grading and diagnostic principles. *Drugs* 2019;79(Suppl 1):S5–S9.
- Vilstrup H, Amodio P, Bajaj J, et al. Hepatic encephalopathy in chronic liver disease: 2014 Practice Guideline by American Association for the Study of Liver Diseases and the European Association for the Study of the Liver. *Hepatology* 2014;60:715–735.
- Kornerup L, Gluud LL, Vilstrup H, et al. Update on the therapeutic management of hepatic encephalopathy. *Curr Gastroenterol Rep* 2018;20(5):21.
- MacLayton DO, Eaton-Maxwell A. Rifaximin for treatment of hepatic encephalopathy. *Ann Pharmacother* 2009;43:77–84.
- Kimer N, Krag A, Moller S, et al. Systematic review with meta-analysis: the effects of rifaximin in hepatic encephalopathy. *Aliment Pharmacol Ther* 2014;40:123–132.
- Mullen KD, Sanyal AJ, Bass NM. Rifaximin is safe and well tolerated for long-term maintenance of remission from overt hepatic encephalopathy. *Clin Gastroenterol Hepatol* 2014;12(8):1390–1397.
- Eltawil KM, Laryea M, Peltekian K, Molinari M. Rifaximin vs conventional oral therapy for hepatic encephalopathy: a meta-analysis. *World J Gastroenterol* 2012;18:767–777.
- Runyon B. Management of adult patients with ascites due to cirrhosis: update 2012. American Association for the Study of Liver Diseases. Available at: https://www.aasld.org/sites/default/files/guideline_documents/adultascitesenhanced.pdf. Accessed November 8, 2018.

48

ACUTE PANCREATITIS

A Sod Story Level III

Scott W. Mueller, PharmD, FCCM, BCCCP

Paul Reynolds, PharmD, BCPS, BCCCP

Robert MacLaren, BSc (Pharm), PharmD, MPH, FCCM, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine the subjective and objective information (include medical history, signs, symptoms, and laboratory values) commonly associated with acute pancreatitis.
- Evaluate precipitating factors associated with acute pancreatitis.
- Describe the potential etiologies and systemic complications associated with acute pancreatitis.
- Recommend appropriate pharmacologic, nonpharmacologic therapies, and supportive care therapies for patients with acute pancreatitis.
- Develop therapeutic goals and a therapeutic plan with appropriate monitoring parameters to assist the healthcare team in realizing desired therapeutic outcomes in a patient with acute pancreatitis.

PATIENT PRESENTATION

■ Chief Complaint

"I've got a really bad pain in my stomach."

■ HPI

Bill Jones is a 42-year-old man who presents to the ED shortly after midnight on a Friday night because of intense midepigastria pain radiating to his back. He states that the pain started shortly after dinner the night before but has progressively worsened. The pain is unrelated to physical activity, and he began vomiting around midnight tonight.

■ PMH

Alcohol withdrawal seizures 5 months ago, which have not recurred. Hypertension, which is medically controlled.

■ FH

Father died at age of 56 from an MVA; mother is 72 years old and has type 2 DM and "cholesterol issues," for which she is taking a "statin." One sister, also with "cholesterol issues," taking an unknown medication. The sister also has a remote history of pancreatitis.

■ SH

Divorced with three children. Employed as a groundskeeper at a golf course. Quit smoking 2 weeks ago, admits to a 40 pack-year history of smoking. He states that he used to consume 6–10 beers per day until 5 months ago when he had a withdrawal seizure. He now drinks only on weekends for a total of about six beers; he reports

sharing a couple of pitchers with two friends last night with dinner. Drinks at least two cups of coffee each morning.

■ Meds

Phenytoin 200 mg twice daily since his seizure
Hydrochlorothiazide 25 mg once daily for blood pressure
Doxycycline 100 mg twice daily for 10 days for "cellulitis" (day 10 of 10)
Ibuprofen 200 mg OTC several doses per day PRN sore back muscles

■ All

Amoxicillin/clavulanate makes his stomach upset

■ ROS

The patient states that he has been feeling well until last night. His back soreness from unloading pallets of heavy sod 1 week ago has resolved with occasional ibuprofen use. He just finished a course of antibiotics this morning for mild cellulitis that was limited to a 1- × 2-in area of the left lower tibia. He has vomited approximately six times since midnight. He has no complaints of diarrhea or blood in the stool or vomitus or knowledge of any prior history of uncontrolled blood sugars or cholesterol.

■ Physical Examination

Gen

The patient is restless and in moderate distress but otherwise is a well-appearing, well-nourished male who looks his stated age.

VS

BP 99/56, P 124, RR 30, T 38.9°C; Wt 89 kg, Ht 5'10"

HEENT

PERRLA; EOMI; oropharynx pink and clear; oral mucosa dry

Skin

Dry with poor skin turgor; location of previous cellulitis appears healed; nontender, (–) erythema, swelling, or warmth

Neck/Lymph Nodes

Supple; no bruits, lymphadenopathy, or thyromegaly

Lungs/Thorax

No external evidence of back injury; (–) spinal/CVA tenderness; normal range of motion; no abnormal breath sounds on auscultation

CV

Sinus tachycardia; no MRG

Abd

Moderately distended with active but diminished bowel sounds; (+) guarding; pain is elicited on light palpation of left upper and midepigastria region. No rebound tenderness, masses, or hepatosplenomegaly.

Rect

Normal sphincter tone; no BRBPR or masses; prostate normal size

MS/Ext

Extremities are warm and well perfused. Good pulses present in all extremities. No clubbing, palmar erythema, or spider angiomas. Cellulitis is no longer evident.

Neuro

A&O $\times$ 3; neuro exam benign; CN II–XII intact; strength is equal bilaterally in all extremities. Normal tone and reflexes. No asterixis.

Labs

Na 128 mEq/L	Hgb 17 g/dL	AST 342 IU/L	Ca 7.2 mg/dL
K 3.4 mEq/L	Hct 50%	ALT 166 IU/L	Mg 1.7 mEq/L
Cl 105 mEq/L	WBC $15.2 \times 10^3/\text{mm}^3$	Alk phos 285 IU/L	Phos 2.2 mg/dL
CO ₂ 18 mEq/L		LDH 255 IU/L	Trig 782 mg/dL
BUN 35 mg/dL	Neutros 72%	T. bili 0.6 mg/dL	Repeat trig
SCr 1.5 mg/dL	Bands 4%	Alb 3.2 g/dL	1010 mg/dL
Glu 375 mg/dL	Eos 1%	Prealb 25 mg/dL	PT 12.8 seconds
	Basos 1%	Amylase 1555 IU/L	INR 1.1
	Lymphs 20%	Lipase 2220 IU/L	aPTT 19.3 seconds
	Monos 2%		Phenytoln total
			13 mg/L
			BAC 4 mg/dL

Other Tests

Negative for presence of serum ketones. Negative for presence of hemoglobin in stool. ASA, acetaminophen, all other alcohols are negative on serum toxicology screen. Negative viral hepatitis titers and negative for HIV.

Arterial Blood Gases

pH 7.31, PaCO₂ 38 mm Hg, PaO₂ 88 mm Hg, HCO₃⁻ 17 mEq/L, O₂ sat 98% in room air

UA

Color yellow; turbidity clear; SG 1.010; pH 7.2; glucose >1000 mg/dL; bilirubin (-); ketones (-); Hgb (-); protein (-); nitrite (-); crystals (-); casts (-); mucous (-); bacteria (-); urobilinogen: 0.25 EU/dL; WBC 0–5/hpf; RBC 0/hpf; epithelial cells: 0–10/hpf.

Chest X-Ray

AP view of chest shows the heart to be normal in size. The lungs are clear without any infiltrates, masses, effusions, or atelectasis. No notable abnormalities.

Ultrasound

Abdominal: Nonspecific gas pattern; no dilated bowel. Questionable opacity/abnormality of common bile duct. Cannot rule out gallstone/obstruction.

Lower extremity: No signs of deep venous thrombosis.

ECG

Sinus tachycardia; rate 140 bpm. No changes from his last ECG (5 months ago), no evidence of myocardial ischemia

Assessment

Acute pancreatitis precipitating hyperglycemia, hypocalcemia, and nonanion gap metabolic acidosis
R/O choledocholithiasis

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of acute pancreatitis?
- What additional information is needed to fully assess this patient's pancreatitis?

Assess the Information

- Assess the severity of acute pancreatitis based on the subjective and objective information available. Utilize a pancreatitis severity scoring system to complete this assessment.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What other etiologies of acute pancreatitis should be considered in this patient?

Develop a Care Plan

- What are the goals of pharmacotherapy for this patient?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating acute pancreatitis and associated problems?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's acute pancreatitis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

A pain control plan is implemented. Partial parenteral nutrition (without lipids) is considered but ultimately withheld as plans are made to initiate enteral nutrition during the daytime (ie, in about 12 hours). After several days of improvement in the hospital, the patient develops a WBC count of $23.4 \times 10^3/\text{mm}^3$ with neutrophils 77%, bands 15%, eosinophils 1%, basophils 0%, lymphocytes 3%, and monocytes 4%. He has a temperature of 39.8°C and is noted to be orthostatic (BP 128/76 sitting, 98/60 standing) with a glucose of 480 mg/dL. He has also experienced several episodes of diarrhea and steatorrhea.

Because of these setbacks in the patient's progress, a contrast-enhanced CT scan is obtained. The results demonstrate peripancreatic and retroperitoneal edema. The pancreas itself appears relatively normal with the exception of small nonenhancing areas around the neck of the pancreas, which are suggestive of necrosis.

FOLLOW-UP QUESTIONS

1. What potential etiologies might explain this patient's fever and relapsing acute pancreatitis?
2. What are the new treatment goals for this patient?
3. Given this new information, what therapeutic interventions should be considered for this patient?
4. How should these new therapies be monitored for efficacy and adverse effects?
5. When this patient is stable, what information should be provided to him to reduce the likelihood of recurrent pancreatitis?

SELF-STUDY ASSIGNMENTS

1. Describe the pathophysiology of autodigestion during acute pancreatitis.
2. Describe the controversies of early enteral nutrition, probiotics, prophylactic antibiotics, and octreotide for management of acute pancreatitis.
3. Summarize published information regarding opioid effects on the sphincter of Oddi.
4. Compose a list of drugs believed to aggravate or cause pancreatitis and assess the level of association for each agent.

CLINICAL PEARL

Invasive placement of a nasojunal tube is not uniformly required, as nasojunal feeding has not consistently shown benefit over nasogastric feeding. Therefore, gastric administration of nutrition is frequently preferred as this route is easily accessible.

REFERENCES

1. Lankisch PG, Apte M, Banks PA. Acute pancreatitis. *Lancet* 2015;386:85–96.
2. Johnson CD, Bessellink MG, Carter R. Acute pancreatitis. *BMJ* 2014;349:g4859. doi: <http://dx.doi.org/10.1136/bmj.g4859>.
3. Tenner S, Baillie J, DeWitt J, Vege SW. American College of Gastroenterology guideline: management of acute pancreatitis. *Am J Gastroenterol* 2013;108:1400–1415.
4. Vege SS, DiMaggio MJ, Forsmark CE, Martel M, Barkun AN. Initial medical treatment of acute pancreatitis: American Gastroenterological Association Institute technical review. *Gastroenterology* 2018; 154:1103–1139.
5. Hung WY, Abreu Lanfranco O. Contemporary review of drug-induced pancreatitis: A different perspective. *World J Gastrointest Pathophysiol* 2014;5:405–415.
6. Crockett SD, Wani S, Gardner TB, et al. American Gastroenterological Association Institute guideline on initial management of acute pancreatitis. *Gastroenterology* 2018;154:1096–1101.
7. Stigliano S, Sternby H, de Madaria E, Capurso G, Petrov MS. Early management of acute pancreatitis: a review of the best evidence. *Dig Liver Dis* 2017;49:585–594.
8. Zerem E. Treatment of severe acute pancreatitis and its complication. *World J Gastroenterol* 2014;20:13879–13892.
9. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *J Parenter Enteral Nutr* 2016;40:159–211.

49

CHRONIC PANCREATITIS

Like a Shot to the Gut Level II

Heather M. Teufel, PharmD, BCCCP

Jaime L. Gray, PharmD, BCCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify subjective and objective findings consistent with chronic pancreatitis and acute exacerbations of chronic pancreatitis.
- Evaluate patient-specific data and develop a problem list for patients with acute exacerbations of chronic pancreatitis.
- Discuss therapeutic alternatives and outline a patient-specific plan for pain management during an acute exacerbation of chronic pancreatitis.
- Recommend appropriate pancreatic enzyme replacement therapy for management of steatorrhea in a patient with chronic pancreatitis.

PATIENT PRESENTATION

Chief Complaint

"I have had pain in my stomach for years, but now I just can't take it anymore. It feels like a shot to the gut."

HPI

Madeline Jane is a 38-year-old woman who presents to the ED complaining of pain in her abdomen with radiation to her back. She also has noticed an increase in loose, foul-smelling stools with an oil-like consistency. Ms Jane has experienced intermittent pain in her abdomen for several years; she has also experienced chronic diarrhea with increased frequency in the last week. Concurrent with the pain are nausea and vomiting, which have increased in intensity and frequency in the past week. She states that she has a chronically dry mouth leading to difficulty swallowing, but with the increased nausea and vomiting, she has had decreased oral intake. Ms Jane presents to the ED today as she now has access to health insurance. She did not seek medical attention previously due to the financial implications of being uninsured.

PMH

There is no formal past medical history because the patient has not sought medical care since college due to being uninsured. Patient reports receiving the "usual" childhood vaccinations and medical care, but she has not seen a physician in over 10 years.

FH

Parents are alive and healthy. She is an only child.

■ SH

Occasional alcohol use (less than one glass of wine per week).
 (+) tobacco use (12 pack years; currently 0.5 pack/day).
 Denies any illicit drugs.
 She is single and not sexually active.
 Ms Jane just started a new job as a medical claims processor at St. Anthony's hospital; she has completed a college-level education.

■ Meds

Multivitamin one tablet by mouth daily, has been taking for several years.
 Acetaminophen 500–1000 mg by mouth Q 6 H PRN for abdominal pain; frequent daily use.
 Loperamide two tablets initially, and then one tablet by mouth PRN diarrhea; she usually takes two to four tablets per day.
 No prescription medications.

■ All

Amoxicillin → rash when she received it as a child for an ear infection, no use since

■ ROS

Mild difficulty swallowing due to chronically dry throat, decreased oral intake due to nausea and vomiting. No indigestion or bloating. Significant abdominal pain and diarrhea as described above. No constipation or fecal incontinence; normal flatus. No blood in the stool. No hemorrhoids. Urine is of normal color, volume, and odor.

■ Physical Examination**Gen**

Thin, ill-appearing Caucasian woman, appearing anxious

VS

BP 106/70, P 104, RR 18, T 37.8°C; Wt 121 lb (55 kg), Ht 5'5" (165 cm), current pain 8 out of 10 on the numerical rating scale

Skin

Normal skin turgor

HEENT

PERRLA, EOMI, oropharynx clear, mucous membranes dry, eyes chronically dry

Neck/Lymph Nodes

Supple; (–) JVD, thyromegaly, lymphadenopathy, or bruits

Lung/Thorax

Audible breath sounds in all lung fields; trachea at midline; normal rate, rhythm, and effort of breathing; (–) vertebral tenderness or deformity

CV

Regular rate and rhythm without gallops or murmur

Abd

Sparse bowel sounds, (+) rebound and guarding

Genit/Rect

No masses, guaiac (–), normal urine output

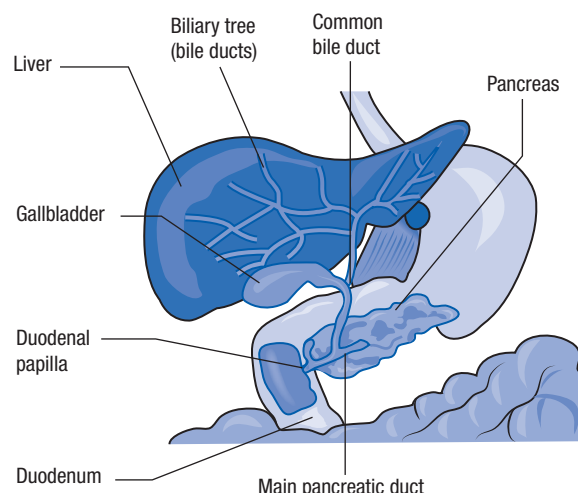


FIGURE 49-1. Anatomic structures depicting joining of common bile duct and the main pancreatic duct before emptying contents into the duodenum. (Source: National Institute of Diabetes and Digestive and Kidney Diseases. Available at: <http://www.niddk.nih.gov/health-information/health-topics/diagnostic-tests/ercp/Pages/diagnostic-test.aspx>.)

MS/Ext

Pulses intact bilaterally; good capillary refill; no cyanosis, clubbing, or edema

Neuro

A&O × 3, CN II–XII intact

■ Labs

Na 140 mEq/L	Hgb 12 g/dL	WBC $8.2 \times 10^3/\text{mm}^3$	T. bili 1.5 mg/dL
K 4.2 mEq/L	Hct 37%	Neutros 65%	Alk phos 140 IU/L
Cl 95 mEq/L	RBC $4.0 \times 10^6/\text{mm}^3$	Bands 5%	Alb 4.4 g/dL
CO ₂ 24 mEq/L	Plt $243 \times 10^3/\text{mm}^3$	Eos 0%	Prealb 20 mg/dL
BUN 8 mg/dL	SCr 0.6 mg/dL	Lymphs 28%	Lipase 203 IU/L
Glu 89 mg/dL	MCV 85.1 μm^3	Monos 2%	Amylase 21 IU/L
ANA pending	MCHC 35 g/dL	Anti-SSA pending	IgG4 pending
	Antiplasminogen-binding protein pending		

■ CT Abdomen With IV Contrast

Changes consistent with chronic pancreatitis: inflammation of the common bile duct with calcifications seen within the pancreas. No evidence of necrosis or fluid collections (Fig. 49-1).

■ Assessment

1. Chronic pancreatitis, idiopathic etiology—with acute exacerbation.
2. Xerostomia and chronic dry eye; rule out autoimmune disorders including Sjögren syndrome.
3. Routine medical care needed.

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of chronic pancreatitis?
- 1.b. What additional information is needed to fully assess this patient's chronic pancreatitis?

Assess the Information

- 2.a. Assess the severity of chronic pancreatitis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating chronic pancreatitis and associated complications?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's chronic pancreatitis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement a Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTION

1. Describe how this patient should be screened for future complications of chronic pancreatitis.

■ SELF-STUDY ASSIGNMENTS

1. Analyze the implication of an idiopathic diagnosis of disease. What other extrapancreatic diseases are associated with chronic pancreatitis?
2. What psychological factors will impact this patient's adherence to medical therapy or her willingness to seek further treatment given the patient's lack of medical care up to this point? How would this impact your ability to provide care for this patient?

CLINICAL PEARL

Chronic pancreatitis is of idiopathic etiology in up to 30% of cases.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Janine E. Then, PharmD, BCPS, and Heather M. Teufel, PharmD, BCPS.

REFERENCES

1. Conwell DL, Lee LS, Yadav D, et al. American Pancreatic Association practice guidelines in chronic pancreatitis: evidence-based report on diagnostic guidelines. *Pancreas* 2014;43:1143–1162.
2. Majumder S, Chari ST. Chronic pancreatitis. *Lancet* 2016;387:1957–1966.
3. Gupte A, Goede D, Tuite R, Forsmark CE. Clinical update: chronic pancreatitis. *BMJ* 2018;361:k2126.
4. Duggan SN, Smyth ND, Murphy A, et al. High prevalence of osteoporosis in patients with chronic pancreatitis: a systematic review and meta-analysis. *Clin Gastroenterol Hepatol* 2014;12:219–228.
5. Lohr JM, Dominguez-Munoz E, Rosendahl J, et al. United European Gastroenterology evidence-based guidelines for the diagnosis and therapy of chronic pancreatitis (HaPANEU). *United European Gastroenterol J* 2017;5:153–199.
6. Duggan S, O'Sullivan M, Feehan S, Ridgway P, Conlon K. Nutrition treatment of deficiency and malnutrition in chronic pancreatitis: a review. *Nutr Clin Pract* 2010;24:362–370.
7. Drewes AM, Bouwense SAW, Campbell CM, et al. Guidelines for the understanding and management of pain in chronic pancreatitis. *Pancreatol* 2017;17:720–731.
8. Motov S, Yasavolian M, Likourezos A, et al. Comparison of intravenous ketorolac at three single-dose regimens for treating acute pain in the emergency department: a randomized controlled trial. *Ann Emerg Med* 2017;70:177–184.
9. Olesen SS, Bouwense SA, Wilder-Smith OH, van Goor H, Drewes AM. Pregabalin reduces pain in patients with chronic pancreatitis in a randomized, controlled trial. *Gastroenterology* 2001;141:536–543.
10. Berry AJ. Pancreatic enzyme replacement therapy during pancreatic insufficiency. *Nutr Clin Pract* 2014;29:312–321.

50

VIRAL HEPATITIS A

Going on Vacation Level II

Juliana Chan, PharmD, FCCP, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine which patient populations are at greatest risk for contracting hepatitis A.
- Recommend hepatitis A immunization for appropriate individuals based on current guidelines of the Centers for Disease Control and Prevention (CDC).
- Assess the efficacy and adverse effects of hepatitis A vaccines.
- Counsel eligible patients on the benefits of hepatitis A vaccination and the possible adverse effects associated with its use.

PATIENT PRESENTATION

■ Chief Complaint

“My family and I are going on vacation.”

HPI

Lorenzo is a 37-year-old white man, born and raised in Italy who now resides in New York. He married his Taiwanese wife 2 years ago. He was diagnosed with NASH and hepatitis C at the age of 34 while undergoing a physical exam. He and the family will be going to China to celebrate Chinese New Year. Lorenzo was instructed to go to the Travel Clinic for vaccinations before leaving the United States in the next 3 weeks.

PMH

NASH diagnosed at age 34
Hepatitis C diagnosed at age 34
Diabetes
Hypertriglyceridemia
HTN

Surgical History

Several surgeries after a motor vehicle accident that required blood transfusions in the early 90s.

FH

Mother with no medical complaints. Father is alive with alcoholic liver disease. One younger sister with DM and older brother with HTN.

SH

Married for 2 years and lives with wife and 2-year-old son. He had smoked in his early 20s, one ppd then quit at age 26. He does not drink (or ever drank, fearing he would end up like his father). He had a tattoo placed professionally 2 years ago. There is no history of IV drug use, cocaine use, or abuse of prescription drugs. He has worked as a banker for the past decade.

Meds

Glipizide 10 mg PO twice daily
Gemfibrozil 600 mg PO twice daily
Enalapril 5 mg PO once daily
Fish oil—OTC, PO once daily

All

Sulfa, ciprofloxacin

ROS

Positive for fatigue, decrease in appetite. Denies weight loss/gain, fevers, chills, headaches, shortness of breath, and coughing. He does have some abdominal pain intermittently, also constipation off and on. No black stools or obvious blood in stools.

Physical Examination**Gen**

The patient is an Italian man in no apparent distress.

VS

BP 126/78, P 72, RR 20, T 36.9°C; Wt 268 lb (121.8 kg), Ht 5'9" (175 cm)

Skin

Warm and dry. Spider angiomas are not present.

HEENT

PERLLA, EOMI; fundi normal; TMs clear. Head is normocephalic and atraumatic; sclerae anicteric.

Neck/Lymph Nodes

Supple; no masses or JVD

Chest

Clear without wheezes, rhonchi, or rales

CV

RRR, S₁, S₂ normal

Abd

(+) Bowel sounds, no masses, nontender, nondistended

Genit/Rect

Rectal exam deferred

MS/Ext

Normal range of motion throughout; no CCE

Neuro

A&O × 3; CN II–XII intact; no focal deficits, negative for asterixis

Labs (Nonfasting)

Na 144 mEq/L	Hgb 15.6 g/dL	AST 31 IU/L	HBsAg (–)
K 4.5 mEq/L	Hct 45%	ALT 63 IU/L	anti-HBs(–)
Cl 107 mEq/L	WBC 6.9 × 10 ³ /mm ³	Alk phos 67 IU/L	anti-HCV(–)
CO ₂ 30 mEq/L		T. bili 1 mg/dL	HCV RNA PCR
BUN 16 mg/dL	Plt 195 × 10 ³ /mm ³	LDH 167 IU/L	not detected
SCr 1.2 mg/dL	T. chol 199 mg/dL	PT 13.1 seconds	Total anti-HAV
Glu 119 mg/dL	Trig 319 mg/dL	Alb 4.5 g/dL	(–)
	LDL 114		
	HDL 21		

Abdominal Ultrasound**Findings**

The liver has a coarse echotexture with smooth contour. No focal liver masses are seen. Hepatic steatosis is observed. There is no intra-hepatic biliary dilatation. The common bile duct measures 3 mm. There is no gallbladder wall thickening or pericholecystic fluid. The head and body of the pancreas are grossly unremarkable; views of the tail are obscured by overlying bowel gas. The right kidney measures 10.2 cm in length. The left kidney measures 11.2 cm. No hydronephrosis is seen in either kidney. There is no splenomegaly.

Impression

1. Coarse heterogeneous appearance of the liver is consistent with patient's history of hepatitis. No evidence for focal liver mass. Hepatic steatosis is present.
2. Cholelithiasis without evidence for cholecystitis.

Assessment

This is a 37-year-old white man with a history of chronic hepatitis C and NASH who is to be evaluated for vaccination prior to his trip to China.

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of current or past hepatitis A infection?

- 1.b. What additional information is needed to fully assess this patient's liver disease?

Assess the Information

- 2.a. Assess for the presence or absence of liver disease based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for preventing hepatitis A infection?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for prevention of hepatitis A and this patient's other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to Lorenzo to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcomes?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE (PART 1)

Lorenzo's wife and 2 year-old son returned to New York from China 10 days ago. His 36-year-old wife complains of nausea, vomiting, weight loss, and fevers. She was admitted to the hospital on day 7 since returning from vacation for medical evaluation. His son is symptom free but was recommended that he follow up with the pediatrician as soon as possible. The following labs were obtained during the first day of hospitalization for Lorenzo's wife:

Na 137 mEq/L	Hgb 11.2 g/dL	AST 3,259 IU/L	anti-HBs (+)
K 4 mEq/L	Hct 33.2%	ALT 3,621 IU/L	HBsAg (–)
Cl 100 mEq/L	WBC 7.7 × 10 ³ /mm ³	Alk phos 247 IU/L	Total anti-HAV (+)
CO ₂ 26 mEq/L		T. bili 20.5 mg/dL	Anti-HAV IgM (+)
BUN 12 mg/dL	Plt 159 × 10 ³ /mm ³	D. bili 12.9 mg/dL	Anti-HCV (–)
SCr 1.3 mg/dL		PT 12.9 s	Acetaminophen <10 mcg/mL
Glu 101 mg/dL		Alb 2.7 g/dL	

CT OF THE ABDOMEN WITH AND WITHOUT IV CONTRAST

Clinical indication: 36 year-old woman with new hepatic failure
Impression:

1. Diffuse thickening of the transverse colon consistent with colitis, likely of infectious or inflammatory etiology.

2. Diffuse low attenuation of the liver, perihepatic ascites, and edematous gallbladder wall consistent with underlying inflammatory process.

FOLLOW-UP QUESTIONS

1. Based on the information provided, what medical condition does Lorenzo's wife have?
2. What is your treatment recommendation for Lorenzo's wife?

CLINICAL COURSE (PART 2)

Lorenzo brought his 2-year-old asymptomatic son to see the pediatrician the same day his mother was admitted to the hospital. Father and son return to the doctor's office the next day to review the labs drawn a day ago.

anti-HBs (+) HBsAg (–) Total anti-HAV (–) anti-HAV IgM (–)

FOLLOW-UP QUESTIONS (CONTINUED)

3. What is your vaccination recommendation for Lorenzo's son? When should the son be vaccinated?

STUDY ASSIGNMENTS

1. Compare and contrast the mechanism of action, immunogenicity rate, and adverse effects of the two commercially available hepatitis A vaccines.
2. Determine which vaccines can be given simultaneously with the hepatitis A vaccine.
3. Compare the cost of administering the Havrix and Engerix-B vaccines separately versus the combination product Twinrix for adults and in children.

CLINICAL PEARL

The hepatitis A vaccine is highly effective in preventing hepatitis A infections when given immediately prior to departing to endemic areas. According to the CDC, all children in the United States over 1 year of age should receive the hepatitis A vaccine.

REFERENCES

1. Advisory Committee on Immunization Practices (ACIP) Centers for Disease Control and Prevention (CDC). Update: prevention of hepatitis A after exposure to hepatitis A virus and in international travelers. Updated recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2007;56(41):1080–1084.
2. Advisory Committee on Immunization Practices (ACIP), Fiore AE, Wasley A, Bell BP. Prevention of hepatitis A through active or passive immunization. Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR Morb Mortal Wkly Rep 2006;55(RR-7):1–23.
3. Hepatitis B Questions and Answers for Health Professionals. Available at: <https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm#vaccFAQ>. Accessed October 31, 2018.
4. Centers for Disease Control and Prevention. Surveillance for Viral Hepatitis, 2013. Available at: <http://www.cdc.gov/hepatitis/statistics/2013surveillance/commentary.htm#hepatitisA>. Accessed September 8, 2018.
5. Centers for Disease Control and Prevention. Hepatitis A questions and answers for health professionals. Available at: <https://www.cdc.gov/hepatitis/hav/havfaq.htm#travel>. Accessed October 29, 2018.

51

VIRAL HEPATITIS B

Arrived in America Level III

Juliana Chan, PharmD, FCCP, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Outline a pharmacologic and nonpharmacologic regimen for patients with chronic hepatitis B.
- Determine clinical and laboratory endpoints for treatment of chronic hepatitis B.
- Assess the efficacy and adverse effects of chronic hepatitis B treatment with pegylated interferon, lamivudine, adefovir dipivoxil, entecavir, tenofovir disoproxil, and tenofovir alafenamide.
- Recommend hepatitis B immunization for appropriate individuals based on current guidelines of the Centers for Disease Control and Prevention (CDC).
- Provide patient education on pegylated interferon, lamivudine, adefovir dipivoxil, entecavir, tenofovir disoproxil, and tenofovir alafenamide treatment.

PATIENT PRESENTATION

■ Chief Complaint

“I’m here for my free hepatitis B screening.”

■ HPI

Ming Hui is a 36-year-old Chinese woman from Mainland China with no significant past medical history. Over the summer, she was required to obtain a physical exam prior to arriving to America. She does not recall the lab results but recalls someone telling her to seek a liver doctor. She is here for her first time in the free health clinic to be evaluated for liver disease.

■ PMH

HTN lifestyle controlled
Chronic hepatitis B

■ Surgical History

None

■ FH

Mother alive, with HCC secondary to HBV. Has one older brother and one younger sister; HBV status unknown for siblings. Father with MI, died at age 56.

■ SH

Not currently in a relationship. She does not smoke or use IV drugs. She drinks one glass of red wine daily for the heart for the past 3 years. She works as an administrative assistant.

■ Meds

Dong quai, three capsules PO daily for menstrual cramps

■ All

None

■ ROS

Denies any symptoms. Her weight is stable with no loss of appetite. No nausea, vomiting, diarrhea, abdominal pain, or constipation. No melena or hematochezia. No changes in urine or stool color and no history of icteric sclerae.

■ Physical Examination

Gen

The patient is not in acute distress.

VS

BP 128/82, P 76, RR 20, T 37.6°C; Wt 127 lb (57.9 kg), Ht 5’1” (155 cm)

Skin

Warm and dry; no signs of jaundice. Good turgor.

HEENT

Head is normocephalic, atraumatic. Sclerae are anicteric bilaterally. Neck is supple. No masses or palpable lymphadenopathy. PERRLA. Funduscopic exam normal.

Lungs

Clear to P&A

Cor

RRR, S₁, S₂ normal; no S₃ or S₄

Abd

Good bowel sounds, soft, nontender; no evidence of ascites; no palpable hepatosplenomegaly

Rect

Guaiac negative

Ext

Normal range of motion throughout; no C/C/E, no gross lesions, ecchymosis, or peripheral edema

Neuro

CN II–XII intact; DTRs 2+ throughout; negative Babinski

■ Labs

Na 139 mEq/L	Hgb 12.4 g/dL	AST 24 IU/L	HBsAg (+)
K 4.0 mEq/L	Hct 37.3%	ALT 25 IU/L	Anti-HBs (–)
Cl 104 mEq/L	Plt 152 ×	Alk phos	HBeAg (+)
CO ₂ 25 mEq/L	10 ³ /mm ³	71 IU/L	HBV DNA PCR
BUN 12 mg/dL	WBC 6.9 ×	T. bili	Quant 9,581,
SCr 0.9 mg/dL	10 ³ /mm ³	0.4 mg/dL	721 IU/mL
Glu (nonfasting) 86 mg/dL	TSH 1.96 µIU/mL	T. prot 7.2 g/dL	Anti-HBc IgM (–)
	T. chol 132 mg/dL	Alb 4.2 g/dL	Anti-HBc
	Trig 281 mg/dL	PT 10.8 s	total (+)
			HCV RNA quant
			not detected
			Anti-HAV,
			total (–)
			Anti-HIV (–)
			HBV genotype A

Other Tests

Complete Ultrasound of the Abdomen

Findings: There is no ascites. The liver is normal in contour and echogenicity. There is no intrahepatic biliary dilatation; the common bile duct is not dilated and measures 0.5 cm. The gallbladder is unremarkable and without calculi, wall thickening, or pericholecystic fluid. The head and body of the pancreas are grossly unremarkable; views of the tail are obscured by overlying bowel gas.

A limited survey of the kidneys was performed. The kidneys are normal in size and echogenicity. The right kidney measures 9.5 cm in length. The left kidney measures 9.6 cm. No hydronephrosis is seen in either kidney. The spleen is normal in echotexture and size, measuring 9.4 cm. The visualized portions of the abdominal aorta and IVC are unremarkable.

Impression: Unremarkable ultrasound of the abdomen, including limited survey of both kidneys.

Assessment

Ming Hui is a 36-year-old Chinese woman with normal LFTs and chronic hepatitis B.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of chronic hepatitis B infection or demonstrates a risk factor for infection?
- What additional information is needed to fully assess this patient's liver disease?

Assess the Information

- Assess the severity of the hepatitis B infection based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating hepatitis B infection?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's hepatitis B infection and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE (PART 1)

The patient tolerated the initial therapy very well with minimal adverse effects. After 52 weeks of therapy, her physician stopped the medication. However, 3 months posttreatment, her serum HBV DNA was detectable. She also states that since finishing her hepatitis B therapy, she has been in a relationship and sexually active. Her lab results for the past few months of treatment were as follows:

Test	12 Weeks After Therapy Started	24 Weeks After Therapy Started	52 Weeks After Therapy Started	9 Months After Therapy Discontinued
AST (IU/L)	54	39	21	55
ALT (IU/L)	78	30	18	84
Alk phos (IU/L)	76	80	83	73
T. bili (mg/dL)	0.5	0.9	0.9	0.8
PT (s)	11.2	11.2	10.7	10.1
Alb (g/dL)	3.9	4.8	4.8	4.2
HBsAg	(+)	(+)	(+)	(+)
Anti-HBs	(-)	(-)	(-)	(-)
HBeAg	(+)	(+)	Nonreactive	(+)
HBeAb	(-)	(+)	(+)	(-)
HBV DNA (IU/mL)	<29 ^a	<29 ^a	<29 ^a	1,122,971

^a<29 IU/mL indicates undetectable HBV DNA level.

FOLLOW-UP QUESTIONS

- What laboratory parameters may suggest that a change in HBV therapy is warranted?
- Based on this new information, develop a drug therapy plan for the patient's hepatitis B. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What information do you need to provide to the patient and her new partner?

CLINICAL COURSE (PART 2)

Eighteen months after the completion of her initial course of therapy, Ming Hui is now married and is 38 years old. She is 3 months pregnant, and she discontinued her hepatitis B therapy. Her HBsAg status is positive with an HBV DNA level of 2,421,789 IU/mL off of the HBV therapy.

FOLLOW-UP QUESTIONS (CONTINUED)

- Would you recommend that the patient restart treatment for hepatitis B because she is pregnant? Justify your answer.
- Would you recommend hepatitis B vaccination and/or other medications for her newborn? If yes, include the drug, doses, and dosage schedule.

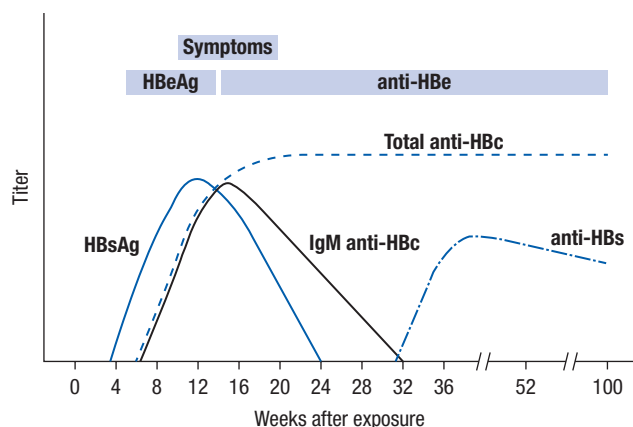


FIGURE 51-1. Typical serologic course of acute hepatitis B virus infection with recovery. *Note:* Serologic markers of infection vary depending on whether the infection is acute or chronic. (Source: Centers for Disease Control and Prevention. Viral Hepatitis Resource Center.)

SELF-STUDY ASSIGNMENTS

1. Describe the ideal patient infected with hepatitis B to respond to antiretroviral HBV therapy and what you would monitor for therapeutic efficacy and adverse effects.
2. Compare and contrast the mechanism of action, immunogenicity rate, and adverse effects of the two available hepatitis B vaccines.
3. Determine the cost of the antiretroviral HBV agents and pegylated interferon therapy for the treatment of hepatitis B.
4. Review the time course of serologic markers after an acute HBV infection and explain their significance to one of your peers (Fig. 51-1).

CLINICAL PEARL

To eliminate HBV transmission that occurs during infancy and childhood, the Immunization Practices Advisory Committee of the CDC recommends that all newborn infants be vaccinated regardless of the hepatitis B status of the mothers.

REFERENCES

1. Tong MJ, Pan CQ, Han SB, et al. An expert consensus for the management of chronic hepatitis B in Asian Americans. *Aliment Pharmacol Ther* 2018;47:1181–1200.
2. Terrault NA, Lok ASF, McMahon BJ, et al. Update on prevention, diagnosis, and treatment of chronic hepatitis B: AASLD 2018 hepatitis B guidance. *Hepatology* 2018;67:1560–1599.
3. World Health Organization (WHO). Guidelines for the prevention, care and treatment of persons with chronic hepatitis B infection. Geneva: WHO. March 2015. Available at: http://apps.who.int/iris/bitstream/10665/154590/1/9789241549059_eng.pdf?ua=1&ua=1. Accessed October 27, 2018.
4. Centers for Disease Control and Prevention. Hepatitis A questions and answers for health professionals. Available at: <https://www.cdc.gov/hepatitis/hav/havfaq.htm#vaccine>. Accessed October 27, 2018.
5. Martin P, Lau DT, Nguyen MH, et al. A treatment algorithm for the management of chronic hepatitis B virus infection in the United States: 2015 update. *Clin Gastroenterol Hepatol* 2015;13:2071–2087.e16.
6. European Association for the Study of the Liver. EASL 2017 clinical practice guidelines on the management of hepatitis B virus infection. *J Hepatol* 2017;67:370–398.

7. Terrault NA, Bzowej NH, Chang KM, Hwang JP, Jonas MM, Murad MH; American Association for the Study of Liver Diseases. AASLD guidelines for treatment of chronic hepatitis B. *Hepatology* 2016;63:261–283.
8. Centers for Disease Control and Prevention. Hepatitis B questions and answers for health professionals. Available at: <https://www.cdc.gov/hepatitis/hbv/hbvfaq.htm#vaccFAQ>. Accessed October 27, 2018.

52

VIRAL HEPATITIS C

Baby-Boomer Beware Level II

Michelle T. Martin, PharmD, FCCP, BCPS, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify and evaluate the clinical manifestations and laboratory parameters relevant to the assessment and treatment of chronic hepatitis C virus (HCV) infection.
- Design a patient-specific pharmaceutical care plan for a patient with chronic HCV, including drugs, doses, and durations of therapy.
- Develop a plan for monitoring efficacy and adverse effects of the pharmacologic agents used in the management of HCV.
- Identify and evaluate the drug interactions with direct-acting antiviral (DAA) agents used in HCV treatment.
- Provide patient education for patients with chronic HCV regarding their medications, nonpharmacologic interventions/behaviors, and vaccinations.

PATIENT PRESENTATION

Chief Complaint

“About three months ago, my primary care physician told me that my liver tests were abnormal. She referred me to your liver clinic and I am here today to talk about the test results from last month.”

HPI

Mr Michael Jones is a 58-year-old African-American man who has been referred by his primary care physician to the liver clinic for assessment of his abnormal liver enzymes. His physician had screened the patient for HCV after a pop-up alert in her institution’s electronic health record system recommended it. After a referral from the primary care physician, Mr Jones presented to liver clinic 1 month ago to see the hepatologist and had a FibroScan and labs drawn. He presents today to discuss the results and next steps.

He denies ever having blood transfusion. He reports use of recreational drugs including marijuana, alcohol, IV heroin, and intranasal cocaine in his teenage years and in his 20s. He states that he stopped use of these drugs around 30 years ago. He had a tattoo placed with a coat hanger while he was in his 20s. He also has a history of heavy alcohol use since his teens. He was treated for drug and alcohol abuse 6 months ago through an inpatient treatment program, and says he

has been sober since that time. He denies any jaundice or right upper quadrant pain. He also denies any hepatic encephalopathy or signs or stigmata of chronic liver disease at this time.

PMH

GERD: Began several years ago, is often exacerbated by spicy food
Right TKA in 2014, with chronic knee pain; recently discontinued naproxen due to stomach upset and was switched to tramadol by his primary care physician
Type 2 diabetes mellitus (diet-controlled now; glargine insulin was discontinued after HgbA1c was 5% last year)

FH

No known family history of liver disease or hepatocellular carcinoma (HCC). Both parents are deceased (father died from prostate cancer at 76, and his mother had a myocardial infarction at age 72). He has one sister (56 years old) and one brother (60 years old). His brother has some depression, and his sister has diabetes.

SH

The patient earned his high school diploma. He has worked at a juvenile detention center for the past 27 years. He is single and lives alone. He is a previous 1 ppd smoker who drank 6+ alcoholic drinks daily and used recreational drugs, including marijuana, alcohol, IV heroin, and intranasal cocaine when he was in his teens and 20s. He stopped using drugs in his late 20s, he quit smoking 4 years ago, and has been sober since his inpatient treatment 6 months ago.

Meds

MVI one tablet PO daily $\times$ 1 year
Omeprazole 20 mg PO daily $\times$ 5 years
Tramadol 50 mg PO BID PRN pain

Allergies and Intolerances

No known drug allergies

ROS

General: He feels that overall his health is “fine” as he made healthy lifestyle choices to quit smoking and alcohol. He has fatigue but attributes this to his age. His GERD symptoms depend on the type of food he eats and have been improved with diet modification. He reports a continued decline in his exercise stamina over the past few months, with knee and shoulder pain that affects his ROM. The remainder of the review of systems was noncontributory, with no additional pertinent positives or negatives.

Physical Examination

Gen

General appearance of a well-nourished, well-built African-American man in NAD

VS

BP 138/92, P 88, RR 18, T 37.2°C; Wt 200 lb (90.9 kg), Ht 5'10" (178 cm)

Skin

Intact without xanthomas, hematomas, or ecchymosis. No jaundice or palmar erythema

HEENT

PERRLA; EOMI; sclerae anicteric; funduscopic exam normal; TM WNL

Neck/Lymph Nodes

Neck supple; no lymphadenopathy or thyromegaly; no carotid bruits

Lungs/Thorax

Clear to auscultation bilaterally. Normal breath sounds.

CV

RRR; S₁, S₂ normal; no S₃ or S₄. No murmurs, rubs, or gallops

Abd

Soft, NT, ND. Normoactive bowel sounds. No evidence of ascites, no HSM.

MS/Ext

Slight edema in right and left knees. Peripheral pulses 2+ throughout; ROM limited by pain in both shoulders and knees.

Neuro

A&O $\times$ 3; CN II–XII intact; DTRs 2+

Labs Obtained 2 Months Ago From Patient's PCP

Na 138 mEq/L	Hgb 14 g/dL	AST 63 IU/L
K 4 mEq/L	Hct 39.8%	ALT 100 IU/L
Cl 103 mEq/L	Plt $237 \times 10^3/\text{mm}^3$	Alk phos 121 IU/L
CO ₂ 27 mEq/L	WBC $5.6 \times 10^3/\text{mm}^3$	T. bili 0.3 mg/dL
BUN 16 mg/dL	54% PMNS	Alb 4.4 g/dL
SCr 1.2 mg/dL	Bands 1%	Anti-HAV (–)
Glu 95 mg/dL	Lymphs 35%	HBsAg (–)
	Monos 10%	Anti-HCV (+)

Labs Obtained at Preclinic Lab Draw About 1 Month Ago

Na 140 mEq/L	Hgb 14.1 g/dL	AST 58 IU/L	HBsAg (–)
K 4.1 mEq/L	Hct 39%	ALT 98 IU/L	Anti-HBs (–)
Cl 100 mEq/L	Plt $235 \times 10^3/\text{mm}^3$	Alk phos 112 IU/L	Anti-HBc (–)
CO ₂ 28 mEq/L	WBC $6 \times 10^3/\text{mm}^3$	T. bili 0.4 mg/dL	Anti-HAV (–)
BUN 15 mg/dL	56% PMNs	Alb 4.1 g/dL	Anti-HCV (+)
SCr 1.2 mg/dL	Bands 1%		HCV RNA 3,500,000 IU/mL
Glu 100 mg/dL	Lymphs 36%	GGT 41 IU/L	HCV Genotype 1a
	Monos 7%		HIV (–)
	PT 12 seconds		
	INR 1.0		

FibroScan (Performed After Liver Clinic Visit 1 Month Ago)

9.8 kPa

Assessment/Diagnosis

Newly diagnosed chronic HCV

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of HCV?
- What additional information is needed to fully assess this patient's HCV?

Assess the Information

- Assess the severity of HCV based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating HCV?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's HCV and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE (PART 1): WEEK 4 PHONE CALL

After results from his labs are available from 4 weeks after HCV treatment initiation, the clinician calls the patient to discuss treatment and his lab results. Mr Jones reports feeling more fatigue than at baseline, but he denies other adverse effects. His AST and ALT are 27 and 30 IU/L, respectively, but his HCV RNA value is now not detected. Other labs are similar to the initial presentation. He states that he has been adherent to HCV therapy.

■ FOLLOW-UP QUESTIONS

1. Based on this information, should the therapy continue as planned? Why or why not?
2. Outline a plan for vaccinating the patient against other forms of viral hepatitis.

■ CLINICAL COURSE (PART 2): END-OF-TREATMENT VISIT

At his end-of-treatment visit, Mr Jones reports feeling better. He states he only had slight fatigue in the past few weeks. Lab values include AST 24 IU/L, ALT 22 IU/L, and HCV RNA not detected. Other labs are similar to the previous visit. He appears well nourished and comfortable. He is seeing his primary care physician regarding his lower extremity pain issues.

■ FOLLOW-UP QUESTIONS (CONTINUED)

3. What are the next steps to assess this patient's response to HCV therapy?
4. What other monitoring do you recommend for this patient?

■ SELF-STUDY ASSIGNMENTS

1. Review the recent AASLD/IDSA guidelines for the treatment of chronic HCV genotype 1 infection and summarize the advantages and disadvantages of the various DAA regimens.
2. Perform a literature search to assess the use of DAAs in patients with ongoing injection drug use or history of substance use.
3. Utilize the University of Liverpool's drug interaction website to assess for the presence and management of additional drug interactions with other DAA options for this patient (ie, phenobarbital, atorvastatin, oxycodone).
4. Consider limitations of risk-based HCV screening and propose modifications to current practice to identify and diagnose patients with HCV.

CLINICAL PEARL

DAA therapy is associated with potential drug interactions due to DAAs being substrates, inducers and/or inhibitors of cytochrome P450 (CYP) 3A, P-glycoprotein (P-gp), and organic anion transporting polypeptide (OATP) 1B1 and 2B1. Additional dosage adjustments and monitoring recommendations are reviewed in the prescribing information of each DAA medication; however, not all potential drug interactions have been studied and/or listed in the prescribing information. To supplement this information, pharmacokinetic properties of medications can be analyzed for the extent and pathway of metabolism, and drug interaction sources should be assessed.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Rima A. Mohammad, PharmD, BCPS, and Randolph E. Regal, BS, PharmD.

REFERENCES

1. Recommendations for testing, managing, and treating hepatitis C. American Association for the Study of Liver Diseases and Infectious Diseases Society of America. Available at: <http://www.hcvguidelines.org/>. Accessed April 1, 2019.
2. Hepatitis C Information for Health Professionals. Division of Viral Hepatitis and National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention. Centers for Disease Control and Prevention Publication. Available at: <http://www.cdc.gov/hepatitis/HCV/index.htm>. Accessed April 1, 2019.
3. Bonder A, Afdhal N. Utilization of FibroScan in clinical practice. *Curr Gastroenterol Rep* 2014;16:372.
4. Hep Drug Interactions. University of Liverpool. Available at: <http://www.hep-druginteractions.org>. Accessed April 1, 2019.
5. Deming P, Martin MT, Chan J, et al. Therapeutic advances in HCV genotype 1 infection: Insights from the Society of Infectious Diseases Pharmacists. *Pharmacotherapy* 2016;36:203–217.
6. Mohammad RA, Bulloch MN, Chan J, et al. Provision of clinical pharmacist services for individuals with chronic hepatitis C viral infection: Joint Opinion of the GI/Liver/Nutrition and Infectious Diseases Practice and Research Networks of the American College of Clinical Pharmacy. *Pharmacotherapy* 2014;34:1341–1354.

This page intentionally left blank

SECTION 5

RENAL DISORDERS

53

DRUG-INDUCED ACUTE KIDNEY INJURY

Not a Cute Consequence Level II

Mary K. Stamatakis, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Evaluate clinical and laboratory findings in a patient with acute kidney injury (AKI).
- Select pharmacotherapy for treatment of complications associated with AKI.
- Assess appropriateness of aminoglycoside serum concentrations in relation to efficacy and toxicity.
- Develop strategies to prevent drug-induced AKI, including the selection of pharmacologic alternatives that do not adversely affect kidney function.
- Adjust drug dosages based on kidney function to maximize efficacy and minimize adverse events.

PATIENT PRESENTATION

■ Chief Complaint

Not available

■ HPI

Wilbur Elliott is a 79-year-old man who originally presented to the hospital 1 month ago with symptoms of heart failure that required open heart surgery for mitral valve replacement. His surgery was complicated by a 1-hour hypotensive episode, with BP of 70/50 mm Hg during surgery. Three days postoperation, purulent drainage was noted from the surgical site, and he was subsequently diagnosed with mediastinitis. At that time, he was in septic shock with severe hypotension. He was found to have *Serratia* bacteremia (blood cultures × 4 positive for *Serratia marcescens*, sensitive to gentamicin, piperacillin, cefepime, ceftriaxone, and ciprofloxacin; resistance was noted to ampicillin). Therapy was initiated with gentamicin and cefepime. Thus far, he has completed day 21 of a 6-week course of antibiotics. A gradual increase in his BUN and serum creatinine concentrations from baseline has been noted (Table 53-1), and signs of volume overload are present.

■ PMH

Mechanical mitral valve replacement surgery 28 days ago
Type 2 DM
CKD
Dyslipidemia
Osteoarthritis
HTN
Heart failure
Depression

■ FH

Father had type 2 DM.

■ SH

Denies smoking or alcohol; retired coal miner (11 years ago)

■ Meds

Gentamicin (see Table 53-1 for dosages and serum drug concentrations; gentamicin is currently on hold)
Cefepime 2 g IVPB Q 12 H
Warfarin 5 mg PO once daily
Enalapril 10 mg PO twice daily
Metoprolol succinate XL 50 mg PO daily
Furosemide 40 mg PO Q 12 H
Atorvastatin 20 mg PO daily
Escitalopram 10 mg PO daily
Glipizide 10 mg PO daily
Spironolactone 12.5 mg PO daily (currently on hold)
Ibuprofen 400 mg PO Q 4–6 H PRN pain (started today for joint pain)

■ All

NKDA

■ ROS

Currently complains of trouble breathing, weakness, general malaise, and pain in right hand. No fever or chills.

■ PE

Gen

Confused-appearing man in mild distress

VS

BP 125/75 mm Hg, P 68 bpm, RR 26, T 37.7°C; current Wt 176 lb (80 kg); admission Wt 165 lb (75 kg), Ht 5'9" (175 cm)

Skin

Surgical incision site healing with no drainage

HEENT

PERRLA, EOMI, poor dentition

TABLE 53-1 SCr, BUN, and Serum Gentamicin Concentrations During Hospitalization

Postoperative Day	SCr (mg/dL)	BUN (mg/dL)	Gentamicin (mcg/mL)		Gentamicin Dosages
			Peak ^a	Trough ^b	
3	1.5	19			140 mg × 1, and then 120 mg Q 12 H
5	1.5	21	6.3	1.1	Continue current regimen
7	1.8	25			
10	2.1	31	6.9	1.8	Continue current regimen
14	2.7	38	8.3	2.5	Decrease to 120 mg Q 24 H
17	3.1	46			
21	3.2	50	9.4	2.7	Gentamicin on hold

BUN, blood urea nitrogen; SCr, serum creatinine.

^aSerum drug concentrations drawn 30 minutes after a 30-minute infusion.^bSerum drug concentrations drawn immediately before a dose.**Neck/Lymph Nodes**

(+) JVD

Chest

Basilar crackles

CVS₁, S₂ normal, no S₃, irregular rhythm**Abd**

Soft, nontender, (+) BS, (–) HSM

Genit/Rect

(–) Masses

MS/Ext

2+ sacral edema; some tenderness and limited motion in right hand

Neuro

A&O to person and place, but not to time

Labs (Current)

Na 139 mEq/L	Hgb 9.7 g/dL	Ca 8.6 mg/dL
K 3.7 mEq/L	Hct 29.5%	Mg 2.1 mg/dL
Cl 103 mEq/L	Plt 303 × 10 ³ /mm ³	Phos 4.4 mg/dL
CO ₂ 24 mEq/L	WBC 8.6 × 10 ³ /mm ³	INR 2.7
BUN 50 mg/dL	(BUN 19 mg/dL on admission)	
SCr 3.2 mg/dL	(SCr 1.5 mg/dL on admission)	
Glu 119 mg/dL		

UA

Color, yellow; character, hazy; glucose (–); ketones (–); SG 1.010; pH 5.0; protein 30 mg/dL; coarse granular casts 5–10/lpf; WBC 0–3/hpf; RBC 0–2/hpf; no bacteria; nitrite (–); osmolality 325 mOsm; urinary sodium 45 mEq/L; creatinine 33 mg/dL, FE_{NA} 3.1%

Repeat Blood Cultures Today

Negative

Fluid Intake/Output and Daily Weights

Day	I/O	Weight (kg)
3 days ago	3200 mL/900 mL	N/A
2 days ago	2600 mL/1000 mL	76
Yesterday	2800 mL/1300 mL	N/A
Today	N/A	80

Assessment

AKI with extracellular fluid expansion

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of AKI with extracellular fluid expansion?
- What additional information is needed to fully assess this patient's AKI?

Assess the Information

- Assess the severity of AKI based on the subjective and objective information available. Assessment of AKI includes the stage and category of AKI (prerenal, intrinsic, postrenal), as well as estimation of creatinine clearance.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case, including goal(s) related to drug dosage adjustments in AKI?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating AKI?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's AKI and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

ADDITIONAL CASE QUESTIONS

- What risk factors did the patient have for gentamicin-induced AKI?

2. What therapeutic interventions could have been initiated to decrease the likelihood of developing drug-induced AKI?
3. Could extended-interval gentamicin dosing have minimized the likelihood of nephrotoxicity?

SELF-STUDY ASSIGNMENTS

1. Create a list of medications that can cause AKI and that should be avoided in patients at risk for AKI.
2. Assume that Mr Elliott's serum creatinine is 1.4 mg/dL at 1 month after discharge. At what point would you restart his medications for treatment of heart failure?

CLINICAL PEARL

A “triple whammy” effect on kidney function can be seen when patients are administered angiotensin converting enzyme inhibitors or angiotensin receptor antagonists, diuretics, and nonsteroidal anti-inflammatory drugs, especially in the elderly.

REFERENCES

1. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for Acute Kidney Injury. *Kidney Int Suppl* 2012;2:1–138.
2. Frazee EN, Personett HA, Wood-Wentz DM, Herasevich V, Lieske JC, Kashani KB. Overestimation of glomerular filtration rate among critically ill adults with hospital-acquired oligoanuric acute kidney injury. *J Pharm Pract* 2016;29:125–131.
3. Xiong L, Lu ZK, Quidley AM, Alford BS, Bookstaver PB. Evaluation of renal function estimation formulas specific to dynamic renal function for drug dosing in critically ill patients. *South Med J* 2018;111:299–306.
4. Chawla LS, Bellomo R, Bihorac A, et al. Acute kidney disease and renal recovery: consensus report of the Acute Disease Quality Initiative (ADQI) 16 Workgroup. *Nat Rev Nephrol* 2017;13:241–257.
5. Lopez-Novoa JM, Quiros Y, Vicente L, Morales AI, Lopez-Hernandez FJ. New insights into the mechanism of aminoglycoside nephrotoxicity: an integrative point of view. *Kidney Int* 2011;79:33–45.
6. Wargo KA, Edwards JD. Aminoglycoside-induced nephrotoxicity. *J Pharm Pract* 2014;27:573–577.
7. Brater DC. Update in diuretic therapy: clinical pharmacology. *Semin Nephrol* 2011;31:483–494.

54

ACUTE KIDNEY INJURY

There's Nothing Cute About It Level II

Scott Bolesta, PharmD, BCPS, FCCM, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Assess a patient with AKI using clinical and laboratory data.
- Classify AKI in a patient.

- Distinguish between AKI resulting from prerenal and that from intrinsic injury.
- Recommend changes to the pharmacotherapeutic regimen of a patient with AKI.
- Justify appropriate therapeutic interventions for a patient with AKI.

PATIENT PRESENTATION

Chief Complaint

“I feel really weak.”

HPI

Everitt Mitchell is a 72-year-old man who presents to the ED with complaints of severe weakness that started this morning and recent stomach pain for the past week. He was feeling normal until he developed stomach pain 1 week ago that worsened with meals. Two days ago the pain worsened to the point where he avoided eating, and last evening he felt more tired than usual and went to bed early. He had difficulty sleeping due to the pain, and since waking this morning he has been in too much pain and too weak to perform his normal ADLs. His wife brought him to the ED because his physician is away on vacation.

PMH

HTN × 30 years
CAD × 20 years
MI × 2 with most recent 2 months ago s/p PCI with drug-eluting stent placement
s/p CABG 20 years ago
HF × 4 years
RA × 1 year

FH

Father died of an acute MI at age 52; mother had diabetes mellitus and died of a stroke at the age of 65.

SH

Retired and living at home with his wife. Before retirement, the patient was employed as an accountant. No alcohol, no tobacco use.

Meds

Aspirin 81 mg PO daily
Amlodipine 10 mg PO once daily
Furosemide 40 mg PO once daily
Metoprolol succinate 50 mg PO once daily
Enalapril 20 mg PO once daily
Prasugrel 10 mg PO daily
Naproxen 500 mg PO BID

All

NKA

ROS

In addition to weakness and stomach pain, the patient complains of feeling cold but denies chills or fever. No changes in vision. Denies SOB, CP, and cough. Complaints of feeling lightheaded. Has been having frequent loose black stools over the past 3 days and abdominal pain that has become severe in the past 2 days. Has noted a decrease in the frequency of his urination over the past 24 hours. Denies musculoskeletal pain or cramping.

■ Physical Examination

Gen

Pale, elderly Caucasian man who appears in moderate distress and generally weak and lethargic

VS

BP 89/43 mm Hg (77/32 mm Hg on standing), P 123 bpm, RR 25, T 36.1°C; Wt 171.6 lb (78 kg), Ht 5'9" (175 cm)

Skin

Pale and cool with poor turgor

HEENT

PERRLA; EOMI; fundi normal; conjunctivae pale and dry; TMs intact; tongue and mouth dry

Neck/Lymph Nodes

No JVD or HJR; no lymphadenopathy or thyromegaly

Lungs

No crackles or rhonchi

CV

Tachycardic with regular rhythm; normal S₁, S₂; no S₃; faint S₄; no MRG

Abd

Rigid with guarding, epigastric tenderness, ND; no HSM; hyperactive BS

Genit/Rect

Stool heme (+); slightly enlarged prostate

MS/Ext

Weak pulses; no peripheral edema; mild swelling of MCP joints of both hands

Neuro

A&O × 3; CNs intact; DTRs 2+; Babinski (–)

■ Labs

Na 132 mEq/L	Ca 8.6 mg/dL
K 5.6 mEq/L	Mg 2.1 mg/dL
Cl 97 mEq/L	Phos 4.3 mg/dL
CO ₂ 22 mEq/L	WBC 8.6 × 10 ³ /mm ³
BUN 53 mg/dL	Hgb 7.6 g/dL
SCr 1.8 mg/dL	Hct 22.5%
Glu 123 mg/dL	Plt 96 × 10 ³ /mm ³

■ Assessment

Admit to hospital for evaluation and management of dehydration, evaluation for acute GI bleed, and potential acute renal failure.

■ Clinical Course

On admission, the patient was resuscitated aggressively with IV normal saline and multiple transfusions (4 units of PRBCs). His home

medications were held, he was started on a continuous IV pantoprazole infusion of 8 mg/hr, and he underwent an emergent EGD. During endoscopy, a large ulcer in the gastric antrum was found with an exposed spurting artery. Endoscopic therapy was unsuccessful, and the patient was taken to the OR for surgical intervention. He was hypotensive in the OR (BP 70 mm Hg systolic on average) and was started on a norepinephrine infusion to maintain a stable BP. Postoperatively, he remained on mechanical ventilation, and his urine output averaged 35 mL/hr over the first 12 postoperative hours despite continued aggressive IV hydration and repeated transfusions in the OR. He also remained on norepinephrine for a continued low BP. On the morning of postoperative day 1, his labs were as follows:

Na 134 mEq/L	Ca 8.2 mg/dL
K 5.4 mEq/L	Mg 2.2 mg/dL
Cl 111 mEq/L	Phos 4.7 mg/dL
CO ₂ 19 mEq/L	WBC 14.6 × 10 ³ /mm ³
BUN 49 mg/dL	Hgb 10.3 g/dL
SCr 2.5 mg/dL	Hct 29.8%
Glu 145 mg/dL	Plt 112 × 10 ³ /mm ³

Urinalysis also showed muddy brown casts, urine sodium of 72 mEq/L, and specific gravity of 1.004. The patient remained on mechanical ventilation and norepinephrine, his urine output had not improved, and his chest radiograph showed diffuse bilateral pulmonary edema with a decrease in O₂ saturation to 86%. An echocardiogram revealed hypokinesis of the anterior portion of the left ventricle and an EF of 25%. The patient was started on dobutamine, and an internal jugular vein catheter was inserted and CVVH-DP was begun.

■ Assessment

A 72-year-old man with an acute UGI bleed, AKI, and volume overload heart failure

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of AKI postoperatively?
- What additional information is needed to fully assess this patient's AKI postoperatively?

Assess the Information

- Assess the severity of AKI based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating AKI?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's AKI and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

On postoperative day 5, his pulmonary edema had resolved, norepinephrine and dobutamine had been weaned off, the dialysis catheter was removed, and he was extubated. His subsequent hospital course was uneventful, and his kidney function gradually improved.

SELF-STUDY ASSIGNMENTS

1. Compare and contrast the RIFLE criteria for defining and classifying AKI to that published by the Acute Kidney Injury Network, and describe how both these definitions of AKI helped form the definition proposed by the KDIGO guidelines.
2. Write a brief paper that discusses the pharmacotherapeutic interventions that have been studied for the prevention of AKI from causes other than IV contrast agents.

CLINICAL PEARL

Patients in the recovery (or “diuretic”) phase of ATN produce large amounts of dilute urine due to resolution of tubular obstruction from sloughed tubular epithelial cells and inability of the recovering tubular cells to reabsorb sodium. This return of urine output does not signal complete recovery of kidney function, and medications eliminated to a large extent by active tubular secretion may still accumulate and require dosage adjustment.

REFERENCES

1. Kidney Disease: Improving Global Outcomes (KDIGO) Acute Kidney Injury Work Group. KDIGO Clinical Practice Guideline for acute kidney injury. *Kidney Int Suppl* 2012;2:1–138.
2. Myburgh JA, Finfer S, Bellomo R, et al. Hydroxyethyl starch or saline for fluid resuscitation in intensive care. *N Engl J Med* 2012;367:1901–1911.
3. Prowle JR, Kirwan CJ, Bellomo R. Fluid management for the prevention and attenuation of acute kidney injury. *Nat Rev Nephrol* 2014;10:37–47.
4. Palevsky PM. Renal replacement therapy in acute kidney injury. *Adv Chronic Kidney Dis* 2013;20:76–84.
5. Ejaz AA, Mohandas R. Are diuretics harmful in the management of acute kidney injury? *Curr Opin Nephrol Hypertens* 2014;23:155–160.
6. Kellum JA, Lameire N. Diagnosis, evaluation, and management of acute kidney injury: a KDIGO summary (part 1). *Crit Care* 2013;17:204.
7. Bellomo R, Wan L, May C. Vasoactive drugs and acute kidney injury. *Crit Care Med* 2008;36(Suppl):S179–S186.
8. Laine L, Jensen DM. Management of patients with ulcer bleeding. *Am J Gastroenterol* 2012;107:345–360.

55

PROGRESSIVE RENAL DISEASE

It Was Only a Matter of Time Level III

Christie Schumacher, PharmD, BCPS, BCACP, BC-ADM, CDE

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify risk factors for progression of chronic kidney disease (CKD) or diabetic kidney disease (DKD).
- Develop a care plan utilizing nonpharmacologic and pharmacologic interventions to slow the rate of progression of CKD.
- Identify clinical and laboratory parameters utilized to evaluate progression of CKD, the efficacy of medication therapy, and to detect or prevent adverse effects.
- Educate patients about the common medications prescribed for CKD.

PATIENT PRESENTATION

Chief Complaint

“I’m here to review the results of my labs.”

HPI

Christine Karter-Davis is a 38-year-old African-American woman with type 2 diabetes mellitus (T2DM), hypertension (HTN), and dyslipidemia who returns to her primary care physician (PCP) for a follow-up visit. At her routine physical examination 3 months ago, her annual nephropathy screening revealed 3+ protein and a urine albumin-to-creatinine ratio (UACR) of 659 mg/g. This is elevated from last year’s screening that showed mildly increased UACR and SCr of 1.2 mg/dL. A second spot urine test from 1 week ago showed a persistently elevated UACR of 673 mg/g. She has returned to the office today to review the results of this testing. Ms Karter-Davis arrives in the office today with no complaints and brought with her a list of her medications and self-monitoring blood glucose readings.

PMH

T2DM × 8 years
HTN × 6 years
Dyslipidemia × 5 years
Seasonal allergies

FH

Father had T2DM and cardiovascular disease (CVD) and died at age 50 secondary to myocardial infarction (MI); mother (age 62) has HTN and dyslipidemia. Has one brother (age 31) who also has T2DM.

SH

The patient is an administrative assistant and has medical coverage and prescription drug benefits. She reports occasional alcohol

consumption on weekends or when out with friends (one to two alcoholic beverages per month). She smokes one pack per day (ppd); decreased from previously reported two ppd last year. No history of illicit drug use.

■ Meds

Metformin 1000 mg PO twice daily
 Liraglutide 1.2 mg subcutaneously daily
 Hydrochlorothiazide 25 mg PO daily
 Atorvastatin 20 mg PO daily
 Mometasone two sprays (100 mcg) in each nostril once daily PRN allergies
 Cetirizine 10 mg PO daily PRN allergies
 Naproxen 220 mg PO BID PRN headaches
 Multivitamin PO daily

■ Immunizations

Tdap—4 years ago

■ All

NKDA, seasonal allergies to grass and pollen

■ ROS

Occasional headaches, generally associated with menstruation; no c/o polyuria, polydipsia, polyphagia, sensory loss, or visual changes
 No dysuria, flank pain, hematuria, pedal edema, chest pain, dizziness, or SOB

■ Physical Examination

Gen

The patient is an African-American woman in no acute distress.

VS

BP 148/84 mm Hg (R arm), repeat BP 146/82 mm Hg (L arm), HR 82 bpm, RR 18, T 37.5°C; Wt 191 lb (87 kg), Ht 5'6" (168 cm)

Skin

Warm, dry, no rashes

HEENT

PERRLA, EOMI, negative for diabetic retinopathy; no retinal edema or vitreous hemorrhage
 TMs intact
 Oral mucosa moist with no lesions

Neck/Lymph Nodes

Supple without adenopathy or thyromegaly

Lungs/Thorax

Clear, breath sounds normal

CV

Heart sounds normal, no murmurs, no bruits

Abd

Soft NT/ND

Genit/Rect

Rectal exam deferred; recent Pap smear negative

MS/Ext

No CCE, normal ROM

Neuro

A&O × 3; CNs intact; normal DTRs

■ Labs (1 Week Ago, Fasting)

Na 140 mEq/L	Hgb 12.2 g/dL	<i>Fasting lipid profile</i>
K 3.9 mEq/L	Hct 36.1%	T. chol 212 mg/dL
Cl 107 mEq/L	WBC $9.5 \times 10^3/\text{mm}^3$	Trig 149 mg/dL
CO ₂ 26 mEq/L	Plt $148 \times 10^3/\text{mm}^3$	LDL 140 mg/dL
BUN 29 mg/dL	Ca 9.4 mg/dL	HDL 42 mg/dL
SCr 1.6 mg/dL	Phos 2.7 mg/dL	Alb 3.4 g/dL
Glu 196 mg/dL	Uric acid 6.2 mg/dL	
A1C 8.2%	eGFR 46.4 mL/min/1.73 m ²	

■ UA (1 Week Ago)

pH 5.2, 1+ glucose, (–) ketones, 3+ protein, (–) leukocyte esterase and nitrite; (–) RBC; 3–4 WBC/hpf, ACR 673 mg/g

■ Assessment

A 38-year-old woman diagnosed today with CKD secondary to T2DM (ie, DKD) and overt macroalbuminuria complicated by inadequately controlled comorbid conditions.

QUESTIONS

Collect Information

- What objective information indicates the presence of CKD in this patient?
- What additional information is needed to fully assess this patient's CKD and other diseases that may contribute to CKD?

Assess the Information

- Assess the severity of CKD based on the subjective and objective information available. Calculate eGFR and CrCl in this patient based on her most recent labs using the Cockcroft–Gault, and CKD-EPI equations.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, efficacy, safety, and patient adherence.

Develop a Care Plan

- What are the goals of therapy for this patient?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating this patient's CKD and other diseases that may contribute to CKD?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's CKD and other drug therapy problems. Include specific drugs, dosage forms, doses, frequency, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, optimize efficacy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the efficacy of the chosen therapies and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Discuss the role of diuretic therapy in patients with normal renal function compared to those with creatinine clearance values <30 mL/min.
2. Review and compare the effects of antihypertensive agents on renal blood flow and glomerular filtration rate in patients with HTN and CKD.

CLINICAL PEARL

The American Diabetes Association (ADA) Standards of Care recommend that a sodium-glucose cotransporter-2 inhibitor be initiated in patients with T2DM and CKD based on benefits seen in secondary renal outcomes in the cardiovascular outcomes trials for these agents.¹

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Michelle D. Furler, BSc Pharm, PhD.

REFERENCES

1. American Diabetes Association. Standards of medical care in diabetes—2019. *Diabetes Care* 2019;42(Suppl 1):S1–S193.
2. National Kidney Foundation. KDOQI clinical practice guideline for diabetes and CKD: 2012 update. *Am J Kidney Dis* 2012;60:850–886.
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Intern Suppl* 2013;3:1–150.
4. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycemia in type 2 diabetes, 2018. A consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2018;41(12):2669–2701.
5. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):1269–1324.
6. National Kidney Foundation. Frequently asked questions about GFR estimates. Available at: https://www.kidney.org/sites/default/files/docs/12-10-4004_abe_faqs_aboutgfrrev1b_singleb.pdf. Accessed November 25, 2018.
7. Grundy SM, Stone NJ, Bailey AL, et al. 2018 ACC/AHA/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018;71:e127–e248.

56

END-STAGE KIDNEY DISEASE

Urine Trouble Level II

Katie E. Cardone, PharmD, BCACP, FNKF, FASN, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify medication-related problems in a patient with end-stage kidney disease maintained on chronic hemodialysis.
- State the desired therapeutic outcomes of each problem.
- List therapeutic alternatives for managing each problem.
- Develop a plan for managing each problem that includes plans for monitoring patient response to interventions.
- Outline a plan for helping the patient understand and effectively implement medication-related interventions.

PATIENT PRESENTATION

Chief Complaint

“I feel tired, nauseated, and constipated.”

HPI

Jane Lopez is a 42-year-old woman who presents to the outpatient dialysis center for her routine HD treatment. She has ESRD secondary to hypertension and has been on HD for 4 years. She has a failed AV fistula and graft and is currently dialyzed via central venous catheter. She has an upcoming appointment with the vascular surgeon to reevaluate her HD access. She also frequently leaves HD 30–60 minutes early against medical advice.

PMH

ESRD secondary to HTN
Anuria
HTN
Anemia
Secondary hyperparathyroidism
H/O gestational diabetes 12 years ago
GERD

PSH

Cesarean section 12 years ago
Tubal ligation 10 years ago
AV fistula creation 5 years ago (failed)
AV graft creation 3 years ago (failed)

FH

Father died of MI at age 60. Mother deceased due to breast cancer. No siblings. Has a 12-year-old son in good health.

■ SH

Married, lives with husband and a 12-year-old son. Occasional social alcohol use. Smokes 1/2 ppd (decreased from one ppd × 10 years). Denies caffeine consumption.

■ ROS

Complains of feeling tired and weak over the past several weeks. Reports some swelling in feet and lower legs. Also reports constipation, nausea, and heartburn.

■ Meds

Furosemide 80 mg PO daily
Metoprolol tartrate 50 mg PO BID
Lisinopril 20 mg PO daily
Calcium acetate 667 mg three caps PO TID with meals
Nephro-Vite PO daily
Omeprazole 20 mg PO daily
Ferrous sulfate 325 mg PO TID
Docusate 100 mg PO daily PRN
Calcium carbonate PO PRN heartburn
Epoetin alfa 10,000 units IV three times weekly with dialysis (dose stable for 3 months)
Iron sucrose 50 mg IV once weekly at dialysis
Calcitriol 0.5 mcg PO three times weekly with dialysis

■ All

NKDA

■ Physical Examination**Gen**

The patient is a WDNW Hispanic woman in NAD who appears her stated age.

VS

BP 175/88 mm Hg (predialysis); 149/89 mm Hg (postdialysis)
Wt 195 lb (88.6 kg) predialysis; 177 lb (84.0 kg) postdialysis
P 91 bpm, RR 16, T 36.5°C; Ht 5'4" (163 cm)

Skin

Dry, scaly arms and legs

HEENT

PEERLA, EOMI, TMs intact

Neck/Lymph Nodes

Supple, no adenopathy, no thyromegaly

Lungs/Thorax

Clear, breath sounds normal

CV

RRR, no murmurs, no bruits

Abd

Soft, NT/ND

Genit/Rect

Deferred

Ext

Mild bilateral lower extremity edema

Neuro**■ Labs**

Na 143 mEq/L	Hgb 9.3 g/dL	AST 21 IU/L	Alb 3.0 g/dL
K 4.3 mEq/L	Hct 27.5%	ALT 4 IU/L	Ca 9.7 mg/dL
Cl 95 mEq/L	RBC 2.84 × 10 ⁶ /mm ³	LDH 139 IU/L	Phos 6.7 mg/dL
CO ₂ 26 mEq/L	MCV 81.8 m ³	Alk phos 175 IU/L	iPTH 855 pg/mL
BUN 59 mg/dL	MCHC 32.4 g/dL	T. bili 0.3 mg/dL	T. sat 12%
SCr 8.9 mg/dL	WBC 5.7 × 10 ³ /mm ³		Ferritin 99 ng/mL

Mrs Lopez's nephrologist provided the following dialysis prescription:
Dialyze 3.5 hours per session, three times per week (T, Th, Sat, morning shift)
Estimated dry weight: 83.5 kg
Dialyzer: F180 (high flux)
Blood flow rate: 400 mL/min
Dialysate flow rate: 800 mL/min
Dialysate: Bicarbonate
Na 145 mEq/L, K 2.0 mEq/L, Ca 2.5 mEq/L, HCO₃ 35 mEq/L
Heparin: 5000 unit IV bolus, and then 1000 units/hr until 1 hour before termination

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of ESRD and complications of ESRD?
- 1.b. What additional information is needed to fully assess this patient's ESRD?

Assess the Information

- 2.a. Assess the severity of ESRD based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's ESRD-related problems?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's ESRD and other drug-related problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to improve medication use patterns, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Mrs Lopez develops a sinus infection for which she goes to an urgent care clinic. She is prescribed levofloxacin 500 mg PO daily $\times$ 14 days. Evaluate the appropriateness of this prescription for Mrs Lopez. What changes, if any, would you suggest regarding this prescription?
2. Mrs Lopez would like a kidney transplant but must first quit smoking to become eligible for transplant. Create a smoking cessation plan for her.

CLINICAL PEARL

The dose of ESAs should always be minimized. In the face of iron deficiency and low hemoglobin, iron should be replenished before increasing the ESA dose.

REFERENCES

1. Georgianos PI, Agarwal R. Pharmacotherapy of hypertension in chronic dialysis patients. *Clin J Am Soc Nephrol* 2016;11:2062–2075.
2. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia of chronic kidney disease. *Kidney Int Suppl* 2012;2:1–335.
3. Epogen (Epoetin Alfa) [Package Insert]. Thousand Oaks, CA, Amgen Inc., 2018.
4. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Kidney Int Suppl* 2017;7:1–59.
5. Rottembourg J, Schellekens H. Non biologic complex drug concept: experiences with iron sucrose and low molecular weight heparin. *J Blood Lymph* 2014;4:123.
6. Triferic (Ferric Pyrophosphate Citrate) [Package Insert]. Wixom, MI, Rockwell, 2018.
7. Pai AB, Jang SM, Wegrzyn N. Iron-based phosphate binders—a new element in management of hyperphosphatemia. *Expert Opin Drug Metab Toxicol* 2016;12:115–127.

57

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE RELEASE

A Sudden Change of Mind Level I

Sarah A. Nisly, PharmD, BCPS, FCCP

Jane M. Gervasio, PharmD, BCNSP, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the etiologies of hyponatremia and specifically the syndrome of inappropriate antidiuretic hormone (SIADH) release.
- Assess risk factors for developing hyponatremia and SIADH.

- Evaluate osmotic and fluid status in patients with hyponatremia.
- Recommend and monitor appropriate therapy and alternative treatments for SIADH.
- Discuss treatment options for SIADH, proper administration of selected treatments, and potential side effects.

PATIENT PRESENTATION

Chief Complaint

“There’s nothing wrong with me, I don’t know why she made me come here!”

HPI

Patrick O’Flannery is a 73-year-old man who presents to the ED after several episodes of “weird” behavior, according to his family and friends. He is accompanied by his wife who stated that Patrick had been the unrestrained driver in a car accident 3 days earlier. Patrick was driving himself home from the Caribou Lodge when he swerved off the road and hit a tree. His wife indicates that he hit his head on the steering wheel and lost consciousness for approximately 2 minutes but appeared otherwise unharmed except for a cut on his forehead. The paramedics cleaned and bandaged the patient’s lesion and noted that he was combative and disoriented but refused to go to the hospital. The wife states that Patrick has not been “acting like himself” since the accident and she had observed him displaying worsening confused and disoriented behavior in the past 24 hours.

PMH

Exercise-induced asthma since childhood
Depression for 7 years

SH

Lives at home with wife; has two children, both living out of state. Employed part time as a cab driver. Social alcohol use. Denies smoking and use of illicit substances.

Meds

Albuterol inhaler 2 puffs by mouth Q 6 H PRN exercise; last used 1 week ago
Fluoxetine 20 mg by mouth daily for 6 years

All

Penicillin (reaction unknown)

ROS

Difficult to obtain because of decreased mental status. Wife states that he has no medical problems except asthma and depression.

Physical Examination

Gen

A&O $\times$ 3 but disoriented about recent events. Patient is agitated and confused.

VS

BP 130/84 mm Hg, P 88 bpm, RR 21, T 37°C; Wt 209 lb (95 kg), Ht 5’9” (175 cm)

Skin

Diaphoretic centrally and very warm; small lesion above left eye

HEENT

NC/AT; EOMI; PERRL; TMs WNL bilaterally

Neck/Lymph Nodes

Supple without lymphadenopathy, masses, goiter, or bruits

Lung/Thorax

Clear to A&P bilaterally

CV

RRR; no MRG

Abd

Soft, NT/ND w/o masses or organomegaly; decreased bowel sounds in all four quadrants

Genit/Rect

Deferred

MS/Ext

Normal ROM; muscle strength 5/5 and equal bilaterally; pulses 2+ throughout; no CCE; capillary refill < 2 seconds

Neuro

CN II–XII intact; DTRs 2/4 and equal bilaterally; sensory intact; (–) Babinski

■ Labs

Na 112 mEq/L	Ca 9.2 mg/dL	T. chol 167 mg/dL
K 3.2 mEq/L	Phos 2.9 mg/dL	TSH 4.12 μ IU/mL
Cl 90 mEq/L	Uric acid 3.2 mg/dL	Serum osmolality 238 mOsm/kg
CO ₂ 27 mEq/L	AST 87 IU/L	
BUN 16 mg/dL	ALT 59 IU/L	
SCr 0.9 mg/dL	T. bili 0.7 mg/dL	
Glu 115 mg/dL	LDH 256 IU/L	

■ UA

SG 1.008, pH 6.8, leukocyte esterase (–), nitrite (–), protein (–), ketones (–), urobilinogen nl, bilirubin (–), blood (–), glucose 80 mg/dL, spot urine sodium 125 mEq/L, osmolality 420 mOsm/kg

■ CT Head

Closed head injury (head trauma)

■ Assessment

1. Closed head injury
2. SIADH
3. Electrolyte disturbances

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of SIADH?
- 1.b. What additional information is needed to fully assess this patient's SIADH?

Assess the Information

- 2.a. Assess the severity of SIADH based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating SIADH?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's SIADH and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate:

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

After Mr O'Flannery's serum sodium returned to baseline, the team began to discuss his discharge regimen.

■ FOLLOW-UP QUESTION

1. Identify the appropriate discharge regimen for this patient. Should he continue fluoxetine?

■ SELF-STUDY ASSIGNMENTS

1. Calculate this patient's serum osmolality and compare this to the measured serum osmolality.
2. What are the risk factors for hyponatremia caused by selective serotonin reuptake inhibitors (SSRIs)?
3. Perform a literature search to determine which SSRIs are most commonly associated with SIADH. Identify the general progression of SSRI-induced SIADH.

CLINICAL PEARL

Cerebral salt wasting (CSW) is another potential cause of hyponatremia, especially if the patient has had a head injury such as subarachnoid hemorrhage or stroke. It is often difficult to differentiate CSW from SIADH due to the overlap in their clinical features. Both CSW and SIADH present with inappropriately high urine osmolality and high urine sodium (usually >40 mEq/L). One difference is that CSW is associated with extracellular fluid depletion, whereas SIADH is associated with normal or slightly increased extracellular fluid volume. CSW can only be diagnosed in patients with clear

evidence of volume depletion (hypotension, decreased skin turgor, and elevated hematocrit). SIADH is usually corrected through fluid restriction; however, establishing euolemia through volume repletion with normal saline usually corrects CSW.

REFERENCES

1. Overgaard-Steensen C, Ring T. Clinical review: practical approach to hyponatraemia and hypernatraemia in critically ill patients. *Crit Care* 2013;17:206. doi: 10.1186/cc11805.
2. Siragy HM. Hyponatremia, fluid–electrolyte disorders, and the syndrome of inappropriate antidiuretic hormone secretion: diagnosis and treatment options. *Endocr Pract* 2006;12:446–457.
3. Assadi F. Hyponatremia: a problem-solving approach to clinical cases. *J Nephrol* 2012;25:473–480.
4. De Picker L, Van Den Eede F, Dumont G, et al. Antidepressants and the risk of hyponatremia: a class by class review of the literature. *Psychosomatics* 2014;55(6):536–547.
5. Potts MB, DeGiacomo AF, Deragopian L, Blevins LS. Use of intravenous conivaptan in neurosurgical patients with hyponatremia from syndrome of inappropriate antidiuretic hormone secretion. *Neurosurgery* 2011;69:268–273.
6. Marik PE, Rivera R. Therapeutic effect of conivaptan bolus dosing in hyponatremic neurosurgical patients. *Pharmacotherapy* 2013;33:51–55.
7. Reddy S, Rangappa P, Jacob I, et al. Efficacy of conivaptan and hypertonic (3%) saline in treating hyponatremia due to syndrome of inappropriate antidiuretic hormone in a tertiary intensive care unit. *Indian J Crit Care Med* 2016;20:714–718.
8. Humayun M, Cranston I. In-patient tolvaptan use in SIADH: care audit, therapy observation and outcome analysis. *BMC Endocrine Disorders* 2017;17:69.
9. Gassanov N, Semmo M, Semmo M, et al. Arginine vasopressin (AVP) and treatment with arginine vasopressin receptor antagonists (vaptans) in congestive heart failure, liver cirrhosis and syndrome of inappropriate antidiuretic hormone secretion (SIADH). *Eur J Clin Pharmacol* 2011;67:333–346.

58

ELECTROLYTE ABNORMALITIES IN CHRONIC KIDNEY DISEASE

Turn Down the 'Lytes Level II

Lena M. Maynor, PharmD, BCPS

Mary K. Stamatakis, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Interpret clinical and biochemical findings in patients with CKD.
- Recommend a patient-specific therapeutic plan for treating electrolyte abnormalities and chronic kidney disease-mineral and bone disorder (CKD-MBD).
- Monitor the effectiveness of the pharmacotherapeutic plan for treating electrolyte abnormalities in CKD.
- Educate patients with CKD on nonprescription medications that can worsen electrolyte abnormalities in CKD.

PATIENT PRESENTATION

Chief Complaint

"I just don't feel like myself."

HPI

Robert Wolfe is a 67-year-old man with type 2 DM, HTN, and stage 5 CKD. He receives hemodialysis (HD) three times a week with a high-flux hemodialysis membrane. His wife brought him into the ED this morning after she noticed increased confusion and lethargy, worsening over the past 2–3 days. According to his wife, the patient missed his HD session 2 days ago. She reports no other new symptoms except for increased pain in his feet from his neuropathy for which his PCP increased his gabapentin dose last week.

PMH

Type 2 DM × 20 years

HTN × 30 years

Stage 5 CKD; he has been receiving HD for the past 5 years with a high-flux cellulose triacetate membrane; he has no residual renal function

Diabetic neuropathy

Anemia of CKD

Dyslipidemia

CKD-MBD

Uremic pruritus

FH

Father with CAD; mother with DM and HTN

SH

Retired from a glass factory; on disability; past history of smoking, quit 3 years ago; (–) ETOH for the past 7 years

Meds

Calcium acetate 667 mg, 2 PO TID

Gabapentin 300 mg PO BID (increased last week from 300 mg PO at bedtime)

Nephrocaps 1 PO daily

Sodium ferric gluconate 62.5 mg IV once weekly with HD

Metoprolol tartrate 25 mg PO BID

Amlodipine 10 mg PO daily

Lipitor 10 mg PO daily

Glipizide XL 10 mg PO daily

Sitagliptin 25 mg PO daily

Epogen 6000 IU IV three times a week with HD

Calcijex 2 mcg IV three times a week with HD

Ensure® Original Vanilla nutritional supplement, one bottle (237 mL) PO TID

All

NKDA

ROS

Increased fatigue and confusion; reduced sensation in lower extremities

PE

Gen

Patient somnolent; does not appear to be in distress

VS

BP 168/82 mm Hg, P 82 bpm, RR 14, T 36.8°C; dry body Wt 150 lb (68 kg), Ht 5'11" (180 cm)

Skin

Normal; intact, warm, and dry

HEENT

NC/AT, PERRLA, EOMI, funduscopy WNL, oropharyngeal mucosa clear

Neck/Lymph Nodes

Positive JVD; no lymphadenopathy, normal thyroid

Lungs

Crackles in bases bilaterally

CV

Normal S₁ and S₂; no S₃ or S₄

Abd

Soft, NT/ND, no HSM

Genit/Rect

Normal prostate, guaiac-negative stool

MS/Ext

1+ bilateral pedal edema, no clubbing or cyanosis

Neuro

A&O to person only, CN II–XII intact, normal DTRs bilaterally

■ Labs

Na 140 mEq/L	Hgb 11.2 g/dL	Ca 10.8 mg/dL
K 6.1 mEq/L	Hct 34.5%	Mg 2.4 mg/dL
Cl 99 mEq/L	Plt $182 \times 10^3/\text{mm}^3$	Phos 7.9 mg/dL
CO ₂ 18 mEq/L	WBC $7.8 \times 10^3/\text{mm}^3$	AST 12 IU/L
BUN 82 mg/dL		ALT 8 IU/L
SCr 8.2 mg/dL		T. bili 0.9 mg/dL
Glu 118 mg/dL		Alk phos 34 IU/L
		Alb 2.2 g/dL
		Intact PTH 602 pg/mL (last month 595 pg/mL)

■ ABG

pH 7.35, PaO₂ 94, PaCO₂ 38, HCO₃ 20 on room air

■ Chest X-Ray

No infiltrates or effusions

■ ECG

Sinus rhythm

■ Assessment

A 67-year-old man with type 2 DM, CKD on HD admitted to the hospital with altered mental status and electrolyte abnormalities.

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of electrolyte abnormalities?

- 1.b. What additional information is needed to fully assess this patient's electrolyte abnormalities?

Assess the Information

- 2.a. Assess the severity of electrolyte abnormalities based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating electrolyte abnormalities?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's electrolyte abnormalities and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

One month later, the following laboratory values and erythropoietin dosages were available from the outpatient hemodialysis unit. (See Table 58-1.) The patient also complains of tingling and numbness in his feet.

■ FOLLOW-UP QUESTIONS

1. Formulate a treatment plan for the patient's anemia of CKD.
2. What alternative regimens could be considered for this patient's painful diabetic neuropathy (include drug[s], dose, route of administration, and frequency)?

■ SELF-STUDY ASSIGNMENT

1. Determine the need for and timing of screening for complications associated with CKD, such as anemia of CKD and CKD-MBD.

TABLE 58-1 Laboratory Values and Erythropoietin Dosages

Time	Hgb (g/dL)	Ferritin (ng/mL)	Transferrin Saturation (%)	Erythropoietin Dosage
1 month ago	11.2	—	—	6000 IU IV three times per week
Current	9.2	210	25	6000 IU IV three times per week

2. Develop a protocol for switching patients from intravenous to subcutaneous erythropoietin administration in the hemodialysis setting.

CLINICAL PEARL

Uremic pruritus is a common and frustrating symptom in patients with CKD, with a poorly understood and complex pathophysiology. Patients who are inadequately dialyzed have secondary hyperparathyroidism, anemia, elevated calcium $\times$ phosphorus product, or elevated serum magnesium and aluminum, and are more likely to suffer from pruritus. While the only definitive treatment for uremic pruritus is kidney transplantation, supportive treatment includes increasing dialysis efficiency, using biocompatible hemodialysis membranes, using emollients with high water content, and applying treatment of known risk factors.

REFERENCES

1. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease-mineral and bone disorder (CKD-MBD). *Kidney Int Suppl* 2017;7:1–59.
2. Kasai S, Sato K, Murata Y, Kinoshita Y. Randomized crossover study of the efficacy and safety of sevelamer hydrochloride and lanthanum carbonate in Japanese patients undergoing hemodialysis. *Ther Apher Dial* 2012;16:341–349.
3. Floege J, Covic AC, Ketteler M, et al. Long-term effects of the iron-based phosphate binder, sucroferric oxyhydroxide, in dialysis patients. *Nephrol Dial Transplant* 2015;30:1037–1046.
4. Block GA, Bushinsky DA, Cheng S, et al. Effect of etelcalcetide vs cinacalcet on serum parathyroid hormone in patients receiving hemodialysis with secondary hyperparathyroidism: A randomized clinical trial. *JAMA* 2017;317:156–164.
5. Kidney Disease: Improving Global Outcomes (KDIGO) Anemia Work Group. KDIGO clinical practice guideline for anemia in chronic kidney disease. *Kidney Int Suppl* 2012;2:279–335.
6. Pop-busui R, Boulton AJ, Feldman EL, et al. Diabetic neuropathy: a position statement by the American Diabetes Association. *Diabetes Care* 2017;40:136–154.

59

HYPERCALCEMIA OF MALIGNANCY

Up, Up, and Away Level II

Laura L. Jung, BS Pharm, PharmD

Lisa M. Holle, PharmD, BCOP, FHOA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of hypercalcemia.
- Evaluate laboratory data and clinical symptoms for assessment and monitoring of hypercalcemia, hypercalcemia treatment, and complications of hypercalcemia.

- Recommend a pharmacotherapeutic plan for the initial treatment of cancer-related hypercalcemia.
- Recognize and develop management strategies for toxicities associated with treatment options for hypercalcemia.

PATIENT PRESENTATION

Chief Complaint

“I can’t stop throwing up.”

HPI

Mary Krupp is a 62-year-old woman who presented to her family practitioner today with a 2-day history of nausea and vomiting. She states that her stomach has not felt normal for the past 3–4 days and is painful. Her daughter states that for the past several days she has complained of constipation, nausea, and extreme thirst, but because she has been vomiting, it has been hard to keep her mother drinking enough liquids. She also reports that her mother stopped taking the sustained-release morphine that was started last week because she thought these were side effects of the morphine. The daughter states that her mom’s last bowel movement was 3 days ago despite administration of a stool softener daily. The daughter also reports her mother has gone “downhill” over the past month and spends 80% of her day in bed and the remainder in the recliner.

PMH

Stage IV non–small cell lung cancer diagnosed 1.5 years ago. At time of diagnosis, a CT scan revealed a 3-cm mass in the hilum of the right lung, extensive mediastinal lymphadenopathy, and a moderate right pleural effusion with pleural studding. A transbronchial biopsy identified the mass as adenocarcinoma, epidermal growth factor (EGFR), anaplastic lymphoma kinase (ALK), ROS1, BRAF V600E mutations, negative, and PD-L1 expression positive (30%). Cytology of the pleural effusion also revealed adenocarcinoma. She was treated with the following regimens: (1) carboplatin/paclitaxel $\times$ 4 cycles; (2) pemetrexed maintenance $\times$ 6 cycles; (3) nivolumab $\times$ 8 cycles; and (4) docetaxel monotherapy $\times$ 3 cycles. The last CT scan performed yesterday revealed a new tumor 3.5 $\times$ 4.2 mm in the left lower lobe and liver metastases.

COPD $\times$ 4 years

Dyslipidemia

FH

Mother died of NSCLC at age 80 years; father died of MI at 64 years; one sister died of breast cancer at 69 years; one sister and three brothers alive.

SH

Tobacco: 2 ppd $\times$ 30 years; chronic alcohol use $\times$ 30 years EtOH (three to four drinks per day). Worked as an office assistant $\times$ 25 years. Lives at home with boyfriend of 16 years; has four grown daughters, ages 47, 44, 39, and 34 years. Had her first child at age 15.

Medications

Morphine sulfate sustained-release 30 mg PO Q 12 H (started 1 week ago)

Morphine sulfate oral solution 5 mg PO Q 2 H PRN pain (estimated use two times in the 24 hours before she stopped taking sustained-released)

Docusate sodium 200 mg PO at bedtime PRN

Simvastatin 20 mg PO daily

■ All

Cephalosporins, penicillin

■ ROS

No fever or chills. Daughter has noted that the patient is more tired than usual and is extremely thirsty, which she believes has affected her appetite over the past week. She denies polyuria, chest pain, unusual shortness of breath, dyspnea, or cough. Ms Krupp states her pain is 8/10 throughout the day.

■ Physical Examination

Gen

Thin Caucasian woman in obvious discomfort

VS

BP 95/70 mm Hg, P 105 bpm, RR 16, T 38°C; Wt 110 lb (50 kg), Ht 5'1" (152.5 cm)

Skin

Slightly warm to touch, fair skin turgor (mild tenting noted)

HEENT

PERRLA, EOMI, fundi benign; nonerythematous TMs; oropharynx clear; mucous membranes dry

Neck/LN

Neck supple, slight axillary lymphadenopathy

Lungs

Decreased breath sounds; bilateral wheezes

Breasts

Breasts nontender. No palpable masses or nipple discharge.

CV

RRR, S₁, S₂ normal; ECG shows shortened ST and QT intervals

Abd

Firm, distended, tender; decreased bowel sounds; stool palpable on left side

Genit/Rect

Normal female genitalia; stool heme (–)

MS/Ext

Bilateral lower extremity weakness graded at 4/5; otherwise normal

Neuro

A&O × 3; sensory and motor intact; strength 5/5 upper, 4/5 lower; CN II–XII intact; Babinski (–)

■ Labs

Na 142 mEq/L	AST 63 IU/L	Ca 14.0 mg/dL	WBC $6.8 \times 10^3/\text{mm}^3$
K 3.5 mEq/L	ALT 35 IU/L	Mg 1.5 mEq/L	Hgb 12.7 g/dL
Cl 109 mEq/L	Alk phos 200 IU/L	Phos 3.5 mEq/L	Hct 40%
CO ₂ 22 mEq/L	T. prot 5.1 g/dL	Alb 2.2 g/dL	Plt $174 \times 10^3/\text{mm}^3$
BUN 40 mg/dL	T. bili 1.6 mg/dL	LDH 160 IU/L	
SCr 1.4 mg/dL	D. bili 0.7 mg/dL		
Glu 100 mg/dL			

■ Chest X-Ray

Osteolytic lesions on the right and left clavicles, masses in right and left lower lobes consistent with NSCLC

■ Assessment/Plan

A 62-year-old woman with metastatic NSCLC s/p three different treatment regimens. Poor performance status. Presenting with first episode of possible tumor-induced hypercalcemia with associated complications and uncontrolled pain.

Admit to inpatient oncology service for further management of hypercalcemia, related complications, and pain control.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of hypercalcemia of malignancy?
- 1.b. What additional information is needed to fully assess this patient's hypercalcemia of malignancy?

Assess the Information

- 2.a. Assess the severity of hypercalcemia of malignancy based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What are the possible etiologies of hypercalcemia in this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating hypercalcemia of malignancy?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's hypercalcemia of malignancy and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of goals of therapy.

■ CLINICAL COURSE

Ms Krupp's serum calcium level decreased to 8.8 mg/dL by day 3 with the treatment you recommended. She was discharged from the hospital on day 5 with improvement in her mental status. However,

she returned to the hospital on day 10 with a serum calcium level of 15.2 mg/dL. She is very somnolent and lethargic.

FOLLOW-UP QUESTIONS

1. What pharmacologic and nonpharmacologic options might be considered at this time and why?
2. How would you monitor the therapy you recommended for efficacy and adverse effects?

SELF-STUDY ASSIGNMENTS

1. What nonmalignant disease states can induce hypercalcemia?
2. What treatment(s) can decrease the risk of developing hypercalcemia in patients receiving calcitriol for anticancer therapy?

CLINICAL PEARL

When evaluating a patient for hypercalcemia, corrected calcium must be used to account for the patient's albumin level.

REFERENCES

1. Wagner J, Arora S. Oncologic metabolic emergencies. *Hematol Oncol Clin N Am* 2017;31:941–957.
2. Mirrakhimov AE. Hypercalcemia of malignancy: an update on pathogenesis and management. *N Am J Med Sci* 2015;7:483–493.
3. Shane E, Berenson JR. Treatment of hypercalcemia. In: Mulder JE, ed. *UpToDate*. <https://www.uptodate.com/contents/treatment-of-hypercalcemia>. Accessed October 25, 2018.
4. Goldner W. Cancer-related hypercalcemia. *J Oncol Pract* 2016;12:426–432.
5. Bentata Y, El Maghraoui H, Benabdelhak M, et al. Management of hypercalcaemic crisis in adults: current role of renal replacement therapy. *Am J Emerg Med* 2018;36:1053–1056.
6. Sternlicht H, Glezerman IG. Hypercalcemia of malignancy and new treatment options. *Ther Clin Risk Manag* 2015;11:1779–1788.
7. Zometa [Package Insert]. Novartis Pharmaceuticals Corporation, East Hanover, NJ, 2014.
8. Sensipar [Package Insert]. Amgen Inc, Thousand Oaks, CA. 2011.
9. Non-Small Cell Lung Cancer NCCN Clinical Practice Guidelines in Oncology. V.1.2019. 2016 National Comprehensive Cancer Network, Inc. Available at: NCCN.org. Accessed November 6, 2019.
10. Asonitis N, Kassi E, Kokkinos M, et al. Hypercalcemia of malignancy treated with cinacalcet. *Endocrinol Diabetes Metab* 2017;17:p117-0118.

60

HYPOKALEMIA AND HYPOMAGNESEMIA

Holiday Lytes Level III

Denise M. Kolanczyk, PharmD, BCPS-AQ Cardiology

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Analyze a patient case history and identify potential causes of electrolyte disorders.

- Select the appropriate route of administration and dose of electrolyte replacement therapy specific for a patient.
- Develop a monitoring plan for efficacy and toxicity in patients receiving electrolyte replacement therapy.
- Outline a patient education plan for a patient receiving electrolyte replacement supplements.

PATIENT PRESENTATION

Chief Complaint

"I'm short of breath."

HPI

Dorothy Snow is a 45-year-old woman with a history of nonischemic cardiomyopathy who presents to the ED with a 3-day history of shortness of breath with mild to moderate exertion. She reports three-pillow orthopnea $\times$ 2 days and cough during sleep. Denies chest pain; occasional palpitations. She has some stomach discomfort that she notices after taking her potassium supplement. She reports a 10-lb weight gain in the past week and an increase in her lower extremity edema.

Two months ago, Mrs Snow was hospitalized briefly with atypical chest pain and had persistent hypokalemia for which her metolazone 5 mg daily was discontinued. Approximately 1 month ago, shortly after Thanksgiving, she subsequently developed significant fluid retention and her PCP restarted metolazone 5 mg PO MWF. About 2 weeks ago, she had an ED visit and her potassium was 7.2 mEq/L (hemolyzed sample). The potassium level was repeated with a result of 5.5 mEq/L. At that time, her potassium supplement dose was reduced from 80 mEq PO QID to 80 mEq PO BID.

PMH (Per Patient Report and Medical Records)

Nonischemic cardiomyopathy—echo LVEF 25% (11 months ago)
ICD placement 2 months ago

HTN

Asthma

Sleep apnea

Type 2 DM with peripheral neuropathy

Obesity

Chronic sinusitis

Anxiety disorder

Hypothyroidism

FH

Both parents are deceased.

SH

Lives with husband. No alcohol use. Former smoker—quit 8 years ago. No illicit drugs.

Meds

Candesartan 32 mg PO daily

Omeprazole 20 mg PO daily

Carvedilol 25 mg PO BID

Digoxin 0.25 mg PO daily

Spironolactone 25 mg PO daily

Furosemide 80 mg PO BID

Citalopram 20 mg PO daily

Atorvastatin 20 mg PO daily

Metformin 1000 mg PO BID

Pregabalin 50 mg PO BID

Metolazone 5 mg PO MWF
 Loratadine 10 mg PO daily
 Tiotropium one capsule (18 mcg) inhaled once daily
 Fluticasone/salmeterol 500/50 one puff BID
 Mometasone one spray each nostril daily
 Magnesium oxide 400 mg PO TID
 Potassium chloride 80 mEq PO BID
 Levothyroxine 75 mcg PO daily
 Lorazepam 0.5 mg PO TID

■ ALL

NKDA

■ ROS

Patient reports becoming short of breath for the past 3 days while walking up one flight of stairs or if she walks too quickly on a flat surface. Previously she could walk two flights of stairs before becoming short of breath. She uses three pillows at night to sleep but does not report PND symptoms. She reports increased swelling in her lower extremities, abdominal fullness, and early satiety. Additionally, she reports mild nausea when taking her potassium supplement. States that she has not changed her diet but did visit her sister and family on Christmas Day about one week ago and ate foods that are not part of her normal diet (eg, ham, canned vegetables, jarred gravy, chips, and dip). Denies ever having an ICD discharge.

■ Physical Examination

Gen

Appears older than her stated age; obese; mild dyspnea at rest

VS

P 106 bpm, RR 20, BP 115/70 mm Hg, T 35.8°C; Wt 192 lb [87.3 kg; baseline weight 184 lb (83.6 kg)], Ht 5'5" (165 cm), O₂ sat 88% room air

Skin

Skin warm, dry

HEENT

PERRLA; conjunctivae clear; moist mucous membranes; tongue midline

Neck/Lymph Nodes

Supple; JVP estimated at 14 cm; no carotid bruit; no lymphadenopathy; (+) thyroid nodules

Lungs

Bibasilar rales R > L; occasional wheezes

CV

Tachycardic; normal S₁, S₂; +S₃; -S₄; 2/6 holosystolic murmur best heard at second left intercostal space

Abd

Obese; good bowel sounds; no bruits; no hepatosplenomegaly, (+) hepatjugular reflux; no evidence of ascites

Genit/Rect

Deferred

Ext

No cyanosis; 3+ pitting edema to knees bilaterally; 2+ pulses bilaterally in upper and lower extremities

Back

No CVA tenderness

Neuro

Alert and oriented × 3; no focal deficits; mild sensory deficit in feet bilaterally; CN II–XII grossly intact

■ Labs

Na 130 mEq/L	Hgb 10.4 g/dL	Ca 8.3 mg/dL	Alb 3.0 g/dL
K 2.8 mEq/L	Hct 29.3%	Mg 1.3 mEq/L	PT 14 seconds
Cl 93 mEq/L	WBC 4.5 × 10 ³ /mm ³	Phos 3.1 mEq/L	INR 1.2
CO ₂ 30 mEq/L	Plt 165 × 10 ³ /mm ³	AST 100 IU/L	aPTT 21 seconds
BUN 17 mg/dL		ALT 110 IU/L	CK 30 IU/L
SCr 1.0 mg/dL	BNP 1533 pg/mL	Troponin I <0.01 ng/mL	
Glu 143 mg/dL	A1C 7.8%		

■ Chest X-Ray

Bilateral pulmonary edema; moderate R pleural effusion; small L pleural effusion; (+) cardiomegaly

■ 12-Lead ECG

Sinus tachycardia; LBBB; no evidence of acute ischemia

■ Assessment

Admit to inpatient telemetry unit.

1. Acute exacerbation of chronic heart failure
2. NYHA class III symptoms, ACC stage C
3. Volume overload
4. Electrolyte abnormalities
5. Hyperglycemia

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of electrolyte abnormalities?
- 1.b. What additional information is needed to fully assess this patient's electrolyte abnormalities?

Assess the Information

- 2.a. Assess the severity of the patient's electrolyte abnormalities based on the subjective and objective information available. Classify this patient's hyponatremia.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful in this patient?

- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the patient's hypervolemia, hypokalemia, and hypomagnesemia?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's electrolyte abnormalities and other drug-related problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The medical team implemented the pharmacotherapy plan you recommended. Today is day 4 of hospitalization, and her clinical status is improved. She states she can walk farther without becoming short of breath and only needs one pillow to sleep. Additionally, she describes less swelling in her legs. On physical exam, her HR is 73, BP is 108/57 mm Hg, and O₂ saturation is 96% on room air. Her lungs are clear, and she has 1+ edema in her legs. Pertinent laboratory results indicate serum potassium 3.8 mEq/L, SCr 1.2 mg/dL, Mg 1.8 mg/dL, CO₂ 26 mEq/L, and Glu 129 mg/dL. Her JVP is 8 cm, and she has no hepa-tojugular reflex. She is scheduled for discharge today.

FOLLOW-UP QUESTIONS

1. What changes should be made to the patient's medication regimen at hospital discharge to prevent future electrolyte imbalances?
2. What changes should be made for outpatient management of the patient's heart failure and hyperglycemia?
3. What vaccinations should this patient receive?

SELF-STUDY ASSIGNMENT

1. Describe how a patient's acid-base status can affect serum electrolyte concentrations.

CLINICAL PEARL

Hypokalemia and hypomagnesemia often coexist. In patients refractory to potassium replacement, magnesium concentrations should be evaluated, and any magnesium deficit must be corrected before potassium can be appropriately replaced.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Denise Sokos, PharmD, BCPS.

REFERENCES

1. Kraft MD, Btaiche IF, Sacks GS, Kudsk KA. Treatment of electrolyte disorders in adult patients in the intensive care unit. *Am J Health-Syst Pharm* 2005;62:1663–1682.
2. Ayuk J, Gittos NJL. How should hypomagnesaemia be investigated and treated? *Clin Endo* 2011;75:743–746.
3. Mount DB. Fluid and electrolyte disturbances. In: Jameson J, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J. eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York, NY: McGraw-Hill; <http://accesspharmacy.mhmedical.com/mwu.idm.oclc.org/content.aspx?bookid=2129&sectioned=192013179>. Accessed March 12, 2019.
4. Cohn JN, Kowey PR, Whelton PK, Prisant M. New guidelines for potassium replacement in clinical practice. A contemporary review by the National Council on Potassium in Clinical Practice. *Arch Intern Med* 2000;160:2429–2436.
5. Huang CL, Kuo E. Mechanism of hypokalemia in magnesium deficiency. *J Am Soc Nephrol* 2007;18:2649–2652.
6. Yancy CW, Jessup M, Bozkurt B, et al. 2013 ACCF/AHA guideline for the management of heart failure: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;128:e240–e327.
7. American Diabetes Association. 15. Diabetes care in the hospital: Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019; 42(Suppl 1):S173–S181.
8. Yancy CW, Januzzi JL Jr, Allen LA, et al. 2017 ACC expert consensus decision pathway for optimization of heart failure treatment: answers to 10 pivotal issues about heart failure with reduced ejection fraction: a report of the American College of Cardiology Task Force on Clinical Expert Consensus Decision Pathways. *J Am Coll* 2018; 71:201–230.
9. American Diabetes Association. 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes-2019. *Diabetes Care* 2019;42(Suppl 1):S103–S123.
10. Kim DK, Hunter P. Advisory Committee on Immunization Practices Recommended Immunization Schedule for Adults Aged 19 Years or Older—United States, 2019. *MMWR Morb Mortal Wkly Rep* 2019;68:115–118. <http://dx.doi.org/10.15585/mmwr.mm6805a>. Accessed March 12, 2019.

61

METABOLIC ACIDOSIS

Oh, My Aching Acidosis Level II

Justin M. Schmidt, PharmD, BCPS

Megan E. Sands, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine the clinical and laboratory manifestations of metabolic acidosis.
- Differentiate the most probable cause(s) of metabolic acidosis.
- Develop a patient-specific pharmacotherapeutic plan for treating chronic metabolic acidosis.
- Provide medication education for patients with chronic metabolic acidosis.

PATIENT PRESENTATION

■ Chief Complaint

"I just feel so weak all the time."

■ HPI

Sue Rider is a 67-year-old woman with progressive CKD due to HTN, who was referred to the nephrology clinic for management of fatigue. Her fatigue started a couple years ago but has progressed to the point that it interferes with her gardening and evening walks. She reports occasional muscle cramps (one every 1–2 months) that last a few seconds to minutes and are not associated with exertion. She reports frequent nonadherence to her furosemide when she feels well.

■ PMH

HTN

CKD stage 4

Seasonal allergic rhinitis

Menopause at 53 years old

■ FH

History of CAD in her mother's family (mother had a heart attack at age 60). No known family history of CKD.

■ SH

The patient is a retired schoolteacher who lives with her husband of 38 years and has three grown children. She denies alcohol use. There is no history of tobacco habituation or recreational drug use.

■ Meds

Amlodipine 5 mg PO daily

Aspirin 81 mg PO daily

Furosemide 40 mg PO daily, taken intermittently for lower extremity edema (reports that she has not taken any for the past few months)

Metoprolol succinate 25 mg PO daily

■ ALL

NKDA

■ ROS

Fatigue worsening over the past two years. Denies weight changes or changes in appetite. Denies fever/chills. No palpitations, shortness of breath or chest pain. Denies abdominal pain, nausea/vomiting, and melena. Admits to weakness and reports occasional myalgia but is not experiencing currently.

■ PE

Gen

Pleasant African-American woman in NAD

VS

BP 155/85 mm Hg, P 78 bpm, RR 16, T 37.2°C; Wt 165 lb (75 kg), Ht 5'4" (162.5 cm)

Skin

Normal color and texture. Intact, warm and dry.

HEENT

No hemorrhages or exudates on fundoscopic examination

Neck/Lymph Nodes

JVP 3 cm; carotid pulses 2+ bilaterally; no thyromegaly or lymphadenopathy

Chest

CTA and P

CV

Unable to palpate PMI; regular rate and rhythm; normal S₁ and S₂; no murmurs

Abd

Obese, soft, nontender; normoactive bowel sounds; no organomegaly

MS/Ext

Minimal sternal tenderness

Neuro

No focal cranial nerve deficits; strength 4/5 in all extremities.

■ Labs

Na 138 mEq/L	Hgb 12.2 g/dL	AST 13 IU/L
K 4.4 mEq/L	Hct 37 %	ALT 7 IU/L
Cl 112 mEq/L	Plt 225 × 10 ³ /mm ³	Alk phos 113 IU/L
CO ₂ 19 mEq/L	WBC 7.6 × 10 ³ /mm ³	GGT 14 IU/L
BUN 37 mg/dL	Ca 7.4 mg/dL	T. bili 0.4 mg/dL
SCr 2.9 mg/dL	Mg 2.2 mg/dL	Alb 3.6 g/dL
Glu 89 mg/dL	Phos 4.3 mg/dL	
eGFR (CKD-EPI)		
19 mL/min		

■ ABG on RA

pH 7.32; PaCO₂ 36 mm Hg; PaO₂ 106 mm Hg; bicarbonate 19 mEq/L

■ Urinalysis macro (dipstick) panel

Color yellow; appearance clear; SG 1.025; pH 5.2; blood (–); glucose (–); ketones (–); leukocyte esterase (–); nitrite (–); bilirubin (–); urobilinogen 0.5 mg/dL; protein > 300 mg/day

■ KUB

No nephrocalcinosis or nephrolithiasis

■ Assessment

1. Acidosis
2. CKD
3. Hypertension
4. Hypocalcemia

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of metabolic acidosis?
- 1.b. What additional information is needed to fully assess this patient's metabolic acidosis and related complications?

Assess the Information

- 2.a. Assess the severity of metabolic acidosis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What factors may have contributed to the development of metabolic acidosis?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating metabolic acidosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's metabolic acidosis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Differentiate between the bone disease of metabolic acidosis versus that associated with chronic kidney disease and osteoporosis.
2. Discuss the types of metabolic acidoses that may be present in patients with CKD and how they may be differentiated.

CLINICAL PEARL

While the chronic metabolic acidosis associated with CKD is usually not progressive, there is increasing evidence that correction of acidosis is related to decreased progression of CKD. Appropriate oral alkali therapy or dietary intervention may result in improved nutritional status, renal function, and quality of life for patients with CKD.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Brian Hodges, PharmD, BCPS, BCNSP.

REFERENCES

1. de Brito-Ashurst I, Varagunam M, Raftery MJ, Yaqoob MM. Bicarbonate supplementation slows progression of CKD and improves nutritional status. *J Am Soc Nephrol* 2009;20:2075–2084.
2. Kraut JA, Madias NE. Metabolic acidosis of CKD: an update. *Am J Kidney Dis* 2016;67:307–317.
3. Kidney Disease: Improving Global Outcomes (KDIGO) CKD Work Group. KDIGO 2012 clinical practice guideline for the evaluation and management of chronic kidney disease. *Kidney Int Suppl* 2013;3:1–150.
4. KDIGO Blood Pressure Work Group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int Suppl* 2012;5:337–414.
5. Goraya N, Simoni J, Jo C, Wesson DE. A comparison of treating metabolic acidosis in CKD stage 4 hypertensive kidney disease with fruits and vegetables or sodium bicarbonate. *Clin J Am Soc Nephrol* 2013;8:371–381.
6. Foque D, Pelletier S, Mafra D, Chauveau P. Nutrition and chronic kidney disease. *Kidney Int Suppl* 2011;80:348–357.
7. Raphael KL. Approach to the treatment of chronic metabolic acidosis in CKD. *Am J Kidney Dis* 2016;67:696–702.
8. McNeil JJ, Wolfe R, Woods RL, et al. Effect of aspirin on cardiovascular events and bleeding in the healthy elderly. *N Eng J Med* 2018;379:1509–1518.
9. Kidney Disease: Improving Global Outcomes (KDIGO) CKD-MBD Work Group. KDIGO 2017 clinical practice guideline update for the diagnosis, evaluation, prevention, and treatment of chronic kidney disease—mineral and bone disorder (CKD-MBD). *Kidney Int Suppl* 2017;7:1–60.

62

METABOLIC ALKALOSIS

Keep Me in the Loop Level I

Natalie I. Rine, PharmD, BCPS, BCCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs and symptoms of metabolic alkalosis.
- Interpret laboratory findings that are consistent with metabolic alkalosis.
- Describe patient-specific factors that contribute to the development of metabolic disorders.
- Recommend appropriate first-line treatment regimens and alternatives for metabolic alkalosis.
- Formulate a patient-specific pharmacotherapeutic plan for the treatment and monitoring of metabolic alkalosis.

PATIENT PRESENTATION

Chief Complaint

“I feel very weak and tired.”

HPI

Brandon O'Byrne is a 60-year-old man who presents to the ED with complaints of generalized weakness, fatigue, myalgias, and polyuria over the past 2 days. He states that recently he has felt bloated and has been taking extra doses of his "water pill." He also mentioned that he may have eaten something bad because he has thrown up three times since dinner last night.

PMH

Hypertension (diagnosed 15 years ago)
HFrEF (diagnosed 3 years ago)
Diabetes, type 2—diet controlled
Dyslipidemia (diagnosed 3 years ago)

FH

Mother is alive with a history of HTN and dyslipidemia. Father is alive with HTN. Younger sister is alive with dyslipidemia.

SH

Patient reports he does not consume alcohol except a glass of wine "at special occasions." He denies tobacco or illicit drug use. Lives at home with his wife of 35 years and their two dogs.

Meds

Lisinopril 20 mg PO once daily
Carvedilol 25 mg PO BID
Furosemide 40 mg PO once daily
Atorvastatin 40 mg PO once daily
Last dose of all medications was this morning 3 hours before arriving at the ED

All

Codeine—patient reports "I get short of breath"

ROS

Denies unusual weight gain or loss. He denies fever, chills, or night sweats, but reports dizziness that has occurred off and on over the past week in addition to generalized fatigue and weakness. No reported chest pain, palpitations, shortness of breath, or cough. He denies diarrhea, constipation, or change in bowel habits. He reports a recent increase in thirst and urination, but no change in urine color. He reports myalgias and perioral numbness that began recently with the fatigue and weakness.

Physical Examination**Gen**

The patient is ill-appearing and feels warm to the touch.

VS

BP 93/62 mm Hg, HR 101, RR 20, T 37.9°C; Wt 176 lb (80 kg), Ht 5'7" (170 cm); O₂ sat 96% on RA

Skin

Soft, intact, warm, dry

HEENT

EOMI; PERLLA; no sinus tenderness; dry mucous membranes; no oral lesions; no nasal congestion present

Neck/Lymph Nodes

No JVD or bruits; no lymphadenopathy or thyromegaly

Chest

CTA bilaterally

CV

RRR; normal S₁, S₂; no S₃ or S₄; no murmurs, rubs, gallops

Abd

Soft, NTND; (+) bowel sounds

GU/Rect

WNL

MS/Ext

No CCE; feet are dry and wrinkled

Neuro

A&O × 3. CN II–XII intact.

Labs

Na 132 mEq/L	Hgb 12.4 g/dL	Alb 3.8 g/dL
K 2.9 mEq/L	Hct 36.7%	AST 19 IU/L
Cl 85 mEq/L	Plt 324 × 10 ³ /mm ³	ALT 16 IU/L
CO ₂ 39 mEq/L	WBC 12.1 × 10 ³ /mm ³	Alk phos 62 IU/L
BUN 24 mg/dL	Mg 1.7 mEq/L	T. bili 0.4 mg/dL
SCr 1.1 mg/dL	Phos 3.6 mg/dL	PT 11.3 s
Glu 118 mg/dL	Ca 7.6 mg/dL	INR 0.96

ABG

pH 7.54, PaCO₂ 46 mm Hg, PaO₂ 86 mm Hg, HCO₃ 38.3 mEq/L on RA

UA

Urine sodium 18 mEq/L; potassium 33 mEq/L; chloride 9 mEq/L, urine pH 6.1

Chest X-Ray

Mild pulmonary congestion, otherwise unremarkable

ECG

Sinus tachycardia, rate 101, no acute ST-segment or T-wave changes

Assessment

Admit patient for hypotension, flulike symptoms, electrolyte and acid–base abnormalities.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of metabolic alkalosis?
- What additional information is needed to fully assess this patient's metabolic alkalosis?

Assess the Information

- Assess the severity of metabolic alkalosis based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

- 2.c. What are some possible nondrug therapy causes of this patient's metabolic alkalosis?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating metabolic alkalosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's metabolic alkalosis and other drug-related problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient was started on IV fluids, and labs were reassessed a few hours later. The patient is observed to have 1+ pitting edema in the lower extremities. Laboratory values are as follows:

Na 140 mEq/L	BUN 14 mg/dL	ABG
K 3.8 mEq/L	SCr 0.8 mg/dL	pH 7.46
Cl 103 mEq/L	Mg 2.1 mEq/L	PaCO ₂ 39 mm Hg
CO ₂ 30 mEq/L		PaO ₂ 92 mm Hg
		HCO ₃ 31 mEq/L

FOLLOW-UP QUESTION

1. Based on the new findings, what modifications in therapy are warranted, if any?

SELF-STUDY ASSIGNMENTS

1. Prepare a paper on the three phases (initiation, maintenance, and compensation) of the pathogenesis of metabolic alkalosis. Describe the mechanisms behind each phase and the treatments, if appropriate.
2. Describe how assessment of urine electrolytes is useful in the diagnosis and treatment of metabolic alkalosis.
3. Research what medications, dietary supplements, and medical procedures could contribute to metabolic alkalosis.

CLINICAL PEARL

Although most cases of metabolic alkalosis are asymptomatic, the disorder can lead to serious complications from electrolyte abnormalities (eg, tetany, arrhythmias, mental status changes). In addition to assessing arterial blood gas and laboratory tests, it is important to obtain a thorough patient history to identify underlying cause of metabolic alkalosis and treat it appropriately.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Jennifer Confer, PharmD, BCPS, BCCCP.

REFERENCES

1. Soifer JT, Kim HT. Approach to metabolic alkalosis. *Emerg Med Clin N Am* 2014;32:453–463.
2. Shah N, Shaw C, Forni LG. Metabolic alkalosis in the intensive care unit. *Neth J Crit Care* 2008;12(3):113–119.
3. Gennari FJ, Weise WJ. Acid-base disturbances in gastrointestinal disease. *Clin J Am Soc Nephrol* 2008;3:1861–1868.
4. Dellinger RP, Levy MM, Rhodes A, et al. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock: 2012. *Crit Care Med* 2013;41:580–637.
5. Seifter JL. Integration of acid-base and electrolyte disorders. *N Engl J Med* 2014;371:1821–1831.
6. Moviat M, Pickkers P, van der Hoeven PHJ, et al. Acetazolamide-mediated decrease in strong ion difference accounts for the correction of metabolic alkalosis in critically ill patients. *Crit Care* 2006;10:R14. doi: 10.1186/cc3970.
7. Oh YK. Acid-base disorders in ICU patients. *Electrolyte Blood Press* 2010;8:66–71.

This page intentionally left blank

SECTION 6

NEUROLOGIC DISORDERS

63

ALZHEIMER DISEASE

Oh Right! I Keep Forgetting Level II

Amie Taggart Blaszczyk, PharmD, BCPS, BCGP, FASCP

Rebecca J. Mahan, PharmD, BCGP, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Assess cognitive deficits and noncognitive/behavioral symptoms of Alzheimer disease (AD).
- Evaluate the drug therapy regimens for medications that could interfere with the AD process and future drug therapy recommendations.
- Design a nonpharmacologic plan for a patient with AD based on target symptoms.
- Recommend appropriate pharmacotherapy to manage the cognitive and behavioral symptoms of AD.
- Determine appropriate education and counseling to provide to patients and care partners about AD, the possible benefits and adverse effects of pharmacotherapy for the disorder, and the importance of adherence to therapy.

PATIENT PRESENTATION

■ Chief Complaint

"I'm not sure why we are here. Ann said I have to move and I don't want to because there are people stealing from my house and I have to catch them before they take it all. My kids are just worriers."

■ HPI

Jane Dale is a 74-year-old Caucasian woman who presents to the geriatric care clinic for a routine visit accompanied by her daughter Ann. Jane was diagnosed with AD 3 years ago. Her initial symptoms included forgetting times and dates easily, misplacing and losing items, repeating questions and current events, the inability to answer questions, and increasing difficulty with managing finances. She was initially treated with oral rivastigmine that was eventually discontinued due to intolerable side effects although it worked well to slow her decline. Treatment with donepezil 10 mg at bedtime has been well tolerated for the past 2 years, and Jane has been participating more actively in family and social functions.

Behavioral problems have been infrequent since diagnosis and have not required treatment. Since her last clinic visit, Jane began using an over-the-counter patch for her urinary incontinence.

Jane lives on her own; her daughter and son share the duties of visiting her twice a day. They have been able to maintain a regular routine with her mother's daily activities, nutrition, and financial responsibilities, using lists and notes to help Jane orient herself. Ann sets up a medication box weekly for Jane but has recently noticed quite a few pills left in the container at the end of the week. When Ann asks her mother about them, Jane has thrown the medication bottles at her and tells her "You take them!" Ann is moving in 1 month to live closer to her own daughter to help with grandchildren and has asked her younger unmarried brother, Sam, to help take care of their mother. Sam has agreed to be his mother's caregiver. He lives and works across town and is not sure if he wants to move his mother into his home. There has been discussion about placing Jane in an assisted living or long-term care facility. Jane displays lack of interest, apathy, and tearfulness lately, especially when Ann and Sam are talking about her care. Ann asks about Jane's current Alzheimer's medication and her recent increase in agitation and mood. During the appointment, Jane turns to Ann and asks "Why are you talking about me?" Ann reminds her that the appointment is for her Alzheimer's. Jane responds "Oh, right! I keep forgetting."

■ PMH

Osteoarthritis in hands and hip × 6 years

Hypertension × 15 years

AD diagnosed × 3 years

Urinary incontinence × 6 months

■ FH

Noncontributory, both parents deceased; two children, both of whom live nearby

■ SH

Lives at home; has been widowed for 10 years (husband died of cancer); negative for tobacco use; occasional alcohol use socially, none for ~5 years

■ Meds

Donepezil 10 mg PO at bedtime

Vitamin E 400 IU PO once daily

Lisinopril 10 mg PO once daily

Aspirin 81 mg PO once daily

Oxybutynin 3.9 mg/24-hr patch applied topically twice weekly (× 2 months)

Protein shakes PRN for weight loss

Acetaminophen 325 mg one to two tablets PO every 6 hours PRN for pain (uses once daily at bedtime)

■ All

NKDA

■ **ROS**

Reports occasional bladder incontinence and knee pain; no c/o heartburn, chest pain, or shortness of breath

■ **Physical Examination****Gen**

Well developed woman who appears her stated age

VS

BP 144/82 mm Hg, P 63 bpm, RR 18, T 37°C; Wt 165 lb (74.8 kg), Ht 5'6"

Skin

Intact, normal color, no suspicious moles or spots, normal skin turgor

HEENT

WNL, TMs intact

Neck/Lymph Nodes

Neck supple without thyromegaly or lymphadenopathy

Lungs/Thorax

Clear, normal breath sounds

Breasts

No masses or tenderness

CV

RRR, no murmurs or bruits

Abd

Soft, NT/ND

Genit/Rect

Deferred

MS/Ext

No CCE, Heberden's nodes on both hands, decreased ROM (L) hip

Neuro

Motor, sensory, CNs, cerebellar, and gait normal. MoCA score 16/30, compared to a score of 19/30 last year. Disoriented to season, month, date, and day of week. Appropriate language and visuospatial skills but impaired attention and very poor short-term memory. Unable to remember any of four words after 3 minutes. Able to follow commands. Displayed apathy, tearfulness, and frustration during assessment.

■ **Labs (Fasting)**

Na 139 mEq/L	Hgb 13.5 g/dL	T. bili 0.9 mg/dL	Vit B ₁₂ 430 pg/mL
K 3.7 mEq/L	Hct 39.0%	D. bili 0.3 mg/dL	TSH 2.5 mIU/L
Cl 108 mEq/L	AST 25 IU/L	T. prot 7.5 g/dL	Free T ₄ 0.9 ng/dL
CO ₂ 25.5 mEq/L	ALT 24 IU/L	Alb 4.5 g/dL	Uric acid 6.8 mg/dL
BUN 16 mg/dL	Alk phos 81 IU/L	Ca 9.7 mg/dL	
SCr 1.4 mg/dL	GGT 22 IU/L	Phos 4.5 mg/dL	
Glu 102 mg/dL	LDH 85 IU/L		

■ **Urinalysis**

Specific gravity 1.010, color dark yellow, appearance clear, glucose (+), bilirubin (-), ketones (-), pH 7.4, protein (-), blood (-), nitrite (+), WBC/hpf 25–50, RBC/hpf 0, leukocyte esterase 2+, bacteria 1+

■ **CT Scan (Head, 4 years ago)**

Mild to moderate generalized cerebral atrophy

■ **Assessment**

1. Behavioral and psychiatric symptoms of dementia (BPSD), uncontrolled, treated
2. Urinary incontinence/drug-disease interaction, uncontrolled, treated
3. Possible UTI, uncontrolled, untreated
4. Possible depression, uncontrolled, untreated
5. Progression of AD, controlled, treated
6. Osteoarthritic pain

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of the cognitive and noncognitive problems of AD?
- 1.b. What additional information is needed to fully assess this patient's AD?

Assess the Information

- 2.a. Assess the severity of AD based on the subjective and objective information available.
- 2.b. Create and prioritize a list of the patient's drug therapy problems. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, safety, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for AD might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's AD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's AD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient/care partner to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome or to detect or prevent adverse effects?

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Ann has moved to be closer to her daughter, and Sam accompanies her to her next appointment. He mentions Jane's agitation and apathy improved with your recommended drug therapy plan. She remains tearful at times and is now not sleeping well at night. She continues to be fearful of someone coming into her house and insists that some of her things are missing. During the appointment, she gets tearful mentioning "I don't know where my little girl is."

FOLLOW-UP QUESTIONS

1. What further evaluation should be done to address the patient's continued tearfulness and sleep problems?
2. Discuss the use of antipsychotic medications for the treatment of BPSD. Include a discussion of the pros and cons of treatment.
3. What is the impact of vitamin B₁₂ and thyroid function on the presentation and progression of dementia symptoms?
4. Determine the clinical utility of combination therapy with a cholinesterase inhibitor and memantine. What improvements in clinical condition may be expected? Is the potential benefit worth the risk?

SELF-STUDY ASSIGNMENTS

1. Compare and contrast the Global Deterioration Scale and the FAST criteria for determining the staging of AD.
2. Discuss the management of chronic medical conditions and primary prevention strategies in a patient with progressing dementia. What are the pros and cons of treatment relative to the patient's quality of life; cost, side effects, and complexity of the drug regimen; and ethical considerations?
3. Discuss the utility of clinical amyloid imaging in the diagnosis of Alzheimer dementia, focusing on the FDA-approved amyloid imaging agents.
4. Investigate the evidence, safety data, and potential issues for valproic acid and the combination product dextromethorphan/quinidine, which are commonly used alternatives to antipsychotics in treating the BPSD.

CLINICAL PEARL

Individuals starting a cholinesterase inhibitor for their dementia should have their pulse monitored closely, as these medications have the potential to decrease heart rate up to 10 bpm. Studies have linked cholinesterase inhibitors to inappropriate pacemaker placement and falls. This is especially important if the patient is on a concomitant medication that can also reduce heart rate (eg, β -blockers).

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Carol A. Ott, PharmD.

REFERENCES

1. Krishnan K, Rossetti H, Hynan LS, et al. Changes in Montreal Cognitive Assessment scores over time. *Assessment* 2017;24(6):772–777.
2. Reus VI, Fochtmann LJ, Eyler AE, et al. The American Psychiatric Association practice guideline on the use of antipsychotics to treat agitation or psychosis in patients with dementia. *Am J Psychiatry* 2016;173(5):543–546.
3. Cummings JL, Isaacson RS, Schmitt FA, Velting DM. A practical algorithm for managing Alzheimer's disease: what, when, and why? *Ann Clin Transl Neurol* 2015;2(3):307–323.
4. Holmes HM, Sachs GA, Shega JW, et al. Integrating palliative medicine into the care of persons with advanced dementia: identifying appropriate medication use. *J Am Geriatr Soc* 2008;56:1306–1311.
5. Rabins PV, Blacker D, Rovner BW, et al. American Psychiatric Association practice guideline for the treatment of patients with Alzheimer's disease and other dementias, 2nd ed. *Am J Psychiatry* 2007;164(Suppl 12):5–56.
6. Campbell N, Boustani M, Limbil T, et al. The cognitive impact of anticholinergics: a clinical review. *Clin Interv Aging* 2009;4:225–233.
7. Dysken MW, Sano M, Asthana S, et al. Effect of vitamin E and memantine on functional decline in Alzheimer disease: The TEAM-AD VA cooperative randomized trial. *JAMA* 2014;311(1):33–44.
8. Ehret MJ, Chamberlin KW. Current practices in the treatment of Alzheimer disease: where is the evidence after the phase III trials? *Clin Ther* 2015;37:1604–1616.
9. Sadowsky CH, Galvin JE. Guidelines for the management of cognitive and behavioral problems in dementia. *J Am Board Fam Med* 2012; 25:350–366.

64

MULTIPLE SCLEROSIS

White Dots and Black Holes Level II

Sarah N. Fischer, PharmD

Jacquelyn L. Bainbridge, BS Pharm, PharmD, FCCP, MSCS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the signs and symptoms of multiple sclerosis (MS) that often mimic those of other neurologic diseases.
- Design a pharmacotherapeutic regimen for treating an acute exacerbation of MS.
- Identify patients for whom disease-modifying therapy (DMT) would be appropriate and recommend the most appropriate alternative for an individual patient.
- Implement a pharmacotherapeutic plan for a patient with worsening MS.
- Educate patients and healthcare practitioners on the proper dosing, self-administration (if appropriate), adverse effects, and storage of various medications used for MS.

PATIENT PRESENTATION

Chief Complaint

"My legs are numb and weak, and I'm having trouble walking and urinating."

HPI

Loretta Mansfield is a 26-year-old woman who was in excellent health until 4 days ago when she developed numbness and tingling in her left foot. Over the course of the next 4 days, the numbness extended higher up her leg to her lower abdomen, stopping at the umbilicus, and then going down the right leg. She also developed weakness in both of her legs, is having trouble walking, and is bothered by urinary urgency.

PMH

Frequent migraine headaches since adolescence that are now well controlled with acetaminophen, aspirin, and caffeine (Excedrin) and oral sumatriptan
Mild recurrent bouts of depression that have not been treated pharmacologically
Obesity most of her life

FH

English descent. She was born in Arizona and moved to Ohio at the age of 12. She has no siblings, and both parents are alive and well. There is no family history of neurologic disease.

SH

Married; employed as an accountant; smoked one pack per day for 8 years; use of alcohol is limited to an occasional glass of wine or beer on weekends.

Meds

Acetaminophen, aspirin, and caffeine (Excedrin) two tablets PO PRN headache
Sumatriptan 50 mg PO PRN migraine, at the onset of pain

Allergies

NKDA

ROS

Unremarkable except that she reports feeling run down and tired most of the day. No previous history of visual disturbance (eg, pain, blurred, double vision), sensory, motor, bowel, bladder, or gait disturbance

Physical Examination**Gen**

The patient is a Caucasian woman who appears to be slightly anxious but is otherwise in NAD.

VS

BP 120/72 mm Hg, P 88 bpm and regular, RR 20, T 36.6°C; Wt 86.4 kg, Ht 5'2", BMI 34.7 kg/m²

Skin

Normal turgor; no obvious lesions, tumors, or moles

HEENT

NC/AT, TMs clear

Neck/Lymph Nodes

Supple, without lymphadenopathy or thyromegaly

CV

RRR; S₁, S₂ normal; no MRG

Lungs

Clear to A&P

Abd

NTND

Genit/Rect

Deferred

MS/Ext

Normal ROM; pulses 2+ throughout

Neuro

CNs II–XII are intact with the exception of abnormal saccadic movements on horizontal gaze; no signs of optic neuropathy.

Motor: Tone, bulk, and strength are 5/5 in both arms, with good fine motor movements. In the legs, she has 4/5 strength in an upper motor neuron pattern, with normal tone and bulk.

Sensory: Moderately diminished light touch, pain, and temperature in both legs with a cord level at the umbilicus, and decreased vibratory sensation in both great toes. (+) Romberg sign.

Coordination: Finger-to-nose and alternating movements with the hands are normal, as is heel to shin bilaterally.

Gait: Mildly unsteady on tandem walking; timed 25-foot walk was 5.2 seconds.

Reflexes: 2/2 in UE, 3/3 in LE; (+) Babinski bilaterally.

The patient is alert, oriented, and cooperative. No Lhermitte's sign is noted.

Labs

Na 142 mEq/L	Anion gap 16 mEq/L	AST 12 IU/L
K 4.1 mEq/L	Ca 9.4 mg/dL	ALT 40 IU/L
Cl 99 mEq/L	Bilirubin 0.8 mg/dL	GGT 33 IU/L
CO ₂ 23 mEq/L	Protein total 8.1 g/dL	ESR 20 mm/hr
BUN 11 mg/dL	Albumin 4.9 g/dL	TSH 1.0 μ IU/mL
SCr 0.9 mg/dL	Vit. B ₁₂ 510 ng/L	ANA negative
Glu 109 mg/dL	Anti-JC virus antibody	CRP 1.0 mg/dL
25(OH) vitamin D	negative	Lyme serology negative
17 ng/mL		

Lumbar Puncture

CSF analysis shows opening pressure 140 mm H₂O, 10 WBC/ μ L, 97% lymphocytes; protein 30 mg/dL, glucose 65 mg/dL; IgG index 1.7; 12 oligoclonal bands unique to CSF.

MRI Scan

Thoracic spine MRI with and without injection of contrast material reveals a one-segment long enhancing lesion in the posterior thoracic spine at level T10.

Brain MRI shows multiple areas of T2 and FLAIR hyperintense lesions; four were periventricular, one was in the left cerebellum, two were juxtacortical; and none of the areas enhance after injection of contrast material. A total of 12 T2 and FLAIR lesions were seen in the brain; see Fig. 64-1.

Assessment

1. Clinically isolated syndrome (CIS) with high risk of disease progression to clinically definite MS presenting with first acute neurologic exacerbation
2. Mild depression
3. Obesity

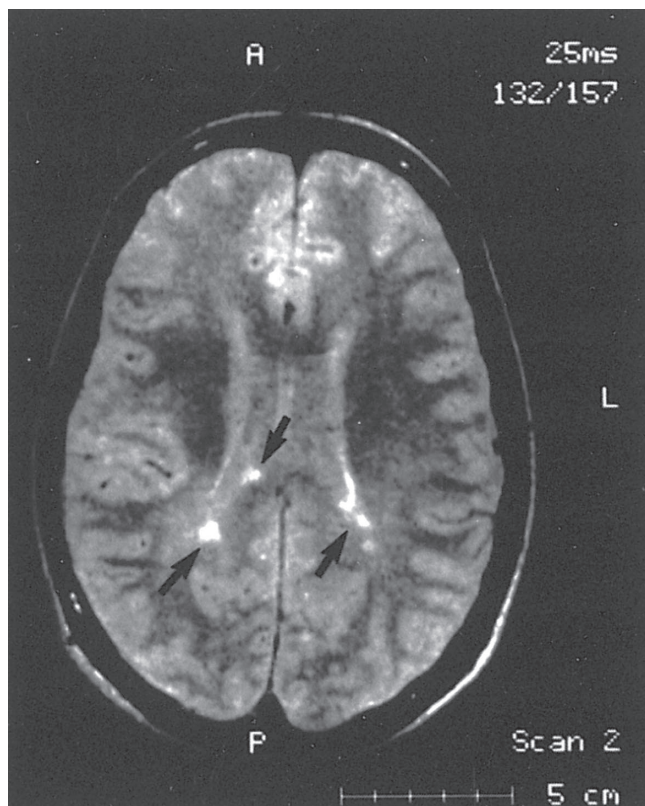


FIGURE 64-1. Brain MRI scan. Arrows highlight typical periventricular white matter lesions seen in multiple sclerosis.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of multiple sclerosis (MS)?
- 1.b. What additional information is needed to fully assess this patient's MS?

Assess the Information

- 2.a. Assess the severity of this patient's MS based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of therapy for this patient?
- 3.b. What nondrug therapies for MS might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic options are available to reduce the risk of recurrent disease activity in this patient?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's MS and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient was treated with the regimen you recommended, with gradual resolution of her symptoms. Six months after the initial presentation, she returns to clinic with complaints of painful loss of vision in her left eye, which evolved over 3 days. On exam, she has a visual acuity of 20/200 in the left eye and 20/20 in the right eye. Visual fields are normal, but she has loss of color sensitivity in the left eye. There is a left relative afferent pupillary defect (Marcus Gunn pupil). There is no disc swelling or atrophy in either eye on fundoscopic examination. The remainder of the physical exam is notable only for a mild Romberg sign and increased reflexes in the lower extremities. Her affect is sad, and she is tearful during the examination. She is concerned that she has now progressed to a diagnosis of clinically definite MS.

- MRI shows four new T2 lesions and 2 Gd enhancing lesion.
- Optical coherence tomography (OCT): OCT was completed because of her complaint of left eye pain and visual loss. OCT was performed on the right and left optic nerves for evaluation of vision loss and eye pain. The signal strength was 9 in the right eye and 6 in the left eye.
 - ✓ Right eye: The average peripapillary retinal nerve fiber layer thickness was 104 μm . There was no retinal nerve fiber layer loss in any quadrant or sector.
 - ✓ Left eye: The average peripapillary retinal nerve fiber layer thickness was 80 μm . There were significant changes in the superior and inferior quadrants consistent with optic neuritis.

FOLLOW-UP QUESTION

1. Would you consider the new information gathered at the follow-up visit to be evidence of significant disease progression that would prompt you to change your treatment strategy? If so, what therapies would be appropriate for the patient?

SELF-STUDY ASSIGNMENTS

1. Obtain relevant information and formulate an opinion on the role of plasmapheresis in the treatment of MS.
2. Review the clinical studies evaluating comparative trials of DMTs for MS. How does glatiramer acetate compare with interferon β -1b and interferon β -1a in terms of both efficacy and toxicity?

3. Outline a plan for providing patient education on the dosing, administration, monitoring, and storage of interferon β -1b, interferon β -1a, and glatiramer acetate.
4. Identify recent clinical trials assessing the efficacy and toxicity of natalizumab, rituximab, alemtuzumab, fingolimod, teriflunomide, and dimethyl fumarate for MS. Considering the data available, define the potential role(s) of these agents for patients with MS.

CLINICAL PEARL

Many patients do not feel better with interferon therapy and may experience unpleasant adverse effects. It is important to reinforce that the first-generation or self-injected DMTs (interferon β -1a, interferon β -1b, glatiramer acetate) do not reduce disease symptoms but will reduce attacks and progression of disability over time. Adequate counseling about the potential benefits and expected side effects is essential to ensuring adherence to the therapy.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Jacquelyn L. Bainbridge, PharmD; Augusto Miravalle, MD; and Felecia Hart, PharmD.

REFERENCES

1. Tullman MJ. A review of current and emerging therapeutic strategies in multiple sclerosis. *Am J Manage Care* 2013;19(2 Suppl):S21–S27.
2. Kaufman DI, Trobe JD, Eggenberger ER, Whitaker JN. Practice parameter: the role of corticosteroids in the management of acute monosymptomatic optic neuritis. Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2000;54:2039–2044.
3. Martinelli V, Rocca MA, Annovazzi P, et al. A short-term randomized MRI study of high-dose oral vs intravenous methylprednisolone in MS. *Neurology* 2009;73(22):1842–1848.
4. Goodin DS, Frohman EM, Garmany GP, et al. Disease modifying therapies in multiple sclerosis. Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology and the MS Council for Clinical Practice Guidelines. *Neurology* 2002;58:169–178.
5. Corboy JR, Goodin DS, Frohman EM. Disease-modifying therapies for multiple sclerosis. *Curr Treat Options Neurol* 2003;5:35–54.
6. Ali R, Nicholas RS, Muraro PA. Drugs in development for relapsing multiple sclerosis. *Drugs* 2013;73(7):625–650.
7. O'Conner P, Wolinsky JS, Confavreux C, et al. Randomized trial of oral teriflunomide for relapsing multiple sclerosis. *N Engl J Med* 2011;365:1293–1303.
8. Gold R, Kappos L, Arnold DL, et al. Placebo-controlled phase 3 study of oral BG-12 for relapsing multiple sclerosis. *N Engl J Med* 2012;367:1098–1107.
9. Schapiro RT. Managing symptoms of multiple sclerosis. *Neurol Clin* 2005;23(1):177–187, vii.
10. Mikol DD, Barkhof F, Chang P, et al. Comparison of subcutaneous interferon beta-1a with glatiramer acetate in patients with relapsing multiple sclerosis (the REBif vs Glatiramer Acetate in Relapsing MS Disease [REGARD] study): a multicentre, randomised, parallel, open-label trial. *Lancet Neurol* 2008;7(10):903–914.

65

COMPLEX PARTIAL SEIZURES

An Overdue Visit to a Neurology Clinic Level I

James W. McAuley, RPh, PhD, FAPhA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify necessary data to collect for patients with complex partial seizures.
- Define potential drug-related problems for antiepileptic drugs.
- List desired therapeutic outcomes for patients with complex partial seizures.
- Based on patient characteristics, choose appropriate pharmacotherapy for treatment of partial seizures and develop a suitable care plan.
- Identify key issues for a woman of childbearing potential taking antiepileptic drugs.

PATIENT PRESENTATION

■ Chief Complaint

"My family doctor told me I should see a neurologist about my seizures."

■ HPI

Peggy Livingston is a 36-year-old woman referred to the neurology clinic by her PCP for evaluation of her seizures and antiepileptic drug therapy. She is enduring quite a heavy seizure burden. Her last seizure was 10 days ago, which resulted in her falling down her basement stairs. Her seizures started at a very early age, and she said no one has been able to identify why she started having seizures. She remembers having them in grade school and being confused a lot throughout her schooling. She was briefly tried on phenobarbital initially but has been on phenytoin most of her life. She has poor seizure control with no extended seizure-free periods. She has not seen a neurologist for years, if ever. She has not had any neuroimaging studies and provides no previous EEG results.

On speaking with the patient and her husband of 2.5 years, most of her events involve "blackouts" and losing track of time. Occasionally, she has "grand mal" seizures. She is more likely to have a seizure if she gets overly tired or stressed. She has no history of severe head injury with loss of consciousness or other significant risk factors for seizures. She states that at some time in her past, she "felt really bad, almost drunk" on higher doses of phenytoin. She states that she is very adherent, although she has run out of medication more than once. Because she is having seizures, she does not drive and therefore must rely on others for transportation. This lack of independence is a major concern for Peggy.

Data gathered from reviewing her seizure calendar over the past 2 months (Fig. 65-1) suggest that she is experiencing approximately eight "small" seizures per month (complex partial seizures

Patient Instructions: Please record the number and type of seizures you have each day.

S = Small, B = Big, ? = Possible seizure

Patient: P. Livingston

March

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
		1	2	3	4	5 S
6	7	8	9	10	11 S	12 S
13	14 S → B	15	16	17	18	19
20	21	22 S, S	23 S	24	25	26
27	28	29	30 S	31		

April

Sunday	Monday	Tuesday	Wednesday	Thursday	Friday	Saturday
					1	2
3	4 S	5	6 S	7 S	8	9
10	11	12	13	14	15 S	16 S, S → B
17	18	19 S	20	21	22	23
24	25 ? S	26	27	28	29 S	30

FIGURE 65-1. Seizure calendar (S = small seizure, B = big seizure, ? = possible seizure).

with no secondary generalization) and one “big” seizure per month (a secondarily generalized tonic-clonic seizure). Her interview details and her overall score on her responses to the QOLIE-31 questions show a significant impact of the seizures on her quality of life. Her scores on the energy/fatigue, seizure worry, and social function domains are especially low in comparison with a cohort of other patients with epilepsy. The score on her NDDI-E was 11, indicating that she had some mood issues, but she was not depressed. On asking if there is anything else the patient would like to discuss, Peggy and her husband state that they desire to start a family in the near future.

■ PMH

Noncontributory, except as described previously

■ FH

Both parents deceased; one younger brother in good health; no seizure disorder, cancer, or CV disease

■ SH

Married; works in a local restaurant; denies tobacco and alcohol use; finished high school with a “C” average; no children

■ Meds

Phenytoin (Dilantin) 300 mg PO at bedtime

■ All

NKDA

■ ROS

Tired a lot but no problems with balance or double vision

■ Physical Examination

Gen

Pleasant woman showing some anxiety during this initial visit

VS

BP 132/87 mm Hg, P 72 bpm, RR 18, T 36.2°C; Wt 66.8 kg, Ht 5'1"

Skin

Normal color, hydration, and temperature

HEENT

Mild hirsutism; (+) gingival hyperplasia

Neck/Lymph Nodes

(–) JVD; (–) lymphadenopathy

Lungs/Thorax

CTA

Breasts

Deferred

CV

Normal S₁ and S₂, RRR, NSR, normal peripheral pulses

Abd

NT/ND, (+) BS, no HSM

Genit/Rect

Deferred

MS/Ext

Significant burn on palm of right hand. This happened within the last week when she had a seizure while frying eggs on the stovetop. Her husband stated that he witnessed her put hand directly in the frying pan during her seizure.

Neuro

CNs II–XII intact; slight lateral gaze nystagmus noted. Motor: 4/5 muscle strength on left side, 5/5 on right side. DTRs: 2+ RUE, 1+ LUE, 0 RLE, 0 LLE. Sensory: normal light touch and pinprick. Station: normal.

■ Labs

Na 137 mEq/L	Hgb 14.5 g/dL	AST 31 IU/L
K 4.1 mEq/L	Hct 41.7%	ALT 22 IU/L
Cl 100 mEq/L	RBC $4.71 \times 10^6/\text{mm}^3$	Alk phos 187 IU/L
CO ₂ 29 mEq/L	MCV 88.6 μm^3	GGT 45 IU/L
BUN 9 mg/dL	MCHC 34.7 g/dL	Ca 7.3 mg/dL
SCr 0.6 mg/dL	Plt $212 \times 10^3/\text{mm}^3$	Alb 3.9 g/dL
Glu 107 mg/dL	WBC $5.4 \times 10^3/\text{mm}^3$	

■ EEG

Abnormal for bitemporal slowing, which is more significant in the left temporal region, as characterized by polymorphic and epileptiform discharges consistent with a history of seizure disorder

■ Assessment

1. Seizure disorder, uncontrolled by phenytoin
2. Potential adverse drug reactions from phenytoin
3. Woman of childbearing potential without folic acid supplementation
4. Possible osteomalacia secondary to long-term phenytoin therapy

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of complex partial seizures?
- 1.b. What additional information is needed to fully assess this patient's complex partial seizures?

Assess the Information

- 2.a. Assess the severity of complex partial seizures based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, cultural, racial, ethical, and psychosocial considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for complex partial seizures might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating complex partial seizures?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's complex

partial seizures and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

A collective decision was made among the healthcare practitioners, the patient, and her husband to add another antiepileptic drug to her current drug regimen and to see her back in 6 weeks. She was given written and verbal information on this new drug and instructed to call or use the patient portal with any questions, problems, or concerns. She and her husband verbalized an understanding. At her next visit, the patient reported that there had been an initial response to the addition of the new antiepileptic drug (ie, fewer seizures), but she still has some “small” seizures and one “big” seizure per month. There are no recent laboratory data. Her neurologic examination is unchanged. She and her husband would like to further discuss their desire to start a family.

FOLLOW-UP QUESTION

1. What is known about long-term effects on cognition and behavior in children exposed to antiepileptic drugs in utero?

SELF-STUDY ASSIGNMENTS

1. Outline a plan for assessing this patient’s adherence with her medication regimen.
2. What risk factors does this patient have for osteoporosis? What interventions should be made?
3. Would switching this patient from brand Dilantin to generic phenytoin be an appropriate alternative? What are the ramifications of making this change?
4. What role can community pharmacists play in the care of patients with epilepsy?

CLINICAL PEARL

Although epilepsy affects men and women equally, there are many women’s health issues, including menstrual cycle influences on seizure activity, drug interactions between contraceptives and antiepileptic drugs, and teratogenicity of antiepileptic drugs.

REFERENCES

1. Taylor RS, Sander JW, Taylor RJ, Baker GA. Predictors of health-related quality of life and costs in adults with epilepsy: a systematic review. *Epilepsia* 2011;52:2168–2180.
2. Gilliam FG, Barry JJ, Hermann BP, Meador KJ, Vahle V, Kanner AM. Rapid detection of major depression in epilepsy: a multicentre study. *Lancet Neurol* 2006;5:399–405.
3. Beghi E. Addressing the burden of epilepsy: many unmet needs. *Pharmacol Res* 2016;107:79–84.
4. England MJ, Liverman CT, Schultz AM, Strawbridge LM. Epilepsy across the spectrum: promoting health and understanding. A summary of the Institute of Medicine report. *Epilepsy Behav* 2012;25:266–276.
5. Voinescu PE, Pennell PB. Delivery of a personalized treatment approach to women with epilepsy. *Semin Neurol* 2017;37:611–623.
6. Meador KJ, Baker GA, Browning N, et al. For the NEAD Study Group. Fetal antiepileptic drug exposure and cognitive outcomes at age 6 years (NEAD study): a prospective observational study. *Lancet Neurol* 2013;12:244–252.
7. Fraser LA, Burneo JG, Fraser JA. Enzyme-inducing antiepileptic drugs and fractures in people with epilepsy: a systematic review. *Epilepsy Res* 2015;116:59–66.
8. Mula M, Kanner AM, Schmitz B, Schachter S. Antiepileptic drugs and suicidality: an expert consensus statement from the Task Force on Therapeutic Strategies of the ILAE Commission on Neuropsychobiology. *Epilepsia* 2013;54:199–203.
9. Long L, Cotterman-Hart S, Shelby J. To reveal or conceal? Adult patient perspectives on SUDEP disclosure. *Epilepsy Behav* 2018;86:79–84.
10. McAuley JW, Miller MA, Klatte E, Shneker BF. Patients with epilepsy’s perception on community pharmacist’s current and potential role in their care. *Epilepsy Behav* 2009;14:141–145.

66

GENERALIZED TONIC-CLONIC SEIZURES

Senior Seizures Level II

Jennifer A. Donaldson, PharmD, BCPPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Define epilepsy.
- Differentiate seizure types based on clinical presentation and description.
- Recommend drugs of choice and alternative therapies for different types of seizures.
- Identify appropriate dosing, the most common adverse effects, and monitoring parameters for anticonvulsants.
- Develop an appropriate pharmaceutical care plan for a patient with epilepsy.

PATIENT PRESENTATION

Chief Complaint

“I had a seizure a few weeks ago and banged up my head.”

HPI

Carter McNeely is a 68-year-old man whose seizures are well controlled with carbamazepine monotherapy. The seizure from 2.5 weeks ago was the first seizure in 20 months. During the seizure, he fell to the floor and sustained a laceration to his occipital region that required staples for closure. The description of his seizures is vague because there have been only six seizures documented since he developed epilepsy 3 years ago. Because Mr McNeely lives alone in an assisted living facility, only half of the documented seizures have been witnessed by another individual who could provide a description. Two seizures were witnessed by other residents who described him as “falling to the ground and starting to shake.” One seizure occurred in the day room when a facility nurse was in the room, and he documented that Mr McNeely fell to the ground, developed rhythmic extensions to both his legs, became incontinent of urine, and was sleepy and disoriented for 2 hours after the episode.

He has only been treated with carbamazepine. This was started by his family practice physician after his second seizure. An EEG was obtained at that time and was unremarkable. Because the seizures are so infrequent, the dose of carbamazepine has never been adjusted.

PMH

Tonic-clonic seizures diagnosed 3 years ago
HTN adequately controlled with lisinopril monotherapy
Dyslipidemia controlled with atorvastatin and low-cholesterol diet
BPH, currently symptom-free on dutasteride

FH

Mother died at age 74 of “natural causes”; had HTN for many years. Father died at age 70 of “natural causes”; did not have any known medical illnesses. All his children and grandchildren are alive and well. One son and one daughter have HTN.

SH

Retired factory worker; resides in an assisted living facility. He is widowed and has six children and nine grandchildren, whom he sees frequently. He denies past or present tobacco and illicit drug use. He reports a history of regular alcohol use but now only drinks one beer that his grandson brings to him every Saturday evening.

Meds

Aspirin 81 mg PO once daily
Atorvastatin 40 mg PO once daily
Carbamazepine XR 200 mg PO twice daily
Dutasteride 0.5 mg PO once daily
Lisinopril 20 mg PO once daily
Multivitamin with minerals one tablet PO once daily

All

NKDA
Adverse drug effect history—none

Physical Examination**Gen**

Exam reveals an elderly Caucasian man who appears his stated age in NAD.

VS

BP 126/78 mm Hg, HR 72, RR 16, temperature not measured; Ht 5'10", Wt 72.5 kg

HEENT

Normocephalic; scalp: healing 3-cm lesion in the occipital region with corresponding mild tenderness and bruising; PERRL

Neck/LN

No thyromegaly, lymphadenopathy, or carotid bruits

Chest/Lungs

Lungs CTA

CV

RRR, no m/r/t

Abd

Soft, nontender; no HSM; (+) BS

MS/Ext

Normal tone; 5/5 strength in all extremities

Neuro

Awake; A&O $\times$ 3; CN II–XII intact, reflexes 2+ and symmetric throughout

Labs

Na 127 mEq/L	Hgb 13.5 g/dL	<i>Fasting Lipid Profile</i>
K 4.7 mEq/L	Hct 41%	T. chol 155 mg/dL
Cl 90 mEq/L	RBC $3.9 \times 10^6/\text{mm}^3$	TG 123 mg/dL
CO ₂ 25 mEq/L	WBC $5.1 \times 10^3/\text{mm}^3$	HDL-C 39 mg/dL
BUN 10 mg/dL	Diff WNL	LDL-C 91 mg/dL
SCr 0.6 mg/dL	MCV 97 μm^3	
Glu 100 mg/dL	Carbamazepine 6 mcg/mL	

EEG

Sleep-deprived EEG unremarkable. Photoc stimulation failed to produce any other changes.

Assessment

1. Epilepsy with generalized tonic-clonic (GTC) seizures
2. Hyponatremia with current serum sodium level of 127 mEq/L
3. Hypertension, controlled with lisinopril 20 mg daily
4. Dyslipidemia currently treated with atorvastatin 40 mg daily
5. Benign prostatic hyperplasia currently treated with dutasteride
6. Osteoporosis with risks for fractures

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of generalized tonic-clonic seizures?
- 1.b. What additional information is needed to fully assess this patient's generalized tonic-clonic seizures?

Assess the Information

- 2.a. Assess the severity of the generalized tonic-clonic seizure based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for generalized tonic-clonic seizures might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat generalized tonic-clonic seizures?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's generalized tonic-clonic seizures and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Antiepileptic medications may interact with a number of other medications used in the elderly patient population. Considering major medical conditions encountered, research potential interactions with classes of medications used to treat those conditions.
2. Perform a literature search to identify articles that have concluded that seizure medications can be withdrawn after a certain seizure-free interval.
3. Write a concise paper outlining the current recommendations for assisting a person who is having a seizure.
4. Assume that a patient taking valproic acid has poorly controlled seizures and a decision is made to add lamotrigine. What precautions, if any, should be taken? How should you initiate lamotrigine therapy?

CLINICAL PEARL

Many important historical figures had epileptic seizures, including Buddha, Socrates, Alexander the Great, Julius Caesar, St. Paul the Apostle, Mohammed, Peter the Great, Handel, Napoleon, Paganini, Kierkegaard, Alfred Nobel, and Dostoyevsky. It may be useful to share some of these names with patients to break the stigma of mental illness associated with epilepsy.

REFERENCES

1. Stefan H. Epilepsy in the elderly: facts and challenges. *Acta Neurol Scand* 2011;124:223–237.
2. Bryson AS, Carney PW. Pharmacotherapy for epilepsy in the elderly. *J Pharm Pract Res* 2015;45:349–356.
3. Bruun E, Kalviainen R, Keranen T. Outcome of initial antiepileptic drug treatment in elderly patients with newly diagnosed epilepsy. *Epilepsy Res* 2016;127:60–65.
4. Johnston A, Smith PEM. Epilepsy and the elderly. *Expert Rev Neurother* 2010;10(12):1899–1910.
5. Leppik IE, Walczak TS, Birnbaum AK. Challenges of epilepsy in elderly people. *Lancet* 2012;380:1128–1130.
6. Ulate-Campos A, Coughlin F, Gainza-Lein M, et al. Automated seizure detection systems and their effectiveness for each type of seizure. *Seizure* 2016;40:88–101.
7. Glauser T, Ben-Menachem E, Bourgeois B, et al. Updated ILAE evidence review of antiepileptic drug efficacy and effectiveness as initial monotherapy for epileptic seizures and syndromes. *Epilepsia* 2013;54:551–563.
8. Berghuis B, van der Palen J, de Haan GJ, et al. Carbamazepine and oxcarbazepine-induced hyponatremia in people with epilepsy. *Epilepsia* 2017;58(7):1227–1233.

67

STATUS EPILEPTICUS

Tempest in a Tom Collins Level I

Jennifer A. Donaldson, PharmD, BCPPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Define status epilepticus and its precipitating causes.
- Identify measures that should be taken in the ED for a patient in status epilepticus.
- Recommend appropriate drug treatment for status epilepticus.
- Recommend an optimal care plan for a patient with status epilepticus.

PATIENT PRESENTATION

Chief Complaint

As given by a friend of the patient: “I walked back into the room after getting breakfast and Josh was having a seizure. He kept shaking for a couple of minutes so I went to get the RA and he said we needed to get him to the ED.”

HPI

Joshua Banch is a 20-year-old man brought to the university hospital emergency department by his college roommate and dormitory resident assistant (RA). The roommate reported that he and Joshua went

out partying the night before because all the fraternities were throwing rush parties. The roommate left Joshua partying at the Delta Tau Chi fraternity house at about 2:00 AM. He heard Joshua return to the room at approximately 4:30 AM and he was clearly intoxicated.

■ PMH

Medical records revealed that the patient developed generalized tonic-clonic seizures in childhood. Phenobarbital was initiated and controlled the seizures for many years. Withdrawal of phenobarbital was attempted 10 years ago after several years of being seizure free. The drug was restarted when seizures occurred during the attempted taper. Phenobarbital was replaced, due to sedation and lethargy, with carbamazepine. Phenytoin was added 8 years ago because of frequent and prolonged breakthrough seizures. He has had occasional breakthrough seizures since his admission to the university 2 years ago. Breakthrough seizures are typically associated with Joshua's nonadherence with medications or sleep deprivation due to prolonged study sessions. He is routinely followed in the university hospital neurology clinic.

■ FH

Negative for epilepsy; the patient has two siblings, all alive and well. No other information on family history was obtained.

■ SH

Single with no children; no tobacco use; reports drinking up to six beers per week

■ Meds

Carbamazepine 500 mg PO TID
Phenytoin 100 mg PO BID

■ All

NKDA

■ ROS

Unobtainable

■ Physical Examination

Gen

WDWN Caucasian man who is unarousable, continues to have intermittent jerking of his extremities; clothes are wet from urinary incontinence.

VS

BP 150/90 mm Hg, P 150 bpm, RR 25, T 37.5°C; Wt 68.3 kg; Ht 5'7"

Skin

Warm, dry, and pale; nail beds are pale

HEENT

Mucous membranes are dry

Neck/Lymph Nodes

Supple; no thyromegaly or lymphadenopathy

Lungs/Chest

Symmetric, lungs CTA

CV

RRR, no m/r/g

Abd

Soft, no HSM, BS normal in all four quadrants

MS/Ext

Muscle mass normal, full ROM

Neuro

Unarousable; reflexes 3+ bilaterally

■ Labs

Na 136 mEq/L	Hgb 12.8 g/dL	Drug screen: pending
K 4.5 mEq/L	Hct 41%	Carbamazepine: pending
Cl 97 mEq/L	Plt $320 \times 10^3/\text{mm}^3$	Phenytoin: pending
CO ₂ 28 mEq/L	WBC $9.0 \times 10^3/\text{mm}^3$	
BUN 16 mg/dL	Diff WNL	
SCr 1.0 mg/dL		
Glu 60 mg/dL		

■ EEG

Baseline from medical record: Diffuse background slowing; no focal changes or epileptiform activity present; photic stimulation failed to produce other changes.

■ Assessment

1. Status epilepticus
2. Generalized tonic-clonic seizures, uncontrolled
3. Medication nonadherence (suspected) with pending drug levels
4. Alcohol use disorder

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of status epilepticus?
- 1.b. What additional information is needed to fully assess this patient's status epilepticus?

Assess the Information

- 2.a. Assess the severity of the status epilepticus based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for status epilepticus might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat status epilepticus?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's status epilepticus and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. There are several drug interactions with phenytoin and carbamazepine. Describe the effects that these drugs have on each other. What, if anything, should be done to compensate for these drug interactions?
2. There are several sports in which patients with epilepsy should not participate. What are some of these sports, and why should these individuals not participate in them?
3. Antiepileptic medications are available in multiple dosage forms. Prepare a table with what dosage forms may be used via a feeding tube, what dosage forms may help with patient adherence, and what IV to PO, or PO to IV conversions exist for products with an intravenous dosage form.
4. Prepare a two-page paper summarizing the hematologic adverse effects of all the anticonvulsants.

CLINICAL PEARL

EEG studies have demonstrated that benign self-limited tonic-clonic seizures in adults last about 1 minute on average and rarely last more than 2 minutes.

REFERENCES

1. Brophy GM, Bell R, Claassen J, et al. Guidelines for the evaluation and management of status epilepticus. *Neurocrit Care* 2012;17(1):3–23.
2. Sharvon S. The treatment of status epilepticus. *Curr Opin Neurol* 2011;24:165–170.
3. Paschal AM, Rush SE, Sadler T. Factors associated with medication adherence in patients with epilepsy and recommendations for improvement. *Epilepsy Behav* 2014;31:346–350.
4. Leach JP, Mohanraj R, Borland W. Alcohol and drugs in epilepsy: pathophysiology, presentation, possibilities, and prevention. *Epilepsia* 2012;53(Suppl 4):48–57.
5. Glauser T, Shinnar S, Gloss D, et al. Evidence-based guideline: Treatment of convulsive status epilepticus in adults and children: report of the Guideline Committee of the American Epilepsy Society. *Epilepsy Curr* 2016;16(1):48–61.
6. Silbergleit R, Durkalski V, Lowenstein D, et al. Intramuscular versus intravenous therapy for prehospital status epilepticus. *N Engl J Med* 2012;366:591–600.
7. Betjemann JP, Lowenstein DH. Status epilepticus in adults. *Lancet Neurol* 2015;14:615–624.
8. Kalss G, Rohrer A, Leiting M, et al. Intravenous brivaracetam in status epilepticus: a retrospective single-center study. *Epilepsia* 2018;59(Suppl 2):228–233.
9. Coppola G, Piccorossi A, Operto FF, et al. Anticonvulsant drugs for generalized tonic-clonic epilepsy. *Expert Opin Pharmacother* 2017;18(9):925–936.

68

ACUTE MANAGEMENT OF THE TRAUMATIC BRAIN INJURY PATIENT

The Agony of Defeat Level III

Denise H. Rhoney, PharmD, FCCP, FCCM, FNCS

Dennis Parker, Jr., PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Discuss the goals of cerebral resuscitation.
- Interpret parameters beneficial in assessing the severity of the brain injury.
- Describe the impact of prior antithrombotic therapy on traumatic brain injury (TBI) and devise an appropriate treatment plan for patients with TBI while on antithrombotic therapy.
- Discuss the therapeutic management of TBI and increased intracranial pressure associated with acute brain injury.
- Recommend appropriate therapy to prevent medical complications after brain injury.

PATIENT PRESENTATION

Chief Complaint

Not available—the patient was brought to the ED by EMS as a trauma code.

HPI

Oliver Johnson is a 55-year-old man who was brought to the ED after suffering a ski accident while on vacation with his wife. His wife reports that he was unarousable at the scene of the accident.

PMH (As Per Patient's Wife)

Dyslipidemia
NSTEMI (1 year ago)

FH

Unknown

SH

Unknown

ROS

Unobtainable

Meds

Aspirin 325 mg PO daily
Clopidogrel 75 mg PO daily
Simvastatin 40 mg PO daily

■ All

NKDA

■ Physical Examination

Gen

WDWN man who does not speak, open his eyes, or move on verbal stimuli. On painful stimuli, he does not speak or open his eyes but does exhibit flexor posturing.

VS

BP 87/60 mm Hg, P 126 bpm, RR 30, T 38.3°C; Wt 85 kg, Ht 6'0"

Skin

Multiple bruises on the face and extremities bilaterally

HEENT

The patient has multiple soft tissue injuries to the face. The left pupil is 5 mm and nonreactive to direct light, and the right pupil is 2 mm and slowly reactive to light. EOMs are not reactive and not moving. External inspection of ears and nose reveals no acute abnormalities. There is some dried blood in the mouth. The head has a large open scalp laceration on the forehead with surrounding ecchymoses. Neck is in a cervical collar; therefore, movement was not attempted. There are no gross masses in the neck.

Lungs

Rhonchi and crackles present bilaterally with thick secretions

Heart

Sinus tachycardia with S₁ and S₂ present

Abd

Soft with no masses or tenderness but decreased bowel sounds. There is no gross hepatosplenomegaly.

Ext

No nontraumatic edema is noted.

Neuro

There is no response other than flexor posturing to pain. The Glasgow coma scale score is 5.

■ Labs

Na 140 mEq/L	Hgb 13.8 g/dL	Ca 8.4 mg/dL	ABG
K 3.7 mEq/L	Hct 40.9%	Mg 1.8 mg/dL	pH 7.49
Cl 106 mEq/L	Plt 166 ×	Phos 2.4 mEq/L	HCO ₃ 22 mEq/L
CO ₂ 20 mEq/L	10 ³ /mm ³	Alb 3.4 g/dL	PaCO ₂ 33 mm Hg
BUN 15 mg/dL	WBC 26.0 ×		PaO ₂ 66 mm Hg
SCr 1.1 mg/dL	10 ³ /mm ³		O ₂ sat 86% on RA
Glu 285 mg/dL	Diff N/A		Urine drug screen (–)
			Blood alcohol <20 mg/dL

■ Portable Chest X-Ray

Right upper lobe atelectasis. No rib fractures. The ET tube is above the carina.

■ Head CT

There is a left parietal open depressed skull fracture. There is an area of hemorrhagic contusion in the left frontal region. There are multiple left temporal and parietal epidural hematomas with midline shift.

■ Assessment

1. S/P head trauma secondary to ski accident with coma and respiratory distress
2. Skull fracture and temporal and parietal epidural hematomas with midline shift while on clopidogrel plus aspirin
3. Hyperglycemia

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of a traumatic brain injury?
- 1.b. What additional information is needed to fully assess this patient's traumatic brain injury?

Assess the Information

- 2.a. Assess the severity of traumatic brain injury based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for traumatic brain injury might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating traumatic brain injury?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's traumatic brain injury and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

Time	Temp (°C)	HR (bpm)	BP (mm Hg)	ICP (mm Hg)	CPP (mm Hg)	BG (mg/dL)	Fluid A (mL)	Fluid B (mL)	Fluid C (mL)	Nutrition	UOP (mL)	Meds given
0600	37.6	85	120/86	18	79	306	80		12	NPO	60	Insulin aspart 8 units
0700		88	128/88	22	77		80		12		105	
0800		89	119/67	15	69		80		12	NPO	100	
0900		85	125/89	16	70		80	100	12		60	Levetiracetam 1000 mg IV
1000	38.2	86	110/65	20	60	288	80		12	NPO	55	Insulin aspart 6 units APAP 325 mg
1100		92	115/79	22	71		80		12		60	Fentanyl 25 mcg × 2
1200		94	129/55	18	62		80		12	NPO	67	
1300		100	100/68	19	60		80		12		100	
1400	38.1	92	113/70	17	67	270	80		12	NPO	55	Insulin aspart 6 units APAP 325 mg
1500		98	130/85	21	79		80		12		70	
1600		89	129/75	18	75		80		12	NPO	60	
1700		94	119/88	20	76		80		12		60	
1800	37.5	85	115/66	22	75	240	80		12	NPO	60	Aspart 2 units
1900		86	124/50	22	53		80		12		80	
2000		83	144/54	16	68		80		12	NPO	60	
2100		89	140/87	24	81		80	100	12		70	Levetiracetam 1000 mg IV
2200	38.6	86	139/84	24	78	220	80		12	NPO	75	Aspart 2 units APAP 325 mg
2300		90	120/86	20	77		80		12		60	
2400		70	132/75	12	82		80		12	NPO	50	
0100		78	140/70	20	73		80		12		110	
0200	37.5	72	135/68	20	70	190	80		12	NPO	120	
0300		79	149/75	19	81		80		12		80	
0400		75	137/68	28	63		80		12	NPO	110	
0500		77	130/68	27	62		80		12		60	

Fluid A = 3% sodium chloride/acetate; Fluid B = levetiracetam IVPB; Fluid C = midazolam infusion (concentration = 1 mg/mL).

HR, heart rate; BP, blood pressure; ICP, intracranial pressure; CPP, cerebral perfusion pressure; BG, blood glucose; UOP, urine output; IVPB, intravenous piggy bag.

FIGURE 68-1. Neurointensive care unit flowsheet. Day 1 (0–24 hours postadmission).

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

On arrival in the ED, IV access was initiated, and the patient was intubated orally using a rapid sequence intubation technique (fentanyl 200 mcg IV followed by lidocaine 100 mg IV, midazolam 2 mg IV, and rocuronium 5 mg IV). The patient was started on 3% sodium/acetate solution at 75 mL/hr and midazolam infusion at 12 mg/hr. Other medications include levetiracetam 2 g IV load followed by 1 g IV Q 12 H, fentanyl 25 mcg IV Q 1 H PRN, and insulin aspart correction dose protocol as needed hourly. A ventriculostomy was placed for monitoring of ICP with an initial ICP reading of 18 mm Hg. The patient was then transferred to the neurointensive care unit for monitoring.

Over the next 48 hours, pertinent laboratory measurements included serum sodium 158 mEq/L, serum osmolality 290 mOsm/L, urine osmolality 250 mOsm/L, and urine specific gravity 1.010 g/cm³. See ICU flowsheet for other important parameters for the first 24 hours (Fig. 68-1) and second 24 hours (Fig. 68-2) in the ICU.

SELF-STUDY ASSIGNMENTS

1. Review the different types of neurologic monitoring devices that are available and how drug therapy might influence these monitoring parameters.
2. Review paroxysmal autonomic instability or “sympathetic storming” and its treatment options and monitoring parameters.
3. Evaluate the role of serum biomarkers in predicting outcome after traumatic brain injury.
4. Review the guidelines for managing the neurobehavioral sequelae of traumatic brain injury.

CLINICAL PEARL

There are only three standards of care for severe brain injury patients: (1) use of corticosteroids is not recommended for improving outcome or reducing ICP; (2) in the absence of increased ICP, chronic prolonged hyperventilation (PaCO₂ < 25 mm Hg) should be avoided; and (3) prophylactic use of antiepileptic drugs is not recommended for preventing late posttraumatic seizures (>7 days).

Time	Temp (°C)	HR (bpm)	BP (mm Hg)	ICP (mm Hg)	CPP (mm Hg)	BG (mg/ dL)	Fluid A (mL)	Fluid B (mL)	Fluid C (mL)	Nutrition	UOP (mL)	Meds given
0600	37.4	85	121/76	19	72	226	80		12	NPO	70	Insulin aspart 4 units IV
0700		78	125/80	20	75		80		12		150	
0800		80	129/66	25	62		80		12	NPO	100	
0900		82	135/87	26	77		80	100	12		200	Levetiracetam 1000 mg IV
1000	38.2	86	120/60	20	60	188	80		12	NPO	350	Insulin aspart 2 units IV APAP 325 mg
1100		95	110/70	28	55		125		12		300	Fentanyl 25 mcg × 2
1200		98	119/65	28	55		125		12	NPO	150	
1300		97	110/78	29	60		125		12		350	
1400	38.3	90	118/77	35	55	286	125		12	NPO	300	Insulin aspart 8 units IV APAP 325 mg
1500		88	135/80	31	67		125		12		500	
1600		89	129/85	28	72		125		12	NPO	350	
1700		77	120/87	20	78		125		12		200	
1800	38.1	80	135/68	23	67	240	125		12	NPO	250	Aspart 2 units IV APAP 325 mg
1900		76	128/60	24	59		125		12		200	
2000		80	141/70	26	68		125		12	NPO	150	
2100		78	140/86	14	90		125	100	12		250	Levetiracetam 1000 mg IV
2200	37.8	80	129/89	24	78	220	125		12	NPO	300	Aspart 4 units IV
2300		80	130/76	18	84		125		12		300	
2400		76	137/70	25	80		125		12	NPO	250	
0100		78	140/80	17	83		125		12		250	
0200	37.9	78	145/78	22	78	190	125		12	NPO	100	Aspart 2 units IV
0300		88	145/70	28	77		125		12		250	
0400		80	127/78	25	76		125		12	NPO	300	
0500		75	138/69	27	75		125		12		250	

Fluid A = 3% sodium chloride/acetate; Fluid B = levetiracetam IVPB; Fluid C = midazolam infusion (concentration = 1 mg/mL).

HR, heart rate; BP, blood pressure; ICP, intracranial pressure; CPP, cerebral perfusion pressure; BG, blood glucose; UOP, urine output; IVPB, intravenous piggy bag.

FIGURE 68-2. Neurointensive care unit flowsheet. Day 2 (24–48 hours postadmission).

REFERENCES

1. Van den Brand CL, Tolido T, Rambach AH, Hunrik MG, Patka P, Jellema K. Systematic review and meta-analysis: is pre-injury antiplatelet therapy associated with traumatic intracranial hemorrhage? *J Neurotrauma* 2017;34:1–7.
2. Devlin JW, Skrobik Y, Celine G, et al. Clinical practice guidelines for the prevention and management of pain, agitation/sedation, delirium, immobility, an sleep disruption in adult patients in the ICU. *Crit Care Med* 2018; 46:e825–e873.
3. Carney N, Totten AM, O'Reilly C, et al. Guidelines for the management of severe traumatic brain injury, fourth edition. *Neurosurgery* 2017;80:6–15.
4. Le Roux P, Menon DK, Citerio G, et al. Consensus Statement of the International Multidisciplinary Consensus Conference on Multimodality Monitoring in Neurocritical Care. *Neurocrit Care* 2014;21 (Suppl 2):S297–S361.
5. Batchelor JS, Grayson A. A meta-analysis to determine the effect of preinjury antiplatelet agents on mortality in patients with blunt head trauma. *Br J Neurosurg* 2013;27:12–18.
6. Frontera JA, Lewin JJ, Rabinstein AA, et al. Guideline for reversal of antithrombotics in intracranial hemorrhage. *Neurocrit Care* 2016; 24:6–46.
7. Beynon C, Hertle DN, Unterberg AW, Sakowitz OW. Clinical review: traumatic brain injury in patients receiving antiplatelet medication. *Crit Care* 2012;16:228.doi: 10.1186/cc11292.
8. Madden LK, Hill M, May TL, et al. The implementation of targeted temperature management: an evidence-based guideline from the Neurocritical Care Society. *Neurocrit Care* 2017;27:468–487.
9. McClave SA, Taylor BE, Martindale RG, et al. Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient: Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.). *J Parenter Enteral Nutr* 2016;40:159–211.
10. Wakai A, McCabe A, Roberts I, Schierhout G. Mannitol for acute traumatic brain injury. *Cochrane Database Syst Rev* 2013;8: CD001049.

69

PARKINSON DISEASE

Slow and Shaky Level III

Mary L. Wagner, PharmD, MS

Yuchen Wang, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize motor and nonmotor symptoms of Parkinson disease (PD).
- Develop an optimal pharmacotherapeutic plan for a patient with PD progressing through different stages of the disease.
- Recommend alternative therapy for a patient experiencing adverse drug effects, drug–drug interactions, and drug–food interactions.
- Educate patients with PD about the disease, pharmacotherapeutic options, and nonpharmacologic treatments.

PATIENT PRESENTATION

■ Chief Complaint

“My work performance has declined because my tremor makes it difficult to type on the computer, and I am slower with most tasks.”

■ HPI

Lori Tanner is a 63-year-old, right-handed woman who presents to the neurology clinic because of a mild tremor in her right hand that has worsened over the past 6 months. It takes her longer to do things because it takes a little more effort to get movement started, and her muscles feel a little stiff. She also admits to difficulty falling asleep but has no issues staying asleep. The stiffness, slowness, tremor, and sleep problems have affected her job performance as a graphic designer, resulting in her contemplating early retirement. She also complains of constipation, depressed mood, lack of pleasure in her usual activities, and loss of sense of smell for about 2 years. Due to complaints of acid reflux, she is currently receiving treatment for it.

■ PMH

GERD × 1 month

Broken left wrist after fall 1 year ago

■ FH

Mother died at age 89 of complications associated with a hip fracture, osteoporosis, and Alzheimer disease (clinical diagnosis without postmortem confirmation); father died from an ischemic stroke at age 58; two daughters are in good health.

■ SH

(–) Alcohol, (–) tobacco, married for 23 years

■ ROS

No complaints other than those noted in the HPI. She denies any other symptoms of autonomic dysfunction such as problems with

swallowing, urination, drooling, or dizziness. She admits to occasional crying spells and low mood but denies panic attacks, hallucinations, vivid dreams, and paranoia.

■ Meds

Pantoprazole 40 mg PO once daily 30 minutes before meals

Calcium carbonate 600 mg PO every morning and night

■ All

None

■ Physical Examination

Gen

The patient is a Caucasian woman who appears older than stated age.

VS

BP 118/74 mm Hg sitting, 116/70 mm Hg standing, P 70 bpm, RR 13; T 36.8°C; Wt 53 kg, Ht 5'2"

Skin

Small amount of dry yellow scales in her eyebrows

HEENT

Decreased facial expression, decreased eye blinking; PERRLA; EOMI

Neck/Lymph Nodes

Supple, no masses, normal thyroid, no bruits

Lungs/Thorax

Clear, normal breath sounds, CTA

CV

RRR, no murmurs, no bruits

Abd

Soft, nontender, no palpable masses

Genit/Rect

No nodules palpated; no rectal polyps

MS/Ext

Normal peripheral pulses and postural stability; no CCE.

Neuro

- General neurologic exam intact, MoCA 30/30, HAM-D scale 11/66 (depressed mood, sleep problems; indicative of mild depression)
- UPDRS: Total 15
 - ✓ Part 1: Mentation, behavior, and mood score 3/16 (1 for depression; 2 for motivation/initiation).
 - ✓ Part 2: ADL score 5/52 (mild trouble with handwriting, cutting food, tremor, and dressing [putting on nylon stockings and buttoning small buttons]). She has no problems with gait. She has some reduced arm swing on the right when she walks. She has no problems with speech, salivation, swallowing, hygiene, turning in bed, falling, freezing, walking, or sensory effects.

✓ Part 3: Motor exam 7/108 (mild problems with facial expression and overall bradykinesia). She has right-sided rigidity and rest tremor, appearing like classic pill-rolling tremor. She has problems with fine motor coordination on her right side noted by the rapid alternating movements, finger taps, hand movements, and foot tap tests. She has no problems arising from a chair or problems with posture or postural stability.

- Handwriting sample: Somewhat slow and progressively smaller in size indicating signs of micrographia

■ Labs

Na 136 mEq/L	Hgb 13.5 g/dL	AST 20 IU/L
K 4.3 mEq/L	Hct 40.5%	ALT 24 IU/L
Cl 101 mEq/L	RBC 4.42×10^6	Alk phos 80 IU/L
CO ₂ 23 mEq/L	WBC $5.0 \times 10^3/\text{mm}^3$	GGT 18 IU/L
BUN 12 mg/dL	Plt $395 \times 10^3/\text{mm}^3$	Ferritin 100 ng/mL
SCr 0.73 mg/dL	Homocysteine 6 $\mu\text{mol/L}$	TSH 2.0 mIU/L
Glu 83 mg/dL	Vitamin D, 25-hydroxy 18 ng/mL	T ₄ total 7.5 mcg/dL

■ Assessment

1. PD, untreated and uncontrolled, with mild depression
2. Insomnia, untreated and uncontrolled
3. Constipation, untreated and uncontrolled
4. Vitamin D deficiency, untreated
5. GERD

■ Clinical Course

The patient is told that she has PD, and the various treatment options are presented to her. She asks about treatment options that may delay disease progression.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of PD?
- 1.b. What additional information is needed to fully assess this patient's PD?

Assess the Information

- 2.a. Assess the severity of PD based on the subjective and objective information available.
- 2.b. Create and prioritize a list of the patient's drug therapy problems. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, safety, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for PD might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's PD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's PD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

- 3.e. What alternatives would be appropriate for this patient's PD symptoms if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient/care partner to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome or to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE—1 YEAR LATER

After the first visit, Ms Tanner was started on rasagiline after 1 month. With partial response of PD symptoms on rasagiline, pramipexole was also started for management of depression. Over the course of that year, pramipexole was gradually increased to 1.5 mg three times a day. Her slowness, stiffness, and tremor have improved since then. She is better able to perform her job, enjoys the work, and is no longer planning her retirement. Her depression and sleep disturbances also improved. Today, however, the patient is complaining of worsening depression and persistent insomnia in the form of increased sleep onset latency. She reports more frequent crying spells and feelings of hopelessness, as well as lack of motivation for her previous hobbies. Her constipation has improved only marginally with the increased fluids and addition of Metamucil that she takes one tablespoonful twice daily. She continues to take pantoprazole despite her stating that her acid reflux has improved. The patient reports no side effects from the pramipexole. However, her husband complains that her personality has changed because she shops excessively, often buying duplicates of things, which is straining their budget.

- Vitals: BP 116/60 mm Hg sitting; P 70 bpm
- Neurologic exams
 - ✓ UPDRS (patient states she is "on"): Mental = 5 (1 for depression and motivation/initiative but 3 for thought disorder), ADLS = 3, and motor = 6, total 14
 - ✓ HAM-D Scale: 18 (scored high on depressed mood, insomnia, and work and interest categories)
- Labs
 - ✓ Vitamin D, 25-hydroxy: 32 ng/mL
 - ✓ T-score: -1.8
- Medications
 - ✓ Multivitamin one tablet PO daily
 - ✓ Calcium carbonate 600 mg PO every morning and night
 - ✓ Vitamin D 1000 IU PO daily
 - ✓ Metamucil one tablespoonful PO twice daily
 - ✓ Pramipexole 1.5 mg PO three times daily
 - ✓ Rasagiline 1 mg PO daily

■ FOLLOW-UP QUESTIONS

1. What is your assessment of the effectiveness of the PD therapy the patient is now receiving?

2. What potential side effects from the therapy is the patient now experiencing?
3. What adjustments in drug therapy should be recommended for each of the patient's problems?
4. What information should the patient receive about her medical problems and therapy at this visit?
5. What additional tests could be performed to assess comorbid conditions?

CLINICAL COURSE—7 YEARS LATER

Ms Tanner returns to the neurology clinic for a routine follow-up visit. She is now 70 years old and is no longer working. Her constipation has stabilized with her bowel regimen. Her symptoms are now bilateral and include tremor, rigidity, stiffness, and gait problems. She also reports that she is slower and clumsier in almost all activities but especially when driving, handling utensils, dressing, turning in bed, and getting out of a chair. She complains of increased "off periods" between doses of her Sinemet. She takes Sinemet at 7 AM, 12 PM, 5 PM, and 10 PM. These off periods occur 30 minutes before her noon, 12 PM, 5 PM, and 10 PM doses of Sinemet. Furthermore, her 12 noon and 5 PM evening dose has a delayed onset of 30 minutes each, and she has dance-like chorea movements from 8 AM to 9 AM. There are no difficulties with mood or hallucinations. Her depression has been well controlled since starting the antidepressant, and her sleep has improved.

She also experiences occasional dizziness with two falls within the last year, one of which resulted in a fractured ankle. The dizziness episodes occur when she wakes up in the morning and when she gets up too quickly from one position to another. She wants to start an exercise program, but she is afraid of falling during her workouts. About a month prior to the visit, she purchased coenzyme Q10, kava, and cowhage (an herbal supplement that contains natural levodopa), thinking they would be a natural way to help her PD. Patient's constipation is now under control with Metamucil twice a day and docusate once a day.

- Vitals: BP 124/74 mm Hg (sitting), 104/70 (standing); and weight 50 kg
- Neurologic exam
 - ✓ She has a positive glabellar reflex (Myerson's sign)
 - ✓ Hamilton Psychiatric Rating Scale for Depression 3/66
 - ✓ MoCA 29/30
 - ✓ UPDRS scores while "on" are: mood 3, ADL 12, and motor 43
- Medications
 - ✓ Carbidopa 25 mg/levodopa 100 mg PO four times daily (7 AM, 12 PM, 5 PM, and 10 PM)
 - ✓ Rasagiline 1 mg PO once daily
 - ✓ Mirtazapine 30 mg PO at bedtime daily
 - ✓ Multivitamin one tablet PO daily
 - ✓ Calcium carbonate 600 mg PO every morning and night
 - ✓ Vitamin D 1000 IU PO daily
 - ✓ Metamucil one tablespoonful PO twice daily
 - ✓ Coenzyme Q10 100 mg PO once daily
 - ✓ Kava 100 mg PO at bedtime
 - ✓ Cowhage 30 g PO once daily
- Labs
 - ✓ Within normal limits and similar to previous labs: Ferritin 150 ng/mL
 - ✓ DXA scan (6 years ago) T-score: spine -1.8 and left hip -1.5
 - ✓ Patient diary (day prior to visit)—Table 69-1

FOLLOW-UP QUESTIONS

1. List the patient's problems at this visit.
2. List and explain any drugs or foods that could be causing any drug-drug or drug-food interactions.

TABLE 69-1 Patient's Diary of Medications and Symptoms

Time	Medications	Symptoms	Comments
7 AM	Carbidopa/levodopa 25/100	Mild stiffness and slowness	Med onset 30 min; feel dizzy when get out of bed
7:30 AM	Rasagiline 1 mg Cowhage (<i>Mucuna pruriens</i>) 30 g Calcium 600 mg Metamucil 1 tablespoon Coenzyme Q10 100 mg	"On" without chorea	7 AM dose last 4.5 hr Breakfast
8–9 AM		Dance-like movements in extremities (chorea)	Noted this since I started supplements
11:30 AM		"Off"	
Noon	Carbidopa/levodopa 25/100	"Off"	Med onset 30 min, noon dose lasts 4.5 hr
12:30 PM		"On" without chorea	Lunch
4:30 PM		"Off" without chorea	
5 PM	MVI Carbidopa/levodopa 25/100 Docusate 100 mg	"Off"	Dinner, Med onset 60 min; dose lasted 4.5 hr
6 PM		"On" without chorea	
9:30 PM		"Off"	
10 PM	Carbidopa/levodopa 25/100 Calcium 600 mg Vitamin D 1000 IU Kava 100 mg Coenzyme Q10 100 mg Metamucil 1 tablespoon		Med onset 30 min
10:30 PM		"On" without chorea	
10:45 PM–6:45 AM			Sleeps well during the night with occasional awakenings, 5 hr of off time (30% of the day)

- For each of the problems identified, what adjustments in drug therapy do you recommend?
- What information should be provided to the patient to ensure successful therapy, enhance adherence, and minimize adverse effects with medications that have been added since the last visit?

■ SELF-STUDY ASSIGNMENTS

- Review the pharmacology and efficacy reports of investigational drugs for PD.
- Investigate the treatment of other nonmotor symptoms of PD such as autonomic dysfunction, depression, anxiety, and psychosis.
- Investigate the use of deep brain stimulation for the treatment of advanced PD.

CLINICAL PEARL

As PD progresses, the timing of medication needs to coincide with symptoms. Evaluate the onset and duration of each dose and make modifications accordingly. Symptoms may worsen when patients are forced to receive medications at predetermined dosing times such as those used in hospitals and nursing homes. Thus, let the patient's symptoms guide the dosing times.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Mary L. Wagner, PharmD, and Margery H. Mark, MD.

REFERENCES

- Kalia LV, Lang AE. Parkinson's disease. *Lancet* 2015;386:896–912.
- Pedrosa DJ, Timmermann L. Review: management of Parkinson's disease. *Neuropsychiatr Dis Treat* 2013;9:321–340.
- Connolly BS, Lang AE. Pharmacologic treatment of Parkinson disease: a review. *JAMA* 2014;311:1670–1683.
- Zesiewicz TA, Sullivan KL, Arnulf I, et al. Practice parameter: treatment of nonmotor symptoms of Parkinson disease: report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology* 2010;74:924–931.
- Seppi K, Weintraub D, Coelho M, et al. The Movement Disorder Society evidence-based medicine review update: treatment for the non-motor symptoms of Parkinson's disease. *Mov Disord* 2011;26(S3):S42–S80.
- Zigmond MJ, Cameron JL, Hoffer BJ, Smeyne RJ. Neurorestoration by physical exercise: moving forward. *Parkinsonism Relat Disord* 2012;18(Suppl 1):S147–S150.
- Fox SH, Katzschlager R, Lim SY, et al. International Parkinson and movement disorder society evidence-based medicine review: update on treatment for the motor symptoms of Parkinson's Disease. *Mov Disord* 2018;33(8):1248–1266.
- Bega D, Zadikoff C. Complementary and alternative management of Parkinson's disease: an evidence-based review of Eastern influenced practices. *J Mov Disord* 2014;7(2):57–66.
- Camacho PM, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologist and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis—2016. *Endocrine Practice* 2016;22(Suppl 4):1–42.
- Gibbons CH, Schmidt P, Biaggioni I, et al. The recommendations of a consensus panel for the screening, diagnosis, and treatment of neurogenic orthostatic hypotension and associated supine hypertension. *J Neurol* 2017;264(8):1567–1582.

70

CHRONIC PAIN MANAGEMENT

Using Opioid Medication in a Troubled Time Level II

Ernest J. Dole, PharmD, PhC, FASHP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Define the goals for pain management in a patient with chronic nonmalignant pain.
- Apply the principles and tools discussed when prescribing, assessing, monitoring, and dispensing chronic opioid therapy (COT) in complex regional pain syndrome (CRPS).
- Identify possible presence of risk factors for aberrant behavior surrounding COT for CRPS.
- Describe strategies to identify and manage medication-related aberrant behavior (MRAB) and risks associated with COT.
- Recommend pharmacotherapy for CRPS, using current guidelines for prescribing COT.

PATIENT PRESENTATION

■ Chief Complaint

"Everything hurts. My pain is 10/10, it is always at a 10/10! I have tried the medications that everyone has prescribed me, but they never seem to work and I'm still in pain. I've tried PT and it makes my pain worse! I'm told to wear my CPAP mask, that it will help my sleep and help my pain. But every time I wear it, I get claustrophobic and my anxiety increases, so I don't wear it anymore. I have been in pain for 30 years, and every time I ask for a medication that works, like oxycodone, which I know works, I am told to try another medication I have never tried, and to see PT and the psychologist. Well, I'm sick of trying medications that don't work, and I'm sick of being told the pain is in my head! The pain isn't in my head, it's all over my body! I just want a shot or a pill that will take all my pain away!"

■ HPI

Danica Mole is a 56-year-old woman with pain from CRPS, fibromyalgia, and ruptured L4–L5 disc. She states that her pain began when she was assaulted by one of her high school students 25 years ago. There was never a report filed of an assault, and she has been on disability since the time of the assault. She has been a patient in this pain clinic for 5 years during which she has failed multiple medications; every time a new nonopioid medication began to work, she developed adverse reactions to it. Thus, she has been prescribed and using opioid medications to control her pain. While she has never overtly misused her opioid medications, she has been calling and asking for early refills of her opioid medications due to overuse and lost or stolen prescriptions. She bristles at any suggestion that she may be "chemically coping." She states proudly that she used to have an alcohol problem, but "took care of herself" and did not need any "12-step program or

rehab hospital.” She has never embraced physical therapy (PT) and states that her pain is made worse by PT. She is antagonistic to behavioral therapy and has been fired as a patient by two of the clinic’s psychiatrists in 5 years. The clinic’s interventionists have declined to offer her epidural or facet injections because they fear further complaints from her regarding complications from the procedure. She has tried trigger-point injections (TPI) only once, stating that they made her pain worse. She states her pain is electrical, shooting, stinging pain from her neck, shoulders, upper and lower back, legs, and feet bilaterally.

■ PMH

CRPS × 30 years
Fibromyalgia × 25 years
Degenerative disc disease × 25 years
Obstructive sleep apnea (OSA) × 20 years
HTN × 10 years
Hyperlipidemia × 10 years
Remote history of substance use disorder, alcohol, “clean” for 6 years
Probable depression

■ FH

Noncontributory

■ SH

The patient is a retired high school teacher. She retired after she was assaulted by one of her students and placed on medical disability over 30 years ago. She has been married for 30 years. She spends her days caring for their 22-year-old daughter who cannot work due to severe migraine headaches and fibromyalgia. She and her husband are pursuing medical disability for their daughter. She often sleeps until one in the afternoon and then stays up most of the night talking to her daughter. She has one younger sister and one younger brother. She makes multiple plans to volunteer and to take care of her elderly in-laws but is never able to complete these plans.

■ Meds

Oxycodone IR 15 mg PO Q 6 H PRN for pain
Morphine ER 30 mg PO TID for pain
Atorvastatin 10 mg PO HS
Hydrochlorothiazide 25 mg PO Q AM
Diazepam 5 mg PO TID PRN

■ All

APAP: increased pain, stomach upset
Amitriptyline: rash
Duloxetine: stomach upset, “mania”
NSAIDs (all): ulcer
Gabapentin: “could not think”
Pregabalin: weight gain
Venlafaxine: stomach upset, increased depression

■ ROS

Positive for total body pain. She states all her muscles hurt, that she has electrical, shooting, stinging pain from her back, legs, and feet bilaterally. Her mood is agitated.

■ Physical Examination

Gen

The patient is a 56-year-old obese woman with wide spread allodynia.

VS

BP 150/96 mm Hg, P 96 bpm, RR 15, T 37.5°C; Wt 50 kg, Ht 142 cm

HEENT

PERRLA, EOMI, TMs intact

Neck

Supple, no JVD, no bruits

Resp

CTA and P; no crackles or wheezes

CV

NSR without MRG

Breasts

Negative

Abd

Soft, NT, liver and spleen not palpable, (+) BS

Genit/Rect

Heme (–) stool, pelvic exam deferred

MS/Ext

Widespread, extreme allodynia with any touch; axial spine had good alignment of the spine. Spine demonstrated excellent range of motion; however, there was widespread allodynia on her spinous muscles. Thoracic spine was normal except for allodynia. Cervical spine demonstrated good range of motion; positive allodynia. She had spasm and tenderness in the trapezius muscles bilaterally (left greater than right), in the rhomboid muscles (right side principally), and in the scalene muscles (the right side of her neck greater than the left side although both sides were affected).

Neuro

CN II–XII intact, A&O × 3
Normal motor strength in the upper extremities with reflexes 1+ and symmetric and normal sensation extremities, no CCE

■ Labs

Chem 7: WNL
LFTs: WNL
CBC: WNL except for elevated Hgb and Hct
MRI: Slight degenerative disk disease that is appropriate for age

■ Assessment

1. CRPS
2. Fibromyalgia
3. OSA
4. Possible MRAB
5. Hypertension
6. Hyperlipidemia

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence or severity of complex regional pain syndrome (CRPS)?
- 1.b. What additional information is needed to fully assess this patient's CRPS?

Assess the Information

- 2.a. Assess the severity of CRPS based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the patient's goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for CRPS might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating CRPS?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the optimal plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The physician in the clinic decides that DM is at a very high risk for accidental opioid overdose because she refuses to wear a CPAP mask and because of her high total daily opioid dose. The physician also states that DM's recent urine drug screening (UDS) came back positive for opiates and oxycodone and asks for a consult.

FOLLOW-UP QUESTIONS

1. What tools can be employed to monitor for medication-related aberrant behavior?
2. What steps can be taken if DM begins to exhibit medication-related aberrant behavior, yet has a valid reason to continue opioid medications?
3. If DM continues to exhibit medication-related aberrant behavior, what strategies can be used to wean her opioid medications?
4. Compare and contrast the terms: physical dependence, tolerance, pseudo-addiction, addiction, and withdrawal.

SELF-STUDY ASSIGNMENTS

1. Prepare a list of opioids and their corresponding equianalgesic dosing.
2. The use of opioid medication is a controversial topic; often it is driven more by passion than by scientific data. In three to four sentences per viewpoint, discuss this issue from the perspective of (1) a provider, and (2) the patient.

CLINICAL PEARL

Opioids are not first-line therapy for any CRPS conditions. No therapeutic guidelines for fibromyalgia advocate for the use of opioids.

REFERENCES

1. Hsu E. Practical management of complex regional pain syndrome. *Am J Ther* 2009;16(2):147–154.
2. Webster LR, Webster RM. Predicting aberrant behaviors in opioid-treated patients: preliminary validation of the opioid risk tool. *Pain Med* 2005;6(6):432–442.
3. Tesarz J, Leisner S, Gerhardt A, et al. Effects of eye movement desensitization and reprocessing (EMDR) treatment in chronic pain patients: a systematic review. *Pain Med* 2014;15:247–263.
4. Hilton L, Hempel S, Ewing B, et al. Mindfulness meditation for chronic pain: systematic review and meta-analysis. *Ann Behav Med* 2017;51:199–213.
5. Wong CS, Wong SH. A new look at trigger point injections. *Anesthesiol Res Pract* 2012;2012:492452. doi: 10.1155/2012/492452.
6. Yeh CH, Chiang YC, Hoffman SL, et al. Efficacy of auricular therapy for pain management: a systematic review and meta-analysis. *Evid Based Complement Alternat Med* 2014;2014:934670. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4140110/>. Accessed April 28, 2019.
7. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep* 2016;65(No. RR-1):1–49.
8. Webster LW, Fine PG. Review and critique of opioid rotation practices and associated risks of toxicity. *Pain Med* 2012;1:1–9.
9. Chou R, Cruciani RA, Fiellin RA, et al. Methadone safety guidelines: methadone safety: a clinical practice guideline from the American Pain Society and College on problems of drug dependence, in collaboration with the Heart Rhythm Society. *J Pain* 2014;15(4):321–337.
10. Christo PJ, Manchikanti L, Ruan X, et al. Urine drug testing in chronic pain. *Pain Physician* 2011;14:123–143.

71

ACUTE PAIN MANAGEMENT

No Pain, Much Gain Level I

Charles D. Ponte, BPharm, PharmD, BC-ADM, BCPS, CDE, CPE, FAADE, FAPhA, FASHP, FCCP, FNAP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Differentiate acute pain from chronic pain.
- Describe the typical clinical findings associated with acute pain.
- Describe the subjective and objective assessment of pain.
- Identify appropriate nonopioid and opioid analgesics for selected patients with acute pain.
- Choose suitable drug and nondrug therapy for the management of common opioid analgesic side effects.
- Develop an appropriate therapeutic plan (including monitoring parameters) for a patient with acute pain.

PATIENT PRESENTATION

■ Chief Complaint

“My belly hurts, and I can’t stand the sight of food.”

■ HPI

Charles Porter is a 68-year-old man who presents to the Family Practice Center with a 2-day history of nausea, vomiting, and epigastric and RUQ abdominal pain. The patient states that the pain began several hours after eating a large platter of extra hot chicken wings with cheese fries and gravy at a local restaurant. The pain intensified and was associated with escalating nausea followed by several episodes of vomiting. The vomiting finally ceased, but the abdominal pain has persisted and is worse after meals. The pain is now dull, constant, and “bores” to his back. Lying up in bed or sitting in a chair seems to relieve some of the pain. Since the initial episode, his appetite has decreased and he has been avoiding fried or fatty foods. He denies any change in stool color or consistency.

■ PMH

HTN × 20 years; poorly controlled
 Type 2 DM × 23 years; under fair control
 History of gout; last attack 15 years ago
 Dyslipidemia × 23 years
 Alcoholic fatty liver disease without cirrhosis × 10 years

■ FH

Father deceased (esophageal varices), age 76; mother deceased (MI), age 83; brother alive and well, age 65; sister with breast cancer and gallbladder disease, age 58

■ SH

He is a retired bar owner and lives with his wife (married for 35 years) on a 10-acre farm a few miles from town. He has two dogs

and a cat. He has a 50 pack-year history of smoking and a history of chronic alcohol abuse.

■ ROS

As per HPI; otherwise negative

■ Meds

Atorvastatin 20 mg PO once daily
 Hydrochlorothiazide 25 mg PO once daily
 Losartan 100 mg PO once daily
 Exenatide ER 2 mg subcutaneously weekly
 Metformin 1000 mg PO BID
 Aspirin 81 mg PO once daily
 Insulin glargine 15 units subcutaneously at bedtime
 Pepcid AC 20 mg PO PRN heartburn
 MVI one tablet PO once daily

■ All

Doxycycline—abdominal pain
 Morphine—hives, mild wheezing and throat “tightness”

■ Physical Examination

Gen

A pleasant, elderly white man in mild to moderate acute distress; appears his stated age

VS

BP 160/95 mm Hg (sitting), P 84 bpm, RR 20, T 37.8°C; pain 6/10; Wt 90 kg, Ht 5’10”

HEENT

PERLLA, fundi with mild AV nicking; TMs intact; mucous membranes moist

Chest

Clear to A&P

Heart

Normal S₁ and S₂; without murmur, rub, or gallop

Abd

Normal bowel sounds, without organomegaly, moderate diffuse epigastric pain with deep palpation with mild guarding

Genit/Rect

Slightly enlarged prostate; guaiac (–) stool

Ext

Good strength throughout, reflexes intact, mild decreased pinprick sensation to both lower extremities; no CCE

■ Labs

Na 138 mEq/L	Hgb 12.6 g/dL	AST 98 U/L
K 3.3 mEq/L	Hct 36%	ALT 77 U/L
Cl 97 mEq/L	Platelets 340 × 10 ³ /mm ³	Alk phos 200 U/L
CO ₂ 23 mEq/L	WBC 14.0 × 10 ³ /mm ³	T. bili 3.4 mg/dL
BUN 15 mg/dL	Neutros 76%	D. bili 2.6 mg/dL
SCr 1.3 mg/dL	Bands 4%	Amylase 435 U/L
Glu 210 mg/dL	Eos 2%	Lipase 367 U/L
	Lymphs 18%	Lipids
		T. chol 210 mg/dL
		HDL 30 mg/dL
		LDL 120 mg/dL
		TG 300 mg/dL

■ Assessment

1. Acute pain due to presumed acute cholecystitis/acute pancreatitis
2. Acute pancreatitis due to presumed biliary obstruction or alcohol abuse
3. Hypertension
4. Hyperglycemia
5. Dyslipidemia
6. Acid reflux
7. Hypokalemia
8. Drug–drug interaction

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of acute pain?
- 1.b. What additional information is needed to fully assess this patient's acute pain?

Assess the Information

- 2.a. Assess the severity of acute pain based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for acute pain management might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's acute pain?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's acute pain and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The patient was admitted to the inpatient service for presumed cholecystitis/acute pancreatitis/hepatitis and pain control. An abdominal ultrasound and abdominal CT were ordered. Blood cultures were obtained. Gastroenterology and general surgery services were consulted. The patient was made NPO except for his home medications. A sliding scale insulin regimen was also ordered.

The drug therapy regimen that a pharmacist recommended for the patient was initiated. At the end of the first hospital day, the patient states that the medication “eases the pain some,” but the pain is inadequately controlled. The pain is rated as an 8/10 using a single-dimensional visual analog pain scale. The patient also complains of some nausea and urinary hesitancy.

■ FOLLOW-UP QUESTIONS

1. What is the most likely cause of this patient's inadequate pain control?
2. What are the revised management goals for this patient?

■ SELF-STUDY ASSIGNMENTS

1. Describe the role of NMDA antagonists in the management of pain.
2. Describe the pathophysiology and management of opioid-induced respiratory depression.
3. What types of pain do not typically respond to opioid analgesics?
4. Explain the pathophysiology behind the development of opioid tolerance.
5. Explain the concepts of equianalgesic doses and relative analgesic potency.
6. Explain the WHO analgesic ladder and list representative analgesic classes (or individual agents) associated with each step of the ladder.
7. Describe the advantages and disadvantages of single- and multi-dimensional pain assessment instruments.

CLINICAL PEARL

Analgesic tolerance can be overcome by switching from one opioid to another. Because cross-tolerance is not complete among opioids, use only 50–75% of the equianalgesic dose of an opioid when changing from one drug to another and titrate accordingly.

REFERENCES

1. Caparrotta TM, Antoine DJ, Dear JW. Are some people at increased risk of paracetamol-induced liver injury? A critical review of the literature. *Eur J Clin Pharmacol* 2018;74:147–160.
2. Brune K, Patrignani P. New insights into the use of currently available non-steroidal anti-inflammatory drugs. *J Pain Res* 2015;8:105–118.
3. Ghelardini C, Di Cesare Mannelli L, Bianchi E. The pharmacological basis of opioids. *Clin Cases Miner Bone Metab* 2015;12:219–221.
4. American Pain Society. Principles of analgesic use in the treatment of acute pain and cancer pain. 6th ed. Glenview, IL, American Pain Society, 2008.
5. Prommer EE. Pharmacological management of cancer-related pain. *Cancer Control* 2015;22:412–425.
6. Thompson DR. Narcotic analgesic effects on the sphincter of Oddi: a review of the data and therapeutic implications in treating pancreatitis. *Am J Gastroenterol* 2001;96:1266–1272.
7. Spiegel B. Meperidine or morphine in acute pancreatitis? *Am Fam Physician* 2001;64:219–220.

8. American Diabetes Association. Standards of medical care in diabetes—2019. *Diabetes Care* 2019;42(S1):S1–S183.
9. Eland IA, Sundström A, Velo GP, et al. Antihypertensive medication and the risk of acute pancreatitis: the European case-control study on drug-induced acute pancreatitis (EDIP). *Scand J Gastroenterol* 2006;41:1484–1490.
10. Azoulay L, Filion KB, Platt RW, et al. Association between incretin-based drugs and the risk of acute pancreatitis. *JAMA Intern Med* 2016;176(10):1464–1473.
11. Pizzimenti V, Giandalia A, Cucinotta D, et al. Incretin-based therapy and acute cholecystitis: a review of case reports and EudraVigilance spontaneous adverse drug reaction reporting database. *J Clin Pharm Ther* 2016;41:116–118.

72

MIGRAINE HEADACHE

It's Not Just a Headache! Level II

Susan R. Winkler, PharmD, BCPS, FCCP

Brittany Hoffmann-Eubanks, PharmD, MBA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Develop pharmacotherapeutic goals for preventing and treating migraine headaches.
- Provide appropriate pharmacotherapeutic recommendations for an individual patient based on the patient's headache type and severity, medical history, previous drug therapy, concomitant problems, and pertinent laboratory data.
- Educate patients on the use of abortive and prophylactic agents for migraine headaches and menstrual migraines.
- Describe the appropriate use of a headache diary and how it may be used to refine headache treatment.

PATIENT PRESENTATION

■ Chief Complaint

"This new medication is not working for my migraines. My headaches are worse around my period and I have gained 10 pounds!"

■ HPI

Sarah Miller is a 34-year-old woman who presents to the Neurology Clinic for a follow-up of migraine headaches. She states that she used to get about two migraines every month; however, she recently went back to work full time and has two young children, ages 3 and 5, to care for. Since then, the frequency of her migraines has increased to about four to five per month. She states her migraines usually occur in the morning and are more frequent around her menses. Her typical headache evolves quickly (within 1 hour) and involves severe throbbing pain that is unilateral and temporal in distribution. Her headaches are preceded by an aura that consists of nausea and pastel lights flashing throughout her visual field. Photophobia occurs frequently, and vomiting may

occur with an extreme headache. She reports experiencing severe migraine attacks that cause her to miss 1 day of work each month. She is unable to complete household chores and has a difficult time caring for her children on the days she has severe migraine attacks. She also complains of having mild migraine attacks lasting 3 days per month during which her productivity at work and at home is reduced by half. She typically has to retreat to a dark room and avoid any noise, or the severity of the migraine increases. She rates her migraines as 7–8 on a headache scale of 1–10, with 10 being the worst. At her previous visit to the neurology clinic 3 months ago, she was prescribed naratriptan 2.5 mg orally to be taken at the onset of headache. However, naratriptan has not been effective for half of the migraines she has had in the past 3 months. During two of the attacks, she experienced partial pain relief, with the pain returning later in the day. She mentions that she was prescribed naratriptan when the Cafergot she was taking stopped working. She states she has taken her medications exactly as advised. She prefers to use medications that can be taken orally. She was also started on valproic acid at her last clinic visit for headache prophylaxis and has noticed a 10-lb weight gain. She inquires about switching from valproic acid to another medication.

■ PMH

Migraine with aura since age 29; previous medical workup, including an EEG and a head MRI, demonstrated no PVD, CVA, brain tumor, infection, cerebral aneurysm, or epileptic component; mild depression for 8 months

■ FH

Positive for migraines (both parents); hypertension and type 2 diabetes (mother)

■ SH

Secretary; recently changed jobs to a full-time position. Mother of two boys, ages 3 and 5. Denies alcohol use; started smoking cigarettes again 3 months ago due to stress, 1 ppd. Reports she also sometimes uses e-cigarettes as she would like to quit smoking. Occasional caffeine intake.

■ Meds

- Currently prescribed:
 - ✓ Naratriptan 2.5-mg tablets, one tablet PO at onset of migraine, repeat dose of 2.5 mg PO in 4 hours if partial response or if headache returns. Maximum dose 5 mg/24 hr.
 - ✓ Metoclopramide 10 mg PO at onset of migraine
 - ✓ Valproic acid 500 mg PO at bedtime
 - ✓ Sertraline 50 mg PO at bedtime
- Past abortive migraine therapies:
 - ✓ Simple analgesics, NSAIDs, and Cafergot (good efficacy until 3 months ago)
 - ✓ Narcotics (good efficacy, but puts her "out of commission for days")
 - ✓ Midrin (no efficacy)
- Past prophylactic therapies prescribed:
 - ✓ Propranolol 20 mg BID (increased episodes of dizziness and lightheadedness; patient self-discontinued medication)
- Mild depression for 8 months, treated in the past with:
 - ✓ Bupropion SR 150 mg PO TID (minimal efficacy, self-discontinued 3 months ago)

■ **All**

NKDA

■ **ROS**

Complains of increased frequency of migraine headaches starting about 6 months ago; increased frequency around menses. Limited efficacy with naratriptan; no nausea, vomiting, diarrhea, or flashing lights at present.

■ **Physical Examination****Gen**

WDWN woman in mild distress

VS

BP 142/86 mm Hg, HR 76, RR 18, T 37.2°C; Wt 75 kg, Ht 5'3"

Skin

Normal skin turgor; no diaphoresis

HEENT

PERRLA; EOMI; no funduscopic exam performed

Neck

Supple; no masses, thyroid enlargement, adenopathy, bruits, or JVD

Chest

Good breath sounds bilaterally; clear to A&P

CV

RRR; S₁, S₂ normal; no murmurs, rubs, or gallops

Abd

Soft, NT/ND, no hepatosplenomegaly; (+) BS

Genit/Rect

Deferred

MS/Ext

UE/LE strength 5/5 with normal tone; radial and femoral pulses 3+ bilaterally; no edema; no evidence of thrombophlebitis; full ROM

Neuro

A&O × 3; no dysarthria or aphasia; memory intact; no nystagmus; no fasciculations, tremor, or ataxia; (–) Romberg; CN II–XII intact; sensory intact; DTRs: 2+ throughout; Babinski (–) bilaterally

■ **Labs**

Na 142 mEq/L	Hgb 13 g/dL	AST 23 IU/L
K 4.2 mEq/L	Hct 40%	ALT 25 IU/L
Cl 101 mEq/L	Plt 302 × 10 ³ /mm ³	Alk phos 35 IU/L
CO ₂ 23 mEq/L	WBC 8 × 10 ³ /mm ³	Urine pregnancy test (–)
BUN 12 mg/dL	Differential WNL	
SCr 0.8 mg/dL		
Glu 95 mg/dL		

■ **Assessment**

1. Migraine with increased frequency
2. Prophylactic therapy for migraine headache

3. Nicotine use

4. Depression

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of migraine headaches?
- 1.b. What additional information is needed to fully assess this patient's migraine headaches? (See Fig. 72-1 for MIDAS questionnaire.)

Assess the Information

- 2.a. Assess the severity of migraine headaches based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for migraine headaches might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for (1) treating the nausea associated with her migraine headaches, (2) acutely treating the migraine headaches, and (3) preventing migraine attacks?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for both the acute and preventive treatment of this patient's migraines and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ **CLINICAL COURSE: ALTERNATIVE THERAPY**

While discussing possible alternatives to her valproic acid therapy, Ms Miller says that a friend who also has migraines had read about some herbal remedies used for migraine prevention. She asks whether any products like that could be used instead of or along with her prescription medications. Ms Miller is very interested in a more "natural"

INSTRUCTIONS: Please answer the following questions about ALL the headaches you have had over the last 3 months. Write your answer in the box next to each question. Write zero if you did not do the activity in the last 3 months.

1. How many days in the last 3 months did you miss work or school because of your headaches?

2. How many days in the last 3 months was your productivity at work or school reduced by half or more because of headaches? (*Do not include days you counted in question 1 where you missed work or school.*)

3. How many days in the last 3 months did you NOT do household work because of your headaches?

4. How many days in the last 3 months was your productivity in household work reduced by half or more because of your headaches? (*Do not include days you counted in question 3 where you did not do household work.*)

5. On how many days in the last 3 months did you miss family, social, or leisure activities because of your headaches?

MIDAS Score: Add the total number of days from questions 1–5. **Total**

NOTE: Scores from A and B below are not included in the MIDAS score, but are used to assess frequency and intensity of pain.

A. How many days in the last 3 months did you have a headache? (*If a headache lasted more than 1 day, count each day.*)

B. On a scale of 0–10, on average how painful were these headaches? (*0 = no pain, and 10 = pain as bad as it can be.*)

Interpretation

The MIDAS questionnaire is scored in units of lost days. Depending on the MIDAS score, patients are assigned to I of IV grades:

MIDAS Grade	Definition	Score
I	Minimal or infrequent disability	0–5
II	Mild or infrequent disability	6–10
III	Moderate disability	11–20
IV	Severe disability	≥21

FIGURE 72-1. MIDAS questionnaire. (Reprinted with permission from Bigal ME, Lipton RB, Krymchantowski AV. The medical management of migraine. *Am J Ther.* 2004;11:130–140. Lippincott Williams & Wilkins, www.lww.com.)

therapy, but only if it would reduce the number of migraines she experiences. For questions related to the use of butterbur and feverfew for the prevention of migraine headaches, see Section 19 (Complementary and Alternative Therapies) of this Casebook.

FOLLOW-UP QUESTION

- Describe how a headache diary could help the treatment of this patient's migraine headaches. (See Fig. 72-2 for headache diary.)

SELF-STUDY ASSIGNMENTS

- Evaluate the literature regarding the efficacy of IV agents (eg, dihydroergotamine, valproate sodium) for acute migraines.
- Evaluate the literature on intranasal ketorolac and intranasal oxytocin for acute migraine.

- Review the literature on the efficacy of the calcitonin gene-related peptide antagonists—erenumab (Aimovig), galcanezumab-gnlm (Emgality), and fremanezumab-vfrm (Ajovy)—for prevention of migraine.
- Explain the role of onabotulinum toxin type A (Botox) for prevention of chronic migraine.

CLINICAL PEARL

Migraines are three times more prevalent in women and are associated with estrogen levels. Sixty percent of women migraineurs report menstrually associated migraines, and 7–14% have migraines exclusively with menses.

Name: _____ Month: _____ Year: _____

Date of Headache														
Headache Intensity														
Excruciating pain	10	10	10	10	10	10	10	10	10	10	10	10	10	10
	9	9	9	9	9	9	9	9	9	9	9	9	9	9
Severe pain	8	8	8	8	8	8	8	8	8	8	8	8	8	8
	7	7	7	7	7	7	7	7	7	7	7	7	7	7
Severe pain	6	6	6	6	6	6	6	6	6	6	6	6	6	6
	5	5	5	5	5	5	5	5	5	5	5	5	5	5
Moderate pain	4	4	4	4	4	4	4	4	4	4	4	4	4	4
	3	3	3	3	3	3	3	3	3	3	3	3	3	3
Mild pain	2	2	2	2	2	2	2	2	2	2	2	2	2	2
Aura only	1	1	1	1	1	1	1	1	1	1	1	1	1	1
Headache Duration (hours)														
Level of Disability														
Hospitalized														
Treatment by health care professional														
Bedrest required														
Decrease in activity by 50%														
Decrease in activity by 25%														
Normal activity														
Other (comment below)														
Associated Symptoms														
Nausea														
Vomiting														
Visual disturbances														
Menstrual period														
Neurological														
Other (comment below)														
Medications Taken														
1.														
2.														
3.														
4.														
5.														
Treatment Results														
Complete relief														
75% relief														
50% relief														
25% relief														
No relief														
Other (comment below)														
General Comments														

Note: A normal diary includes space to record a full month of headache activity. This form has been truncated for space purposes.

FIGURE 72-2. A headache diary.

REFERENCES

- Bigal ME, Lipton RB, Krymchantowski AV. The medical management of migraine. *Am J Ther* 2004;11:130–140.
- Kropp P, Meyer B, Meyer W, Dresler T. An update on behavioral treatments in migraine—current knowledge and future options. *Expert Rev Neurother* 2017;11:1059–1068.
- Lipton RB. Risk factors for and management of medication-overuse headache. *Continuum (Minneapolis)* 2015;21(4):1118–1131.
- Banzi R, Cusi C, Randazzo C, Sterzi R, Tedesco D, Moja L. Selective serotonin reuptake inhibitors (SSRIs) and serotonin-norepinephrine reuptake inhibitors (SNRIs) for the prevention of migraine in adults. *Cochrane Database Syst Rev* 2015. doi: 10.1002/14651858.CD011681.
- Evans RW, Tepper SJ, Shapiro RE, Sun-Edelstein C, Tietjen GE. The FDA alert on serotonin syndrome with use of triptans combined with selective serotonin reuptake inhibitors or selective serotonin-norepinephrine reuptake inhibitors: American Headache Society position paper. *Headache* 2010;50:1089–1099.
- Silberstein SD. Preventive migraine treatment. *Continuum (Minneapolis)* 2015;21(4):973–989.
- Silberstein SD, Holland S, Freitag F, et al. Evidence-based guideline update: pharmacologic treatment for episodic migraine prevention in adults. Report of the Quality Standards Subcommittee of the American Academy of Neurology and the American Headache Society. *Neurology* 2012;78:1337–1345.
- Linde M, Mulleners WM, Chronicle EP, McCrory DC. Gabapentin or pregabalin for the prophylaxis of episodic migraine in adults. *Cochrane Database Syst Rev* 2013;(6):CD010609. doi: 10.1002/14651858.CD010609.
- Nierenburg HDel C, Ailani J, Malloy M, Siavoshi S, Hu NN, Yusuf N. Systematic review of preventive and acute treatment of menstrual migraine. *Headache* 2015;55:1052–1071.
- Mitsikostas DD, Reuter U. Calcitonin gene-related peptide monoclonal antibodies for migraine prevention: comparisons across randomized controlled studies. *Curr Opin Neurol* 2017;30(3):272–280.

SECTION 7

PSYCHIATRIC DISORDERS

73

ATTENTION-DEFICIT HYPERACTIVITY DISORDER

He Is So Energized, He Keeps Going and
Going and Level I

Laura F. Ruekert, PharmD, BCPP, BCGP

Syed Khan, MD, MBA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Determine the signs and symptoms of attention-deficit/hyperactivity disorder (ADHD) as defined by the *Diagnostic and Statistical Manual of Mental Disorders*, Edition 5 (DSM-5).
- Differentiate treatment options for ADHD with regard to effectiveness, tolerability, safety, monitoring parameters, and potential for drug interactions.
- Compare the advantages and disadvantages of once-daily stimulant preparations with short-acting stimulants.
- Develop useful dosing schedule strategies that may be employed in the management of patients with ADHD to enhance medication adherence.
- Perform patient assessment to determine efficacy with selected therapy and appropriate monitoring for any adverse effects.

PATIENT PRESENTATION

■ Chief Complaint

"My son has trouble focusing and sitting still while completing his afternoon homework."

■ HPI

David Handlon is a 10-year-old boy who returns for a routine visit to his psychiatrist with his mother. He was diagnosed 2 years ago with ADHD and is currently being treated with Adderall XR 20 mg every morning. His mother states that during the last parent-teacher meeting, his teacher indicated that David's behavior is well controlled during the day. Despite David's good behavior during the day, his mother reports difficulty getting David to complete any afternoon tasks or assignments after school. David's rules include no playtime activities until he has completed his afternoon homework assignments. Instead of focusing on homework, David insists on playing Guitar Hero® in his room, and he sometimes

carelessly throws his guitar. David has also exhibited impulsive and reckless behavior when interacting with his younger 8-year-old brother. Initially David's mother thought the medication was working. However, within the past year, David's afternoon antics have progressively gotten worse. Mrs Handlon is afraid that uncontrolled afternoon antics will have serious repercussions on David's daytime behavior and grades. She questions, "What are my options?"

■ PMH

Asthma × 3 years
ADHD × 2 years
Tonsillectomy (1 year ago)
Broken wrist at age 8 (fell from tree)
Vaccinations up to date

■ FH

Both father and uncle have a history of hyperactivity and are currently receiving treatment as adults.

■ SH

Lives with both parents and younger brother in the suburbs

■ Meds

Adderall XR 20 mg daily (given every morning at 7:00 AM)
Albuterol inhaler two puffs Q 4–6 H PRN shortness of breath
Montelukast 5 mg PO daily

■ All

NKDA

■ ROS

Physical assessment was difficult to assess for David as he could not sit still for more than 30 seconds and was jumping off of the exam table. Asthma symptoms appear controlled with PRN inhaler use at bedtime only and daily montelukast.

■ PE

Gen

Well-nourished, healthy-appearing male child, normal physical development

VS

BP 110/72 mm Hg, P 82 bpm, RR 25, T 37.5°C; Wt 50 kg, Ht 5'2"

Skin

No signs of rash, skin irritation, or bruising noted. Scar noticed on left wrist from where he fell from tree. Minor cuts on knees from frequent falls on school playground.

HEENT

Unable to assess

Neck/Lymph Nodes

Unable to assess

Lungs/Thorax

No rales, rhonchi, or wheezing

CV

RRR

Abd

Deferred

Genit/Rect

Deferred

MS/Ext

Unable to assess

Neuro

A&O $\times$ 3; no underlying tics noted

Labs

Na 138 mEq/L	Hgb 14 g/dL	WBC $9 \times 10^3/\text{mm}^3$	Mag 1.8 mg/dL
K 3.8 mEq/L	Hct 44.5%	Neutros 66%	Serum iron
Cl 106 mEq/L	RBC $4.6 \times 10^6/\text{mm}^3$	Bands 2%	95 mcg/dL
CO ₂ 23 mEq/L		Eos 3%	TSH 3.6 mIU/L
BUN 18 mg/dL	Plt $278 \times 10^3/\text{mm}^3$	Lymphs 24%	
SCr 0.8 mg/dL		Monos 5%	
Glu 110 mg/dL	MCV 85 μm^3		
	MCHC 33 g/dL		

ECG

NSR; changes not clinically significant

Assessment

1. ADHD
2. Mild-persistent asthma, well controlled with PRN albuterol and daily montelukast

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence or severity of ADHD?
- 1.b. What additional information is needed to fully assess this patient's ADHD?

Assess the Information

- 2.a. Assess the severity of ADHD based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be beneficial for those diagnosed with ADHD?

- 3.c. What feasible pharmacotherapeutic alternatives are available for the treatment of ADHD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's ADHD and other drug problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for the follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Many parents are apprehensive about starting stimulants in children as a result of abuse warnings in the prescribing information and media reports. After performing a literature search, prepare an educational brochure addressing the question, "What is the relationship between both untreated and treated ADHD and drug abuse? Does stimulant treatment for ADHD increase the risk of drug abuse?"
2. Provide a summary that addresses the long-term effect stimulants have on growth and appetite, cardiovascular risks, sleep, and any psychiatric or behavioral effects.
3. ADHD is considered a chronic condition. Discuss various etiologies (including genetics) and population characteristics. Compare and contrast how symptoms and presentations change over the course of a lifetime. Include discussion of the different consequences from untreated ADHD spanning from childhood to adulthood.
4. Develop an appropriate recommendation for product conversion in a patient who is switching from oral methylphenidate (Concerta) 36 mg PO daily to methylphenidate (Daytrana) transdermal patch. Also, convert doses of mixed amphetamine salts (Adderall IR/Adderall XR) to lisdexamfetamine (Vyvanse).
5. Perform a literature search and defend or refute the role of modafinil, selective serotonin reuptake inhibitors, tricyclic antidepressants, and atypical antipsychotics in the treatment of ADHD.

CLINICAL PEARL

Because of well-established efficacy and tolerability, stimulant medications are considered first-line therapy in children with ADHD. The American Academy of Pediatrics reports at least an 80% response rate when these agents are used appropriately in the management of ADHD. If a patient does not respond adequately to initial stimulant therapy, a second or even third stimulant should be tried before initiating a nonstimulant medication. Most patients will be successfully treated by an alternative stimulant. Factors to consider when selecting a stimulant include age, tolerability, and dosage formulation preferences.

ACKNOWLEDGMENTS

This case is based on the patient case written for the 10th edition by Darin C. Ramsey, PharmD, and Laura F. Ruekert, PharmD.

REFERENCES

1. American Psychiatric Association. Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association, 2013.
2. Wolraich M, Brown L, Brown RT, et al. ADHD: clinical practice guideline for the diagnosis, evaluation, and treatment of attention-deficit/hyperactivity disorder in children and adolescents. *Pediatrics* 2011; 128(5):1007–1022.
3. The European Union. Attention Deficit Hyperactivity Disorder Drug Use Chronic Effect (ADDUCE) project, 2016. <https://cordis.europa.eu/docs/results/260/260576/final1-public-final-report-all-sections.pdf>. Accessed April 20, 2019.
4. The Medical Letter. Drugs for ADHD. *Med Lett Drugs Ther* 2015;57(1464):37–40.
5. Sonuga-Barke EJ, Brandeis D, Cortese S, et al. Nonpharmacological interventions for ADHD: Systematic review and meta-analyses of randomized controlled trials of dietary and psychological treatments. *Am J Psychiatry* 2013;170: 275–289.
6. Cortese S, Adamo N, Del Giovane C, et al. Comparative efficacy and tolerability of medications for attention-deficit hyperactivity disorder in children, adolescents, and adults: a systematic review and network meta-analysis. *Lancet Psychiatry* 2018;5:727–738.
7. Pliszka S; AACAP Work Group on Quality Issues. Practice parameter for the assessment and treatment of children and adolescents with attention-deficit-hyperactivity disorder. *J Am Acad Child Adolesc Psychiatry* 2007;46:894–921.
8. Stuhel M, Munda B, Svab V, et al. Comparative efficacy and acceptability of atomoxetine, lisdexamfetamine, bupropion and methylphenidate in treatment of attention deficit hyperactivity disorder in children and adolescents: a meta-analysis with focus on bupropion. *J Affect Disord* 2015;178:149–159.
9. Henniseen L, Bakkar MJ, Banaschewski T, et al. Cardiovascular effects of stimulant and non-stimulant medication for children and adolescents with ADHD: a systematic review and meta-analysis of trials of methylphenidate, amphetamines, and atomoxetine. *CNS Drugs* 2017;31:199–215.

- Recommend effective pharmacologic and nonpharmacologic treatment options for the management of BN.
- Compare and contrast short-term and long-term complications of BN and discuss the associated therapeutic options for prevention and management.
- Design a treatment plan including monitoring parameters and counseling points for a patient with BN.

PATIENT PRESENTATION

■ Chief Complaint

“I’m so unpopular, I just want to die!”

■ HPI

Cady Greenwald is a 21-year-old woman presenting to a behavioral acute care hospital referred by her outpatient psychiatrist for suicidal ideations and symptoms of an eating disorder. She reported worsening depressive symptoms after she was cut from the college dance team 6 months ago. She expressed anxious feelings of inadequacy and obsessions with her image after that incident, and she is now binge eating and purging up to eight episodes a week. She explains she tries to withhold food for as long as possible and then loses control and impulsively binges on large amounts of food usually in private. She becomes overwhelmed with guilt and anxiety and subsequently purges. In addition, she uses laxatives about three to four times a week and engages in self-injurious behavior by cutting her forearm. She has now dropped out of school and expresses suicidal ideations with a plan, stating “no one would miss me.” She admitted daily use of alcohol and marijuana to help her depressive thoughts, calm her anxieties, and regulate her appetite. Compounding the eating disorder is that Cady has a diagnosis of bipolar disorder, type II, treated with escitalopram, bupropion, and ziprasidone, and she has been experiencing a depressive episode.

■ PMH

Bipolar disorder, type II
Cluster B personality disorder traits
Substance use disorder
Tobacco use disorder
All diagnosed three years ago by patient’s outpatient psychiatrist

■ FH

Parents married for 25 years. Father has a history of depression. Maternal aunt diagnosed with bipolar disorder. Maternal uncle and paternal aunt have a history of depression and substance use.

■ SH

Completed 2 years of college as a dance major but dropped out 2 weeks ago due to increasing stress. She lives alone in her apartment. She admits to smoking marijuana daily because she claims “everything is OK after I smoke.” She also drinks until she passes out about two nights a week and just occasionally drinks otherwise. She uses tobacco 1 ppd × 2 years.

■ Meds

Ziprasidone 40 mg PO BID × 3 years
Bupropion SR 200 mg PO BID × 1 year
Escitalopram 20 mg PO once daily × 3 years

■ All

NKDA

74

BULIMIA NERVOSA

Self-Conscious Socialite Level II

Laura F. Ruekert, PharmD, BCPP, BCGP

Cheen T. Lum, PharmD, BCPP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Define bulimia nervosa (BN) according to the *Diagnostic and Statistical Manual of Mental Disorders*, Edition 5 (DSM-5) criteria.
- Assess signs and symptoms commonly associated with the presentation of BN.

■ **ROS**

Cady expresses feelings of hopelessness and frustration with her life in general. She states she has never experienced relief from depressive symptoms and uses marijuana and alcohol daily to cope. She endorses suicidal ideations with a plan of cutting her wrists, but denies any previous attempts. She reports high anxieties and obsessions with her image. She reports fatigue, weakness, dizziness, and low energy increasing the past couple of weeks. Her LMP was 2 months ago, and her periods have been irregular.

■ **PE****Gen**

Tearful, thin, anxious-appearing Caucasian woman

Skin

Abrasion on dorsum of right hand (Russell sign), numerous superficial scars and cuts on the left forearm. No findings of lanugo on arms/upper body area.

VS

BP 98/72 mm Hg, P 52 bpm, RR 20, T 36.4°C; Wt 48 kg, Ht 5'4"

HEENT

Normocephalic; brittle/coarse hair; PERRLA, EOMI; mild parotid gland enlargement

Neck/Lymph Nodes

No JVD

Lungs/Thorax

Lungs CTA; no rales, rhonchi, wheezes

CV

Hypotensive; bradycardic

Abd

Slightly distended, (–) BS

Genit/Rect

Unremarkable

MS/Ext

No cyanosis, clubbing, edema

Neuro

A&O × 3

■ **Labs**

Na 135 mEq/L	Hgb 14 g/dL	WBC $7.3 \times 10^3/\text{mm}^3$	AST 20 IU/L
K 3.3 mEq/L	Hct 39%	Neutros 60%	ALT 15 IU/L
Cl 100 mEq/L	RBC $5 \times 10^6/\text{mm}^3$	Bands 3%	Ca 8.6 mg/dL
HCO ₃ 22 mEq/L	Plt $247 \times 10^3/\text{mm}^3$	Eos 2%	Mg 1.3 mg/dL
BUN 25 mg/dL	MCV 83 fL	Lymphs 31%	Serum iron 96 mcg/dL
SCr 1.0 mg/dL	MCHC 34 g/dL	Monos 4%	Folic acid 9.3 ng/mL
Glu 74 mg/dL	Albumin 3.4 g/dL		Ferritin 110 ng/mL

Other:

UDS: +THC BAL <0.2 ECG shows QTc interval of 506 seconds
HAM-D score 20 HCG (–)

■ **Assessment**

1. BN, severe, complicated by self-mutilating behaviors
2. Bipolar type II with a depressive episode
3. Substance use disorder
4. Tobacco use disorder

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence or severity of eating disorder and related psychiatric conditions?
- 1.b. What additional information is needed to fully assess this patient's BN?

Assess the Information

- 2.a. Assess the severity of BN and any secondary complications from BN, based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for BN might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating BN?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's BN and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for the follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Compare and contrast the differences in the etiologies and presentations of the various eating disorders.
2. Review the literature and discuss the incidence, types, and implications of psychiatric comorbidities associated with eating disorders and how these may affect treatment.
3. Prepare a table highlighting the different laboratory parameters seen in a patient presenting with acidosis secondary to laxative abuse versus a patient presenting with alkalosis secondary to excessive purging.
4. Review the literature and prepare a one-page paper describing the complications of eating disorders and the overall implications of eating disorders on long-term health.

CLINICAL PEARL

Therapeutic management of eating disorders involves both comprehensive and intensive therapy with a multidisciplinary team using a combination of methods to address the complex nature of the disorder. Nonpharmacologic and pharmacologic approaches are intended to address the symptoms of eating disorders and any comorbid psychiatric disease states (substance abuse, depression, and anxiety are highly concomitant) as well as to prevent or treat potential complications.

ACKNOWLEDGMENT

Magdolene Daas, MD, assisted with the content and review of this case.

REFERENCES

1. Lock J, La Via MC; American Academy of Child and Adolescent Psychiatry (AACAP) Committee on Quality Issues (CQI). Practice parameters for the assessment and treatment of children and adolescent with eating disorders. *J Am Acad Child Adolesc Psychiatry* 2015;54(5):412–425.
2. Campbell K, Peebles R. Eating disorders in children and adolescents: state of the art review. *Pediatrics* 2014;134:582–592.
3. American Psychiatric Association. Practice guidelines for the treatment of patients with eating disorders, 3rd ed. *Am J Psychiatry* 2006;163(7 Suppl):4–54.
4. Aigner M, Treasure J, Kaye W, Kasper S; WFSBP Task Force on Eating Disorders. World Federation of Societies of Biological Psychiatry (WFSBP) guidelines for the pharmacological treatment of eating disorders. *World J Biol Psychiatry* 2011;12:400–443.
5. Hilbert A, Hoek HW, Schmidt R. Evidence-based clinical guidelines for eating disorders: international comparison. *Curr Opin Psychiatry* 2017;30:423–437.
6. Bello NT, Yeomans BL. Safety of pharmacotherapy options for bulimia nervosa and binge-eating disorder. *Expert Opin Drug Saf* 2018;17(1):17–23.
7. Tortorella A, Fabrazzo M, Monteleone AM, Steardo L, Monteleone P. The role of drug therapies in the treatment of anorexia and bulimia nervosa: a review of the literature. *J Psychopathol* 2014;20:50–65.
8. Garner DM, Anderson ML, Keiper CD, Whynott R, Parker L. Psychotropic mediations in adult and adolescent eating disorders: clinical practice versus evidence-based recommendations. *Eat Weight Disord* 2016;21:395–402.
9. Yager J, Devlin MJ, Halmi KA, et al. Guideline Watch (August 2012): Practice guideline for the treatment of patients with eating disorders. 3rd ed. American Psychiatric Association, 2012. <https://focus.psychiatryonline.org/doi/abs/10.1176/appi.focus.120404>. Accessed March 12, 2019.
10. Flament MF, Bissada H, Spettigue W. Evidence-based pharmacotherapy of eating disorders. *Int J of Neuropsychopharm* 2012;15:189–207.

75

ALCOHOL WITHDRAWAL

Cold Turkey Can Land You in Hot Water Level I

Kevin M. Tuohy, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the signs and symptoms of acute alcohol withdrawal syndrome.
- Explain the common laboratory abnormalities seen in alcohol-dependent patients.
- Develop a treatment plan for acute alcohol withdrawal and alcohol-related seizures.
- Recommend an appropriate pharmacotherapeutic regimen for electrolyte replacement in an alcohol-dependent patient.

PATIENT PRESENTATION

Chief Complaint

“My husband has been acting strange, sweating, and shaking all day. I think he had a seizure an hour ago.”

HPI

Seamus Leahy is a 54-year-old man who is brought to the ED by his wife. She states that her husband has abused alcohol since she met him while in college. She states that his typical daily consumption for the past 25 years has averaged about 14–18 alcoholic beverages. She reports that he has not been able to afford to drink recently due to a recent layoff from his job. In an effort to save money, he has decided to quit drinking “cold turkey.” He has not consumed any alcohol in the previous 48 hours.

PMH

Alcohol abuse and dependence
Alcohol withdrawal with seizure 4 years prior
Hypertension × 10 years
GERD × 4 years

SH

The patient is an unemployed construction worker. He has not worked for the past 6 months. He has been married for 22 years. He has been a heavy drinker for past 25 years. Drinks an average of 16 drinks (usually beer- or whiskey-containing drinks) per day. (+) Tobacco use: quit 5 years ago.
Denies any illicit drug use.

Meds

Hydrochlorothiazide 25 mg PO daily
Amlodipine 5 mg PO daily
OTC omeprazole 20 mg PO as needed for heartburn symptoms (usually requires a dose about four times a week)

■ All

NKDA

■ ROS

The patient exhibits overall confusion and is not responsive to questions. Wife states his mental status was normal until this afternoon when his confusion, sweating, and shakiness started.

■ PE

Gen

Tall, thin, undernourished-appearing male, in mild distress who is acutely confused and tremulous

VS

BP 150/85 mm Hg, P 107 bpm, RR 20, T 38.3°C; Wt 76 kg, Ht 6'6"

Skin

Moist, diaphoretic

HEENT

Head—atraumatic, icteric sclera, PERRLA, EOMI, mild AV nicking on fundoscopic exam

Neck/Lymph Nodes

Supple, no thyromegaly or lymphadenopathy

Lungs/Thorax

Symmetric, lungs CTA

CV

RRR, no MRG

Abd

Soft, nontender; (+) bowel sounds; (+) hepatomegaly

Genit/Rect

(–) Occult blood in stool

MS/Ext

Confused, tremor in both hands

Neuro

A&O only to person, DTRs exaggerated

■ Labs

Na 139 mEq/L	Phos 2.8 mg/dL	PT 14.5 seconds
K 3.2 mEq/L	Ca 9.5 mg/dL	INR 1.30
Cl 88 mEq/L	GGT 310 units/L	ETOH (–)
CO ₂ 26 mEq/L	AST 250 units/L	
BUN 14 mg/dL	ALT 120 units/L	
SCr 1.1 mg/dL	T. bili 1.7 mg/dL	
Glu 99 mg/dL	D. bili 1.1 mg/dL	
Mg 1.6 mg/dL	Alb 2.1 g/dL	

■ Assessment

1. Acute alcohol withdrawal with possible witnessed seizure
2. Alcohol use disorder
3. Hypertension
4. GERD

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of acute alcohol withdrawal syndrome?
- 1.b. What additional information is needed to fully assess this patient's alcohol withdrawal syndrome?

Assess the Information

- 2.a. Assess the severity of acute alcohol withdrawal syndrome based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient's acute alcohol withdrawal syndrome?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating acute alcohol withdrawal syndrome?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Research alcohol-related treatment on the Internet that can be recommended to patients with alcohol use disorder.
2. Discuss the pharmacologic options that are currently marketed in the United States (FDA-approved drugs) for the treatment of alcohol use disorder.

CLINICAL PEARLS

1. All benzodiazepines appear similarly efficacious in reducing signs and symptoms of alcohol withdrawal. The choice of the agent should be determined based on patient-specific factors and the pharmacokinetic profile of the drug.
2. Very high doses of benzodiazepines are often needed to control the symptoms of alcohol withdrawal. This is due to cross tolerance between alcohol and benzodiazepines.

REFERENCES

1. Mayo-Smith MF. Pharmacological management of alcohol withdrawal: a meta-analysis and evidence-based practice guideline. American Society of Addiction Medicine Working Group on Pharmacological Management of Alcohol Withdrawal. *JAMA* 1997;278:144–151.
2. Sullivan JT, Sykora K, Schniederman J, Naranjo CA, Sellers EM. Assessment of alcohol withdrawal: the revised clinical institute withdrawal assessment for alcohol scale (CIWA-Ar). *Br J Addict* 1989; 84:1353–1357.
3. Schuckit MA. Recognition and management of withdrawal delirium (delirium tremens). *N Engl J Med* 2014;371:2109–2113.
4. Muzyk AJ, Leung JG, Nelson S, Embury ER, Jones SR. The role of diazepam loading for the treatment of alcohol withdrawal syndrome in hospitalized patients. *Am J Addict* 2013;22:113–118.
5. Martinotti G, diNicola M, Frustaci A, et al. Pregabalin, tiapride, and lorazepam in alcohol withdrawal syndrome: a multi-centre, randomized, single-blind comparison trial. *Addiction* 2010;105:288–299.
6. Rosenson J, Clements C, Simon B. Phenobarbital for acute alcohol withdrawal: a prospective randomized double-blind placebo controlled study. *J Emerg Med* 2013;44:592–598.
7. Lyon JE, Khan RA, Gessert CE, Larson PM, Renier CM. Treating alcohol withdrawal with oral baclofen: a randomized, double-blind, placebo-controlled trial. *J Hosp Med* 2011;6:469–474.
8. Muzyk AJ, Fowler JA, Norwood DK, Chilipko A. Role of α_2 -agonists in the treatment of acute alcohol withdrawal. *Ann Pharmacother* 2011;45:649–657.
9. Mueller SW, Preslaski CR, Kiser TH, et al. A randomized, double-blind, placebo-controlled dose range study of dexmedetomidine as adjunctive therapy for alcohol withdrawal. *Crit Care Med* 2014;42:1131–1139.
10. National Institute on Alcohol Abuse and Alcoholism. Alcohol's effects on the body. U.S. Department of Health and Human Services. www.niaaa.nih.gov/alcohol-health/alphabets-effects-body. Accessed April 10, 2019.

76

NICOTINE DEPENDENCE

I'm Over It! Level II

Gabriella A. Douglass, PharmD, BCACP, AAHIVP, BC-ADM

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify a patient's location in the stages of change process to develop a tailored intervention plan to promote smoking cessation and nicotine abstinence.
- Design a patient-specific plan for initiating lifestyle modifications and pharmacologic treatment to assist a patient in quitting smoking.
- Compare the side-effect profiles of individual nicotine replacement products.
- Develop appropriate educational information on the use of pharmacotherapy for treatment of nicotine dependence.
- Formulate monitoring and follow-up plans for a patient attempting to quit smoking based on patient-specific information and the prescribed regimen.

PATIENT PRESENTATION

■ Chief Complaint

"My sugars are still running high, and I feel tired all the time. I think these cigarettes have something to do with how I'm feeling and I'm over it! I tried to quit once using nicotine gum for two days, but it made me sick to my stomach and made my jaw hurt; plus I was still craving cigarettes. I have two kids and a wife, and I want to get better so I can take care of my family. I've seen commercials on what smoking can do to you and I'm scared that could happen to me!"

■ HPI

Phil Morris is a 41-year-old African-American man who presents to the primary care clinic to review his most recent laboratory results. He reports a 2-week history of extreme thirst and hunger, excessive urination and is generally feeling unwell. His symptoms are interfering with his job. He has missed 2–3 days of work each week in the last month. He is concerned that he will not have enough money to cover his family's expenses. He states that his insurance premiums and deductibles are high, and he struggles to pay for medical expenses. He reports difficulty remembering to take his medication for blood glucose as prescribed. He wants to feel better because he wants to be able to work and provide for his family.

■ PMH

Type 2 diabetes mellitus without complications
Nicotine dependence $\times$ 18 years
Obesity
Stage 1 hypertension

■ FH

Father: 67 years old, prior myocardial infarction at age greater than 60; hypertension
Mother: 64 years old; type 2 diabetes mellitus, ovarian cancer
Son: 12 years old; asthma
Daughter: 7 years old; ADHD

■ SH

Caffeine Use: Daily cola consumption of 8+ cans a day
Tobacco use: Current everyday smoker for 18 years. Smokes a pack of cigarettes daily when he can afford to buy them. He wishes to stop smoking due to family pressure. He reports a previous unsuccessful attempt to stop smoking (See Table 76-1).
Alcohol: Alcohol use one drink per day
Drug Use: Not using drugs
Habits: He sleeps on average 7 hr per day. He does not exercise.
Home environment: He lives with his spouse and two children. The living environment is secure and supportive.
Education: He has a high school diploma.
Work: He works full time at a local convenience store.
Financial: His income is marginal, enough to buy only necessities.
Language: Native language is English
Marital Status: He is currently married. He is sexually active in a monogamous relationship.

■ Meds

Metformin 500 mg PO twice daily with meals

■ All

NKDA

■ ROS

Systemic: Feeling as well as can be expected, preoccupied with current illness, and feels tired
Otolaryngeal: Discoloration of teeth to yellow
Gastrointestinal: He reports polyphagia.
Genitourinary: Increased urinary frequency, polyuria
Endocrine: He reports polydipsia.

■ PE

Gen

Patient is alert and oriented and in no acute distress.

VS

BP 128/85, P 89, RR 20, T 98.7°F; Wt 125 kg, Ht 5'8"

Skin

No lesions noted, the skin showed no erythema, showed no ecchymosis, and the skin of the extremities was not cold. Yellow nail plates noted on his hands.

HEENT

Normocephalic with no lesions. Pupils are equal, round, and reactive to light and accommodation. The extraocular movements were normal. The pupils were normal. The conjunctiva exhibited no abnormalities. Visual fields normal. Nares appear normal. Mouth is well hydrated and without lesions. Mucous membranes are moist. Posterior pharynx is clear of any exudate or lesions. Canal and tympanic membranes are clear. Tympanic membrane was normal. No hearing abnormalities.

Neck/Lymph Nodes

No malformation or tenderness noted, no tenderness on palpation of the back, no muscle spasm of the back, and no costovertebral angle tenderness.

Lungs/Thorax

Clear to auscultation bilaterally with no rales, rhonchi, or wheezing. Respiration rhythm and depth was normal, the chest was normal to percussion, the lungs were clear to auscultation, and no decrease in breath sounds was heard. No rales/crackles were heard.

Breasts

Clinical breast exam: normal

CV

JVP was normal. Heart rate and rhythm normal. Heart sounds normal, no S₃ was heard, and no S₄ was heard. No murmurs were heard. Arterial pulses were equal bilaterally and normal. Edema not present. Veins unremarkable.

Abd

Soft, nontender, and nondistended, with normal bowel sounds. No palpable masses or hepatosplenomegaly. The abdomen was normal on visual inspection. Abdominal auscultation revealed no abnormalities. Abdominal percussion was normal. Abdominal palpation revealed no abnormalities and no direct suprapubic tenderness. No rebound tenderness in the abdomen. The liver was normal to palpation and not enlarged. The spleen was normal to palpation.

Genit/Rect

Urinary system: normal.
Rectal exam: The prostate was normal.

MS/Ext

No cyanosis, clubbing, lesions, or edema. Pulses normal bilaterally. Foot exam performed including visual inspection and sensory exam with monofilament and pulse exam. No abnormalities detected.

Neuro

Cranial nerves II–XII are grossly intact. No focal deficits and oriented to time, place, and person. The cranial nerves were normal. Gait and stance were normal. The reflexes were normal. No peripheral neuropathy was noted.

■ Labs

Na 142 mEq/L	Hgb 15.8 g/dL	T. chol 160 mg/dL
K 4.3 mEq/L	Hct 46.4%	Triglycerides 190 mg/dL
Cl 98 mEq/L	RBC $5.06 \times 10^6/\text{mm}^3$	HDL-C 32 mg/dL
CO ₂ 21 mEq/L	MCV 92 μm^3	VLDL-C 38 mg/dL
BUN 15 mg/dL	Plt $186 \times 10^3/\text{mm}^3$	LDL-C 90 mg/dL
SCr 0.8 mg/dL	WBC $6.4 \times 10^3/\text{mm}^3$	ALT (SGPT) 18 IU/L
Glu 190 mg/dL		AST (SGOT) 12 IU/L
HgA _{1c} = 7.5%		Bilirubin, Total
		0.3 mg/dL
		Alkaline Phosphatase
		40 IU/L

■ Assessment

1. Nicotine dependence, currently untreated and desiring to quit smoking
2. Type 2 diabetes mellitus without complications, uncontrolled
3. Stage 1 hypertension, untreated
4. Dyslipidemia, untreated
5. Obesity, unchanged status since last encounter

TABLE 76-1 Stages of Change and Smoking Cessation Counseling

Stage of Change	Patient's Mindset	Response
Precontemplation	Not interested in quitting, fails to recognize smoking as a problem	Provide concise and relevant statement about why the smoker should think about quitting smoking
Contemplation	Smoking is a problem and might consider quitting	State that there is good evidence that cigarette smoke and secondhand smoke are dangerous. Encourage smoker to quit
Preparation	Cigarette smoking is problematic and now ready to think about quitting	Discuss options for treatment—both pharmacotherapeutic and nonpharmacotherapeutic
Action	Motivated to quit, instituting a plan with an identified quit date and developing a plan to cope with stressors	Encourage quit attempt, offer to be a resource during the quit attempt, and praise former smokers' abstinent status
Maintenance	Former smokers who have not smoked for a period of time	Great job staying quit. Continued cessation is a positive move in becoming healthier

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of nicotine dependence?
- 1.b. What additional information is needed to fully assess this patient's nicotine dependence?

Assess the Information

- 2.a. Assess the severity of nicotine dependence based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for nicotine dependence might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating nicotine dependence?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's nicotine dependence and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Evaluate current literature concerning the use of quitlines to enhance quit-smoking attempts. What is the status of quitlines in your state? In a one-page paper, explain how you could educate your community about quitlines.
2. Describe the legal status (both federal and state) and explain the role of commercially used e-cigarettes.

CLINICAL PEARL

Blood glucose levels may increase while using the nicotine patch because of an impaired cellular response to insulin. This effect is less pronounced than the endocrine changes seen with cigarette

smoking. Moreover, a person using the nicotine patch is not exposed to all the toxins in cigarette smoke.

REFERENCES

1. Siu AL; U.S. Preventive Services Task Force. Behavioral and pharmacotherapy interventions for tobacco smoking cessation in adults, including pregnant women: U.S. Preventive Services Task Force Recommendation Statement. *Ann Intern Med* 2015;163(8):622–634.
2. Stead LF, Koilpillai P, Lancaster T. Additional behavioural support as an adjunct to pharmacotherapy for smoking cessation. *Cochrane Database Syst Rev* 2015, Issue 10.
3. American Diabetes Association. 8. Pharmacologic approaches to glycaemic treatment: Standards of Medical Care in Diabetes—2018. *Diabetes Care* 2018;41(Suppl 1):S73–S85.
4. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/ APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71:e13–e115.
5. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129(25 Suppl 2):S1–S45.
6. Centers for Disease Control and Prevention. Current cigarette smoking among adults—United States, 2016. *MMWR Morb Mortal Wkly Rep* 2018;67(2):53–59.
7. Fiore MC, Jaén CR, Baker TB, et al. Treating tobacco use and dependence: 2008 update. Content last reviewed October 2018. Agency for Healthcare Research and Quality, Rockville, MD. <http://www.ahrq.gov/professionals/clinicians-providers/guidelines-recommendations/tobacco/index.html>. Accessed April 1, 2019.
8. Cahill K, Stevens S, Perera R, Lancaster T. Pharmacological interventions for smoking cessation: an overview and network meta-analysis. *Cochrane Database Syst Rev* 2013;(5):CD009329.
9. Anthenelli RM, Benowitz NL, West R, St Aubin L, McRae T, Lawrence D, et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. *Lancet* 2016;387:2507–2520.
10. Varenicline (Chantix) prescribing information. https://www.accessdata.fda.gov/drugsatfda_docs/label/2018/021928s045_046lbl.pdf. Accessed April 1, 2019.

77

SCHIZOPHRENIA

A Thousand Worms Inside My Body Level I

Leigh Anne Nelson, PharmD, BCPP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the target symptoms of schizophrenia.
- Manage an acutely psychotic patient with appropriate pharmacotherapy.

- Identify and manage the adverse effects of antipsychotics.
- Discuss the role of second-generation antipsychotics in the treatment of schizophrenia.

PATIENT PRESENTATION

■ Chief Complaint

"I want to see my lawyer."

■ HPI

This is the first inpatient admission for Anita Gonzalez, a 32-year-old Hispanic woman who was brought to the psychiatric hospital by the police. Earlier today she was brought to the crisis center by a friend in her apartment building after the landlord threatened to call the police since Anita was creating a disturbance. At the crisis center, Anita became increasingly agitated and suspicious; the police were called; however, she left before being evaluated by staff. The patient apparently has been delusional and believes people sneak into her room at night when she is asleep and place a thousand worms inside her body. She also believes that she is being raped by passing men on the street. She is quite preoccupied about having massive wealth. She claims to have bought some gold and left it at the grocery store. She believes that her ideas have been given to a Cuban communist who has had plastic surgery to look like her and is using her identification to take possession of all of her property. She states that she is having difficulty getting her property back.

Apparently, the precipitating event today that eventually resulted in her hospitalization was that she created a disturbance at a local fast-food restaurant, claiming that she owned it. Because of the disturbance, police were called, and she subsequently was sent here on an order of protective custody. According to the patient, she bought a hamburger and sat down to eat it, and for some reason, somebody called the police and charged her with illegal trespassing. She claims that 6 years ago she was raped by a relative of a sister and broke her hip in the process. She states that her feet were cut off because she would not do what her impostors wanted her to do, and her feet were subsequently sent back to her from Central America and were reattached.

Her speech is quite rambling. She speaks of having been part of an experiment in Monterey, Mexico, in which 38 eggs were taken from her body, and children were produced from them and then killed by the government. She claims that she has worms in her that are the type that kill dogs and horses and says that they have been put there by the government. She also claims that at one time she had transmitters in her backbone and that it took 3 years to have them taken out by the government. She claims to have had surgery in the past, and the surgeon did not know what he was doing and took out her gallbladder and put it in the intestines where it exploded. The patient also states that on one occasion, a physician was removing the snakes from her abdominal cavity, and the snakes killed the doctor and a nurse. She also claims that she worked as a surgeon herself before 1963.

■ Past Psychiatric History

Denies any prior hospitalization for mental health problems

■ PMH

Gallbladder surgery (cholecystectomy) 2 months ago

Hypertension × 2 years

No record of her ever being raped or having a broken hip is found.

No further medical history is known.

■ Family Psychiatric History

The patient claims that her alleged family is not really her family and that she is not sure who her family is.

■ SH

Divorced; heterosexual; lives in an apartment alone; employment history unknown

Denies any illicit drug or alcohol use. Smokes two packs of cigarettes per day.

■ Meds

Lisinopril 20 mg PO once daily

■ All

Penicillin (rash)

■ Mental Status Examination

The patient is a woman of Hispanic ethnicity, modestly dressed, with some disarray. She is morbidly obese. Her hair is black and unwashed. She is alert, oriented, and in no acute distress. Her speech is clear, constant, and pressured, with many grandiose delusions and illogical thoughts. She is quite rambling, going from one subject to the other without interruption. Her affect is mood-congruent, her mood is euphoric, and there is a marked degree of grandiosity. Her thought processes are quite illogical, with markedly delusional thinking. There is no current evidence of auditory hallucinations, and she denies visual hallucinations. She denies any suicidal or homicidal ideation, but she is quite verbal and pressured in her thought content, verbalizing a great deal about the things that have been taken away from her illegally by people impersonating her. She has marked delusional symptoms with paranoid ideation prominent. Her memory (immediate, recent, and remote) is fair. Her cognition and concentration are adequate. Her intellectual functioning is within the average range. Insight and judgment are markedly impaired.

■ ROS

Reports occasional GI upset; complains that worms are inside her stomach; otherwise negative

■ PE

VS

BP 140/85 mm Hg, P 80 bpm, RR 17, T 37.1°C; Wt 97 kg; Ht 5'3"

Skin

Scratches on both hands

HEENT

PERRLA; EOMI; fundi benign; throat and ears clear; TMs intact

Neck

Supple, no nodes; normal thyroid

Lungs

CTA & P

CV

RRR, normal S₁ and S₂

Abd

(+) BS, nontender

Ext

Full ROM, pulses 2+ bilaterally

Neuro

A&O × 3; reflexes symmetric; toes downgoing; normal gait; normal strength; sensation intact; CNs II–XII intact

■ Labs

See Tables 77-1 to 77-3.

■ Assessment

- Schizophrenia, acute episode
- Hypertension
- Obesity
- Tobacco use disorder

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of an acute episode of schizophrenia?
- What additional information is needed to fully assess this patient's schizophrenia?

Assess the Information

- Assess the severity of the acute episode of schizophrenia based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient's schizophrenia?
- What feasible pharmacotherapeutic alternatives are available for treating schizophrenia?

TABLE 77-2 Antipsychotic Treatment Recommendations

Recommendation	APA 2004 (commentary 2009)	PORT 2009	NICE 2014
First episode	SGA	SGA (except clozapine and olanzapine), FGA	SGA, FGA (in combination with psychological interventions)
Second episode	SGA, FGA, clozapine	SGA, FGA	SGA, FGA (only if an SGA has already been tried)

FGA = first-generation antipsychotics, SGA = second-generation antipsychotics.

- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- What information should be provided to the patient to enhance medication adherence, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

- Perform a literature search regarding the metabolic side-effect risk associated with the second-generation antipsychotics. Which ones are more likely to cause weight gain, hyperglycemia,

TABLE 77-1 Laboratory Values

Na 140 mEq/L	Hgb 14.6 g/dL	WBC $11.0 \times 10^3/\text{mm}^3$	AST 34 IU/L	Ca 9.6 mg/dL
K 3.9 mEq/L	Hct 45.7%	Neutros 66%	ALT 22 IU/L	Phos 5.1 mg/dL
Cl 104 mEq/L	RBC $4.7 \times 10^6/\text{mm}^3$	Lymphs 24%	Alk phos 89 IU/L	TSH 4.5 $\mu\text{IU/mL}$
CO ₂ 22 mEq/L	MCV 90.2 μm^3	Monos 8%	GGT 38 IU/L	RPR negative
BUN 19 mg/dL	MCH 31 pg	Eos 1%	T. bili 0.9 mg/dL	Serum alcohol <10 mg/dL
SCr 1.1 mg/dL	MCHC 34.5 g/dL	Basos 1%	Alb 3.6 g/dL	Urine pregnancy (–)
Glu 100 mg/dL		Plt $232 \times 10^3/\text{mm}^3$	T. chol 208 mg/dL	
Urinalysis		Urine drug screen		
Color yellow		Amphetamines (–)		
Appearance slightly cloudy		Barbiturates (–)		
Glucose (–)		Benzodiazepines (–)		
Bilirubin (–)		Cannabinoids (–)		
Ketones, trace		Cocaine (–)		
SG 1.025		Opiates (–)		
Blood (–)		PCP (–)		
pH 6.0		Oxycodone (–)		
Protein (–)				
Nitrites (–)				
Leukocyte esterase (–)				

TABLE 77-3 Recommended Monitoring Parameters for Patients Receiving SGA

Parameter	Baseline	4 Weeks	8 Weeks	12 Weeks	Quarterly	Annually
Personal/family history	X					
Weight (BMI)	X	X	X	X	X	
Blood pressure	X			X		X
Fasting plasma glucose	X			X		X
Fasting lipid profile	X			X		X
Waist circumference	X					X
Tardive dyskinesia evaluation	X					X
Hematologic profile ^a	X					X
CV status ^b	X					X

^aDesirable for all SGA but required for clozapine according to a strict monitoring protocol.

^bECG if > 40 years or h/o CV disease.

and hyperlipidemia? Which ones are less likely to cause weight gain, hyperglycemia, and hyperlipidemia?

2. Perform a literature search regarding QTc changes with both first- and second-generation antipsychotics. Which antipsychotics are more likely to alter the QTc interval?
3. Review the pharmacoeconomic literature for the second-generation antipsychotics. For your geographic area, compare costs for the average daily (monthly for long-acting injectable [LAI]) doses of haloperidol (oral and LAI formulation), chlorpromazine (oral formulation), clozapine (oral and orally disintegrating formulation), olanzapine (oral and orally disintegrating formulation), risperidone (oral, orally disintegrating, and LAI formulation), aripiprazole (oral, orally disintegrating, and LAI formulation), quetiapine and extended-release quetiapine (oral formulation), ziprasidone (oral formulation), paliperidone (oral and LAI formulation), asenapine (sublingual formulation), lurasidone (oral formulation), brexpiprazole (oral formulation), and cariprazine (oral formulation).

CLINICAL PEARL

A benzodiazepine (eg, lorazepam) may be used during the initiation of an antipsychotic to minimize anxiety, agitation, or aggression secondary to psychosis and allow time for the antipsychotic to take effect. For management of acute agitation or aggression, the addition of a benzodiazepine may also allow lower dosages of the antipsychotic to be used and help prevent antipsychotic-induced side effects such as extrapyramidal symptoms (eg, dystonia).

REFERENCES

1. American Psychiatric Association. Schizophrenia spectrum and other psychotic disorders. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013:87–122.
2. Castle DJ, Buckley PF. Schizophrenia. 2nd ed. Oxford, UK: Oxford University Press; 2015.
3. Lehman AF, Lieberman JA, Dixon LB, et al. American Psychiatric Association Practice Guidelines; Work Group on Schizophrenia. Practice guideline for the treatment of patients with schizophrenia, 2nd ed. Am J Psychiatry 2004;161(2 Suppl):1–56.
4. Dixon LB, Perkins B, Calmas C. Guideline Watch (September 2009): practice guideline for the treatment of patients with schizophrenia. Psychiatry Online. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/schizophrenia-watch.pdf. Accessed November 12, 2018.
5. Buchanan RW, Kreyenbuhl J, Kelly DL, et al. The 2009 schizophrenia PORT psychopharmacological treatment recommendations and summary statements. Schizophr Bull 2010;36:71–93.
6. Hasan A, Falkai P, Wobrock T, et al. World Federation of Societies of Biological Psychiatry guidelines for biological treatment of schizophrenia, part 1: update on the acute treatment of schizophrenia and management of treatment resistance. World J Biol Psychiatry 2012;13(14):2–44.
7. National Institute for Health and Care Excellence. Psychosis and schizophrenia in adults: prevention and management. <https://www.nice.org.uk/guidance/cg178>. Accessed November 12, 2018.
8. Lieberman JA, Stroup TS, McEvoy JP, et al., for the Clinical Antipsychotic Trials of Intervention Effectiveness (CATIE) Investigators. Effectiveness of antipsychotic drugs in patients with chronic schizophrenia. N Engl J Med 2005;353:1209–1223.
9. American Diabetes Association, American Psychiatric Association, American Association of Clinical Endocrinologists, and North American Association for the Study of Obesity. Consensus development conference on antipsychotic drugs and obesity and diabetes. Diabetes Care 2004; 27:596–601.

78

MAJOR DEPRESSION

A Life Worth Living Level I

Katelynn Mayberry, PharmD

Brian L. Crabtree, PharmD, BCPP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs and symptoms of depression.
- Develop a pharmacotherapy plan for a patient with depression.
- Compare side-effect profiles of various antidepressant drugs.
- Discuss pharmacoeconomic considerations when selecting antidepressant therapy.

PATIENT PRESENTATION

■ Chief Complaint

“I don’t know if I can handle this anymore.”

■ **HPI**

Geneva Flowers is a 41-year-old Caucasian woman who is referred by her family physician to an outpatient mental health clinic. She complains of feeling down and sad, with crying spells, trouble sleeping, increased eating, impaired concentration, and fatigue. She has not worked in over 2 months and has used up her vacation and sick leave from work.

She went through treatment for alcohol use disorder over 1 year ago. Things were going fairly well for her after her treatment, and she remarried approximately 8 months ago. Arguments with her teenage sons about family issues and past incidents have made her increasingly depressed over the past few months. Her older son, 17, moved out to live with his father. Her younger son, 12, moved to live with his paternal grandparents.

She divorced the boys' father after approximately 10 years of marriage when she discovered that he was having an affair with another woman. She left her second husband after approximately 2 years because of problems involving his children that caused increasing conflict with her then-husband. Without a second income in the household, she accumulated large credit card debts. She began drinking and soon developed a pattern of using alcohol to relieve stress. Just before entering alcoholism treatment, there was a sexual fondling incident involving one of her son's friends while the friend was visiting her son at her house, but she was amnesic for the incident the next day. Her present husband, her third, has been supportive of her, but she feels guilty about her failed previous marriages and her sons, worries about her debt, and has become more despondent. She has taken a leave of absence from her job as an administrative assistant at an elementary school.

The patient sought treatment for depression 3 months ago from her family physician, who prescribed mirtazapine. Her spirits have not improved, and she says the medication made her gain weight. Because of vague references that the physician believed could possibly indicate suicidal ideas, she has been referred for psychiatric evaluation.

■ **PMH**

Childhood illnesses: she has had all the usual childhood illnesses.

She was hospitalized at age 3 for bacterial meningitis but knows of no residual effects.

Adult illnesses: no current nonpsychiatric adult illnesses; no previous psychiatric treatment

Trauma: fractured arm due to bicycle accident at age 9, otherwise unremarkable

Surgeries: Hx childbirth by C-section; tonsillectomy at age 6

Travel: no significant travel history

Diet: no dietary restrictions. Despite not having much of an appetite, reports eating more since taking mirtazapine

Exercise: no regular exercise program

Immunizations: no personal records of childhood vaccinations; had tetanus booster 9 years ago; does not remember when she had most recent influenza immunization

■ **FH**

Father is deceased, had coronary artery disease, but ultimately died of colon cancer. Mother has well-controlled HTN. A sister has depression and anxiety and takes antidepressant medication (patient does not know its name). A second sister committed suicide.

■ **SH**

High school graduate; works as an administrative assistant but on leave for approximately 2 months. Married approximately 8 months, two previous divorces. Lived with husband and sons

until sons moved out in the past few weeks. Health insurance is through the school district where she is employed; includes adjusted copay on prescriptions. Reports heavy credit card debt. Attended church regularly in the past (Protestant), but not recently. Attends AA weekly.

Denies drinking alcohol since chemical dependence treatment. Denies smoking. Drinks three to four cups of caffeinated coffee per day; usually drinks iced tea with evening meal; drinks colas as leisure beverage. Used marijuana a few times after high school, denies use in more than 10 years; denies present or past use of other illicit substances.

■ **Meds**

Mirtazapine 30 mg PO QHS (started on mirtazapine 15 mg PO QHS approximately 3 months ago)

St. John's wort 300 mg PO TID for the past 2 weeks at suggestion of husband (purchased at health food store)

OTC antihistamines and decongestants for colds or allergies; none in recent months

■ **All**

NKDA

■ **ROS**

General appearance: pt c/o feeling tired much of the time

HEENT: wears contact lenses; no tinnitus, ear pain, or discharge; no c/o nasal congestion; Hx of dental repair for caries

Chest: no Hx of asthma or other lung disease

CV: reports occasional feelings of "pounding heart"; no Hx of heart disease

GI: reports infrequent constipation; takes MOM PRN; has gained 9 lb in last 2 months

GU: has regular menses; LMP ended a week ago

Neuromuscular: occasional headaches, worse over the past few months; no syncope, vertigo, weakness or paralysis, numbness or tingling

Skin: no complaints

■ **PE**

Performed by nurse practitioner

Gen

Overweight WF, slightly unkempt

VS

BP 132/78 mm Hg, P 88 bpm, RR 22, T 36.9°C; Wt 187 lb, Ht 5'8"

Skin

Normal skin, hair, and nails

HEENT

PERRLA; EOM intact, no nystagmus. Fundus—disks sharp, no retinopathy; no nasal discharge or nasal polyps; TMs gray and shiny bilaterally; minor accumulation of cerumen.

Neck/Lymph Nodes

Supple without thyromegaly or lymphadenopathy

Chest/Lungs

Frequent sighing during examination, but no tachypnea or SOB; chest CTA

Breasts

No masses, tenderness, or discharge

Heart

RRR without murmur

Abd

Soft, nontender; (+) BS; no organomegaly

Genit/Rect

Deferred

Ext

Unremarkable

Neuro

CN: EOM intact, no nystagmus, no weakness of facial or tongue muscles. Casual gait normal. Finger-to-nose normal.

Motor: normal symmetric grip strength. DTRs 2+ and equal.

Sensory: intact bilaterally.

Mental Status

When seen in the clinic, the patient is pale and appears moderately overweight, dressed in casual slacks and sweater. Grooming is fair and without makeup. She speaks slowly, often not responding to questions for approximately 30 seconds before beginning answers. She describes depressed mood and lack of energy and says she feels no pleasure in life. Her husband is good to her, but she feels everyone else she loves has left her. She has no social contacts other than occasional visits by her parents. She spends most of her time in bed. She feels worthless and blames herself for her problems. She feels particularly anguished about the incident with her son's friend even though she does not remember it. She is often anxious and worries about the future. She wonders if her sons love her and if they will ever return. She worries how she will repay her financial debts. Her speech is logical, coherent, and goal-oriented. She denies suicidal intent but says the future seems dim to her, and she wonders sometimes if life is worth living. She admits she sometimes wishes she could just go to sleep and not wake up. She denies hallucinations. Paranoid delusions, FOI, IOR, and LOA are absent. There is no dysarthria or anomia.

Labs (Collected 11:45 AM)

Na 139 mEq/L	Hgb 14.0 g/dL	AST 34 IU/L
K 4.2 mEq/L	Hct 46.2%	ALT 42 IU/L
Cl 102 mEq/L	MCV 92 μm^3	GGT 38 IU/L
CO ₂ 24 mEq/L	MCH 29 pg	T. bili 0.8 mg/dL
BUN 12 mg/dL	Plt $234 \times 10^3/\text{mm}^3$	T. prot 7.0 g/dL
SCr 0.9 mg/dL	WBC $7.3 \times 10^3/\text{mm}^3$	Alb 4.4 g/dL
Glu 98 mg/dL	Segs 49%	CK 57 IU/L
Ca 9.5 mg/dL	Bands 1%	T ₄ 8.6 mcg/dL
Mg 1.7 mEq/L	Lymphs 42%	T ₃ uptake 29%
Uric acid 4.0 mg/dL	Monos 2%	TSH 2.8 mIU/L
	Eos 6%	

UA

Glucose (–); ketones (–); pH 5.8; SG 1.016; bilirubin (–); WBC 1/hpf; protein (–), amorphous—rare; epithelial cells 1/hpf; color yellow; blood (–), RBC 0/hpf; mucus—rare; bacteria—rare; casts 0/lpf; appearance clear

Assessment

1. Major depressive disorder, single episode, with melancholic features
2. Drug-drug interactions with St. John's wort

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of depression?
- 1.b. What additional information is needed to fully assess this patient's depression?

Assess the Information

- 2.a. Assess the severity of depression based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for depression might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's depression?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's depression and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE: ALTERNATIVE THERAPY

Mrs Flowers understands that she must stop the St. John's wort she has been taking because of an interaction with her prescribed mirtazapine, but she wonders if it would have been helpful if she had started it when she first began feeling depressed. See Section 19 in this Casebook for questions about the use of St. John's wort for treatment of depression.

SELF-STUDY ASSIGNMENTS

1. The selective serotonin reuptake inhibitor (SSRI) antidepressants are commonly used and have the same serotonin reuptake pharmacology; contrast the agents in this class, considering relative side effects, dosing, and drug interactions.
2. Compare other antidepressants with SSRIs with regard to adverse effects and relative advantages and disadvantages.

3. Discuss the role of combination drug therapy in the treatment of depression, including the use of drugs not usually classified as antidepressants.
4. Review the medical literature and evaluate the scientific evidence for the efficacy of St. John's wort in the treatment of depression.

CLINICAL PEARL

Although SSRIs are of one pharmacologic class, they are not of one chemical class. Therefore, failure to respond to one SSRI does not reliably predict failure to respond to others.

REFERENCES

1. American Psychiatric Association. Depressive disorders. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Washington, DC: American Psychiatric Association; 2013:155–188.
2. Teter CJ, Kando JC, Wells BG. Chapter 68, Major depressive disorder. In: DiPiro JT, Talbert RL, Yee GC, et al, eds. Pharmacotherapy: A Pathophysiologic Approach. 10th ed. New York, NY: McGraw-Hill; 2017:1047–1066.
3. Cuijpers P, Dekker J, Hollon SD, Anderson G. Adding psychotherapy to pharmacotherapy in the treatment of depressive disorders in adults: a meta-analysis. *J Clin Psychiatry* 2009;70:1219–1229.
4. Linde K, Kriston L, Rucker G, et al. Efficacy and acceptability of pharmacological treatments for depressive disorders in primary care: systematic review and network meta-analysis. *Ann Fam Med* 2015;13:69–79.
5. Hoffelt C, Gross T. A review of significant pharmacokinetic drug interactions with antidepressants and their management. *Ment Health Clin* 2016;6:35–41.
6. Perry PJ. Pharmacotherapy for major depression with melancholic features: relative efficacy of tricyclic versus selective serotonin reuptake inhibitor antidepressants. *J Affect Disord* 1996;39:1–6.
7. Bishop JR, Stevenson JM, Burghardt KJ. Pharmacogenetics in mental health. In: Johnson JA, Ellingrod VL, Kroetz DL, Kuo GM, eds. Pharmacogenomics: Application to Patient Care. 3rd ed. Lenexa, KS: American College of Clinical Pharmacy; 2015:115–134.
8. U.S. Food and Drug Administration. FDA approves new nasal spray medication for treatment-resistant depression; available only at a certified doctor's office or clinic. U. S. Food and Drug Administration, 2019. <https://www.fda.gov/news-events/press-announcements/fda-approves-new-nasal-spray-medication-treatment-resistant-depression-available-only-certified>. Accessed May 1, 2019.

79

BIPOLAR DISORDER

Up All Night Level II

Jason M. Noel, PharmD, BCPP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Given a description of a patient case, identify and assess the symptoms of an acute episode of bipolar disorder.
- Recommend appropriate pharmacotherapy for patients with acute mania.

- Generate parameters for monitoring mood stabilizer and/or antipsychotic therapy for bipolar disorder.
- Identify the pharmacotherapeutic options for treating the subtypes of bipolar disorder.

PATIENT PRESENTATION

■ Chief Complaint

"I am trying to keep the evil spirits away!"

■ HPI

Tyler Clemens is a 28-year-old man who brought by the police to the crisis center for an emergency evaluation. According to neighbors who called the police, the patient has been acting increasingly strange. The lights in the house are left on all night, and loud music is played at all hours. Last evening, he dug a trench around his front yard with an electric lawn edger and filled it with various herbal plants. This evening, he hung wreaths and horseshoes on his front door and threw many of his belongings into his yard and the street. When approached by neighbors, he apparently began screaming and preaching at them. When the police arrived, they found the patient standing naked on the dining room table in his front yard preaching. When the police approached, he began throwing garlic cloves at them and screaming, "I refuse to let you all curse me in my own home." He became increasingly hostile during the arrest shouting, "You can't do this—I have rights!" He then tried to bite one of the officers.

■ PMH

Manic episodes first occurred while he was in college, leading to psychiatric admissions at ages 21 and 23 for acute mania. Patient was treated with haloperidol and lithium, with adequate response and discharged on both occasions after about a month. Adherence to outpatient treatment has been inconsistent, with several documented missed appointments and prescription refills.

He also receives outpatient treatment for migraine headaches and shift work disorder.

■ Patient Interview

Patient is disheveled with pungent body odor. He is pacing the room, waving his hands in the air and preaching in an elated, loud, sing-song voice. He is wearing a dirty T-shirt and jeans. When asked how he felt, he stated, "Playful, with intense clarity, sharp, spiffy, and clean." He then became hostile and angry, insisting that he be discharged before sunrise or he would "be tormented by the demons forever." He claims to have witnessed spirits that attached themselves to various people and that now control their thoughts and actions. He spoke in long run-on sentences with many political, religious, and sexual references. He was very difficult to interrupt. For example, at one point he stated, "Can't you see, or are you an idiot?! I am being persecuted by the evil spirits I must stop them now and if you don't get that, you're an idiot."

When asked about his sleep, he angrily replied, "Would you sleep at a time like this? If I sleep, this whole town will be taken over! I cannot allow that to happen." The patient stated that he has not been eating and has not taken his lithium in several days because, "Lithium is of the ground, the underworld. The Lord will sustain me." When his interviewers challenged him on these beliefs, he suspected them of being part of plot to undermine his mission. When told that he might need to be in the hospital so we can help him with his problems, he screamed, "You can't help me! You're nonbelievers."

■ Abnormal Involuntary Movements

Excessive eye blinking and mild grimacing; unclear whether abnormal (patient states this is the “demon blood trying to take over my body”). He is bothered by it in that to him, it represents his “sinful nature.”

■ FH

Father has a history of depression; paternal grandmother was placed in an “asylum” for hysteria secondary to childbirth. Mother and brother have type 2 diabetes.

■ SH

Recently fired from his job as a nursing assistant at a local hospital, where he worked the night shift on a “7 on/7 off” schedule. Patient states that he drinks “only occasionally,” but he was noted to be intoxicated, with a BAC 0.14%, on a previous admission.

■ Meds

Haloperidol 5 mg PO daily

Lithium carbonate 600 mg PO twice daily

Acetaminophen/butalbital/caffeine two tablets PO as needed for headaches

Modafinil 200 mg PO at 9 PM for shift work disorder

■ All

NKDA

■ ROS

Migraine headaches about twice a month, no aura, (+) nausea and photophobia. Occasional GI upset with no clear relationship to meals or time of day; frequent loose stools.

■ PE

VS

BP 118/73 mm Hg, P 83 bpm, RR 16, T 37.1°C; Wt 94 kg, Ht 5'2"

HEENT

PERRLA; EOMI; fundi benign; throat and ears clear; TMs intact; rapid eye blinking and facial grimacing (may indicate early tardive dyskinesia)

Skin

Psoriasis evident on both elbows

Neck

Supple, bite mark, no nodes

Lungs

CTA & P

CV

RRR; S₁, S₂ normal; no MRG

Abd

(+) BS, nontender

Ext

Full ROM, pulses 2+ bilaterally

Neuro

A&O × 3; reflexes symmetric; toes downgoing; normal gait; normal strength; sensation intact; CNs II–XII intact

■ Labs

Na 141 mEq/L	Hgb 14.6 g/dL	WBC 12.0 × 10 ³ /mm ³	AST 32 IU/L
K 3.8 mEq/L	Hct 45.7%	Neutros 67%	ALT 21 IU/L
Cl 103 mEq/L	RBC 4.73 × 10 ⁶ /mm ³	Lymphs 23%	Alk phos 87 IU/L
CO ₂ 24 mEq/L	MCV 90.2 μm ³	Monos 7%	GGT 46 IU/L
BUN 19 mg/dL	MCH 31 pg	Eos 2%	T. bili 0.9 mg/dL
SCr 1.1 mg/dL	MCHC 34.4 g/dL	Basos 1%	Alb 3.7 g/dL
Glu 89 mg/dL	Plt 256 × 10 ³ /mm ³		TSH 4.1 μIU/mL
Ca 9.7 mg/dL			RPR: neg
Phos 5.3 mg/dL			Lithium 0.1 mEq/L

■ UA

Color yellow; appearance slightly cloudy; glucose (–), bili (–), ketones trace; SG 1.025, blood (–), pH 6.0, protein (–), nitrites (–), leukocyte esterase (–)

■ Assessment

1. Bipolar I disorder, current episode manic, with psychotic features
2. Nonadherence to prescribed medication
3. Possible adverse drug reactions
4. Migraine headaches
5. Shift work disorder

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of a manic episode?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of the current manic episode based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient's bipolar disorder?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating bipolar disorder?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Perform a literature search and explore the anticonvulsants that are not specifically approved for use in bipolar disorder (eg, gabapentin, oxcarbazepine, topiramate) in the treatment of bipolar disorder.
2. Standardized rating scales are often used in clinical trials and occasionally in clinical practice to quantify the presence of symptoms in people with psychiatric disorders and drug-induced movement disorders. Perform an Internet search for each of the following rating scales. For each scale, determine the symptom domains measured, the overall score ranges, and severity score cutoff ranges (eg, mild, moderate, severe).

Mania:

Young Mania Rating Scale (YMRS)

Depression:

Hamilton Depression Rating Scale (HAM-D)

Montgomery-Åsberg Depression Rating Scale (MADRS)

Movement Disorders:

Abnormal Involuntary Movement Scale (AIMS)

Dyskinesia Identification System: Condensed User Scale (DISCUS)

CLINICAL PEARL

When a patient admitted with acute mania is taking activating drugs such as antidepressants or stimulants, those drugs should be tapered and withdrawn. In some patients, antidepressants and stimulants may activate mania or increase the rate of cycling and, potentially, delay response to antimanic/mood stabilizers.

REFERENCES

1. American Psychiatric Association. Bipolar and related disorders [Internet]. In: Diagnostic and Statistical Manual of Mental Disorders. 5th ed. Arlington, VA: American Psychiatric Association; 2013. <http://dx.doi.org/10.1176/appi.books.9780890425596.dsm03>. Accessed April 27, 2019.
2. Suppes T, Dennehy E, Hirschfeld R, et al. The Texas implementation of medication algorithms. *J Clin Psychiatry* 2005;66:870–886.
3. Perlis R, Ostacher M, Patel J, et al. Predictors of recurrence in bipolar disorder: primary outcomes from the Systematic Treatment Enhancement Program for Bipolar Disorder (STEP-BD). *Am J Psychiatry* 2006;163:217–224.
4. Yatham L, Kennedy S, Parikh S, et al. Canadian Network for Mood and Anxiety Treatments (CANMAT) and International Society for Bipolar Disorders (ISBD) collaborative update of CANMAT guidelines for the management of patients with bipolar disorder: update 2013. *Bipolar Disorders* 2012;15(1):1–44.
5. National Institute for Health and Care Excellence. Bipolar disorder: assessment and management. NICE Clinical Guideline 2014. <https://www.nice.org.uk/guidance/cg185>. Accessed April 27, 2019.
6. Hirschfeld R, Bowden C, Gitlin M, et al. Practice guideline for the treatment of patients with bipolar disorder (revision). *Am J Psychiatry*

2002;159(4 Suppl):1–50. <http://dx.doi.org/10.1176/foc.1.1.64>. Accessed April 19, 2016.

7. Hirschfeld RM, Baker JD, Wozniak P, et al. The safety and early efficacy of oral-loaded divalproex versus standard-titration divalproex, lithium, olanzapine, and placebo in the treatment of acute mania associated with bipolar disorder. *J Clin Psychiatry* 2003;64:841–846.
8. Calabrese JR, Sullivan JR, Bowden CL, et al. Rash in multicenter trials of lamotrigine in mood disorders: clinical relevance and management. *J Clin Psychiatry* 2002;63:1012–1019.
9. Sachs GS, Nierenberg AA, Calabrese JR, et al. Effectiveness of adjunctive antidepressant treatment for bipolar depression. *N Engl J Med* 2007;356:1711–1722.
10. Goodwin GM, Bowden CL, Calabrese JR. A pooled analysis of 2 placebo-controlled 18-month trials of lamotrigine and lithium maintenance in bipolar I disorder. *J Clin Psychiatry* 2004;65:432–441.

80

GENERALIZED ANXIETY DISORDER

Nervous Nellie Level I

Sarah T. Melton, PharmD, BCPP, BCACP, FASCP

Cynthia K. Kirkwood, PharmD, BCPP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify target symptoms associated with generalized anxiety disorder (GAD).
- Construct pharmacotherapeutic goals for GAD.
- Recommend appropriate pharmacotherapy and duration of treatment for the acute, continuation, and maintenance phases of GAD.
- Develop a care plan and coordinate care with other healthcare providers.
- Develop a monitoring plan for a patient treated for GAD based on the treatment regimen.

PATIENT PRESENTATION

Chief Complaint

“I am so worried all the time that I can’t do anything else. I need some serious help.”

HPI

Ned Johnson is a 55-year-old man who presents to his family physician with complaints of severe irritability, feelings of “being on edge,” and inability to fall asleep at night. He states that he always feels tense and exhausted with constant muscle tension and body aches. He was laid off from his job as a manager at a building supply store 9 months ago. Over the past year, he has had difficulty

concentrating when filling out job application forms, and his mind often “goes blank” when talking with people. His irritability has impacted his relationship with his wife, and he is worried that she will leave him. He has developed frequent abdominal pain and daily episodes of diarrhea. He constantly worries about the lack of financial resources, his wife losing her job, and his relationship with his wife. He is afraid that he and his wife will lose their house and cars. He states that he cannot control his constant worry and that his anxiety has increased in intensity over the past 6 months. He denies having obsessive-compulsive thoughts or behaviors or symptoms of panic disorder or social anxiety disorder. He recently went to the emergency department (ED) because he was so worried about multiple issues in his life that he could not eat or sleep for 2 days. He was given an IM injection of hydroxyzine and sent home with a prescription for hydroxyzine 25-mg capsules orally four times daily as needed for anxiety. He stopped this medication last week secondary to constipation and decreased urinary flow. He tried kava kava from an herbal store a few months ago. It was not effective, and he discontinued it after 2 weeks because of severe abdominal pain.

■ PMH

Records from the family physician indicate frequent visits over the past 9 months for insomnia, headaches, abdominal pain, and diarrhea. He has been treated with buspirone for anxiety for the past 6 months. He has a history of peptic ulcer disease treated with ranitidine 6 years ago. He is currently taking omeprazole as needed for dyspepsia.

After a recent visit to the ED, he was prescribed hydroxyzine to be taken up four times daily as needed for anxiety.

Past psychiatric history is significant for episode of depression and alcohol use disorder when he was 33 years old, which were treated with fluoxetine. He took the fluoxetine for 2 weeks and discontinued it secondary to insomnia.

■ FH

Father, 80-year-old, on “nerve medication” for several years. Mother deceased at age 73 from breast cancer with history of major depression and alcohol use disorder. Patient has one sister who was treated with multiple medications in the past for anxiety and depression, and was treated for sedative, hypnotic, or anxiolytic use disorder 5 years ago.

■ SH

Married for 25 years; no children; high school graduate; past nicotine use disorder (quit 5 years ago with 40 pack-year history); alcohol use disorder (has been sober for 10 years and attends Alcoholics Anonymous on a weekly basis); little exercise because of time constraints; drinks four to five cups of coffee per day and three to four Mountain Dew soft drinks throughout the day. He admits to occasional cannabis use when his anxiety is “out of control.” (Note: cannabis is not legal for medical or recreational use in his state.) He does not have any prescription drug coverage at this time.

■ Meds

Buspirone 30 mg PO BID for anxiety
Phenylephrine 10 mg PO QID PRN for nasal congestion
Loperamide 2 mg PO Q 6 H PRN for diarrhea
Calcium carbonate chewable tablets 750 mg BID PRN for indigestion
Omeprazole 20 mg PO daily PRN for dyspepsia

■ All

Sulfa (hives); codeine (nausea)

■ ROS

Positive for paresthesia, headaches and mild diaphoresis; negative for dizziness, palpitations, SOB, chest pain

■ PE

Gen

Anxious, well-groomed man sitting on examination table; cooperative; oriented $\times 3$

VS

BP 125/85 mm Hg, P 98 bpm, RR 18, T 36.5°C; Wt 90 kg, Ht 5'11"

Skin

Clammy; no rashes, lesions, or track marks

HEENT

EOMI; PERRLA; fundi benign; ear and nose clear; dentition intact; tonsils 1+

Neck/Lymph Nodes

Supple, no lymphadenopathy; thyroid symmetric and of normal size

Lungs/Chest

Symmetric chest wall movement; BS equal bilaterally; no rub; clear to A&P

CV

RRR, normal S₁ and S₂, no MRG

Abd

Symmetric; NTND; normal BS; no organomegaly or masses

Genit/Rect

Deferred

MS/Ext

Average frame; normal bones, joints, and muscles

Neuro

CNs II–XII intact; motor and sensory grossly normal; coordination intact

MSE

Appearance and behavior: well groomed, fair eye contact, wringing hands, and bouncing legs

Speech: well spoken and coherent with normal rate and rhythm

Mood: anxious, worried about everything in his life, and concerned that he is very sick

Affect: full

Thought processes: linear, logical, and goal-directed

Thought content: negative for suicidal or homicidal ideations, obsessions/compulsions, delusions, or hallucinations

Memory: 3/3 at 0 minutes, 2/3 at 5 minutes; spelled “world” backward

Abstractions: good

Judgment: good by testing

Insight: fair

Score on Hamilton Anxiety Scale = 34 points (see Appendix A)

■ Labs

Na 142 mEq/L	Hgb 14.0 g/dL
K 4.3 mEq/L	Hct 38%
Cl 105 mEq/L	TSH 4.1 mIU/L
CO ₂ 28 mEq/L	AST 29 IU/L
BUN 15 mg/dL	ALT 28 IU/L
SCr 1.0 mg/dL	Alk phos 23 IU/L
Glu 80 mg/dL	Vit D 25-OH 51 ng/mL

■ ECG

NSR; rate 88 bpm

■ Urine Toxicology Screen

Positive for 9-carboxy-THC

■ Assessment

1. GAD treated and uncontrolled with buspirone
2. Substance use disorder
3. Nasal congestion self-treated with phenylephrine PRN
4. Diarrhea self-treated with loperamide PRN
5. Dyspepsia treated with omeprazole PRN and calcium carbonate PRN

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence or severity of GAD?
- 1.b. What additional information is needed to fully assess this patient's GAD?

Assess the Information

- 2.a. Assess the severity of GAD based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for GAD might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating GAD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the optimal plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE: ALTERNATIVE THERAPY

Mr Johnson is still worried about the side effects of prescription drugs to treat his anxiety and whether he will be able to afford them. He states that he has read a lot of information about kava that "it really works for anxiety." Mr Johnson says, "Maybe I was just using a bad product last time I tried it and that's why it didn't help much and hurt my stomach. Should I get a better product and try it again?" Please see Section 19 of this Casebook for questions about the use of kava kava for the treatment of GAD.

■ SELF-STUDY ASSIGNMENTS

1. Perform a literature search to review the role of pregabalin in the treatment of GAD. Write a summary of the controlled trials that evaluated the use of pregabalin in GAD as monotherapy.
2. Individuals with GAD may misuse alcohol, cannabis, or other substances in an effort to ameliorate their anxiety. Review and summarize the recommendations put forth by the International Psychopharmacology Algorithm Project on treating patients with GAD and a history of or current substance use disorder.
3. Many patients with mental illness do not have prescription drug insurance coverage, and this impacts the choice of pharmacotherapy. Using this case example, go to a Web-based pharmacy discount site or patient assistance program and document how you would go about helping this patient obtain a first-line agent that he otherwise would not be able to afford (eg, escitalopram, duloxetine, venlafaxine extended-release capsules).

CLINICAL PEARL

With effective pharmacotherapy available for the acute and long-term therapy of GAD, the treatment goal for anxiety is remission. Many patients exhibit treatment response but still have anxiety symptoms and social and functional impairment. Remission is a more rigorous treatment goal that requires a HAM-A score of ≤ 7 or reduction of at least 70% in baseline levels of symptoms.

REFERENCES

1. Hamilton M. Hamilton Anxiety Scale. In: Guy W, ed. ECDEU Assessment Manual for Psychopharmacology. Rockville, MD: U.S. Department of Health, Education, and Welfare; 1976:193–198.
2. Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Pharmacology. *J Psychopharmacol* 2014;28:403–439.
3. Davidson JR, Zhang W, Connor KM, et al. A psychopharmacological treatment algorithm for generalized anxiety disorder (GAD). *J Psychopharmacol* 2010;24:3–26.
4. Zhang Y, Huang G, Yang S, Liang W, Zhang L, Wang C. Duloxetine in treating generalized anxiety disorder in adults: a meta-analysis of published randomized, double-blind, placebo-controlled trials. *Asia Pac Psychiatry* 2016;8(3):215–225.

5. Bandelow B, Sher L, Bunevicius R, et al. Guidelines for the pharmacological treatment of anxiety disorders, obsessive-compulsive disorder and posttraumatic stress disorder in primary care. *Int J Psychiatry Clin Pract* 2012;16:77–84.
6. Frampton JE. Pregabalin: a review of its use in adults with generalized anxiety disorder. *CNS Drugs* 2014;28:835–854.
7. Evoy KE, Morrison MD, Saklad SR. Abuse and misuse of pregabalin and gabapentin. *Drugs* 2017;77(4):403–426.
8. Maneeton N, Maneeton B, Woottituk P, et al. Quetiapine monotherapy in acute treatment of generalized anxiety disorder: a systematic review and meta-analysis of randomized controlled trials. *Drug Des Devel Ther* 2016;10:259–276.
9. Sarris J, LaPorte E, Schweitzer I. Kava: a comprehensive review of efficacy, safety, and psychopharmacology. *Aust N Z J Psychiatry* 2011;45:27–35.

81

OBSESSIVE–COMPULSIVE DISORDER

It's Never Enough Level I

Lindsey Miller, PharmD, BCPP

Chris Paxos, PharmD, BCPP, BCPS, BCGP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify target symptoms associated with obsessive–compulsive disorder (OCD).
- Determine goals of pharmacotherapy for OCD.
- Develop an appropriate plan and duration of therapy for the management of OCD.
- Educate patients and consult with providers about the pharmacotherapy used for OCD.
- Develop a monitoring plan for a patient treated for OCD based on the treatment regimen.

PATIENT PRESENTATION

■ Chief Complaint

“I am going to lose my job—if I don’t stop!”

■ HPI

Makela Jones is a 34-year-old woman presenting to her primary care provider along with her husband. Her husband has become increasingly concerned about Makela’s behaviors at home, prompting the visit to her provider. Makela will not walk through any doorways before counting to ten, turning in a complete circle, then stepping three steps to the left and two to the right for fear that someone will be hurt if she fails in performing this ritual. Makela has stated, “No matter how much I try to ignore these compulsions, I must complete them! My coworkers are starting to talk about me.” The patient has been experiencing

a great deal of anxiety over the past several months, but it has become progressively worse since she was given a promotion at work approximately one month ago. At home, Makela will not allow her husband and daughter to eat until she has checked their food multiple times for signs of poisoning, yet this never seems to be enough. The patient states that her anxiety has risen to a level that she has never experienced before, and she no longer knows what to do. When asked about suicidal ideation, Makela says she has had fleeting thoughts of suicide but does not have a plan. She reports intrusive thoughts of running to the doorway during work meetings just to make sure she has performed her ritual and everyone is safe. She understands that these thoughts are irrational and wants them to go away. She is concerned because her thoughts and rituals consume 4–5 hours each day and have impeded her ability to complete her work and be “present” at home. She stopped preparing meals for her family because she has to check the ingredients so many times that dinner is never complete. She also reports checking the stove in multiples of three to feel some relief from the overwhelming anxiety that develops throughout the day from the intrusive thoughts and behavior. She states that she has tried to hide her ritual from her husband, but it has become so time-consuming and distressful that he has brought it to her attention. Her husband’s concern has only added to her anxiety.

■ PMH

G₂P₁A₁—normal spontaneous vaginal delivery

Overweight

Surgeries: Dental surgery in college

Trauma: Patient denies

Immunizations: Patient believes she is current with all vaccinations

■ PPH

No formal diagnoses, however, the patient recalls doing strange counting and checking rituals during childhood. She has always felt a need to “control things.”

■ FH

Father has a history of major depression and hypertension.

Mother has multiple sclerosis and major depression.

Older brother is a “perfectionist” and has to have everything “just right.”

■ SH

Married for 8 years with a 4-year-old daughter; bachelor degree in accounting and Masters of Business Administration and works full-time as the human resource manager for a local law firm; denies tobacco use but admits to occasional alcohol use. After her daughter was born, she had excessive worrying that the baby was being harmed by her breast milk, leading her to exclusively use formula to feed her starting at 2 weeks. She has commercial insurance coverage.

■ Meds

Prenatal vitamin, one tablet PO daily

Acetaminophen 500 mg PO PRN headache (patient uses one to two times per month)

Diphenhydramine 25 mg PO PRN insomnia (patient uses two times per month)

Previously took an oral contraceptive (medication name unknown) but has stopped it within the last several months.

■ All

Sulfa drugs (rash), kiwi and mango (rash)

■ ROS

Unremarkable except patient reports that she feels she is “under extreme duress” and cannot continue with these obsessions. Patient denies fatigue, change in appetite or sleep pattern, and crying spells, but she does express difficulty concentrating. No palpitations or dyspnea.

■ PE

Gen

Anxious, overweight woman sitting on examination table, cooperative, oriented × 3

VS

BP 112/67 mm Hg, P 92 bpm, RR 18, T 36.5°C; Wt 77.3 kg, Ht 5’7”

Skin

Hands are dry; no rashes, lesions, or track marks; nails and hair are normal.

HEENT

EOMI; PEERLA; fundi benign; ear and nose clear; dentition intact; tonsils 1+

Neck/Lymph Nodes

Supple, no lymphadenopathy; thyroid symmetric and of normal size

Lungs/Chest

Symmetric chest wall movement, BS equal bilaterally, no rub; clear to A&P

Breasts

Normal, expecting menstruation

CV

RRR, normal S₁ and S₂, no MRG

Abd

Symmetric; NT/ND; normal BS; no organomegaly or masses

Gyn

Deferred

MS/Ext

Large frame; normal bones, joints, muscles

Neuro

CNs II–XII intact, no nystagmus; motor and sensory grossly normal; coordination intact; no tremor; normal gait

MSE

Appearance and behavior: well groomed, poor eye contact

Speech: coherent, logical and goal-oriented

Mood: anxious, worried that she “will lose her job”

Affect: anxious

Thought processes: linear, logical, and goal-directed

Thought content: negative for suicidal or homicidal ideations; positive for obsessions about the well-being of others; compulsions including counting and performing rituals; denies delusions and hallucinations

Memory: 3/3 at 0 minutes, 3/3 at 5 minutes (ball, pencil, chair); spelled “world” backward

Abstractions: good

Judgment: good by testing

Insight: good

Score on Yale–Brown Obsessive Compulsive Scale = 33 points

■ Labs

Na 139 mEq/L

K 4.0 mEq/L

Cl 107 mEq/L

CO₂ 28 mEq/L

BUN 14 mg/dL

SCr 0.9 mg/dL

Glu 75 mg/dL

HCG negative

Hgb 15.0 g/dL

Hct 40%

WBC $6.3 \times 10^3/\text{mm}^3$

AST 30 IU/L

ALT 25 IU/L

Alk phos 42 IU/L

Albumin 3.9 g/dL

TSH 2.8 IU/L

■ ECG

NSR; QTc—460 milliseconds

■ Urine Toxicology Screen

Negative

■ Drug Levels

Acetaminophen 10 mcg/mL

■ Assessment

1. OCD, uncontrolled and untreated
2. Insomnia, managed with PRN medication
3. Headache, managed with PRN medication
4. Overweight, untreated

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of OCD?
- 1.b. What additional information is needed to fully assess this patient's OCD?

Assess the Information

- 2.a. Assess the severity of OCD based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for OCD might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating OCD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's OCD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTIONS

- When is a decrease in the Y-BOCS score considered clinically significant?
- If this patient had presented to the prescriber desiring to become pregnant after 6 months of pharmacotherapy, what would your recommendations be regarding pharmacotherapy?

■ SELF-STUDY ASSIGNMENTS

- Prepare a grid contrasting the pros and cons of each SSRI in the management of OCD.
- Perform a literature search and write a short paper on the treatment options used to augment antidepressant monotherapy in patients with OCD who have a partial response or are resistant to treatment.
- Visit the International OCD Foundation website and review the patient brochure “What you need to know about obsessive-compulsive disorder,” especially the section on children and teens with OCD.

CLINICAL PEARL

Higher dosages of antidepressant medication than those typically used for depression are often required to obtain antiobsessional effects. A response to pharmacotherapy may not occur until a therapeutic dose has been maintained for at least 10–12 weeks.

ACKNOWLEDGMENTS

This case is based on the patient case written for the 10th edition by Cynthia K. Kirkwood, PharmD, and Sarah T. Melton, PharmD.

REFERENCES

- Fineberg NA, Reghunandanan S, Simpson HB, et al. Obsessive-compulsive disorder (OCD): practical strategies for pharmacological and somatic treatment in adults. *Psychiatry Res* 2015;227:114–125.
- Rush AJ, First MB, Blacker D, eds. *Handbook of Psychiatric Measures*. 2nd ed. Washington, DC: American Psychiatric Publishing; 2008:547–549.
- Koran LM, Simpson HB. Guideline watch (March 2013): Practice guideline for the treatment of patients with obsessive-compulsive disorder. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd-watch.pdf. Accessed April 20, 2019.
- American Psychiatric Association. *Diagnostic and Statistical Manual of Mental Disorders*. 5th ed. Washington DC: 2013.
- American Psychiatric Association. Practice guideline for the treatment of patients with obsessive-compulsive disorder. Arlington, VA: American Psychiatric Association; 2007. http://psychiatryonline.org/pb/assets/raw/sitewide/practice_guidelines/guidelines/ocd.pdf. Accessed February 19, 2019.
- Katzman MA, Bleau P, Blier P, et al. Canadian clinical practice guidelines for the management of anxiety, posttraumatic stress and obsessive-compulsive disorders. *BMC Psychiatry* 2014;14(Suppl 1):S1.
- Fonseka TM, Richter MA, Müller DJ. Second generation antipsychotic-induced obsessive-compulsive symptoms in schizophrenia: a review of the experimental literature. *Curr Psychiatry Rep* 2014;16(11):510.
- Alwan S, Friedman JM, Chambers C. Safety of selective serotonin reuptake inhibitors in pregnancy: review of current evidence. *CNS Drugs* 2016;30:499–515.
- Orsolini L, Bellantuono C. Serotonin reuptake inhibitors and breastfeeding: a systematic review. *Hum Psychopharmacol Clin Exp* 2015; 30:4–20.
- Baldwin DS, Anderson IM, Nutt DJ, et al. Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder, and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. *J Psychopharmacol* 2014;28:403–439.

82

INSOMNIA

Restless Nights and the Blue Moon Level II

Suzanne C. Harris, PharmD, BCPP, CPP

Rachel Marie E. Salas, MD, MedHP, FAAN

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the psychosocial, disease-related, and drug-induced causes of insomnia.
- Explain the impact of poor medication adherence on chronic illnesses.
- Design a therapeutic plan for the treatment of insomnia.
- Educate a patient regarding nonpharmacologic treatments for insomnia.

PATIENT PRESENTATION

■ Chief Complaint

“I can’t sleep.”

■ HPI

Judy Miller is a 55-year-old woman who is referred by her family medicine physician to a pharmacotherapy clinic for medication

therapy management for insomnia. She receives help paying for her medications from medication assistance programs. She has been experiencing long-standing insomnia for approximately 9 months. Specifically, she is having difficulty falling and staying asleep at least four to five times during the week, and then sleeps all day on Sunday. Ms Miller is currently taking temazepam 30 mg daily at bedtime that was recently increased from 15 mg. She said that she started taking valerian root 600 mg 6 weeks ago based on a friend's recommendation but does not feel any benefit. Additionally, she has been experiencing vivid dreams that she attributes to the valerian root. When she had health insurance, she started cognitive behavioral therapy for insomnia (CBT-I); however, when she lost her insurance, she was only able to complete six out of eight sessions, with last session over 4 weeks ago. She endorsed moderate benefit from CBT-I but still complained of residual symptoms. She is also experiencing depression due to not having any employment and a stress of a partner who recently moved in with her because he could not pay his apartment rent. Her most recent Patient Health Questionnaire-9 (PHQ-9) result was 20. She admits to being intermittently nonadherent and missing doses of scheduled inhaled medications for COPD and sertraline, olanzapine/fluoxetine, and valerian root one to two times per week. She reports that she is no longer able to see her psychiatrist due to cost of the visits.

■ PMH

Insomnia for many years
COPD
Depression
Migraine headaches
GERD
Allergic rhinitis

■ FH

Mother is alive and well and lives nearby. Father died of MI at age 65.

■ SH

She is in a new relationship with her partner who recently moved in due to his own financial difficulties. Unemployed, leading to stress at home to pay bills but receives some money from her mother. She smokes approximately five cigarettes per day now but has smoked up to two ppd in the past. She does not drink alcohol. She sees a deacon at her church for counseling regularly. She receives medication assistance for several of her medications from a local agency.

■ Medications

Temazepam 30 mg PO QHS PRN sleep
Fluticasone/salmeterol DPI 250/50 one inhalation twice daily
Albuterol MDI two puffs Q 6 H PRN SOB
Tiotropium Handihaler one inhalation daily
Sertraline 200 mg PO Q AM
Olanzapine 3 mg/fluoxetine 25 mg PO Q PM
Sumatriptan 100 mg PO PRN for migraine
Atenolol 25 mg PO Q AM for migraine prophylaxis
Ibuprofen 200–400 mg PO Q 6 H PRN for pain/migraines
Tramadol 50 mg PO Q 6 H PRN for pain/migraines
Hydrocodone 5 mg/acetaminophen 325 mg PO Q 4-6H PRN for pain/migraines
Dexlansoprazole 60 mg PO Q AM
Pseudoephedrine 30 mg PO Q 6 H PRN allergies
Valerian root supplement 600 mg PO QHS

■ Allergies

NKDA

■ ROS

Patient reports that she does not sleep at all during the week and only sleeps on Sunday. She also reports some improvement in sleep hygiene based on previous recommendations, such as avoiding eating too close to bedtime and long naps, but she continues to exercise in late evenings and reads and watches television in bed. She has cut back to three cups of coffee throughout the day, reduced from six to eight cups of coffee throughout the day. She continues to experience difficulty going to sleep and staying asleep and reports having had this problem for several years. Additionally, the temazepam does not seem to help much. Due to reports of awakening during the night and risk factors for obstructive sleep apnea (ie, postmenopausal, family history of OSA, GERD, increased BMI), her primary care provider ordered a sleep study that was normal other than some minimal snoring. She has a long history of depression but has never been hospitalized. She currently is not experiencing a “blue mood” or any thoughts of suicide, and her PHQ-9 score today is 20. She has been prescribed sertraline, which she tolerates well, and the combination of olanzapine and fluoxetine to help with her depressive symptoms. Her COPD is secondary to a long history of smoking but is currently controlled on tiotropium, fluticasone/salmeterol, and albuterol PRN. She has experienced migraine headaches for several years and uses sumatriptan and ibuprofen PRN and atenolol daily for prophylaxis. She sometimes uses tramadol and hydrocodone/acetaminophen as well for migraines. Her GERD, which she experiences when she is supine, is currently controlled on dexlansoprazole. She has runny nose, congestion, and itchy eyes in the spring.

■ PE (from the last visit with her PCP)

Gen

Obese (per BMI criteria), black woman in NAD who looks her stated age

VS

BP 125/80 mm Hg, P 76 BPM, RR 16, T 37°C; Wt 105 kg; Ht 5'6"

Skin

Normal skin color and turgor, no lesions noted

HEENT

Normocephalic, PERRLA, EOMI

Neck/Lymph Nodes

Supple with normal size thyroid, (–) adenopathy

Lungs

CTA bilaterally

CV

Normal S₁, S₂; no MRG

Abd

NTND, no HSM

Genit/Rect

Deferred. Last PAP smear was WNL 6 months ago.

Ext

No C/C/E; normal muscle bulk and tone; muscle strength 5/5 and equal in all extremities; normal pulses

Neuro

Oriented to person, place, and time; CN II–XII intact; Mini-Mental State Examination results: 30/30

Labs

Na 141 mEq/L	Hgb 13 g/dL	AST 36 IU/L	Lipid panel
K 3.9 mEq/L	Hct 38%	ALT 32 IU/L	T. chol 215 mg/dL
Cl 105 mEq/L	RBC 4.4 ×	LDH 112 IU/L	LDL 100 mg/dL
CO ₂ 26 mEq/L	10 ⁶ /mm ³	GGT 47 IU/L	HDL 45 mg/dL
BUN 12 mg/dL	Plt 236 ×	T. bili 0.6 mg/dL	TG 160 mg/dL
SCr 0.7 mg/dL	10 ³ /mm ³	T. prot 7.1 g/dL	
Glu 85 mg/dL	WBC 6.8 ×	Alb 4.0 g/dL	
	10 ³ /mm ³		
	TSH 3.9 mIU/L		
	Free T ₄		
	4.0 ng/dL		

Assessment

1. Insomnia, with poor sleep hygiene and sleep environment, that is inadequately managed with long-term use of benzodiazepine
2. Depression evidenced by PHQ-9 score of 20
3. Allergic rhinitis and pseudoephedrine use
4. Migraine headache
5. GERD
6. Health maintenance and nonadherence to medication
7. Multiple stressors and poor access to healthcare

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of insomnia?
- 1.b. What additional information is needed to fully assess this patient's insomnia?

Assess the Information

- 2.a. Assess the severity of insomnia based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for this patient?
- 3.b. What nonpharmacologic therapies might be useful for this patient's insomnia?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's insomnia?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's insomnia and other drug therapy problems. Include specific drugs, dosage form, dose, schedule, and durations of therapy.

- 3.e. What alternatives would be appropriate if the initial therapy fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. Which clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE: ALTERNATIVE THERAPY

Ms Miller states she knows her neighbor had suggested that using a melatonin product would help her be able to stay asleep. She would like to learn about if that is a good option to help keep her from waking up after she has fallen asleep. See Section 19 of this Casebook for questions about the use of melatonin to help manage insomnia.

SELF-STUDY ASSIGNMENTS

1. Discuss pharmacist's interventions that can improve medication adherence.
2. Explain important monitoring parameters for patients receiving atypical antipsychotics.

CLINICAL PEARL

Patients with underlying depression frequently have insomnia, and poor medication adherence to antidepressants can exacerbate sleep disorders.

ACKNOWLEDGMENTS

This case is based on the patient case written for the 10th edition by Mollie Ashe Scott, PharmD, and Amy M. Lugo, PharmD.

REFERENCES

1. Qaseem A, Kansagara D, Forcica MA, et al. Management of chronic insomnia disorder in adults: a clinical practice guideline from the American College of Physicians. *Ann Intern Med* 2016;165(2):125–133.
2. Maness DL, Khan M. Nonpharmacologic management of chronic insomnia. *Am Fam Physician* 2015;92:1058–1064.
3. Sateia MJ, Buysse DJ, Krystal AD, et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine Clinical Practice Guideline. *J Clin Sleep Med* 2017;13(2):307–349.
4. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel. American Geriatrics Society 2015 updated beers criteria for potentially inappropriate medication use in older adults. The American Geriatrics Society 2015 Beers Criteria Update Expert Panel *J Am Geriatr Soc* 2015;63:2227–2246.

5. U.S. Food and Drug Administration. Postmarket drug safety information for patients and providers. Sleep disorder (sedative-hypnotic) drug information. <https://www.fda.gov/drugs/postmarket-drug-safety-information-patients-and-providers/sleep-disorder-sedative-hypnotic-drug-information>. Accessed January 1, 2020.
6. U.S. Food and Drug Administration. FDA Drug Safety Communication: FDA warns of next-day impairment with sleep aid Lunesta (eszopiclone) and lowers recommended dose. <https://www.fda.gov/drugs/drug-safety-and-availability/fda-drug-safety-communication-fda-warns-next-day-impairment-sleep-aid-lunesta-eszopiclone-and-lowers>. Accessed January 1, 2020.
7. Schroeck JL, Ford J, Conway EL, et al. Review of safety and efficacy of sleep medicines in older adults. *Clin Ther* 2016;38(11):2340–2372.
8. Cleare A, Pariante CM, Young AH, et al. Evidence-based guidelines for treating depressive disorders with antidepressants: a revision of the 2008 British Association for Psychopharmacology guidelines. *J Psychopharmacol* 2015;29(5):459–525.
9. Kripke DF, Langer RD, Kline LE. Hypnotics' association with mortality or cancer: a matched cohort study. *BMJ Open* 2012. doi:10.1136/bmjopen-2012-000850.
10. Finan PH, Richards JM, Gamaldo CE, et al. Validation of a wireless, self-application, ambulatory electroencephalographic sleep monitoring device in healthy volunteers. *J Clin Sleep Med* 2016;12(11):1443–1451.

This page intentionally left blank

SECTION 8

ENDOCRINOLOGIC DISORDERS

83

TYPE 1 DIABETES MELLITUS AND KETOACIDOSIS

Disconnected Level II

Holly S. Divine, PharmD, BCACP, BCGP, CDE, FAPhA

Carrie L. Isaacs, PharmD, CDE, MLDE

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize signs and symptoms of diabetic ketoacidosis (DKA).
- Determine laboratory parameters for the diagnosis and monitoring of DKA.
- Identify anticipated fluid and electrolyte abnormalities associated with DKA and their treatment.
- Recommend appropriate insulin therapy for treating DKA.
- Identify therapeutic decision points in DKA treatment and provide parameters for altering therapy at those points.

PATIENT PRESENTATION

■ Chief Complaint

"I felt weak and nauseated during softball practice. I checked my blood glucose and it read HI" (blood glucose >600 mg/dL).

■ HPI

Mary McGee is a 21-year-old woman with a history of type 1 diabetes, diagnosed 3 years ago. She is a college senior at the local university where she also plays softball. She started using an insulin pump approximately 6 months ago.

She noticed she was unusually tired and short of breath at the beginning of her practice and then began feeling weak and nauseated. She was also very thirsty during practice. Her softball coach said she seemed "a little confused." He advised her to check her blood glucose and it read "HI". She checked her insulin pump and noticed the pump had become disconnected. She is unsure how long she has been without insulin. She vomited two times since shortly thereafter and was transported via EMS to the ED.

■ PMH

Type 1 DM diagnosed 3 years ago. No prior hospitalizations for DKA or prior surgeries.

■ FH

Parents are alive and healthy. One twin sister who also has type 1 DM.

■ SH

College student; no tobacco, alcohol, or illicit drug use. Sexually active; in a monogamous relationship.

■ Meds

NovoLog 100 U/mL, per insulin pump

Basal rates:

0.6 U/hr 0000–0300

0.9 U/hr 0300–0700

0.8 U/hr 0700–1100

0.7 U/hr 1100–1730

0.8 U/hr 1730–0000

Correction factor: 1 U:40 mg/dL >120 mg/dL

Insulin:carbohydrate ratios:

1:10 insulin:carbohydrate before breakfast

1:15 insulin:carbohydrate before lunch and dinner

Glucagon injection kit, as needed

Ortho-Cyclen (35 mcg ethinyl estradiol/0.25 mg norgestimate) one tablet PO once daily × 3 years

■ Allergies

NKDA

■ ROS

Complaints of blurry vision, lethargy, shortness of breath, nausea, polyuria, and polydipsia. Denies constipation, diarrhea, and headache.

■ Physical Examination

Gen

WDWN Caucasian woman appearing her stated age, with deep respirations, ketones on her breath, and slurred speech; slightly confused, but responds appropriately to questions

VS

BP 101/72 mm Hg, P 123 bpm, RR 32, T 37.0°C; Wt 56 kg, Ht 5'6"; BMI 19.9 kg/m²

Skin

Unremarkable

HEENT

PERRLA, EOMI; mucous membranes are dry

Neck/Lymph Nodes

Supple without lymphadenopathy or thyromegaly

Lungs

CTA, Kussmaul respirations

CV S_1 and S_2 are normal without S_3 , S_4 , murmur or rub; RRR**Abd**

NT/ND

Genit/Rect

Deferred

MS/Ext

No edema, pulses 2+ throughout, mild calluses

NeuroA&O $\times$ 3; DTRs 2+ throughout; feet with normal sensation and vibration**Labs**

Na 136 mEq/L
K 4.8 mEq/L
Cl 101 mEq/L
 CO_2 10 mEq/L
BUN 23 mg/dL
SCr 1.4 mg/dL
Glu 479 mg/dL

WBC $15.0 \times 10^3/mm^3$
RBC $4.61 \times 10^6/mm^3$
Hgb 14.2 g/dL
Hct 40.7%
Platelets $239 \times 10^3/mm^3$
Ketones positive
hCG negative

ABG

pH 7.26; $PaCO_2$ 21 mm Hg; PaO_2 128 mm Hg; HCO_3^- 7.1 mEq/L;
 O_2 sat 97%

UA

(+) Ketones; (+) glucose

Chest X-Ray

Normal

ECG

Sinus tachycardia

Assessment

DKA precipitated by insulin deficiency

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence and severity of DKA?
- 1.b. What are the precipitating risk factors for DKA, and which of those risk factors are present in this patient?
- 1.c. What are the diagnostic criteria for DKA?

Assess the Information

- 2.a. What problems need to be addressed in DKA besides hyperglycemia?
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What therapeutic options are available to correct the metabolic derangements of DKA?
- 3.c. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's DKA and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient regarding prevention of future DKA?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcomes?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy. Specifically once DKA is resolved, identify the plan for conversion of IV insulin therapy to subcutaneous therapy.

SELF-STUDY ASSIGNMENTS

1. What does the ADA state about DKA and hyperosmolar hyperglycemic state (HHS) in patients with type 2 DM? Compare these two disorders with respect to prevention, precipitating causes, signs and symptoms, pathophysiology, and treatment.
2. Investigate other causes of DKA, such as illness, and write a sick day management plan for this patient.
3. How might the use of continuous glucose monitors (CGMs) be beneficial in patients with type 1 DM?
4. Review euglycemic DKA and its relationship to the sodium-glucose cotransporter-2 (SGLT2) inhibitor drug class.

CLINICAL PEARL

DKA is the second most common complication seen with insulin pump therapy. Young persons who have recurrent DKA should be evaluated for psychological problems, including eating disorders, as a potential contributing factor.

REFERENCES

1. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. *Diabetes Care* 2009;32:1335–1343.
2. Umpierrez G, Korytkowski M. Diabetic emergencies-ketoacidosis, hyperglycaemic hyperosmolar state and hypoglycemia. *Nat Rev Endocrinol* 2016;12:222–232.
3. Dingle HE, Slovis C. Diabetic ketoacidosis and hyperosmolar hyperglycemic syndrome management. *Emerg Med* 2018;50(8):161–171.
4. American Diabetes Association. Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019;42(Suppl 1):S1–S193.
5. American Association of Clinical Endocrinologists and American College of Endocrinology. Clinical practice guidelines for developing a diabetes mellitus comprehensive care plan—2015. *Endocr Pract* 2015;21(Suppl 1):1–87.

6. Duhon B, Attridge RL, Franco-Martinez AC, Maxwell PR, Hughes DW. Intravenous sodium bicarbonate therapy in severely acidotic diabetic ketoacidosis. *Ann Pharmacother* 2013;47:970–975.
7. Potti LG, Haines ST. Continuous subcutaneous insulin infusion therapy: a primer on insulin pumps. *J Am Pharm Assoc* 2009;49:e1–e17.
8. Scheiner G, Sobel RJ, Smith DE, et al. Insulin pump therapy: guidelines for successful outcomes. *Diabetes Educ* 2009;35(Suppl 2):29S–41S.
9. Beck J, Greenwood DA, Blanton L, et al; 2017 Standards Revision Task Force. 2017 national standards for diabetes self-management education and support. *Diabetes Care* 2017;40:1409–1419.

84

TYPE 2 DIABETES MELLITUS: NEW ONSET

The Candy Man Level II

Nicole C. Pezzino, PharmD, CDE, BCACP

Scott R. Drab, PharmD, CDE, BC-ADM

Deanne L. Hall, PharmD, CDE, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs, symptoms, and risk factors associated with type 2 diabetes mellitus (DM).
- Identify the comorbidities in type 2 DM associated with insulin resistance (metabolic syndrome).
- Compare the pharmacotherapeutic options in the management of type 2 DM including mechanism of action, contraindications, and side effects.
- Develop appropriate educational information for a patient regarding self-monitoring of blood glucose (SMBG).
- Design a patient-specific pharmacotherapeutic plan for the treatment and monitoring of type 2 DM.

PATIENT PRESENTATION

■ Chief Complaint

“My vision has been blurred lately and it seems to be getting worse.”

■ HPI

Alfonso Giuliani is a 68-year-old man who presents to his family physician’s office complaining of periodic blurred vision for the past month. He further complains of fatigue and lack of energy that prohibits him from working in his garden and participating in physical activity.

■ PMH

HTN × 18 years

Dyslipidemia × 8 years

Gouty arthritis × 16 years with complicated course of uric acid urolithiasis

Hypothyroidism × 15 years

Overweight × 25 years

■ FH

Diabetes present in mother. Immigrated to the United States with his mother and sister after their father died suddenly from unknown causes at age 45. One younger sibling died of breast cancer at age 48.

■ SH

Retired candy salesman, married × 46 years with three children and two grandchildren. No tobacco use. Drinks one to two glasses of homemade wine with meals. He reports adherence with his medications.

■ Meds

Lisinopril 20 mg PO once daily

Allopurinol 300 mg PO once daily

Levothyroxine 0.088 mg PO once daily

■ All

NKDA

■ ROS

Occasional polydipsia, polyphagia, fatigue, weakness, and blurred vision. Denies chest pain, dyspnea, tachycardia, dizziness or light-headedness on standing, tingling or numbness in extremities, leg cramps, peripheral edema, changes in bowel movements, GI bloating or pain, nausea or vomiting, urinary incontinence, or presence of skin lesions.

■ PE

Gen

The patient is a centrally obese, Caucasian man who appears to be restless and in mild distress.

VS

BP 124/76 mm Hg without orthostasis, P 80 bpm, RR 18, T 37.2°C; Wt 77 kg, Ht 66”; BMI 27.4 kg/m²

Skin

Dry with poor skin turgor; no ulcers or rash

HEENT

PERRLA; EOMI; TMs intact; no hemorrhages or exudates on fundoscopic examination; mucous membranes normal; nose and throat clear w/o exudates or lesions

Neck/Lymph Nodes

Supple; without lymphadenopathy, thyromegaly, or JVD

Lungs/Thorax

CTA

CV

RRR; normal S₁ and S₂; no S₃, S₄, rubs, murmurs, or bruits

Abd

Soft, NT, central obesity; normal BS; no organomegaly or distention

Genit/Rect

Normal external male genitalia

MS/Ext

Normal ROM and sensation; peripheral pulses 2+ throughout; no lesions, ulcers, or edema

Neuro

A&O × 3, CN II–XII intact; DTRs 2+ throughout; feet with normal vibratory and pinprick sensation (5.07/10 g monofilament)

Labs

Na 141 mEq/L	Ca 9.9 mg/dL	A1C 7.8%
K 4.0 mEq/L	Phos 3.2 mg/dL	<i>Fasting lipid profile</i>
Cl 96 mEq/L	AST 21 IU/L	T. chol 280 mg/dL
CO ₂ 22 mEq/L	ALT 15 IU/L	HDL 27 mg/dL
BUN 24 mg/dL	Alk phos 45 IU/L	LDL 193 mg/dL
SCr 1.1 mg/dL	T. bili 0.9 mg/dL	Trig 302 mg/dL
Random glu 202 mg/dL		

UA

(–) Ketones, (–) protein, (–) microalbuminuria

Assessment

1. Elevated random glucose and A1C, diagnostic for type 2 DM, new onset
2. Dyslipidemia requiring treatment
3. Overweight requiring lifestyle modifications
4. HTN apparently well controlled
5. Gouty arthritis; patient claims not to have had an acute attack in over 3 years; will obtain a uric acid level to evaluate
6. Hypothyroidism; will obtain a thyroid panel to evaluate
7. Preventative health; obtain current immunization status from provider

Clinical Course

The patient returned to clinic 3 days later for lab work, which revealed: TSH 1.8 mIU/L, free T₄ 1.2 ng/dL, and UA 1.2 mg/dL. Additionally, provider provided updated immunization status, which revealed up-to-date on all childhood vaccines, annual influenza and pneumococcal polysaccharide administered at 65 years old.

QUESTIONS**Collect Information**

- 1.a. What risk factors for type 2 DM are present in this patient?
- 1.b. What subjective and objective information indicates the presence of new-onset type 2 DM?
- 1.c. What information indicates the presence of insulin resistance?
- 1.d. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. Considering his other medical problems, what other treatment goals should be established?
- 3.c. What nonpharmacologic therapies might be useful in the management of this patient?
- 3.d. What feasible pharmacotherapeutic alternatives are available for treating type 2 DM?
- 3.e. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's diabetes and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.f. What changes in therapy would you recommend if your initial plan fails to achieve adequate glycemic control?

Implement the Care Plan

- 4.a. What information should be provided to the patient about diabetes and its treatment to enhance adherence, ensure successful therapy, minimize adverse effects, and prevent future complications?
- 4.b. How would you educate the patient regarding how and when to check his blood glucose?
- 4.c. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate glycemic efficacy and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.
- 5.c. The patient's physician suggested that he obtain a blood glucose meter for self-testing. What evidence supports SMBG, and what are the healthcare provider's responsibilities with respect to patients and SMBG?
- 5.d. Identify at least four potential situations in which the information provided by SMBG would be useful to patients and healthcare providers.
- 5.e. What factors should be considered in the selection of an appropriate blood glucose meter?

CLINICAL COURSE: ALTERNATIVE THERAPY

While discussing Mr Giuliani's diagnosis with him, he states that his neighbor with diabetes told him that she just follows her diabetic diet and takes cinnamon and something called "alip acid" and does not have to take any prescriptions for her blood sugar. He also says that he has read about fish oil being used for diabetes. Mr Giuliani asks if he should start any of those to help get his blood sugar under control. See Section 19 in this Casebook for questions about the use of fish oil, cinnamon, and alpha-lipoic acid for treatment of diabetes.

FOLLOW-UP QUESTIONS

1. What nonprescription products could be recommended for patients to use in treating hypoglycemic episodes?
2. List several potential sources of error in SMBG.

3. When starting patients on insulin, the use of combination oral antihyperglycemic agents and insulin offers several advantages over switching entirely to insulin:
 - (a) What are the advantages of adding insulin to existing therapies with oral agents?
 - (b) List an appropriate method of starting insulin therapy to adequately control fasting hyperglycemia in patients on combination oral agents.

■ SELF-STUDY ASSIGNMENTS

1. Describe how you would evaluate and monitor this patient's quality of life.
2. Characterize the relationship between insulin resistance and the risk for ASCVD.
3. Prepare a list of medications that have been associated with increasing blood glucose. Provide literature evidence on the strength of the association with each medication.
4. Review the literature and conduct a comparative review of the efficacy of inhaled insulin therapy relative to the insulin products commercially available for subcutaneous injection.

CLINICAL PEARL

Approximately 30.3 million Americans have diabetes, and approximately one-third are undiagnosed. An estimated 1.5 million Americans are newly diagnosed with diabetes every year, providing further evidence that diabetes is a major public health threat of epidemic proportions. Excess caloric intake, low physical activity, and increasing levels of obesity are the main contributors to the increased incidence.

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019;42(1 Suppl):S1–S193.
2. Bloomgarden ZT. Insulin resistance: current concepts. *Clin Ther* 1998;20:216–231.
3. American College of Endocrinology and American Association of Clinical Endocrinologists. Clinical practice guidelines for developing a diabetes mellitus comprehensive care plan—2015. *Endocr Pract* 2015;21(Suppl 1):1–87.
4. American College of Endocrinology and American Association of Clinical Endocrinologists. Consensus Statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the Comprehensive Type 2 Diabetes Management Algorithm—2019 Executive Summary. *Endocr Pract* 2019;25(1):69–100.
5. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018 November doi: 10.1016/j.jacc.2018.11.003.
6. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APHA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2018;138(17):e426–483.
7. Davies MJ, D'Alessio DA, Fradkin J, et al. Management of hyperglycemia in type 2 diabetes, 2018: a consensus report by the American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD). *Diabetes Care* 2018;41(12):2669–2701.
8. Cho TM, Wideman RD, Kieffer TJ. Clinical application of glucagon-like peptide 1 receptor agonists for the treatment of type 2 diabetes mellitus. *Endocrinol Metab* 2013;28:262–274.

85

TYPE 2 DIABETES MELLITUS: EXISTING DISEASE

Establishing Optimal Control Level II

Sharon S. Gatewood, PharmD, BCACP, FAPhA

Margaret A. Landis, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the goals of therapy for the treatment of type 2 diabetes mellitus (DM).
- Discuss the risk factors and comorbidities associated with type 2 DM.
- Compare options for drug therapy management of type 2 DM, including mechanisms of action, combination therapies, comorbidities, and patient-friendly treatment plans.
- Develop an individualized drug therapy management plan, including dosage regimens, therapeutic endpoints, and monitoring parameters.
- Provide patient education regarding medications and the importance of adhering to the treatment plan, monitoring the disease state, maintaining blood glucose control, and seeking advice from healthcare providers when necessary.

PATIENT PRESENTATION

■ Chief Complaint

“I have had diabetes for about six months and would like to have my blood sugar tested. I think that my blood sugar is running low because I have a terrible headache.”

■ HPI

Sarah Martin is a 45-year-old white woman who comes to the pharmacy for a diabetes education class taught by the pharmacist. She would like for the pharmacist to check her blood sugar before the class begins. She was diagnosed with type 2 DM about 6 months ago. She had been attempting to control her disease with diet and exercise, but had no success. Her physician started her on metformin 1000 mg twice daily with food about 3 months ago. She has gained 10 lb over the past year. She monitors her blood sugar once a day, and her results have ranged from 215 to 280 mg/dL. Her fasting blood sugars have averaged 200 mg/dL.

■ PMH

Type 2 DM × 6 months
HTN × 17 years
Bipolar disorder × 25 years
Dyslipidemia × 12 years
Morbid obesity × 20 years

FH

Father has a history of HTN, dyslipidemia, and bipolar disorder. Mother has a history of dyslipidemia and hypothyroidism. Brother has DM thought to be secondary to alcoholism.

SH

Has been married for 23 years. She has two children who are teenagers and one child in college. She works as a sales associate in the electronics department of a local mass merchandiser. She denies any use of tobacco products after stopping smoking 10 years ago, but does drink alcohol occasionally (three beers or glasses of wine per week).

Meds

Metformin 1000 mg PO BID with food
 Lisinopril 20 mg PO once daily
 Olanzapine 5 mg PO QHS
 Carbamazepine ER 200 mg PO BID
 Lorazepam 1 mg PO TID PRN (takes once a month)
 Fluoxetine 20 mg PO Q AM
 Pravastatin 40 mg PO once daily

All

Penicillin—hives

ROS

Complains of nocturia, polyuria, and polydipsia on a daily basis. Denies nausea, constipation, diarrhea, signs or symptoms of hypoglycemia, paresthesias, and dyspnea.

Physical Examination**Gen**

WDWN severely obese, white woman in NAD

VS

BP 154/90 mm Hg, P 98 bpm, RR 18, T 37.0°C; Wt 109 kg, Ht 5'8", waist circ 38"

HEENT

PERRLA, EOMI, R&L fundus exam without retinopathy

Neck/Lymph Nodes

No LAN

Lungs

CTA & P

CV

RRR, no m/r/g

Abd

NT/ND

Genit/Rect

Deferred

MS/Ext

Carotids, femorals, popliteals, and right dorsalis pedis pulses 2+ throughout; left dorsalis pedis 1+; feet show mild calluses on MTPs

Neuro

DTRs 2+ throughout, feet with normal sensation (5.07 monofilament) and vibration

Labs

Na 138 mEq/L	Ca 9.4 mg/dL	<i>Fasting lipid profile</i>
K 3.7 mEq/L	Phos 3.3 mg/dL	T. chol 244 mg/dL
Cl 103 mEq/L	AST 16 IU/L	LDL 141 mg/dL
CO ₂ 31 mEq/L	ALT 19 IU/L	HDL 58 mg/dL
BUN 16 mg/dL	Alk phos 62 IU/L	Trig 225 mg/dL
SCr 0.9 mg/dL	T. bili 0.4 mg/dL	TC/HDL ratio 4.2
Glu (random) 243 mg/dL	A1C 10.0%	

UA

1+ protein, (+) microalbuminuria

Assessment

The patient reports that she exercises at most once a week and her diet is difficult to maintain due to being busy with her children's schedules and having an erratic eating schedule at both work and home. Her glycemic control has worsened from an A1C of 8.9% 6 months ago. She has had a moderate weight gain of 10 lb over the past year. Her blood pressure and cholesterol are not at goal on the current drug therapy. Her bipolar disorder is controlled on the current drug therapy. When the patient is in a depression or manic phase, she tends to use food to "treat" the symptoms.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of uncontrolled diabetes?
- What additional information is needed to fully assess this patient?

Assess the Information

- Assess the severity of the diabetes based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient?
- What feasible pharmacotherapeutic alternatives are available for treating type 2 diabetes mellitus?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's diabetes and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Discuss the phenomenon known as the metabolic syndrome and the role that insulin resistance is postulated to play in its sequelae.
2. Explore and discuss the importance of monitoring postprandial blood glucose levels and its impact on overall glucose control, A1C levels, and progression of diabetes complications.
3. Research the various blood glucose monitors available, and compare, among available monitors, the features that meet the needs of individual patients and improve adherence to testing regimens.
4. Research new therapies for diabetes and discuss their potential role in the management of patients with type 2 DM.
5. Keep a food diary, including carbohydrate counting for each meal, and exercise log for 1 week. Evaluate and discuss your experience from the viewpoint of a patient with type 2 DM.
6. Investigate continuous blood glucose monitoring systems (CGMS) technology, and discuss the role of CGMS in a patient with type 2 DM.
7. Research and compare current insulin pumps in the market. Discuss the role of insulin pump therapy in a patient with type 2 DM and what patient characteristics make or eliminate the patient as an insulin pump candidate.

CLINICAL PEARL

Although metformin is considered the first-line therapy for a patient with type 2 DM, not all patients with type 2 DM are appropriate candidates for metformin. Metformin has several contraindications, and patients generally must have good renal, hepatic, cardiac, and respiratory function to be considered a candidate for metformin therapy. Thus, a thorough assessment of the patient's comorbid conditions must be made. Early initiation of insulin therapy in patients who do not meet target goals is recommended.

REFERENCES

1. American Diabetes Association. Standards of Medical Care in Diabetes—2019. *Diabetes Care* 2019;42(1 Suppl):S1–S187.
2. Grundy SM, Stone NJ, Bailey AL, et al. AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: executive summary: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *J Am Coll Cardiol* 2018 November doi: 10.1016/j.jacc.2018.11.003.
3. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary. *J Am Coll Cardiol* 2018 May;71(19):e127–e248.
4. Executive Summary: Guidelines (2013) for the management of overweight and obesity in adults. A report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Obesity* 2014 Jul;22(Suppl 2):S5–S39.

5. Burghardt KJ, Seyoum B, Mallisho A, et al. Atypical antipsychotics, insulin resistance and weight; a meta-analysis of healthy volunteer studies. *Prog Neuropsychopharmacol Biol Psychiatry* 2018 April 20;83:55–63.
6. Koski RR. Practical review of oral antihyperglycemic agents for type 2 diabetes mellitus. *Diabetes Educ* 2006;32(2):869–876.
7. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes, 2015: a patient-centered approach. Update to a position statement of the American Diabetes Association and the European Association for the Study of Diabetes. *Diabetes Care* 2015;38:140–149.
8. Jamerson K, Weber MA, Bakris GL, et al. Benazepril plus amlodipine or hydrochlorothiazide for hypertension in high-risk patients. *N Engl J Med* 2008;359:2417–2428.
9. Pepine CJ, Handberg EM, Cooper-DeHoff RM. A calcium antagonist vs a noncalcium antagonist hypertension treatment strategy for patients with coronary artery disease: the International Verapamil-Trandolapril Study (INVEST): a randomized control trial. *JAMA* 2003;290:2805–2816.
10. Edwards SJ, Smith CJ. Tolerability of atypical antipsychotics in the treatment of adults with schizophrenia or bipolar disorder: a mixed treatment comparison of randomized controlled trials. *Clin Ther* 2009;31:1345–1359.

86

HYPERTHYROIDISM: GRAVES DISEASE

Gland Central Level II

Kristine S. Schonder, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the signs, symptoms, and laboratory parameters associated with hyperthyroidism, and relate them to the pathophysiology of the disease.
- Select and justify appropriate patient-specific initial and follow-up pharmacotherapy for patients with hyperthyroidism.
- Develop a plan for monitoring the pharmacotherapy for hyperthyroidism.
- Provide appropriate education to patients receiving drug therapy for hyperthyroidism.

PATIENT PRESENTATION

Chief Complaint

“My heart feels like it is racing, and I feel jittery.”

HPI

Carrie Gibson is a 23-year-old woman who presents to her PCP with complaints of palpitations and a fine tremor. The palpitations started a few months ago and would come and go until the past week when they began occurring more frequently, almost daily. She denies CP.

TABLE 86-1 Lab Values

Na 140 mEq/L	Hgb 12.8 g/dL	RDW 10.2%	AST 14 IU/L	Total T ₄ 24 mcg/dL
K 4.1 mEq/L	Hct 38.4%	WBC $4.8 \times 10^3/\text{mm}^3$	ALT 16 IU/L	Free T ₄ 4 ng/dL
Cl 98 mEq/L	RBC $3.08 \times 10^6/\text{mm}^3$	Polys 72%	T. bili 0.2 mg/dL	TSH 0.02 mIU/L
CO ₂ 23 mEq/L	Plt $298 \times 10^3/\text{mm}^3$	Lymphs 27%	Amylase <30 IU/L	T ₃ resin uptake 35%
BUN 9 mg/dL	MCV 86.4 μm^3	Monos 1%	Ca 9.5 mg/dL	Total T ₃ 550 ng/dL
SCr 0.6 mg/dL	MCH 27.1 pg	Basos 2%	Mg 2.0 mEq/L	Free thyroxine index 28.7
Glu 78 mg/dL	MCHC 31.8 g/dL		Phos 3.7 mg/dL	Thyrotropin receptor antibody 1.8 IU/L (≤ 1.75 IU/L)

She reports that she began noticing a fine tremor approximately 3 weeks ago. She also reports loose stools and a 5-kg weight loss over the past 6 months, despite a good appetite and food intake. She feels hot all of the time and sweats a lot. She further states that she has been losing her hair recently and that she is more irritable than usual.

■ PMH

She has been healthy up to this point with no medical conditions. She reports having had “the flu” last November but states that she did not seek medical attention at that time.

■ FH

Father has HTN; mother had a history of Graves disease and passed away 1 year ago from breast CA at age 53. Her oldest sister is 32 years of age and has breast CA; she has two other sisters, ages 29 and 25, and one brother, age 27, all of whom are healthy. Her aunt (mother’s sister) and grandmother both had Graves disease.

■ SH

She smokes 1.5 ppd $\times$ 5 years and drinks alcohol socially on the weekends (“a few drinks on Fridays and Saturdays”).

■ Meds

Drospirenone/ethinyl estradiol PO daily

■ All

None

■ ROS

She reports no visual changes, CP, or dyspnea. She has occasional N/V/D.

■ Physical Examination

Gen

Patient is a thin, tanned WF in NAD. She appears anxious and has a fine motor tremor in her hands.

VS

BP 136/80 mm Hg, P 120 bpm, RR 18, T 38.1°C; Wt 48 kg, Ht 5’6”

Skin

Hair is fine and sparse in the temporal area.

HEENT

PERRLA, EOMI, (+) lid lag, no proptosis (no ophthalmoplegia) or periorbital edema

Neck/Lymph Nodes

Supple, (+) smooth, symmetrically enlarged thyroid (approximately 1.5 times the normal size), prominent pulsations in neck vessels

Lungs

CTA bilaterally, no wheezes or rales

Breasts

Nontender, no discharges, no palpable masses or nodes

CV

Regular rhythm, tachycardic without murmurs; (–) bruits

Abd

Soft, NT/ND; (+) hyperactive BS; no HSM or masses. Aortic pulsations palpable.

Genit/Rect

Denies frequency, urgency, hematuria, vaginal discharge or lesions; pelvic exam normal; guaiac (–) stool

Ext

Normal pulses bilaterally, no calf tenderness. No cyanosis. Fingernails and toenails are flaking. Thumbnails have prominent ridges.

Neuro

A&O $\times$ 3; fine tremor with outstretched hands; no asterixis; hyperreflexia at knees; no proximal muscle weakness

■ Labs

See Table 86-1.

■ ECG

NSR, with HR of 120 bpm

■ Assessment

A 23-year-old woman with small goiter, probable hyperthyroidism. Most likely cause is Graves disease.

QUESTIONS

Collect Information

1. What subjective and objective information indicates the presence of hyperthyroidism?

Assess the Information

- 2.a. Assess the severity of hyperthyroidism based on the subjective and objective information available.
- 2.b. Create a list of the patient’s drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating hyperthyroidism?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's hyperthyroidism and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement for the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient is started on the treatment you recommended and returns for a 6-month follow-up visit. She reports that she has noticed marked improvement in her symptoms. The palpitations and tremor have both resolved. She states that she missed her last menses and is concerned that she may be pregnant. The following vital signs and laboratory results are obtained:

VS: BP 124/70 mm Hg, P 88 bpm, RR 16, T 37.2°C

Hgb 12.5 g/dL	WBC $5.8 \times 10^3/\text{mm}^3$	AST 18 IU/L
Hct 37.5%	Polys 65%	ALT 16 IU/L
MCV 85.6 μm^3	Lymphs 30%	T. bili 0.2 mg/dL
MCH 26.5 pg	Monos 2%	Total T ₄ 14.2 mcg/dL
MCHC 30.9 g/dL	Basos 2%	TSH <0.17 mIU/L
RDW 9.4%	Basos 1%	hCG 2637 mIU/mL

FOLLOW-UP QUESTIONS

1. What changes to the patient's treatment for Graves disease, if any, would you suggest at this point?
2. What other interventions would you recommend for this patient?

SELF-STUDY ASSIGNMENTS

1. Develop a monitoring protocol for the pharmacotherapy of hyperthyroidism.
2. Design a systematic approach for a patient counseling technique for the drug therapy of hyperthyroidism.

CLINICAL PEARL

Ophthalmopathy associated with Graves disease can produce significant morbidity in patients and can cause blindness in severe cases that affect the optic nerve or cornea. Graves ophthalmopathy

is thought to be an autoimmune disorder mediated by autoreactive T lymphocytes and cytokine release. The most common symptoms include diplopia, photophobia, tearing, and pain. Correction of the underlying hyperthyroidism can improve symptoms of Graves ophthalmopathy in most cases. However, symptoms can temporarily worsen with radioactive iodine treatment, until the hyperthyroidism is corrected. Severe cases of Graves ophthalmopathy should be treated with systemic or intraocular glucocorticoids. Alternative therapies include orbital radiotherapy and other immunomodulating drugs, such as cyclosporine and rituximab. Surgery is reserved for the most severe cases or those refractory to steroids.

REFERENCES

1. Ross DS, Burch HB, Cooper DA, et al. 2016 American Thyroid Association guidelines for diagnosis and management of hyperthyroidism and other causes of thyrotoxicosis. *Thyroid* 2016;26(10):1343–1421.
2. De Leo S, Lee SY, Braverman LE. Hyperthyroidism. *Lancet* 2016;388(10047):906–918.
3. Alexander EK, Pearce EN, Brent GA, et al. 2017 guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017;27(3):315–389.
4. Wiersinga WM. Smoking and thyroid. *Clin Endocrinol* 2013;79:145–151.
5. Committee on Underserved Women, Committee on Obstetric Practice. Committee opinion no. 721: smoking cessation during pregnancy. *Obstet Gynecol* 2017;130(4):e200–e204.

87

HYPOTHYROIDISM

Trying to Have a Baby Is Making Me Tired!. Level II

Michael D. Katz, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs, symptoms, and associated complications of mild and overt hypothyroidism.
- Identify the goals of therapy for hypothyroidism.
- Develop an appropriate treatment and monitoring plan for thyroid replacement based on individual patient characteristics.
- Select an appropriate product for thyroid replacement therapy.
- Properly educate a patient taking thyroid replacement therapy.

PATIENT PRESENTATION

Chief Complaint

"We are trying so hard to have a baby. Maybe that's why I'm so tired all the time . . . too much pressure."

HPI

Vickie Greene is a 31-year-old African-American woman who presents with her husband Eric (age 33) to the endocrinology clinic after being referred by her OB-GYN based on the results of some recent blood work. The Greens have been trying to have a baby for almost 2 years, without Vickie becoming pregnant. The infertility workup done by the OB-GYN showed that Eric had a normal sperm count and sperm motility, and that Vickie had no anatomical abnormalities of her reproductive tract and no evidence of endometriosis. Vickie's serum sex hormone and gonadotropin levels were all normal. The couple is contemplating in vitro fertilization but wants to make sure that there are no hormone-related causes of her infertility. Vickie says that for the past few months she has felt increasingly fatigued, which she attributes to the stress of her unsuccessful attempts to become pregnant. She wonders if she is becoming depressed. She also notes that for the past few months, she has had more difficulty concentrating at work, and she has "gained a few pounds." Over the past 6 months, Vickie has noticed that her periods are a little heavier than normal and are somewhat more irregular. She notes that 2 years ago, she attended a local health fair that provided a variety of laboratory tests. The result of her TSH at that time was 4.2 mIU/L. Her PCP at that time felt that the TSH value was within the normal range and required no follow-up.

PMH

Infertility $\times$ 2 years
Iron deficiency anemia as a teenager

FH

Father, age 55, has mild COPD; mother, age 54, has type 2 DM, HTN; she has one sister, age 32, who has hypothyroidism. No history of sickle cell trait or disease.

SH

Married $\times$ 6 years, first marriage for both. No history of STDs. Works as an immigration attorney for a private firm. Social drinker in past but has not used alcohol since attempting to become pregnant; (–) tobacco or illicit drug use.

Meds

MiraLAX PO daily PRN constipation
Seasonale one PO daily (stopped 2 years ago)
FeSO₄ 300 mg PO daily
Calcium carbonate 500 mg PO twice daily
Acetaminophen 325–650 mg PO PRN headache, body aches

All

Skin rash from sulfa drug

ROS

(+) Fatigue that she attributes to stress, (+) occasional insomnia, (+) constipation relieved with MiraLAX; (+) occasional headaches relieved with nonaspirin pain reliever; (–) tinnitus, vertigo, or infections; (–) urinary symptoms; (+) dry skin

Physical Examination**Gen**

Well-appearing African-American woman in NAD

VS

BP 112/74 mm Hg, P 64 bpm, RR 12, T 36.8°C; Wt 62 kg, Ht 5'7"

Skin

Slightly dry-appearing skin; (–) rashes or lesions

HEENT

PERRLA, EOMI; (–) sinus tenderness; TMs appear normal

Neck/Lymph Nodes

(–) Thyroid nodules, possible slight thyroid enlargement; (–) lymphadenopathy, (–) carotid bruits

Lungs/Thorax

CTA

Breasts

(–) Lumps/masses

CV

RRR, normal S₁, S₂; (–) S₃ or S₄

Abd

NT/ND, (–) organomegaly

Neuro

A&O $\times$ 3; CN II–XII intact; DTRs 2+, symmetric

GU

Deferred given recent extensive w/u by OB-GYN

Labs (Fasting)

Na 138 mEq/L	Hgb 13.1 g/dL	Anti-TPO antibody +
K 4.2 mEq/L	Hct 39.2%	TSH 9.8 mIU/L
Cl 98 mEq/L	WBC $6.8 \times 10^3/\text{mm}^3$	Free T ₄ 0.72 ng/dL
CO ₂ 25 mEq/L	MCV 89 μm^3	T. chol 212 mg/dL
BUN 8 mg/dL	Ca 9.6 mg/dL	LDL chol 142 mg/dL
SCr 0.7 mg/dL	Mg 2.0 mEq/L	HDL chol 45 mg/dL
Glu 98 mg/dL	PO ₄ 3.8 mg/dL	TG 125 mg/dL
	Albumin 4.0 g/dL	
	AST 22 IU/L	
	ALT 19 IU/L	
	T. bili 0.4 mg/dL	
	Alk phos 54 IU/L	

Assessment

A 31-year-old woman with infertility, fatigue, other nonspecific symptoms, and an elevated TSH level, suggestive of hypothyroidism

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of hypothyroidism?
- What additional information is needed to fully assess this patient?

Assess the Information

- Assess the severity of this patient's hypothyroidism based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating hypothyroidism?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize the medication therapy for this patient's hypothyroidism and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTION

1. What changes in her thyroid therapy might be necessary if she does become pregnant?

■ SELF-STUDY ASSIGNMENTS

1. Review the effects of untreated hypothyroidism during pregnancy on both mother and baby.
2. Research information on the US bioequivalence testing of levothyroxine (LT₄) products. How does US bioequivalence testing of LT₄ products differ from that of other oral products? Does LT₄ bioequivalence ensure therapeutic equivalence? Is there a consensus regarding the substitution of LT₄ product?
3. Review the factors that may alter LT₄ dose requirements, including drug interactions.

CLINICAL PEARL

Pregnant women who are receiving LT₄ replacement must undergo monthly monitoring of the TSH level to ensure adequate replacement. The majority of such women will require an increase of their LT₄ dose during pregnancy to ensure adequate replacement for both mother and fetus.

REFERENCES

1. Aoki Y, Belin RM, Clickner R, Jeffries R, Phillips L, Mhafey KR. Serum TSH and total T4 in the United States population and their association with participant characteristics. National Health and Nutrition Examination Survey (NHANES 1999–2002). *Thyroid* 2007;17:1211–1223.
2. Canaris GJ, Manowitz NR, Mayor G, Ridgway EC. The Colorado thyroid disease prevalence study. *Arch Intern Med* 2000;160:526–534.
3. Stagnaro-Green A, Pearce E. Thyroid disorders in pregnancy. *Nat Rev Endocrinol* 2012;8:650–658.

4. Jonklaas J, Bianco AC, Bauer AJ, et al. Guidelines for the treatment of hypothyroidism: prepared by the American Thyroid Association Task Force on thyroid hormone replacement. *Thyroid* 2014;24:1670–1751.
5. Peeters RP. Subclinical hypothyroidism. *N Engl J Med* 2017;376:2556–2565.
6. Blakesley V, Awni W, Locke C, Ludden T, Granneman GR, Braverman LE. Are bioequivalence studies of levothyroxine sodium formulations in euthyroid volunteers reliable? *Thyroid* 2004;14:191–200.
7. Dong BJ, Hauck WW, Gambertoglio JG, et al. Bioequivalence of generic and brand-name levothyroxine products in the treatment of hypothyroidism. *JAMA* 1997;277:1205–1213.
8. Mayor GH, Orlando T, Kurtz NM. Limitations of levothyroxine bioequivalence evaluation: an analysis of an attempted study. *Am J Ther* 1995;2:417–432.
9. Alexander EK, Pearce EN, Brent GA, et al. 2017 guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017;27:315–389.
10. Hennessey JV. The emergence of levothyroxine as a treatment for hypothyroidism. *Endocrine* 2017;55:6–18.

88

CUSHING SYNDROME

A Tale of Two Glands Level II

Scott G. Garland, PharmD

Steven M. Smith, PharmD, MPH, BCPS, CHC, FCCP

John Gums, PharmD, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize and differentiate the signs, symptoms, and laboratory changes associated with the various forms of Cushing syndrome.
- Recognize the biochemical, anatomic, and emotional changes that can occur with Cushing syndrome.
- Recommend appropriate treatment regimens for patients with Cushing syndrome.
- Provide patient counseling on proper dosing, administration, and adverse effects of treatment for Cushing disease.

PATIENT PRESENTATION

■ Chief Complaint

“I have been tired and weak lately, and I’ve noticed some swelling in my legs recently.”

■ HPI

Susan Taylor is a 31-year-old woman who presents to her family physician complaining of fatigue, weakness, and edema. She also reports weight gain (50 lb over 2 years) and depression with insomnia.

PMH

Patient has been healthy with no other major medical illnesses, except seasonal allergic rhinitis. She had two healthy children by uncomplicated vaginal deliveries.

FH

Mother is alive at age 54 with type 2 DM; father is living at age 56 with HTN. She has two sisters: one is healthy and the other has depression.

SH

Patient does not smoke and drinks occasionally. She is a photographer. Children are ages 6 years and 3 years.

Meds

Seasonique one tablet PO once daily as directed
Nasonex two sprays in each nostril once daily PRN allergic symptoms
Unisom SleepTabs 25 mg PO QHS PRN sleep
Advil 200 mg one to two tablets PO Q6H PRN headache

All

Sulfa—rash

ROS

(+) For fatigue, weakness, occasional back pain, and weight gain; also reports episodes of sadness, depressed mood, and insomnia; skin bruises easily; occasional headache, blurred vision, and heartburn; no CP, wheezing, or SOB. Normal menstruation with regular periods. LMP 7 weeks ago.

Physical Examination**Gen**

WDWN obese, cushingoid-appearing white woman in NAD

VS

BP 165/86 mm Hg, HR 85 bpm, RR 14/min, T 37.0°C, Wt 82.1 kg, Ht 5'3"

Skin

Thin skin with some bruising and scratches; purple striae visible on abdomen

HEENT

Rounded face; moderate facial hair; PERRLA; EOMI; funduscopic exam shows normal retinal background, optic cup-to-disc ratios 0.4; visual fields appear to be grossly intact; OP moist and pink

Neck/Lymph Nodes

Supple; (+) JVD at 30° (7 cm); (–) bruits, adenopathy, or thyromegaly

Chest

CTA bilaterally

Breasts

No lumps or masses

CV

RRR, no MRG

Abd

Obese, soft, NT, (–) masses or organomegaly

Genit/Rect

Guaic (–); normal external genitalia; no masses

MS/Ext

Appears to have decreased strength bilaterally; DTR 1–2+ and symmetric throughout all four extremities; 2+ pitting pedal edema bilaterally; pedal pulses palpable with moderate intensity

Neuro

Oriented × 3; flat affect; CNs II–XII intact

Labs

Na 138 mEq/L	Hgb 13.4 g/dL	AST 9 IU/L	TSH 2.33 mIU/L
K 3.3 mEq/L	Hct 38.5%	ALT 7 IU/L	A1C 7.1%
Cl 105 mEq/L	RBC $4.0 \times 10^6/\text{mm}^3$	Alk phos	<i>Fasting lipid profile</i>
CO ₂ 25 mEq/L	Plt $264 \times 10^3/\text{mm}^3$	180 IU/L	T. chol 261 mg/dL
BUN 12 mg/dL	WBC $14.5 \times 10^3/\text{mm}^3$	T. bili	HDL 62 mg/dL
SCr 0.9 mg/dL		0.5 mg/dL	LDL 120 mg/dL
Glu 160 mg/dL		Alb 4.5 g/dL	Trig 396 mg/dL
		UA 5.6 mg/dL	

Assessment

Probable Cushing syndrome of unknown etiology requiring further evaluation by an endocrinologist

Clinical Course

The patient was seen by an endocrinologist for further evaluation. Baseline 24-hour UFC was 356 and 362 mcg on separate days. A midnight salivary cortisol concentration was 0.54 mcg/dL. An overnight 1-mg DST showed a plasma cortisol concentration of 9.2 mcg/dL. Plasma ACTH concentrations on 2 consecutive days at 1:00 PM were 103 and 110 pg/mL. A CRH stimulation test revealed a baseline plasma cortisol of 10.4 mcg/dL and ACTH of 108 pg/mL, with an increase to a plasma cortisol of 13.5 mcg/dL and ACTH of 187 pg/mL following CRH administration. An MRI revealed an enlarged pituitary gland; the same finding was seen on a focused repeat MRI. There was no focal inhomogeneity that would suggest an isolated adenoma (ie, the tumor cannot be localized).

The risks and benefits of all the treatments were explained to Ms Taylor. She preferred to undergo radiation treatments rather than exploratory-type surgery. She indicated that she would like to have more children and would prefer to try other treatments prior to surgery.

QUESTIONS**Collect Information**

- What information (signs, symptoms, laboratory values) indicates the presence of Cushing syndrome?
- What information (presentation, history, laboratory values, imaging) can be used to identify the most likely etiology of Cushing syndrome?

Assess the Information

- Assess the severity of the Cushing syndrome based on the subjective and objective information available.

- 2.b. Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What psychosocial and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for the treatment of Cushing syndrome?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's Cushing syndrome and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What adjunctive pharmacotherapy may be required if the therapy identified in 3.d. above is successful?
- 3.f. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse events?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse events?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

FOLLOW-UP QUESTIONS

1. What advantages does measuring late-night salivary cortisol have over measuring late-night serum cortisol concentrations?

CLINICAL COURSE

The patient received radiation therapy with adjuvant pharmacotherapy to reduce cortisol levels. Given that it may take several months for therapy to normalize cortisol, several other interventions were initiated to ameliorate the complications of Cushing disease. She received hydrochlorothiazide 25 mg daily for hypertension, pioglitazone 30 mg daily for elevated blood glucose, rosuvastatin 5 mg daily for dyslipidemia, and escitalopram 10 mg daily for depression. A DXA scan revealed a Z-score of -2.4 standard deviations at the hip and -2.6 vertebrally. Accordingly, she received a diagnosis of steroid-induced osteoporosis. One month following initiation of the above agents, she presented to her physician for follow-up. She reported increased weakness, leg cramps, and palpitations. Lab work revealed a serum potassium concentration of 2.7 mEq/L.

2. What pharmacologic therapy would you recommend to reduce her risk of fracture?
3. What medication changes would you suggest at this time?

SELF-STUDY ASSIGNMENTS

1. Many of the tests used in the differential diagnosis of Cushing syndrome require drug therapy (eg, DST, CRH). Create a table to assist healthcare providers in performing these tests correctly (include possible adverse events, timing, critical values, and evaluation of the results).
2. Compare the retail costs in your area for each of the pharmacotherapeutic alternatives for the treatment of Cushing syndrome. Write a brief summary of your findings, and describe whether this information would cause you to change your recommendation for the initial drug therapy for this patient.
3. Describe methods that may be used to minimize drug-induced Cushing syndrome.

CLINICAL PEARL

Most patients with Cushing disease are treated with transsphenoidal surgery because of its high cure rate (80–90%). Pharmacotherapy is usually used as adjunctive therapy rather than primary therapy.

REFERENCES

1. Newell-Price J, Bertagna X, Grossman AB, Nieman LK. Cushing syndrome. *Lancet* 2006;367:1605–1617.
2. Sharma ST, Nieman LK, Feelders RA. Cushing syndrome: epidemiology and developments in disease management. *Clin Epidemiol* 2015;7:281–293.
3. Nieman LK, Biller BMK, Findling JW, et al. Treatment of Cushing Syndrome: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2015;100:2807–2831.
4. Lacroix A, Feelders RA, Stratakis CA, Nieman LK. Cushing syndrome. *Lancet* 2015;386(9996):913–927.

89

ADDISON DISEASE

I May Look Great, but I Don't Feel Well Level II

Zachary A. Weber, PharmD, BCPS, BCACP, CDE

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the clinical presentation, symptoms, and laboratory changes associated with Addison disease.
- Optimize pharmacologic and nonpharmacologic therapy for patients with Addison disease and comorbid conditions.
- Provide education and counseling to patients and family members about Addison disease and the proper administration, side effects, and adverse effects of corticosteroids and mineralocorticoids, and the importance of adherence to therapy.

- Provide counseling and education about common side effects associated with high and low cortisol serum concentrations.
- Compare corticosteroids with respect to relative glucocorticoid and mineralocorticoid potencies.

PATIENT PRESENTATION

■ Chief Complaint

"I've noticed that over the past six months, my son's skin is getting darker, and he has been more lethargic, somewhat withdrawn, and sleeping more. I have also noticed that he has been making some poor choices, in terms of friends and activities."

■ HPI

Gregory Waters is a 19-year-old man who is brought to the ED by his mother after she found him crying, confused, and disoriented. His mother states that she has recently noticed that he has not had the same level of energy, and has been complaining about not being able to run and play basketball with his friends at the park. She has also noticed he has been hanging out with a different group of friends, and she is concerned he may be involved in some abhorrent activities and has not been taking his medications appropriately.

■ PMH

Type 1 DM × 7 years
Hypothyroidism × 3 years

■ FH

Mother, 52 years old, has HTN; father, 54 years old, has hypothyroidism; sister, 24 years old, has both HTN and type 1 DM.

■ SH

Denies use of alcohol, tobacco, or illicit drugs; lives with his mother.

■ Meds

Lantus 24 units subcutaneously at bedtime
NovoLog 1:15 scale carbohydrate counting ratio, subcutaneously with meals
Levothyroxine 100 mcg PO daily

■ All

NKDA

■ ROS

Increased tanning of the skin noted over the past 6 months. Increased fatigue, nausea, and a 2.5-kg weight loss over the past month.

■ Physical Examination

Gen

Alert, somewhat disoriented and confused

VS

BP 84/47 mm Hg, HR 91 bpm, RR 16/min, T 36.2°C; Wt 62.5 kg, Ht 5'4"

Skin

Warm, dry, and intact. Slightly tanned color

HEENT

Normocephalic; oral mucosa moist. PERRL. EOMI.

Neck

No JVD. Nontender. No thyroid nodularity.

Lungs

CTA. Respirations are nonlabored.

CV

Normal rate and rhythm. No murmurs. Normal perfusion. No edema.

Abd

Soft, NT/ND. Normal BS.

MS/Ext

No CCE; normal ROM

Neuro

Alert, somewhat disoriented

Psych

Somnolent, but cooperative

■ Labs (Fasting, Drawn at 10:15 AM)

Na 116 mEq/L	Hgb 14.2 g/dL	AST 111 IU/L	T. chol 168 mg/dL
K 4.9 mEq/L	Hct 43.8%	ALT 59 IU/L	Trig 120 mg/dL
Cl 99 mEq/L	RBC $4.88 \times 10^6/\text{mm}^3$	Alk phos 75 IU/L	Fe 93 mcg/dL
CO ₂ 26 mEq/L	Plt $244 \times 10^3/\text{mm}^3$	GGT 63 IU/L	TSH 25.8 mIU/L
BUN 14 mg/dL	WBC $3.6 \times 10^3/\text{mm}^3$	LDH 173 IU/L	Free T ₄ 0.41 ng/dL
SCr 0.9 mg/dL	Neutros 41%	T. bili 1.1 mg/dL	Cortisol 0.4 mcg/dL
Glu 140 mg/dL	Lymphos 43%	D. bili 0.5 mg/dL	ACTH 2003 pg/mL
Ca 9.2 mg/dL	Monos 13%	T. prot 7.3 g/dL	A1C 8.2%
Phos 5.1 mg/dL	Eos 2%	Alb 4.1 g/dL	
Uric acid 4.1 mg/dL	Basos 1%		

Reference range for cortisol: AM 8–25 mcg/dL, PM 4–20 mcg/dL; ACTH 0–130 pg/mL

■ UA

Clear, pale yellow, SG 1.020, pH 6.8

■ Other

CT scan negative; ECG normal

■ Assessment

1. Primary adrenal insufficiency, most likely due to an autoimmune disease
2. Hypothyroidism with an elevated TSH, likely secondary to non-adherence to prescribed levothyroxine regimen
3. Type 1 DM with an elevated A1C, likely secondary to nonadherence to prescribed insulin regimen

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of Addison disease?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of Addison disease based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What psychosocial considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating Addison disease?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's Addison disease and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Review the signs and symptoms of an acute adrenal crisis, and describe the treatment.
2. Differentiate the glucocorticoids with respect to duration of activity, glucocorticoid potency, and mineralocorticoid potency.
3. Differentiate the biologic functions of cortisol and aldosterone.
4. Explain why the skin becomes pigmented in adrenal insufficiency.
5. Identify drugs that may precipitate acute adrenal insufficiency or adrenal crisis.

CLINICAL PEARL

Although rare, a decrease in insulin requirements and unexplained hypoglycemia in patients with type 1 DM may be initial signs of Addison disease.

REFERENCES

1. Bornstein SR, Allolio B, Arlt W, et al. Diagnosis and treatment of primary adrenal insufficiency: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2016;101(2):364–389.
2. Griffing GT. Addison Disease. Available at: <https://emedicine.medscape.com/article/116467-overview>. Accessed November 26, 2018.
3. Baker SJ, White K. Addison's Disease Owner Manual. Available at: <http://www.addisons.org.uk/info/manual/adshguidelines.pdf>. Accessed November 28, 2018.
4. Michels A, Michels N. Addison disease: early detection and treatment principles. *Am Fam Phys* 2014;89(7):563–568.
5. Abdel-Motleb M. The neuropsychiatric aspect of Addison's disease: a case report. *Innov Clin Neurosci* 2012 Oct;9(10):34–36. Available at: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC3508960/>. Accessed November 28, 2018.
6. Kordonouri O, Maguire AM, Knip M, et al. Other complications and associated conditions with diabetes in children and adolescents. *Ped Diab* 2009;10(Suppl 12):204–210.
7. Barker JM, Fain PR, Eisenbarth GS. Addison's disease and type 1 diabetes. *Curr Opin Endocr Diabetes* 2005;12(4):280–284.
8. Reisch N, Arlt W. Fine tuning for quality of life: 21st century approach to treatment of Addison's disease. *Endocrinol Metab Clin N Am* 2009;38:407–418.
9. Arlt W. The approach to the adult with newly diagnosed adrenal insufficiency. *J Clin Endocrinol Metab* 2009;94(4):1059–1067.
10. Elbelt U, Hahner S, Allolio B. Altered insulin requirement in patient with type 1 diabetes and primary adrenal insufficiency receiving standard glucocorticoid replacement therapy. *Eur J Endocrinol* 2009;160:919–924.

90

HYPERPROLACTINEMIA

The Missing Period Level I

Amy Heck Sheehan, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of hyperprolactinemia.
- Recommend appropriate treatment options for hyperprolactinemia.
- Design a plan to monitor the response to the pharmacologic treatment of hyperprolactinemia.

PATIENT PRESENTATION

Chief Complaint

"I haven't had my period for almost a year."

HPI

Susan Oliver is a 31-year-old woman with a history of oligomenorrhea (menstrual cycle every 2–6 months) since menarche at age 14. She presents to her gynecologist after 11 months of amenorrhea and a small amount of milky discharge from her left breast, which she first noticed 1–2 months ago. The patient and her husband would like to have a baby, but she is concerned that she may be unable to have children. The patient states that she and her husband have not used birth control for more than 1 year, and she has had several negative home pregnancy tests.

■ PMH

GERD
Seasonal allergies
Depression

■ FH

Father died at age 58 from an AMI; mother (age 62) has type 2 DM and HTN. Patient has two brothers (ages 33 and 35) who are alive and well.

■ SH

The patient is employed as an administrative assistant. She does not smoke and has less than one drink of alcohol per month. She has been married for 5 years and lives with her husband and two stepdaughters (ages 7 and 9).

■ Meds

Omeprazole 20 mg PO daily
Desloratadine 5 mg PO daily
Fluoxetine 20 mg PO daily
Prenatal vitamins one tablet PO daily
Acetaminophen 500 mg PO PRN

■ All

Codeine (hives)

■ ROS

Galactorrhea of the left breast and amenorrhea for 11 months as described in the HPI. No active GERD.

■ Physical Examination**Gen**

The patient is a WDW white woman in NAD.

VS

BP 124/71 mm Hg, P 72 bpm, RR 13, T 37.1°C; Wt 72 kg, Ht 5'8"

Skin

Normal, intact, warm, and dry

HEENT

PERRLA, EOMI, normal funduscopic exam, normal visual fields

Neck/Lymph Nodes

Normal thyroid, no lymphadenopathy

Lungs/Chest

CTA & P

Breasts

Galactorrhea of left breast, no masses

CV

RRR, S₁ and S₂ normal, no MRG

Abd

Soft, nontender, no organomegaly, (+) bowel sounds

GU

LMP 11 months ago, normal pelvic exam and Pap smear

MS/Ext

Normal ROM, no edema, pulses 2+ throughout

Neuro

A&O × 3, bilateral reflexes intact, normal gait, CNs II–XII intact

■ Labs

Na 138 mEq/L	AST 23 IU/L	TSH 2.1 mIU/L
K 4.0 mEq/L	ALT 31 IU/L	T ₃ 111 ng/dL
Cl 101 mEq/L	Alk phos 110 IU/L	Total T ₄ 7.5 mcg/dL
CO ₂ 25 mEq/L	T. bili 0.5 mg/dL	Free T ₄ 1.3 ng/dL
BUN 13 mg/dL		Serum β-hCG negative
SCr 0.8 mg/dL		FSH 12 IU/L
Glu 89 mg/dL		

Serum prolactin on 3 separate days: 133, 159, and 142 mcg/L

■ Other Test Results

DXA T-score −0.90 at the lumbar spine (no previous DXA results)
MRI of the pituitary gland revealed an 8-mm pituitary adenoma.

■ Assessment

Hyperprolactinemia due to a microprolactinoma

QUESTIONS**Collect Information**

- What signs, symptoms, and laboratory values indicate the presence of hyperprolactinemia?
- What additional information is needed to fully assess this patient's hyperprolactinemia?

Assess the Information

- Assess the severity of hyperprolactinemia based on the subjective and objective information available.
- Create a list of this patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy for a woman with hyperprolactinemia?
- What nondrug therapies can be considered for the treatment of hyperprolactinemia?
- What pharmacotherapeutic options are available for the treatment of hyperprolactinemia in this woman?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's hyperprolactinemia and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance adherence, optimize therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to monitor the patient's response to therapy and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient was started on the regimen you recommended, and she returned to the clinic 4 weeks later complaining of significant nausea and abdominal pain that was temporally associated with medication administration. Serum prolactin concentrations measured 10 minutes apart were 140, 151, and 137 mcg/L. Galactorrhea and amenorrhea were unchanged.

FOLLOW-UP QUESTIONS

1. Identify the possible reasons for the patient's poor initial response to therapy.
2. Given the new patient information, what alternative therapies should be considered?
3. How long will this patient require drug treatment for the prolactinoma?

SELF-STUDY ASSIGNMENTS

1. Review the available information on the safety of dopamine agonist pharmacotherapy in pregnant women. If this patient eventually becomes pregnant, should a dopamine agonist be continued throughout the pregnancy?

2. Research information on the use of hormone replacement therapy in patients with hyperprolactinemia. Is this patient a candidate for hormone replacement therapy? Why or why not?
3. Describe the treatment of hyperprolactinemia in the presence of a macroadenoma. How would the management of hyperprolactinemia be different if the patient were diagnosed with a macroprolactinoma instead of a microprolactinoma?

CLINICAL PEARL

Although dopamine agonists are the mainstay of therapy for hyperprolactinemia, approximately 5–10% of patients do not respond to these agents because of poor compliance, suboptimal dosing, or the presence of a treatment-resistant prolactinoma.

REFERENCES

1. Melmed S, Casanueva FF, Hoffman AR, et al. Diagnosis and treatment of hyperprolactinemia: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2011;96:273–288.
2. Molitch ME. Management of the pregnant patient with a prolactinoma. *Eur J Endocrinol* 2015;172:R205–R213.
3. Glezer A, Bronstein MD. Prolactinomas. *Endocrinol Metab Clin N Am* 2015;44:71–78.
4. dos Santos Nunes V, El Dib R, Boquszewski CL, Noqueira CR. Cabergoline versus bromocriptine in the treatment of hyperprolactinemia: a systematic review of randomized controlled trials and meta-analysis. *Pituitary* 2011;14(3):259–265.
5. Klibanski A. Prolactinomas. *N Engl J Med* 2010;362:1219–1226.

This page intentionally left blank

SECTION 9

GYNECOLOGIC AND OBSTETRIC DISORDERS

91

PREGNANCY AND LACTATION

Pregnant and Then Some Level II

Sneha Baxi Srivastava, PharmD, BCACP, CDE

Ziemowit Mazur, EdM, MS, PA-C

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe each FDA pregnancy category using the US Food and Drug Administration Drug Classification System and the new Pregnancy and Lactation Labeling Rule (PLLR).¹
- Determine the factors (clinical vs pharmacologic) that should be considered when treating a pregnant or lactating patient.
- List the risks and benefits associated with medication use during pregnancy for hyperthyroidism, depression, mechanical heart valve requiring chronic anticoagulation for thromboembolism prophylaxis, and gestational diabetes.
- Identify alternative therapies that are considered safe during pregnancy for the treatment of depression and thromboembolism prophylaxis in a patient with a mechanical heart valve.
- Design a pharmacotherapeutic plan for a pregnant patient with depression, hypertension, and a mechanical heart valve including treatment options, appropriate monitoring, and therapeutic goals.
- Educate a patient on the treatment options, benefits, risks, and monitoring of antidepressants, antihypertensives, and anticoagulants during pregnancy.

PATIENT PRESENTATION

■ Chief Complaint

"I have been nauseated and vomiting for the past week. I took a pregnancy test yesterday, and it was positive! How am I going to handle a pregnancy at this age? Plus, I am taking a lot of different medications. Could I have harmed my baby?"

■ HPI

Chloe Avett is a 34-year-old woman who reports experiencing two to three episodes of nausea per day with vomiting occasionally in the mornings and evenings. She typically wakes up feeling nauseous and will vomit one to two times a week. Her GI symptoms began about 2 weeks ago and have remained consistent, preventing

her from going to work consistently or being able to work effectively. She states that she feels "run down" all the time and needs to start feeling better soon, or she will lose her job. She took a pregnancy test today, and it is positive. She is very concerned about her "blood thinner" medication, remembering that she could not take it with her previous pregnancy. She was diagnosed with depression 2 years ago and has not had any depressive symptoms in the last year—she has noted that since she incorporated exercise, she has seen improvement in her mood. She states she does not take her paroxetine anymore. Overall, she lives a healthy lifestyle, eating well (follows a vegan diet) and exercising three to four times a week.

■ PMH

Depression

History of multiple, unprovoked, lower extremity DVTs

Hyperthyroidism (diagnosed 9 months ago)

S/P gestational diabetes

■ FH

Mother alive with DM2 and HTN, father alive with celiac disease. Patient has one twin sister who is alive and well.

■ SH

Married, mother to one daughter. She is a physician assistant at an outpatient clinic. She runs and does strength training three to four times a week and follows a plant-based diet. She was a smoker (half pack per day) but is currently tobacco-free and occasionally drinks a glass of wine or alcoholic beverage on the weekends.

■ Meds

Self-discontinued paroxetine 20 mg PO once daily

Methimazole 10 mg PO once daily

Warfarin 5 mg PO MWF, 7.5 mg rest of the week

Acetaminophen 375 mg PO PRN (takes once a month for a rare headache)

■ All

NKDA

■ ROS

Fatigue

■ PE

Gen

WDWN concerned woman

VS

BP 120/62 mm Hg, P 72 bpm, RR 18, T 36.3°C; Wt 50 kg, Ht 5'3"

Skin

Warm, dry, no eruptions, boils, or lesions

HEENT

WNL

Neck/Lymph Nodes

No adenopathy, no thyromegaly, supple

Lungs

CTA bilaterally

Breasts

Tender to palpation; no masses

CV

Mechanical click systolic murmur, grade 2/4

Abd

Soft, NT, (+) BS; no masses, no bruits

Genit/Rect

Pelvic exam confirms pregnancy; stool heme/guaiac (–)

Urine (–) for protein/glucose

Ext

(–) CCE; pulses intact

Neuro

Normal sensory and motor levels

■ Labs

Ultrasound: confirmed pregnancy

Na 138 mEq/L	Hgb 13 g/dL	Blood type: O–
K 4 mEq/L	Hct 40%	PT/INR 10.0 sec/3.0
Cl 102 mEq/L	WBC $8.0 \times 10^3/\text{mm}^3$	Fasting glucose 80 mg/dL
CO ₂ 27 mEq/L	Plt $345 \times 10^3/\text{mm}^3$	A1c 5.9%
BUN 10 mg/dL	TSH 1.45 mIU/L	
SCr 0.9 mg/dL		

■ Assessment

1. Nausea and vomiting due to pregnancy
2. Thromboprophylaxis
3. Hyperthyroidism
4. Depression
5. S/P gestational diabetes

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of nausea and vomiting secondary to pregnancy?
- 1.b. What additional information is needed to fully assess this patient's nausea and vomiting secondary to pregnancy?

Assess the Information

- 2.a. Assess the severity of nausea and vomiting based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for nausea and vomiting secondary to pregnancy might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's nausea and vomiting?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's nausea and vomiting and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The patient returns to your office 4 weeks after she delivers her healthy baby girl. She reports that her clinical symptoms of depression have intensified postpartum and would like to know if she should reinstitute her antidepressant, and if so, at what dose. She also states that she was diagnosed with gestational diabetes and was treated with insulin during the last 4 weeks but is no longer using any insulin.

■ FOLLOW-UP QUESTIONS

1. Based on the American College of Obstetricians and Gynecologists (ACOG) guidelines, what would you recommend to the patient for the postpartum depression?
2. What is the Pregnancy and Lactation Labeling Rule?

CLINICAL PEARLS

Electronic resources for information related to fetal and neonatal effects in pregnancy and lactation include Reprotox (www.reprotox.org) and TERIS (<http://depts.washington.edu/terisweb>). There are also postmarketing pregnancy exposure registries available through the US Food and Drug Administration Pregnancy Labeling Task Force. Alternatively, there is General Practice Research Database (GPRD) that can be utilized as data sources for investigating drug exposure during pregnancy.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Lisa R. Garavaglia, PharmD.

REFERENCES

1. American College of Obstetricians and Gynecologists. Committee on Practice Bulletins-Obstetrics. ACOG Practice Bulletin No. 189: Nausea and vomiting of pregnancy. *Obstet Gynecol* 2018;131(1):e15–e30.
2. Bates SM, Greer IA, Middeldorp S, Veenstra DL, Prabulos AM, Vandvik PO. VTE, thrombophilia, antithrombotic therapy, and pregnancy: antithrombotic therapy and prevention of thrombosis, 9th ed: American College of Chest Physicians evidence-based clinical practice guidelines. *Chest* 2012;141(2 Suppl):e691S–e736S.
3. Alexander EK, Pearce EN, Brent GA, et al. 2017 Guidelines of the American Thyroid Association for the diagnosis and management of thyroid disease during pregnancy and the postpartum. *Thyroid* 2017; 27(3):315–389.
4. De Groot L, Abalovich M, Alexander EK, et al. Management of thyroid dysfunction during pregnancy and postpartum: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2012; 97(8):2543–2565.
5. Peleg D, Cada S, Peleg A, Ben-Ami M. The relationship between maternal serum thyroid-stimulating immunoglobulin and fetal and neonatal thyrotoxicosis. *Obstet Gynecol* 2002;99(6):1040–1043.
6. Nguyen CT, Sasso EB, Barton L, Mestman JH. Graves' hyperthyroidism in pregnancy: a clinical review. *Clin Diabetes Endocrinol* 2018;4:4.
7. Morales DR, Slattery J, Evans S, Kurz X. Antidepressant use during pregnancy and risk of autism spectrum disorder and attention deficit hyperactivity disorder: systematic review of observational studies and methodological considerations. *BMC Med* 2018;6(1):6.
8. Yonkers KA, Wisner KL, Stewart DE, et al. The management of depression during pregnancy: a report from the American Psychiatric Association and the American College of Obstetricians and Gynecologists. *Gen Hosp Psychiatry* 2009;31(5):403–413.
9. American Diabetes Association. Management of diabetes in pregnancy: standards of medical care in diabetes—2019. *Diabetes Care* 2019; 42(Suppl 1):S165–S172.
10. U.S. Food and Drug Administration. Pregnancy and lactation labeling (drugs) final rule. www.fda.gov/drugs/labeling-information-drug-products/pregnancy-and-lactation-labeling-drugs-final-rule. Accessed January 2, 2020.

92

CONTRACEPTION

Stork Landing Prohibited Level II

Julia M. Koehler, PharmD, FCCP

Jennifer R. Guthrie, MPAS, PA-C

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Discuss the absolute and relative contraindications to the use of hormonal contraceptives.
- Discuss the advantages and disadvantages of the various forms of contraceptives, including both oral and nonoral hormonal formulations as well as intrauterine devices.

- Compare and contrast the marketed contraceptive options and select the best product for an individual patient.
- Develop strategies for managing the possible side effects of oral contraceptives (OCs) and prepare appropriate alternative treatment plans.
- Provide specific patient education on the administration and expected side effects of selected hormonal contraceptives.

PATIENT PRESENTATION

Chief Complaint

"My fiancé and I are getting married soon, and we're not ready for kids just yet."

HPI

Maddie Freney is a 24-year-old female graduate student who presents to the women's health clinic for her annual exam and contraceptive counseling. She and her fiancé, Fritz, are planning to be married in approximately 4 months. Maddie states that she and Fritz have been in a monogamous sexual relationship for the past 3 years, and that their primary method of contraception has been via the inconsistent use of male condoms. She is here today to be evaluated for the use of hormonal contraceptives. The patient states she began menses at age 14 years, with irregular cycles occurring every 25–36 days and 8–10 days in length. Her last menses was 2 weeks ago and described as "normal." The patient states she has heard about contraceptive options that "decrease your number of periods," and she wants to know more about those options and if they would be okay for her to try.

PMH

Migraine headaches without aura or focal neurologic symptoms, well controlled for the past 12 months on prophylactic therapy; no history of HTN, dyslipidemia, or heart disease.

FH

Mother, age 53 years, has HTN and osteoporosis and went through natural menopause at age 50 years. Grandmother, age 74 years, has a history of breast cancer which was diagnosed at age 60 years. Father, age 55 years, has osteoarthritis, HTN, and dyslipidemia. Grandfather, age 76, has coronary artery disease and a history of MI at age 60 years.

SH

Currently lives in a house on campus, which she rents with three other graduate students. Once she and Fritz are married, they plan to rent an apartment together until she finishes graduate school. She admits to occasional social use of alcohol ("a few drinks at parties on the weekends"). Otherwise, she denies regular alcohol use during the week. Denies tobacco and illicit drug use.

Meds

Propranolol LA 160 mg PO once daily for migraine prophylaxis
Naproxen 220 mg, one to two tablets PO Q 8 H PRN mild menstrual cramps

All

NKDA

ROS

Nulliparous with no history of abnormal Pap smears. Last Pap smear was normal at age 21 years. Denies missed periods, excessive

vaginal bleeding, abnormal vaginal discharge, or significant pelvic pain with menses. Menstrual periods are the most irregular during midterm and final exam times. No history of STIs. She has mild acne on her forehead and nose, which are treated with facial wash. Denies weight change, recent skin changes, breast tenderness, nausea, or vomiting. Migraine headaches are not accompanied by aura or focal neurologic symptoms, and have been well controlled on prophylactic medication—patient states she has not had a migraine for more than 12 months; however, prior to being placed on propranolol for migraine prophylaxis, she reported experiencing menstrual-related headaches in addition to frequent migraines. No history or current symptoms of depression or anxiety. Immunizations are up to date, including HPV and hepatitis B vaccinations.

■ PE

VS

BP 108/68 mm Hg, P 66 bpm, RR 14, T 37°C; Wt 59 kg, Ht 5'7", BMI 20.4 kg/m²

Gen

Thin, well-developed woman in NAD

Skin

Warm, dry, and without rashes; mild noninflammatory facial acne limited to forehead and nose; normal pigmentation

HEENT

Deferred

Neck/Lymph Nodes

Supple without lymphadenopathy or masses. No thyroid tenderness or thyromegaly

Lungs

CTA, no wheezing

CV

RRR; no MRG

Breasts

Symmetric in size without nodularity or masses, nontender; nipples appear normal, everted and without discharge

Abd

Soft, NT, no masses or organomegaly

Genit/Rect

Normal-appearing external genitalia without lesions; uterus anteverted, mobile, and without masses or tenderness; no cervical discharge or motion tenderness; ovaries palpable, of normal size, and without tenderness; rectal exam not performed. Pap test collected.

MS/Ext

Normal ROM and strength of bilateral extremities; no peripheral edema

Neuro/Psych

A&O × 3; CN II–XII grossly intact and without focal deficits of sensation or strength; normal mood and affect

■ Labs

Negative UPT

■ Assessment

1. Contraception
2. Irregular menses and menstrual headaches
3. Migraine headache
4. Acne vulgaris, mild

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates consideration for hormonal contraception for this patient?
- 1.b. What additional information is needed to fully assess this patient's request for hormonal contraception?

Assess the Information

- 2.a. Assess the urgency for provision of pharmacologic contraception based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug contraceptive options might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for prevention of pregnancy?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's contraceptive needs and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

5. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

■ CLINICAL COURSE

Maddie returns to the clinic in 2 months complaining of worsening acne and breakthrough bleeding.

■ FOLLOW-UP QUESTIONS

1. What medical conditions can be the cause of breakthrough bleeding?

2. If breakthrough bleeding is not caused by an underlying medical condition, how can it be managed?
3. What recommendations can be made to address this patient's complaint of worsening acne?

SELF-STUDY ASSIGNMENTS

1. Compare the costs of each method of birth control and prepare a report that contains your conclusions as to which method provides the best efficacy at the most reasonable cost.
2. Visit a pharmacy and review the various home pregnancy tests; determine how you would counsel a patient to use each one, and evaluate them for ease of use.

CLINICAL PEARL

Oral, transdermal, transvaginal, injectable, and implantable hormonal contraceptives, as well as intrauterine devices and most barrier contraceptives (with the exception of latex and synthetic condoms), do not protect against the acquisition of STIs. Thus, it is important to properly educate patients who are sexually active about the importance of taking necessary precautions to minimize their risk for acquiring an STI, regardless of the type of hormonal contraceptive used.

REFERENCES

1. Hatcher RA, Trussell J, Nelson AL, Cates W Jr, Kowal D, Policar M. Contraceptive Technology. 20th revised ed. New York, NY: Ardent Media; 2011.
2. U.S. Preventive Services Task Force. USPSTF A and B recommendations. Updated February 2019. <http://www.uspreventiveservicestaskforce.org/Page/Name/uspstf-a-and-b-recommendations/>. Accessed March 12, 2019.
3. Curtis KM, Tepper NK, Jatlaoui TC, et al. U.S. medical eligibility criteria for contraceptive use, 2016. MMWR Recomm Rep 2016;65 (No. RR-3): 1-104. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6503a1.htm>. Accessed January 2, 2020.
4. Schoenen J, Sándor PS. Headache with focal neurological signs or symptoms: a complicated differential diagnosis. Lancet Neurol 2004;3:237-245.
5. Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. selected practice recommendations for contraceptive use, 2016 MMWR Recomm Rep 2016;65 (No. RR-4):1-66. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6504a1.htm>. Accessed March 12, 2019.
6. Vinogradova Y, Coupland C, Hippisley-Cox J. Use of combined oral contraceptives and risk of venous thromboembolism: nested case-control studies using the QResearch and CPRD databases. BMJ 2015; 350:h2135. doi:10.1136/bmj.h2135.
7. Oedingen C, Scholz S, Razum O. Systematic review and meta-analysis of the association of combined oral contraceptives on the risk of venous thromboembolism: the role of the progestogen type and estrogen dose. Thromb Res 2018;165:68-78.
8. Machado RB, Pereira AP, Coelho GP, Neri L, Martins L, Luminoso D. Epidemiological and clinical aspects of migraine in users of combined oral contraceptives. Contraception 2010;81:202-208.
9. Practice Bulletin No. 157. Cervical cancer screening and prevention. Obstet Gynecol 2016;127:e1-e20.
10. Committee on Practice Bulletins—Gynecology. Practice Bulletin No. 179: Breast cancer risk assessment and screening in average-risk women. Obstet Gynecol 2017;130:e1-e16.

93

EMERGENCY CONTRACEPTION

More Than Just Plan B Level II

Rebecca H. Stone, PharmD, BCPS, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the advantages and disadvantages of the various options for emergency contraception.
- Describe the efficacy of each emergency contraception method and factors that may influence the efficacy.
- Discuss the possible adverse effects and contraindications of the various forms of emergency contraceptives, including both oral and nonoral options.
- Educate patient regarding the use of emergency contraception and adherence to contraceptive regimen.

PATIENT PRESENTATION

Chief Complaint

"I forgot to restart my birth control pill pack. I have gone 9 days without a 'real' pill. I'm not ready to be pregnant yet!"

HPI

Olivia Furtel is a 19-year-old woman who presents to the family medicine clinic in a panic. She states that she typically throws out the last week of pills in her pack, "since they are not 'real' pills anyway," and she forgot to start her new oral contraceptive pack on time. She had intercourse with her husband 2 days ago and wants to know what she should do to avoid pregnancy.

PMH

Seasonal allergies

FH

Mother, age 47, with type 2 diabetes. Father, age 45, with hypertension. Maternal grandmother, age 69, with COPD.

SH

Denies smoking
Enjoys an occasional glass of wine
Married × 1 year—mutually monogamous relationship

Meds

Cetirizine 10 mg PO once daily × 5 years
Ethinyl estradiol 20 mcg/ levonorgestrel 0.1 mg (Aviane) 1 tablet PO once daily × 2 years

All

NKDA

■ **ROS**

Patient is a nulligravida woman whose menstrual periods are regular with the use of the combined oral contraceptive (OC). She denies any breakthrough bleeding or spotting with routine use. She is tolerating the OC well.

■ **PE***Gen*

WDWN woman appearing anxious

VS

BP 106/70 mm Hg, P 60 bpm, RR 13, T 37°C; Wt 53.5 kg, Ht 5'5", BMI 19.6 kg/m²

Skin

Normal; intact; warm and dry

Exam

Deferred; she had a complete examination 3 months ago that was normal

■ **Labs***3 months ago*

Negative Pap smear

1 year ago

Tests negative for chlamydia, gonorrhea, syphilis, and HIV

■ **Assessment**

1. Emergency contraception
2. Contraception
3. Seasonal allergies

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates that this patient is appropriate for emergency contraception?
- 1.b. What additional information is needed to fully assess this patient's need for emergency contraception?

Assess the Information

- 2.a. Assess the urgency of emergency contraception access based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for addressing this patient's risk of unintended pregnancy?

- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ **CLINICAL COURSE**

A few weeks later, Ms Furtel calls into the clinic to report that she started her period and is not pregnant. She states that she is thankful for the advice provided to her.

■ **SELF-STUDY ASSIGNMENTS**

1. For other forms of hormonal contraception, such as the patch, the ring, progestin-only OCs and injectables, create a table identifying when emergency contraception may be needed if these methods are not used appropriately.
2. Identify strategies to minimize the hormone-free interval with the use of hormonal contraception and thereby diminish the potential need for emergency contraception.
3. For patients not using hormonal contraception, identify additional scenarios for which emergency contraception may be utilized.
4. Explain how BMI or body weight may influence efficacy of emergency contraceptive products.

CLINICAL PEARL

Although not FDA-approved for this purpose, a copper IUD may also be used as emergency contraception within the first 120 hours after inadequately protected intercourse.

ACKNOWLEDGEMENT

This case is based on the patient case written for the 10th edition by Emily C. Papineau, PharmD.

REFERENCES

1. Curtis KM, Jatlaoui TC, Tepper NK, et al. U.S. Selected practice recommendations for contraceptive use, 2016. *MMWR Recomm Rep* 2016;65(4):1–66.

- American College of Obstetricians and Gynecologists. Practice Bulletin No. 152: Emergency contraception. *Obstet Gynecol* 2015;126(3):e1–11.
- Curtis KM, Tepper NK, Jatlaoui TC, et al. U.S. Medical eligibility criteria for contraceptive use, 2016. *MMWR Recomm Rep* 2016;65(3):1–103.
- Haeger KO, Lamme J, Cleland K. State of emergency contraception in the U.S., 2018. *Contracept Reprod Med* 2018;3:20.
- Gemzell-Danielsson K, Berger C. Emergency contraception—mechanisms of action. *Contraception* 2013;87(3):300–308.
- American College of Obstetricians and Gynecologists. Practice Bulletin No. 186: Long-acting reversible contraception: implants and intrauterine devices. *Obstet Gynecol* 2017;130(5):e251–e269.
- Berger C, Boggavarapu NR, Menezes J, Lalitkumar PG, Gemzell-Danielsson K. Effects of ulipristal acetate on human embryo attachment and endometrial cell gene expression in an in vitro co-culture system. *Hum Reprod* 2015;30(4):800–811.
- Ulipristal (Ella) prescribing information. Charleston, SC: Afaxys; 2018.
- Noe G, Croxatto HB, Salvatierra AM, et al. Contraceptive efficacy of emergency contraception with levonorgestrel given before or after ovulation. *Contraception* 2011;84(5):486–492.
- Glazier A, Cameron ST, Blithe D, et al. Can we identify women at risk of pregnancy despite using emergency contraception? Data from randomized trials of ulipristal acetate and levonorgestrel. *Contraception* 2011;84(4):363–367.

94

PREMENSTRUAL DYSPHORIC DISORDER

A Gloomy Girl Level II

Larissa N. H. Bossaer, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Differentiate between the clinical presentation and diagnosis of premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD).
- Identify the desired therapeutic outcomes for patients with PMDD.
- Design an appropriate therapeutic plan for a patient with PMDD.
- Design an appropriate monitoring plan for a patient with PMDD, considering patient-specific factors.
- Educate patients and other healthcare professionals about PMDD and therapeutic options.

PATIENT PRESENTATION

■ Chief Complaint

“I think my boss may fire me if I don’t get some help.”

■ HPI

Gloria Gray, a 29-year-old woman, is an established patient at the family medicine clinic who returns with complaints of bloating,

breast tenderness, angry outbursts, irritability, depression, and fatigue. She has kept a record of her symptoms over the past 3 months, and it appears that her symptoms occur during the last week of her menstrual cycle each month. During this time, she has a difficult time at work. She gets angry easily and yells at coworkers. She feels very fatigued during this time, which causes her to lose focus and fall behind on her work. She is really concerned that she may lose her job. In addition, even though her husband has been very patient with her during these episodes, she can tell that it is negatively affecting their relationship because they argue more frequently. She has tried over-the-counter ibuprofen and *Midol Teen*, but these agents helped only minimally. Her symptoms typically resolve within the first few days of her menses. She says that she is depressed about her current situation, and she would really like some help. On an additional note, she states that she and her husband are not ready to have children as they previously thought. She says that there has just been too much stress in their lives lately, so she is interested in taking birth control. She and her husband use condoms but want to take every precaution currently to effectively prevent pregnancy.

■ PMH

Migraines without aura
Irritable bowel syndrome

■ FH

Mother has dyslipidemia. Father has irritable bowel syndrome.

■ SH

Married for 4 years. No children. Previous smoker 10 years ago, but no current tobacco use. She drinks alcohol socially on the weekends. She works full time as a professor at a small community college.

■ Meds

Metamucil one teaspoonful of powder in 8 oz of water daily
Propranolol 20 mg PO Q 6 H
Sumatriptan 100 mg PO PRN migraine headache, may repeat × one dose
Women’s multivitamin one tablet daily

■ All

NKDA

■ PE

Gen

Tearful, petite woman

VS

BP 108/66 mm Hg, P 55 bpm, RR 17, T 98.3°F; Wt 112 lb (50.8 kg), Ht 5’6”

Skin

Normal; intact; warm and dry

HEENT

PERRLA; EOMI; moist mucous membranes; TMs intact

Neck/Lymph Nodes

Supple without evidence of JVD, lymphadenopathy, or thyromegaly

Lungs/Thorax

CTA & P

Breasts

Symmetric; no lumps or masses; nipples without discharge; tender to touch

CV

RRR without MRG

Abd

Soft, NT/ND; +BS; no masses

Genit/Rect

Normal pelvic exam and Pap smear

Ext

Normal ROM; pulses 2+; No CCE

Neuro

A&O $\times$ 3; CN II–XII intact; DTRs 2+

Labs

Na 141 mEq/L	Ca 9.2 mg/dL	<i>Fasting lipid profile</i>	WBC $6 \times 10^3/\text{mm}^3$
K 3.5 mEq/L	AST 20 IU/L	T. chol 190 mg/dL	Hgb 13 g/dL
Cl 104 mEq/L	ALT 17 IU/L	TG 120 mg/dL	Hct 39%
CO ₂ 27 mEq/L	Alb 3.9 g/dL	LDL 95 mg/dL	MCV 92.8 μm^3
Glu 81 mg/dL	TSH 0.74 mIU/L	HDL 71 mg/dL	MCH 31.7 pg
BUN 14 mg/dL			MCHC 34.2 g/dL
SCr 0.9 mg/dL			Plt $249 \times 10^3/\text{mm}^3$
			Urine Hcg: Negative

Assessment

1. PMDD
2. Contraception
3. Migraines without aura
4. Irritable bowel syndrome

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of PMDD (See Table 94-1).
- 1.b. What additional information is needed to fully assess this patient's PMDD?

Assess the Information

- 2.a. Assess the severity of PMDD based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for PMDD might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's PMDD?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's PMDD and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

TABLE 94-1 Item Content of the Daily Record of Severity of Problems (DRSP)³

- 1.a. Felt depressed, sad, "down," or "blue"
- 1.b. Felt hopeless
- 1.c. Felt worthless or guilty
2. Felt anxious, tense, "keyed up," or "on edge"
- 3.a. Had mood swings (eg, suddenly felt sad or tearful)
- 3.b. Was more sensitive to rejection or my feelings were easily hurt
- 4.a. Felt angry, irritable
- 4.b. Had conflicts or problems with people
5. Had less interest in usual activities (eg, work, school, friends, and hobbies)
6. Had difficulty concentrating
7. Felt lethargic, tired, fatigued, or had a lack of energy
- 8.a. Had increased appetite or overate
- 8.b. Had cravings for specific foods
- 9.a. Slept more, took naps, found it hard to get up when intended
- 9.b. Had trouble getting to sleep or staying asleep
- 10.a. Felt overwhelmed or that I could not cope
- 10.b. Felt out of control
- 11.a. Had breast tenderness
- 11.b. Had breast swelling, felt "bloated," or had weight gain
- 11.c. Had headache
- 11.d. Had joint or muscle pain

At work, at school, at home, or in daily routine, at least one of the problems noted above caused reduction of productivity or inefficiency.

At least one of the problems noted above interfered with hobbies or social activities (eg, avoid or do less).

At least one of the problems noted above interfered with relationships with others.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers?

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Develop a patient educational handout that outlines the differences between PMS and PMDD and provides resources for patients to get more information on PMDD.
2. List diseases or conditions that mimic the symptoms of PMDD that must be ruled out before the diagnosis of PMDD can be confirmed in a patient.
3. Discuss how migraine headaches and irritable bowel syndrome may be affected by the menstrual cycle.

CLINICAL PEARL

PMDD and PMS are similar in many ways, but they differ in diagnostic criteria and severity. While approximately 80% of women experience PMS, only about 2% of women meet criteria for the diagnosis of PMDD. It is important to differentiate PMDD from PMS to appropriately treat patients who suffer from the disease.

REFERENCES

1. American Psychiatric Association. Desk reference to the diagnostic criteria from DSM-5. Washington, DC: American Psychiatric Publishing; 2013:100–101.
2. Futterman LA, Rapkin AJ. Diagnosis of premenstrual disorders. *J Reprod Med* 2006;51:349–358.
3. Endicott J, Nee J, Harrison W. Daily record of severity of problems (DRSP): reliability and validity. *Arch Women Ment Health* 2006;9:41–49.
4. Kroll R, Rapkin AJ. Treatment of premenstrual disorders. *J Reprod Med* 2006;51:359–370.
5. Yonkers KA, Simoni MK. Premenstrual disorders. *Am J Obstet Gynecol* 2018;218(1):68–74.
6. Biggs WS, Demuth RH. Premenstrual syndrome and premenstrual dysphoric disorder. *Am Fam Physician* 2011;84:918–924.
7. Marjoribanks J, Brown J, O'Brien PM, Wyatt K. Selective serotonin reuptake inhibitors for premenstrual syndrome. *Cochrane Database Syst Rev* 2013;6:CD001396.
8. Yonkers KA, Kornstein SG, Gueorguieva R, Merry B, Van Steenburgh K, Altemus M. Symptom-onset dosing of sertraline for the treatment of premenstrual dysphoric disorder: a randomized clinical trial. *JAMA Psychiatry* 2015;72(10):1037–1044.
9. U.S. Food and Drug Administration. FDA Drug Safety Communication: Updated information about the risk of blood clots in women taking birth control pills containing drospirenone. <http://www.fda.gov/Drugs/DrugSafety/ucm299305.htm>. Accessed February 22, 2019.
10. Freeman EW, Halbreich U, Grubb GS, et al. An overview of four studies of a continuous oral contraceptive (levonorgestrel 90 mcg/ethinyl estradiol 20 mcg) on premenstrual dysphoric disorder and premenstrual syndrome. *Contraception* 2012;85:437–445.

95

ENDOMETRIOSIS

Persistent Pelvic Pain Level I

Erin C. Raney, PharmD, FCCP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs and symptoms associated with endometriosis.
- Compare and contrast the benefits and risks associated with various hormonal medications used for the treatment of endometriosis-associated pelvic pain.
- Determine a treatment approach for this case taking into account other health issues and potential health benefits.
- Discuss possible side effects associated with treatment for endometriosis.

PATIENT PRESENTATION

■ Chief Complaint

"I am not getting relief from my endometriosis pain with Tylenol and I would like to see what other options I have."

■ HPI

Kelly Lancaster is a 26-year-old woman who was diagnosed with endometriosis 1 year ago by a previous healthcare provider based on a history of dysmenorrhea, intermittent pain with defecation, and past history of dyspareunia. She presents to the nurse practitioner today to establish care and evaluate continued endometriosis-related pain despite treatment with acetaminophen which she has been using when the pain is most severe during her menstrual period. During these times, the acetaminophen reduces her pain from a 6 on a 10-point scale to a 5.

■ PMH

S/P deep vein thrombosis at age 20 after ankle surgery; treated for 6 months with warfarin; no coagulopathy identified; no recurrence
Seasonal allergic rhinitis
GOP0A0

■ FH

Mother (aged 60 years) has a history of endometriosis, no other health conditions; father (aged 62 years) has hypertension; one male sibling (aged 30 years) has asthma.

■ SH

Patient is an information technology specialist. She has no children. She is single; currently not sexually active. She does not smoke and consumes no more than two alcohol-containing beverages per week. She exercises 30 minutes five times a week and teaches a yoga class 2 nights per week.

■ Meds

Acetaminophen 1000 mg PO four times daily for menstrual pain
Fluticasone propionate 50 mcg nasal spray: 1 spray in each nostril once daily during allergy season
Multivitamin one tablet PO daily

■ All

Ibuprofen (hives, anaphylaxis)

■ ROS

(+) For moderate pain in pelvic region, (–) for constipation, menstrual periods occur at regular intervals of 28 days

■ PE

Gen

WDWN woman in NAD

VS

BP 108/72 mm Hg, P 65 bpm, RR 15, T 37°C; Wt 60 kg, Ht 5'6"; patient has maintained same weight for the last 5 years

Skin

No lesions

HEENT

WNL, normal nasal mucosa, no rhinorrhea

Neck/Lymph Nodes

Supple, no bruits, no adenopathy, no thyromegaly

Lungs/Thorax

CTA bilaterally; no wheezes

Breasts

Supple; no masses

CV

RRR, normal S₁ and S₂

Abd

Soft; patient states, at baseline, she experiences pain that averages a 2–3 on a 10-point pain scale (with 10 being the worst possible pain), this worsens to a 6 during the first 2–3 days of her menstrual period. (+) BS; no masses noted.

Genit/Rect

Pelvic exam: (+) adnexal pain elicited and rated at 5 on a 10-point pain scale, no masses

MS/Ext

Pulses intact

Neuro

Normal sensory and motor levels

■ Labs

Na 135 mEq/L

K 4.3 mEq/L

Cl 104 mEq/L

CO₂ 25 mEq/L

BUN 10 mg/dL

SCr 0.8 mg/dL

Random glu 84 mg/dL

Fasting lipid profile

T. chol 149 mg/dL

LDL 60 mg/dL

HDL 65 mg/dL

Trig 120 mg/dL

■ Other

PAP test: Normal

HPV/chlamydia/gonorrhea: Negative

Urine pregnancy test: Negative

Vaginal ultrasound (from previous medical records): Normal

■ Assessment

1. Endometriosis
2. Seasonal allergic rhinitis

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of endometriosis?
- 1.b. What additional information is needed to fully assess this patient's endometriosis?

Assess the Information

- 2.a. Assess the severity of endometriosis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for the treatment of pain associated with endometriosis?

- 3.c. What pharmacotherapeutic alternatives are available for the treatment of pain associated with endometriosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The patient returns to her nurse practitioner 6 months after starting medroxyprogesterone acetate 150 mg intramuscular injections every 3 months. She reports that her pelvic pain is better controlled with an overall average pain rating of 1 on the 10-point scale. She states that she had intermittent spotting initially but now has no menstrual periods.

■ FOLLOW-UP QUESTIONS

1. What is the optimal length of time for a patient to continue on medroxyprogesterone acetate injections for the treatment of endometriosis-related chronic pelvic pain?
2. Would your recommendation change if this patient had risk factors for osteopenia or osteoporosis?
3. Would your recommendation change if this patient had indicated an interest in having a child in the next 1–2 years?

■ SELF-STUDY ASSIGNMENTS

1. Research complementary therapies that have been studied for the relief of endometriosis and compare the evidence for their efficacy with standard treatments.
2. Review the contraindications of the various contraceptive agents used for the treatment of endometriosis.

CLINICAL PEARL

Pharmacologic treatment of endometriosis may be useful for decreasing pain. Pharmacotherapeutic agents that mimic pregnancy or menopause are the cornerstone of treatment. All these agents have comparable efficacy in treating pain but have different side-effect profiles. Treatment with hormonal therapy does not improve fertility, which can also be a potential consequence of the disease.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Connie K. Kraus, PharmD.

REFERENCES

1. Dunselman GAF, Vermeulen N, Becker C, et al. ESHRE guideline: management of women with endometriosis. *Hum Reprod* 2014;29:400–412.
2. Mira, RAA, Buen MM, Borges MG, Yela D, Benetti-Pinto CL. Systematic review and meta-analysis of complementary treatments for women with symptomatic endometriosis. *Int J Gynecol Obstet* 2018;143:2–9.
3. Kodaman PH. Current strategies for endometriosis management. *Obstet Gynecol Clin N Am* 2015;42:87–101.
4. Vercellini P, Buggio L, Berlanda N, Barbara G, Somigliana E, Bosari S. Estrogen-progestins and progestins for the management of endometriosis. *Fertil Steril* 2016;106:1552–1571.
5. Hatcher RA, Nelson AL, Trussell J, et al. *Contraceptive technology*, 21st ed. New York: Ayer Company Publishers, 2018.
6. Centers for Disease Control and Prevention. U.S. medical eligibility criteria for contraceptive use, 2016. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6503a1.htm>. Accessed January 2, 2020.
7. Taylor HS, Giudice LC, Lessey BA, et al. Treatment of endometriosis-associated pain with elagolix, an oral GnRH antagonist. *N Engl J Med* 2017;377:28–40.
8. Bedaiwy MA, Alfaraj S, Yong P, Casper R. New developments in the medical treatment of endometriosis. *Fertil Steril* 2017;107:555–565.
9. American College of Obstetricians and Gynecologists. Committee opinion: aromatase inhibitors in gynecologic practice. *Obstet Gynecol* 2018;131:e194–e199.
10. American College of Obstetricians and Gynecologists. Committee opinion: depot medroxyprogesterone acetate and bone effects. *Obstet Gynecol* 2014;123:1398–1402.

96

MANAGING MENOPAUSAL SYMPTOMS

Is It Getting Hot in Here? Level II

Andrea S. Franks, PharmD, BCPS

Julie W. Jeter, MD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs and symptoms associated with menopause.
- List the risks and benefits associated with hormone therapy (HT), and identify appropriate candidates for HT.
- Describe differences between transdermal, vaginal, and oral forms of HT and their place in therapy.
- Recommend nonpharmacologic therapy for managing menopausal symptoms.
- Identify alternative, nonhormonal therapies for managing menopausal symptoms.

- Design a comprehensive pharmacotherapeutic plan for a patient on HT including treatment options, monitoring, and duration of therapy.
- Determine the desired therapeutic outcomes for a patient taking HT.
- Educate patients on the treatment options, benefits, risks, and monitoring of HT.

PATIENT PRESENTATION

■ Chief Complaint

“I have been having hot flashes for a few months, and they are interfering with my life at home and work.”

■ HPI

Nancy Wilson is a 51-year-old woman who reports experiencing two to three hot flashes per day. She also states she is awakened from sleep about two to three times per week feeling hot and “drenched with sweat.” She has trouble falling back asleep after these episodes and it leaves her feeling exhausted the next day. Her symptoms began about 6 months ago, and over that time, they have increased in frequency and severity and they are interfering with her daily function. When she is doing presentations or participating in important meetings at work, it seems to trigger a hot flash. She also complains of vaginal dryness and painful intercourse. She states that her older sister was prescribed a medication for similar symptoms, but she is hesitant to take the same thing because she heard on the news and from friends that the medication may not be safe. She states she does not want to “start having periods again.” Her anxiety is currently controlled with paroxetine. She exercises three times a week and tries to follow a healthy diet with lean protein and lots of fruits and vegetables. She admits to “stress eating” and eating unhealthy foods when she travels for work.

■ PMH

Generalized anxiety disorder
GERD
HTN

■ FH

Mother, age 70, has HTN; father died of CVA at age 68. Patient has one sister, age 54, who is in good health but has HTN.

■ SH

Recently divorced, mother of two healthy sons living at home, ages 16 and 20. She is a marketing executive and often travels for important meetings and presentations. She walks on her local greenway three times a week, does yoga occasionally, and is trying to follow a dietitian-designed healthy diet although inconsistently. She does not smoke and occasionally drinks a glass of red wine with dinner or one cocktail when she goes out with friends.

■ Meds

Hydrochlorothiazide 25 mg PO once daily
Omeprazole 20 mg PO once daily
Paroxetine 20 mg PO once daily at bedtime

■ All

NKDA

■ **ROS**

(+) Hot flashes, night sweats, vaginal dryness/dyspareunia. (–) weight gain, constipation. LMP 18 months ago.

■ **PE****Gen**

WDWN woman in NAD

VS

BP 128/86 mm Hg, P 78 bpm, RR 15, T 36.4°C; Wt 76.2 kg, Ht 5'6"

Skin

Warm, dry, no lesions

HEENT

WNL

Neck/LN

Supple, no bruits, no adenopathy, no thyromegaly

Lungs/Thorax

CTA bilaterally

Breasts

Supple; no masses

CV

RRR, normal S₁ and S₂; no MRG

Abd

Soft, NT/ND, (+) BS; no masses

Genit/Rect

Pelvic exam normal except (+) mucosal atrophy; stool guaiac (–)

Ext

(–) CCE; pulses intact

Neuro

Normal sensory and motor levels

■ **Labs**

Na 136 mEq/L	Hgb 12.7 g/dL	Ca 9.3 mg/dL	<i>Fasting lipid profile</i>
K 3.9 mEq/L	Hct 39.3%	AST 32 IU/L	T. chol 190 mg/dL
Cl 104 mEq/L	WBC 6.5 × 10 ³ /mm ³	ALT 30 IU/L	LDL 132 mg/dL
CO ₂ 25 mEq/L	Plt 208 × 10 ³ /mm ³	TSH 2.46 mIU/L	HDL 50 mg/dL
BUN 10 mg/dL		FSH 87.8 mIU/mL	Trig 180 mg/dL
SCr 0.7 mg/dL		UPT (–)	
Random glu			
98 mg/dL			

■ **Other**

Pap smear and mammogram: Normal

■ **Assessment**

1. Menopausal symptoms
2. Generalized anxiety disorder
3. Hypertension
4. Gastroesophageal reflux disease
5. Elevated triglycerides
6. Osteoporosis prevention

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of menopausal symptoms?
- 1.b. What additional information is needed to fully assess this patient's menopausal symptoms?

Assess the Information

- 2.a. Assess the severity of menopausal symptoms based on the subjective and objective information available.
- 2.b. Create a prioritized list of the patient's drug therapy problems, including assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for this patient's menopausal symptoms?
- 3.b. What nondrug therapies for menopausal symptoms might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating menopausal symptoms?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's menopausal symptoms and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence to the medication, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ **CLINICAL COURSE**

The patient returns to her provider after 1 year of HT. She reports that her hot flashes and night sweats have decreased in number and intensity, and her vaginal dryness is not bothering her. She is wondering if she should continue her HT regimen, and if so, for how long?

■ **FOLLOW-UP QUESTIONS**

1. What is the optimal dose and length of time for a patient to continue on HT?
2. How should HT be discontinued after successful treatment?

3. Would your recommendation for HT change if the patient had been complaining of genital symptoms only? Why or why not?
4. Would your recommendation for HT change if this patient were to have had significant risk factors for CHD or a personal history of breast cancer? Why or why not?
5. How would you respond to the patient if she asked you about taking compounded bioidentical HT?

CLINICAL COURSE: ALTERNATIVE THERAPY

Ms Wilson is considering stopping her HT because her cousin was recently diagnosed with breast cancer. She still desires relief from hot flashes and asks for additional information on other alternatives. She has heard that black cohosh should not be used in women with breast cancer, but she has a friend who also has a family history of breast cancer who has been on black cohosh for about 9 months on the recommendation of her physician. Her friend has a checkup with lab tests every 6 months. Ms Wilson asks if black cohosh or soy would be an appropriate option to help keep her hot flashes under control. See Section 19 in this Casebook for questions about the use of black cohosh for managing menopausal symptoms.

SELF-STUDY ASSIGNMENTS

1. Research nonhormonal therapies that have been studied for the relief of menopausal symptoms and compare the scientific evidence of their efficacy to traditional hormonal medications.
2. Review the results of the Women's Health Initiative (WHI) study from 2002 and the 2007 reanalysis of the WHI results regarding the impact of HT on cardiovascular disease related to age and duration of HT use. Provide a summary of the overall findings regarding HT and cardiovascular and breast cancer risk.

CLINICAL PEARL

Women should receive a thorough history and physical exam, including assessing ASCVD and breast cancer risk factors, before HT is considered. If a woman does not have any contraindications to HT, including CHD, stroke, and VTE, and also does not have a personal history of breast cancer, short-term HT would be an appropriate therapy option as it remains the most effective treatment for vasomotor symptoms.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Nicole S. Culhane, PharmD.

REFERENCES

1. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APHA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association Task Force on practice guidelines. *J Am Coll Cardiol* 2018; pii: S0735-1097(18)39033-8. doi: 10.1016/j.jacc.2018.11.002.
2. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporos Inter* 2014;25:2359–2381.
3. North American Menopause Society. The 2017 hormone therapy position statement of the North American Menopause Society. *Menopause* 2017;24:728–753.
4. North American Menopause Society. Nonhormonal management of menopause-associated vasomotor symptoms: 2015 position statement of The North American Menopause Society. *Menopause* 2015; 22:1155–1172.
5. Manson JE, Chlebowski RT, Stefanick ML, et al. Menopausal hormone therapy and health outcomes during the intervention and extended poststopping phases of the Women's Health Initiative randomized trials. *JAMA* 2013;310:1353–1368.
6. Marjoribanks J, Farquhar C, Roberts H, Lethaby A, Lee J. Long-term hormone therapy for perimenopausal and postmenopausal women. *Cochrane Database Syst Rev* 2017;1:CD004143.
7. Rossouw JE, Prentice RL, Manson JE, et al. Postmenopausal hormone therapy and risk of cardiovascular disease by age and years since menopause. *JAMA* 2007;297:1465–1477.
8. Handley AP, Williams M. The efficacy and tolerability of SSRI/SNRI in the treatment of vasomotor symptoms in menopausal women: a systematic review. *J Am Assoc Nurse Pract* 2015;27:54–61.
9. Leach MJ, Moore V. Black cohosh (*Cimicifuga* spp.) for menopausal symptoms. *Cochrane Database Syst Rev* 2012;9:CD007244.
10. Barzilay JI, Davis BR, Pressel SL, et al. The impact of antihypertensive medications on bone mineral density and fracture risk. *Curr Cardiol Rep* 2017;19:76.

This page intentionally left blank

SECTION 10

UROLOGIC DISORDERS

97

ERECTILE DYSFUNCTION

Where There's a Pill, There's a Way Level III

Cara Liday, PharmD, CDE

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize risk factors associated with development of erectile dysfunction (ED).
- Provide brief descriptions of the advantages and disadvantages of the common therapies available for treating ED.
- Recommend appropriate first- and second-line therapy for treatment of ED.
- Provide appropriate patient education on administration and expected side effects of selected treatment modalities for ED.

PATIENT PRESENTATION

■ Chief Complaint

"I'm having trouble in the bedroom lately...."

■ HPI

Peter Johnson is a 63-year-old man who presents to his PCP with the above complaint. On questioning, he states that for the past year he has been able to achieve only partial erections that are insufficient for intercourse. He notices occasional nocturnal penile tumescence. He feels that the problem is leading to a strained relationship with his wife. He has tried a couple of herbal products or "natural supplements" that he ordered over the Internet, but they did not help.

■ PMH

Type 2 DM × 14 years
Diabetic peripheral neuropathy
HTN
Dyslipidemia
CKD stage 3

■ FH

Father deceased at age 72 secondary to MI; mother alive with HTN

■ SH

Married for 38 years; no history of marital problems; 20 pack-year smoking history; does not drink alcohol; walks for 30 minutes 3 days per week

■ Meds

Insulin glargine 60 units SC at bedtime
Metformin 1000 mg PO BID
Dulaglutide 1.5 mg SQ once weekly
Gabapentin 600 mg PO TID
Lisinopril 40 mg PO once daily
Hydrochlorothiazide 25 mg PO once daily
Atorvastatin 80 mg PO once daily
ASA 81 mg PO once daily

■ All

NKDA

■ ROS

Denies significant life stressors, fatigue, urgency, or symptoms of prostatitis. Complains of occasional nocturia, numbness, burning and tingling in his feet, and difficulty achieving and maintaining erections.

■ Physical Examination

Gen

Alert, well-developed, cooperative man in NAD

VS

BP 131/78 mm Hg, P 60 bpm, RR 18, T 37.2°C; Wt 120 kg, Ht 5'10"

Skin

Warm, dry; no lesions

HEENT

NC/AT; EOMI; PERRLA; funduscopic examination shows no arteriolar narrowing, hemorrhages, or exudates

Neck/Lymph Nodes

Supple without JVD, lymphadenopathy, masses, or goiter

Lungs/Chest

Clear to A&P bilaterally

CV

RRR; normal S₁ and S₂; no MRG

Abd

Soft, obese; NTND; normal bowel sounds; no masses or organomegaly

Genit/Rect

Normal scrotum, testes descended; NT w/o masses; penis without discharge or curvature

MS/Ext

Muscle strength 5/5 throughout; full ROM in all extremities; pulses 2+ throughout; no edema present; multiple toenails with yellow discoloration and thickening

Neuro

CNs II–XII intact; DTRs 2+ and equal bilaterally. No motor deficits; feet with reduced sensation (monofilament), vibration and Ipswich touch test bilaterally; normal pain sensation with sharp pinprick bilaterally

Labs

Na 139 mEq/L	Hgb 16.0 g/dL	Ca 9.5 mg/dL	<i>Fasting lipid profile</i>
K 3.9 mEq/L	Hct 50%	Mg 1.8 mEq/L	T. chol
Cl 102 mEq/L	AST 35 IU/L	A1C 8.5%	192 mg/dL
CO ₂ 24 mEq/L	ALT 18 IU/L	Testosterone	HDL 41 mg/dL
BUN 27 mg/dL		700 ng/dL	LDL 94 mg/dL
SCr 1.8 mg/dL		TSH 1.54 mIU/L	TG 167 mg/dL
Glu (fasting)			VLDL 19 mg/dL
166 mg/dL			

UA

SG 1.00; pH 5.1; leukocyte esterase (–); nitrite (–); protein 100 mg/dL; glucose 2+; ketones (–); urobilinogen normal; bilirubin (–); blood (–); albumin/Cr ratio 28 mg/g

IIEF-5 (International Index of Erectile Function-5)

Score 8/25

Assessment

A 63-year-old man with ED, hypertension, chronic kidney disease, dyslipidemia, peripheral neuropathy, poor long-term control of type 2 diabetes, and probable diagnosis of onychomycosis

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of ED?
- What risk factors for ED are present in this patient?
- What additional information is needed to fully assess this patient's ED?

Assess the Information

- Assess the severity of ED based on the information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of therapy for ED in this case?
- What nondrug therapies might be useful for treating ED in this patient?
- What feasible pharmacotherapeutic alternatives are available for treating ED?
- Create an individualized, patient-centered, team-based care plan to optimize initial therapy for this patient's ED and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects with ED therapy?

- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

- If therapy for onychomycosis is desired, what medication would be optimal, and how would the addition of this agent change your treatment of the patient's ED?
- β -Blockers are typically associated with an increased incidence of ED. Determine why nebivolol may have a lower incidence of ED and may possibly improve erectile function.
- Discuss the possible benefits of using a PDE-5 inhibitor in patients with symptomatic benign prostatic hyperplasia (BPH).
- Determine a treatment plan for a patient presenting with ED with a documented low testosterone concentration.

CLINICAL PEARL

Patients with cardiovascular (CV) disease have a greater risk of developing ED. In addition, the presence of ED in otherwise healthy individuals may indicate an increased risk of subsequent CV disease. Development of ED may precede the onset of CV symptoms by 3 years or more. Providers should use this opportunity to screen or treat CV disease appropriately.

REFERENCES

- Gandaglia G, Briganti A, Jackson G, et al. A systematic review of the association between erectile dysfunction and cardiovascular disease. *Eur Urol* 2014;65(5):968–978.
- Rosen RC, Cappelleri JC, Smith MD, Lipsky J, Pena BM. Development and evaluation of an abridged, 5-item version of the International Index of Erectile Function (IIEF-5) as a diagnostic tool for erectile dysfunction. *Int J Impot Res* 1999;11(6):319–326.
- Razdan S, Greer AB, Patel A, Alameddine M, Jue JS, Ramasamy R. Effect of prescription medications on erectile dysfunction. *Postgrad Med J* 2018;94(1109):171–178.
- Hatzimouratidis K, Giuliano F, Moncada I, Muneer A, Salonia A, Verze P. Guidelines on male sexual dysfunction. Available at the European Association of Urology Website. <http://uroweb.org/guideline/male-sexual-dysfunction/#3>. Updated 2018. Accessed November 10, 2018.
- Burnett AL, Nehra A, Breaux RH, et al. Erectile dysfunction: AUA guideline. *J Urol* 2018;200(3):633–641.
- Nehra A, Jackson G, Miner M, et al. The Princeton III Consensus recommendations for the management of erectile dysfunction and cardiovascular disease. *Mayo Clin Proc* 2012;87:766–778.
- Cui T, Kovell RC, Brooks DC, Terlecki RP. A urologist's guide to ingredients found in top-selling nutraceuticals for men's sexual health. *J Sex Med* 2015;12(11):2105–2117.
- U.S. Food and Drug Administration. Consumer updates. 'All natural' alternatives for erectile dysfunction: a risky proposition. <https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm465024.htm>. Accessed November 10, 2018.
- Diehm N, Borm AK, Keo HH, Wyler S. Interdisciplinary options for diagnosis and treatment of organic erectile dysfunction. *Swiss Med Wkly* 2015;145:1–12.

98

BENIGN PROSTATIC
HYPERPLASIA

Trouble With Dribbles Level II

Kathryn Eroschenko, PharmD

Michael Biddle, PharmD, BCPS

Kevin W. Cleveland, PharmD, ANP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the clinical manifestations of benign prostatic hyperplasia (BPH) and lower urinary tract symptoms (LUTS) secondary to BPH.
- Differentiate between obstructive and irritative symptoms in patients with BPH.
- Recommend appropriate pharmacotherapeutic treatment for BPH.
- Identify and manage drug interactions associated with BPH pharmacotherapy.
- Recognize when surgical therapies should be considered for patients with BPH.
- Understand how some drugs can exacerbate BPH symptoms.

PATIENT PRESENTATION

■ Chief Complaint

"I'm up four to five times a night feeling that I have to urinate, and then when I get to the bathroom all I do is dribble. I'm very light-headed when I stand up, and sometimes I don't make it to the bathroom in time. I have a girlfriend now, but I am finding it difficult to be intimate with her. Also, going to the bathroom all night is really impacting my love life."

■ HPI

Jimmy McCracken is a 65-year-old man with a long-standing history of UTIs. He has a history of urosepsis requiring hospitalization. He is being evaluated because of complaints of worsening urinary hesitancy, nocturia, and dribbling. He also has a new complaint of ED. He would like information on prescription medications to treat his urinary symptoms but is not opposed to using natural products.

■ PMH

HTN
Laminectomy 10 years ago
BPH
Chronic UTIs
Type 2 DM
ED
Obesity
Osteoarthritis (new onset)
Cat allergy (new onset)

■ FH

Educated through the 12th grade. Father died of massive MI at age 78; mother died of natural causes at age 91.

■ SH

Worked for 35 years in a grocery store; retired 7 years ago. Married once. Wife deceased 6 months ago (stroke); one daughter, two granddaughters. Lives alone but is starting to become more socially active. He recently joined a senior dating website and has started dating a 60-year-old woman. He also just adopted a 3-year-old cat from the humane society. Although he reports being allergic to cat dander, he feels that she has added happiness back in to his life and uses medications to keep his allergies under control because he doesn't want to give up the cat. Used smokeless tobacco × 35 years (quit 10 years ago); heavy ETOH in the past, occasional glass of wine now.

■ ROS

In conversation, he is alert, friendly, and courteous. He has no c/o dyspepsia, dysphagia, abdominal pain, hematemesis, urinary incontinence, or visible blood in the stool.

■ Meds

Metformin 1000 mg PO BID
Rosuvastatin 20 mg PO once daily
Terazosin 10 mg PO once daily
Amitriptyline 25 mg PO at bedtime (insomnia)
Metoprolol succinate 50 mg PO once daily
Ibuprofen 800 mg PO BID
Claritin-D 24-hour one tablet PO daily (allergy to cats)

■ All

NKDA; allergic to cat dander

■ Physical Examination

Gen

White male in NAD; well-kept appearance; A&O × 3

VS

BP 110/60 mm Hg, P 65 bpm, RR 18, T 37°C; Wt 115.2 kg, Ht 6'0"

Skin

Vertical scars on neck and lower back from laminectomies

HEENT

PERRLA; EOMI; TMs intact; nose and throat clear w/o exudate or lesions

Neck/Lymph Nodes

Supple w/o LAD or masses; thyroid in midline

Lungs/Thorax

CTA, distant sounds

CV

RRR w/o murmurs

Abd

Soft, NTND w/o masses or scars; (+) BS

Genit/Rect

Testes ↓↓, penis circumcised w/o DC; guaiac (+) stool

TABLE 98-1 Laboratory Values

Na 136 mEq/L	Hgb 12.6 g/dL	WBC $5.6 \times 10^3/\text{mm}^3$	AST 12 IU/L	Ca 8.5 mg/dL
K 4.1 mEq/L	Hct 37.9%	Neutros 75%	ALT 16 IU/L	Phos 3.5 mg/dL
Cl 103 mEq/L	MCV 78 μm^3	Lymphs 16%	Alk phos 55 IU/L	Uric acid 3.5 mg/dL
CO ₂ 41 mEq/L	MCH 29 pg	Monos 5%	LDH 121 IU/L	T ₄ 7.3 mcg/dL
BUN 9 mg/dL	MCHC 33.0 g/dL	Eos 3%	T. bili 0.6 mg/dL	TSH 1.04 mIU/L
SCr 0.7 mg/dL	Plt $191 \times 10^3/\text{mm}^3$	Basos 1%	T. prot 6.1 g/dL	A1C 7%
Glu 120 mg/dL			T. chol 146 mg/dL	PSA 4.5 ng/mL

MS/Ext

Distal pulses 1–2+, knees appear to be inflamed with decreased range of motion and tenderness on palpation.

Neuro

DTRs 2+; CNs II–XII grossly intact

Labs

See Table 98-1.

UA

Color straw; appearance clear; SG 1.010; pH 6.5; glucose (–); bilirubin (–); ketones (–); blood (–); urobilinogen 0.2 mg/dL; nitrite (–); leukocyte esterases (–); epithelial cells—occasional per hp; WBC—occasional per hp; RBC—none seen; bacteria—trace; amorphous—none seen; crystals—1+ calcium oxalate; mucus—none seen. Culture not indicated.

GU Consult

Patient treated for UTI 2 weeks ago with Cipro 250 mg PO Q 12 H $\times$ 3 days. Urine clear; negative for glucose. Bladder examination with ultrasound revealed postvoid residual estimate of 300 mL. Prostate approximately 35 g, benign. AUA Symptom Score = 20. Uroflowmetry (Qmax) = 8 mL/sec. A 3-day urine frequency volume chart was completed and showed no polyuria.

Assessment

BPH

ED

Symptomatic hypotension

Microcytic anemia possibly secondary to ulceration from ibuprofen use

HTN

Type 2 DM

Obesity

OA

Cat allergy (recent onset with adoption of new cat)

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. Describe the natural history and epidemiologic characteristics of BPH.
- 2.d. What other medical conditions should be ruled out before treating this patient for BPH?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating BPH?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE: ALTERNATIVE THERAPY

As the pharmacist in the team, you perform a literature search on the use of saw palmetto for BPH. You discover that there are reports of the dietary supplement both improving and worsening symptoms of ED. In addition, your readings indicate that saw palmetto should really only be used by patients with mild to moderate BPH. Based on this information, you do not recommend use of saw palmetto for the patient's BPH symptoms. However, because the patient is requesting information on natural products, you search for alternative dietary supplements that may provide some benefit for this patient's BPH without contributing to ED. Would *Pygeum africanum* be a reasonable option to consider? For questions related to the use of *P. africanum* for the treatment of BPH, please see Section 19 of this Casebook.

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information is consistent with the presence of BPH?
- 1.b. What additional information is needed to fully assess this patient's BPH (Figure 98-1)?

Assess the Information

- 2.a. Assess the severity of BPH based on the subjective and objective information available.

Patient Name: _____ DOB: _____ ID: _____ Date of assessment: _____							
Initial Assessment () Monitor during: _____ Therapy () after: _____ Therapy/surgery () _____							
AUA BPH Symptom Score							
	Not at all	Less than 1 time in 5	Less than half the time	About half the time	More than half the time	Almost always	
1. Over the past month, how often have you had a sensation of not emptying your bladder completely after you finished urinating?	0	1	2	3	4	5	
2. Over the past month, how often have you had to urinate again less than two hours after you finished urinating?	0	1	2	3	4	5	
3. Over the past month, how often have you found you stopped and started again several times when you urinated?	0	1	2	3	4	5	
4. Over the past month, how often have you found it difficult to postpone urination?	0	1	2	3	4	5	
5. Over the past month, how often have you had a weak urinary stream?	0	1	2	3	4	5	
6. Over the past month, how often have you had to push or strain to begin urination?	0	1	2	3	4	5	
	None	1 time	2 times	3 times	4 times	5 or more times	
7. Over the past month, how many times did you most typically get up to urinate from the time you went to bed at night until the time you got up in the morning?	0	1	2	3	4	5	
Total Symptom Score							

FIGURE 98-1. The American Urologic Association (AUA) symptom index for benign prostatic hyperplasia (BPH). (Reproduced from article in the public domain: Barry MJ, Fowler FJ Jr, O'Leary MP, et al. The American Urological Association symptom index for benign prostatic hyperplasia. The Measurement Committee of the American Urological Association. *J Urol* 1992;148(5):1549–1557.)

CLINICAL COURSE

After your recommendations were implemented, Mr McCracken's BP increased to 130/80 mm Hg, and the BPH and ED symptoms improved remarkably. Over the ensuing weeks, he continued to experience occasional urgency and hesitancy. After 6 months of watchful waiting, he opted for laser prostatectomy. This procedure was successful in alleviating his symptoms.

SELF-STUDY ASSIGNMENTS

1. Compare the efficacy of saw palmetto (*Serenoa repens*) to finasteride and $\alpha 1$ -antagonists for the treatment of BPH.
2. Compare treatment options for ED in patients with BPH. Identify the risks and potential benefits of using $\alpha 1$ -antagonists and 5 α -reductase inhibitors in treating comorbid ED and BPH.
3. Identify the BPH patient subpopulation that would benefit most from finasteride/dutasteride therapy.
4. Perform a literature search for evidence that supports use of phosphodiesterase type 5 inhibitors and $\alpha 1$ -antagonists as combination therapy for BPH/ED.
5. Perform a literature search for the use of phosphodiesterase type 5 inhibitors as monotherapy for LUTS secondary to BPH.

CLINICAL PEARL

Physiologic measurements such as postvoid residuals, uroflowmetry, and pressure-flow studies often do not correlate well with the patient's perception of BPH symptom severity.

REFERENCES

1. McVary KT, Roehrborn CG, Avins AL, et al. Update on AUA guideline on the management of benign prostatic hyperplasia. *J Urol* 2011; 185(5):1793–1803.
2. Miner M, Rosenberg MT, Perelman MA. Treatment of lower urinary tract symptoms in benign prostatic hyperplasia and its impact on sexual function. *Clin Ther* 2006;28:13–25.
3. Kaminetsky JC. Comorbid LUTS and erectile dysfunction: optimizing their management. *Curr Med Res Opin* 2006;22:2407–2506.
4. Hollingsworth J, Wilt T. Lower urinary tract symptoms in men. *BMJ* 2014;349:g4474. doi:10.1136/bmj.g4474.
5. Narayan P, Evans CP, Moon T. Long-term safety and efficacy of tamsulosin for the treatment of lower urinary tract symptoms associated with benign prostatic hyperplasia. *J Urol* 2003;170(Pt 1):498–502.
6. Sarma AV, Wei JT. Clinical practice. Benign prostatic hyperplasia and lower urinary tract symptoms. *N Engl J Med* 2012;19:367(3): 248–257.
7. Greco KA, McVary KT. The role of combination medical therapy in benign prostatic hyperplasia. *Int J Impot Res* 2008;20(Suppl 3): S33–S43.
8. Van Asseldonk B, Barkin J, Elterman D. Medical therapy for benign prostatic hyperplasia: a review. *Can J Urol* 2015;22(Suppl 1):7–17.
9. Donatucci CF, Brock GB, Goldfischer ER, et al. Tadalafil administered once daily for lower urinary tract symptoms secondary to benign prostatic hyperplasia: a 1-year, open-label extension study. *BJU Int* 2011; 107(7):1110–1116.
10. Tacklind J, MacDonald R, Rutks I, Stanke JU, Wilt TJ. *Serenoa repens* for benign prostatic hyperplasia. *Cochrane Database Syst Rev* 2012 (Dec 12);12:CD001423.

99

URINARY INCONTINENCE

Bladder Matters Level II

Mary W. L. Lee, PharmD, BCPS, FCCP

Roohollah R. Sharifi, MD, FACS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Differentiate among overactive bladder syndrome, stress urinary incontinence, overflow urinary incontinence, and functional urinary incontinence.
- Recommend appropriate nondrug therapy for managing overactive bladder syndrome.
- Determine when anticholinergic drugs should be recommended for managing overactive bladder syndrome.
- Compare and contrast muscarinic receptor selectivity, lipophilicity, and pharmacokinetic properties of commonly used antimuscarinic agents for managing overactive bladder syndrome and discuss the clinical implications of these properties.
- Explain how concomitant medications may exacerbate overactive bladder syndrome.
- Recommend medication options for patients who poorly tolerate initial anticholinergic therapy for overactive bladder syndrome.

PATIENT PRESENTATION

■ Chief Complaint

"I can't seem to control my urine. I feel like I have to urinate all the time. However, when I do go to the bathroom, I often pass only a small amount of urine. Sometimes I wet myself. I was started on a medication for my leaking a few weeks ago, but it doesn't seem to be working. I also can't seem to remember anything. It is a wonder that I remembered to come to the clinic today."

■ HPI

Susan Jones is a 65-year-old woman with urinary urgency, frequency, and incontinence. She reports soiling her underwear at least two to three times during the day and night and has resorted to wearing panty liners or changing her underwear several times a day. The patient has curtailed much of her volunteer work and social activities because of this problem. Urinary leakage is not worsened by laughing, coughing, sneezing, carrying heavy objects, or walking up and down stairs. She does not report wetting herself without warning. She has been taking Detrol LA 2 mg PO daily for the past month with no improvement in her voiding symptoms, and she complains of new-onset confusion and difficulty remembering routine tasks.

■ PMH

HTN for many years, treated with medications for 10 years. Dyslipidemia for 5 years, controlled with a low-cholesterol diet, weight control, regular exercise, and medication. Menopausal; stopped ovulating at age 52; no longer has hot flashes. Has difficulty falling

asleep and often has sleepless nights. She has no history of spinal or pelvic surgery.

■ FH

Noncontributory

■ SH

Nonsmoker; social drinker; married

■ Meds

Hydrochlorothiazide 25 mg PO once daily with supper

Irbesartan 150 mg PO daily

Pravastatin 40 mg PO at bedtime

Detrol LA 2 mg PO daily

Somnol (diphenhydramine) 15 mg PO at bedtime as needed, usually about five times a week

Amitriptyline 50 mg PO at bedtime as needed

■ All

NKDA

■ ROS

Complaints of urinary incontinence that has not responded to Detrol LA. Feels confused and has difficulty remembering routine tasks. Patient states that her ability to remember what she has to do became impaired in the past 3 weeks after Detrol was started.

■ Physical Examination

Gen

WDWN woman

VS

BP 135/84 mm Hg, P 90 bpm, RR 16, T 37°C; Wt 65 kg, Ht 5'2"

Skin

No rashes, wounds, or open sores

HEENT

PERLLA; EOMI; no AV nicking or hemorrhages

Neck/Lymph Nodes

No palpable thyroid masses; no lymphadenopathy

Pulm

Clear to A&P

Breasts

Normal; no lumps

CV

Regular S₁, S₂; (+) S₄; (-) S₃, murmurs, or rubs

Abd

Soft, NTND, (+) bowel sounds

Genit/Rect

Genital examination shows atrophic vaginitis consistent with menopausal status. Perineal sensation and anal sphincter tone are normal.

Pelvic examination shows no uterine prolapse and a mild degree of cystocele. Cervix is normal. No pelvic, adnexal, or uterine masses found.

External hemorrhoids; heme (–) stool.

Ext

Normal; equal motor strength in both arms and legs

Neuro

Although alert, the patient is not oriented to correct month, day, or year. CNs II–XII grossly intact; DTRs 3/5 bilaterally; negative Babinski. When asked to recall a series of five objects after 5 minutes, the patient had difficulty and could only recall one object.

Labs

Na 140 mEq/L
K 4.2 mEq/L
Cl 105 mEq/L
CO₂ 28 mEq/L
BUN 17 mg/dL
SCr 1.2 mg/dL
Glu 100 mg/dL

Hgb 12 g/dL
Hct 37%
Plt $400 \times 10^3/\text{mm}^3$
WBC $5.0 \times 10^3/\text{mm}^3$

UA

No bacteria; no WBC

Other

Using an ultrasonic bladder scan, a residual urine volume was measured after the patient voided. No residual urine was found. The bladder was then filled with 300 mL saline. The patient felt the first desire to void at 100 mL. The catheter was removed. The patient was asked to cough in different positions. No stress urinary incontinence was demonstrated. The patient voided the entire volume of saline that was instilled.

Assessment

Overactive bladder with symptoms of urinary urgency, frequency, and incontinence, which has not responded to Detrol LA 2 mg PO daily for 1 month. Patient is also having new-onset confusion and forgetfulness, which are probably related to Detrol LA and to the total anticholinergic burden. Will evaluate carefully and consider alternative medication options.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of urge incontinence?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. Assess the severity of incontinence based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. Differentiate urge incontinence from stress incontinence, overflow incontinence, and functional incontinence.
- 2.d. Define overactive bladder syndrome.

- 2.e. In addition to the medications the patient is currently taking, what other drugs could exacerbate the symptoms of overactive bladder syndrome?
- 2.f. What are the possible consequences of persistent CNS adverse effects of anticholinergic agents in this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What pharmacotherapeutic alternatives are available for treating overactive bladder? Compare and contrast antimuscarinic agents for treatment of overactive bladder syndrome.
- 3.d. Which anticholinergic agents have a low potential to cause CNS adverse effects? Describe the physicochemical or pharmacokinetic characteristics of these agents that contribute to this favorable profile.
- 3.e. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Assume that the physician stopped Detrol LA and started the patient on trospium extended-release (Sanctura XR) 60 mg daily by mouth. After 3 weeks of the new medication regimen, the patient returns to the clinic. Although her confusion and forgetfulness have resolved, her symptoms of overactive bladder syndrome have worsened. The patient complains of multiple episodes of nocturia that disturb her sleep. She says that she cannot tolerate this and wants different drug treatment.

FOLLOW-UP QUESTIONS

1. Why should medications with anticholinergic effects be used cautiously in older patients?
2. What alternative medication could you recommend for this patient to manage her voiding symptoms?

SELF-STUDY ASSIGNMENTS

1. Patients have been classified as extensive versus poor metabolizers of tolterodine. Describe the characteristics of these patients and the clinical implications of this patient classification.
2. Botulinum toxin has been reported to be effective for relieving symptoms of overactive bladder. Explain how it is administered and the adverse effects associated with its use.

3. Mirabegron and anticholinergic agents have been used in combination to treat overactive bladder syndrome. What are the advantages and disadvantages of combination therapy?

CLINICAL PEARL

A uroselective antimuscarinic agent generally exerts systemic clinical effects. Although inhibition of M_3 receptors may cause bladder relaxation and decrease involuntary detrusor contraction, M_3 receptors are also located in the colon and salivary glands. Therefore, antagonism of M_3 receptors may relieve overactive bladder symptoms but may also produce dose-related anticholinergic adverse effects including constipation and dry mouth.

REFERENCES

1. Chung A, Noguchi N, Chan L, Tse V. Voiding dysfunction in older men. *Curr Opin Urol* 2016;26(2):177–183.
2. White N, Iglesia CB. Overactive bladder. *Obstet Gynecol Clin North Am* 2016;43(1):59–68.
3. Vo A, Kiehl SJ. Female voiding dysfunction and urinary incontinence. *Med Clin North Am* 2018;102(2):313–324.
4. Orme S, Morris V, Gibson W, Wagg A. Managing urinary incontinence in patients with dementia: pharmacological treatment options and considerations. *Drugs Aging* 2015;32(7):559–567.
5. Araklitis G, Cardozo L. Safety issues associated with using medication to treat overactive bladder. *Expert Opin Drug Saf* 2017;16(11):1273–1280.
6. Nambiar AK, Bosch R, Cruz F, et al. EAU guidelines on assessment and nonsurgical management of urinary incontinence. *Eur Urol* 2018;73(4):596–609.
7. Shamlivan T, Wyman JF, Ramakrishnan R, Sainfort F, Kane RL. Benefits and harms of pharmacologic treatment of urinary incontinence in women. *Ann Intern Med* 2012;156(12):861–874.
8. Chancellor MB, Staskin DR, Kay GC, et al. Blood-brain barrier permeation and efflux exclusion of anticholinergics used in the treatment of overactive bladder. *Drugs Aging* 2012;29(4): 259–273.
9. Gormley EA, Lightner DJ, Faraday M, Vasavada SP. Diagnosis and treatment of overactive bladder (non-neurogenic) in adults: AUA/SUFU guideline amendment. *J Urol* 2015;193(5):1572–1580.
10. Robinson D, Thiagamoorthy G, Cardozo L. A drug safety evaluation of mirabegron in the management of overactive bladder. *Expert Opin Drug Saf* 2016;15(5):689–696.

SECTION 11

IMMUNOLOGIC DISORDERS

100

SYSTEMIC LUPUS ERYTHEMATOSUS

Sometimes, It's Lupus Level II

Nicole Paolini Albanese, PharmD, CDE, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Discuss the clinical presentation of SLE, including its complications.
- Design appropriate therapy for the treatment of SLE and the complications of antiphospholipid syndrome (APS) and iron deficiency anemia.
- Construct a monitoring plan for SLE, including disease activity, drug efficacy, and drug toxicity.
- Recommend appropriate therapy for the treatment of SLE during pregnancy.

PATIENT PRESENTATION

■ Chief Complaint

"My knees are killing me, I'm tired all the time, and I've got horrible pain in my stomach."

■ HPI

Ann Baker is a 32-year-old woman who has been having knee pain on and off for about 2 years. She has been to the doctor a few times since then with the same complaint. Workups showed no radiologic changes to the knees, and the doctor settled on a diagnosis of early arthritis. She was not evaluated by a rheumatologist. Despite scheduled APAP and ibuprofen throughout the day, the pain has not decreased much. The pain seems to be cyclical; it is very bad for a period of weeks, and then it wanes over time. It is also worse in the summer. She thinks the rashes she gets occasionally on her face and arms have something to do with the pain, since the rash happens around the same time of a bad flare-up. No matter how much sleep she gets, it does not seem to be enough; a couple of sleep medications later, she is no better than before she tried them. She has also noticed a darkening of her stool over the past couple of months.

■ PMH

Knee pain × 2 years
HTN × 1 year
Depression × 3 years
Fatigue × 1 year

■ FH

Father alive in his mid-60s; has HTN and dyslipidemia. Mother alive in her mid-60s; has asthma and seasonal allergies.

■ SH

Employed as a travel agent; married 5 years; occasional EtOH use and no current or past tobacco use. On inquiry, Ms Baker states she and her husband are trying to conceive.

■ Meds

Hydrochlorothiazide 12.5 mg PO once daily
Amlodipine 5 mg PO once daily
Fluoxetine 20 mg PO once daily
Ibuprofen 800 mg PO four times daily
Acetaminophen 500 mg PO three times daily
Past meds: Zolpidem 10 mg PO at bedtime and ramelteon 8 mg PO at bedtime (stopped using both after inefficacy)

■ All

NKDA

■ ROS

(+) Fatigue, rash; (–) fever, chills, peripheral edema, or alopecia

■ Physical Examination

Gen

Tired-looking woman in moderate pain.

Pain scale: Presently 6/10; per patient, her worst pain is 10/10; her best score is 0/10.

VS

BP 136/82 mm Hg, P 74 bpm, RR 17, T 38°C, Wt 59 kg, Ht 5'4"

Skin

Warm; moist to touch; slight red, scaly rash on forearms and across both cheekbones but sparing the nasolabial folds

HEENT

PERRLA; EOMI

Neck/Lymph Nodes

Supple without adenopathy

Lungs/Thorax

CTA; no rales/rhonchi

CV

RRR; S₁ and S₂ normal

Abd

Tender, nondistended; (+) bowel sounds; (+) stool guaiac

Ext

Peripheral pulses intact; no edema

Joint examination: (–) bony proliferation, synovitis, crepitus, muscle atrophy, or deformities; no limitations on range of motion

Neuro

A&O × 3; CN II–XII intact; Babinski negative

Labs

Na 136 mEq/L	RBC 3.2 $10^6/\text{mm}^3$	ESR 66 mm/hour
K 4.7 mEq/L	Hgb 11.0 g/dL	RF titer 1:40
Cl 105 mEq/L	Hct 25%	Anti-CCP antibody (–)
CO ₂ 25 mEq/L	MCV 78 fL	ANA titer 1:320 (rim pattern)
BUN 13 mg/dL	WBC $7.2 \times 10^3/\text{mm}^3$	C3 50 mg/dL
SCr 0.8 mg/dL	Plt $250 \times 10^3/\text{mm}^3$	C4 10 mg/dL
Uric acid 5.5 mg/dL	Fe 35 mcg/dL	Lupus anticoagulant (+)
Glucose 82 mg/dL	TIBC 455 mcg/dL	Anticardiolipin Ab (+)
	Ferritin 8 ng/mL	dsDNA Ab (+)

UA

(–) WBC, RBC, RBC casts; (+) microalbuminuria; (–) protein

Radiologic Joint Evaluation

(–) Patellar or tibial fracture, (–) displacement, (–) fragments, (–) ligament damage, no evident soft tissue damage

Assessment

Mild SLE with biomarkers for APS; iron deficiency anemia possibly secondary to NSAID use; possible NSAID-associated gastropathy

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of SLE?
- 1.b. What information indicates the presence of iron deficiency anemia?
- 1.c. What additional information is needed to fully assess this patient's SLE?

Assess the Information

- 2.a. Assess the severity of SLE based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for SLE in this patient?
- 3.b. What are the goals of pharmacotherapy for antiphospholipid syndrome (APS) in this patient?
- 3.c. What are the goals of pharmacotherapy for iron deficiency anemia in this patient?
- 3.d. What nondrug therapies might be useful for treating SLE?
- 3.e. What feasible pharmacotherapeutic alternatives are available for treating SLE in this patient?

- 3.f. What options are available for prophylaxis of thrombotic events due to APS?
- 3.g. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.h. Does the regimen you selected pose any concerns if the patient were to become pregnant?
- 3.i. What are your recommendations for treating this patient's iron deficiency anemia and NSAID-associated gastropathy?
- 3.j. Should any changes be made in this patient's antihypertensive therapy?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, minimize relapses, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

FOLLOW-UP QUESTIONS

1. What can this patient do to increase the chances of having a successful pregnancy?
2. If your initial medication regimen does not work, what is the next step in treating this patient?

SELF-STUDY ASSIGNMENTS

1. How do B-lymphocyte stimulator antagonists work, and where do they fit in with the pharmacotherapy of SLE?
2. Devise a comprehensive patient education plan for women with SLE who wish to start a family.

CLINICAL PEARL

Because UV light exacerbates SLE, drugs that induce photosensitivity should be avoided in patients with the disease.

REFERENCES

1. Short MW, Domagalski JE. Iron deficiency anemia: evaluation and management. *Am Fam Physician* 2013;87(2):98–104.
2. Lam NC, Ghetu MV, Bieniek ML. Systemic lupus erythematosus: primary care approach to diagnosis and management. *Am Fam Physician* 2016;94(4):284–294.
3. Sciascia S, Hunt BJ, Talavera-Garcia E, Lliso G, Khamashta MA, Cuadrado MJ. The impact of hydroxychloroquine treatment on pregnancy outcome in women with antiphospholipid antibodies. *Am J Obstet Gynecol* 2016;214(2):273.e1–e8.

4. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *J Am Coll Cardiol* 2014;63(25 Pt B):2889–2934.
5. Lewis MJ, Jawad AS. The effect of ethnicity and genetic ancestry on the epidemiology, clinical features and outcome of systemic lupus erythematosus. *Rheumatology* 2017;56(Suppl 1):i67–i77.
6. Petri M, Orbai AM, Alarcón GS, et al. Derivation and validation of the Systemic Lupus International Collaborating Clinics classification criteria for systemic lupus erythematosus. *Arthritis Rheum* 2012;64(8):2677–2686.
7. Thong B, Olsen NJ. Systemic lupus erythematosus diagnosis and management. *Rheumatology (Oxford)* 2017;56(Suppl 1):i3–i13.
8. Lanas A, Chan FKL. Peptic ulcer disease. *Lancet* 2017;390(10094):613–624.
9. Lopes MRU, Danowski A, Funke A, Rego J, Levy R, Andrade DCO. Update on antiphospholipid antibody syndrome. *Rev Assoc Med Bras* 2017;63(11):994–999.
10. Vreede AP, Bockenstedt PL, Knight JS. Antiphospholipid syndrome: an update for clinicians and scientists. *Curr Opin Rheumatol* 2017;29(5):458–466.
11. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA Guideline for the Prevention, Detection, Evaluation, and Management of High Blood Pressure in Adults. A Report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Hypertension* 2018;71(6):1269–1324.

101

ALLERGIC DRUG REACTION

Return of the 3-Day Itch Level II

Lynne M. Sylvia, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Interpret drug allergy information (eg, timing of the reaction, signs, and symptoms) to identify the likelihood of an IgE-mediated reaction.
- Assess the potential for cross-sensitivity between penicillins and carbapenems.
- Differentiate desensitization from graded challenge dosing procedures and identify patients who are appropriate candidates for each procedure.
- Select appropriate antibiotic therapy for a patient with multiple antibiotic allergies.

PATIENT PRESENTATION

■ Chief Complaint

“My cough is back and I feel like I did when I was admitted three weeks ago.”

■ HPI

Alan Adams is a 55-year-old man with a history of COPD who is an inpatient on the general medicine service at an academic medical center. He has had four admissions this year for COPD and pneumonia. Three weeks ago, he presented to the ED complaining of a 3-day history of tiredness and a cough productive of greenish sputum. Sputum cultures at that time revealed *Pseudomonas aeruginosa* sensitive to aztreonam and cefepime with intermediate sensitivity to piperacillin–tazobactam and tobramycin. Due to his multiple antibiotic allergies, the patient underwent desensitization to cefepime. He was subsequently treated as an inpatient for 10 days with IV cefepime without incident. He has remained an inpatient for continued COPD management.

■ PMH

COPD × 17 years

Chronic empyema secondary to bronchial pleural fistulae with chest tube placement 7 months ago

RUL lung abscess secondary to *Candida* and *Aspergillus*; S/P upper lobe lobectomy 11 years ago

HTN × 10 years

S/P MI 15 years ago

■ SH

Lives with his mother; he is unemployed. He has a 40 pack-year smoking history. Admits to occasional alcohol use; denies use of recreational drugs.

■ Meds

Albuterol MDI two puffs Q 6 H PRN

Ipratropium MDI two puffs Q 6 H

Aspirin 81 mg PO once daily

Amlodipine 10 mg PO once daily

Atorvastatin 40 mg PO once daily (FLP 1 year ago: TC 142, LDL 67, HDL 46, TG 145)

Prednisone 20 mg PO daily (initiated as 60 mg PO daily earlier in this hospital stay for COPD exacerbation; plan is to taper the dose and discontinue therapy within 2 weeks of hospital discharge)

■ All

Ampicillin–sulbactam: facial edema, tongue swelling, and periorbital edema

Ceftazidime: urticarial rash on chest and face with shortness of breath

Codeine: nausea, pruritus

■ ROS

(+) Fatigue, fever, sore throat, shortness of breath, and cough with thick sputum; (–) nausea, vomiting, diarrhea, chills, or chest pain

■ Physical Examination

Gen

A 55-year-old Caucasian man appearing older than his stated age in moderate respiratory distress. He is lethargic and hard of hearing.

VS

BP 100/60 mm Hg, P 85 bpm, RR 16, T 39°C; Wt 52 kg, Ht 5'5"

Skin

Dry scaly skin; no tenting

HEENT

PERRLA, EOM intact, dry mucous membranes, difficulty hearing
L > R

Neck/Lymph Nodes

(-) Bruits, (-) lymphadenopathy

Lungs/Thorax

(+) Diffuse crackles at the left base; wheezes throughout with poor breath sounds

CV

Normal S₁ and S₂, RRR, (-) MRG

Abd

Distended with (+) bowel sounds; (-) hepatosplenomegaly

Genit/Rect

Deferred

Ext

(+) Clubbing; (-) cyanosis or edema; poor muscle tone

Neuro

Alert, oriented, and cooperative. CNs II–XII are intact. Tone and strength are 4/5 in both arms, and 4/5 in both legs. Sensory exam is normal. Reflexes are 2+ in UE and 3+ in LEs.

■ Labs

Na 137 mEq/L	Hgb 14.8 g/dL	WBC $17 \times 10^3/\text{mm}^3$
K 3.7 mEq/L	Hct 44.6%	Neutros 72%
Cl 96 mEq/L	RBC $5.36 \times 10^6/\text{mm}^3$	Bands 5%
CO ₂ 29 mEq/L	Plt $244 \times 10^3/\text{mm}^3$	Eos 4%
BUN 22 mg/dL	MCV 83.2 μm^3	Lymphs 11%
SCr 1.0 mg/dL	MCHC 33.2 g/dL	Monos 8%
Glu 119 mg/dL		Basos 0%

■ ABG

pH 7.44, PaO₂ 55 mm Hg, PaCO₂ 38 mm Hg, O₂ sat 90%

■ Chest X-Ray

Haziness in the left lower lobe; S/P right upper lobe resection

■ Sputum Gram Stain

Pending

■ Sputum Cultures

Pending

■ Blood Cultures

Pending

■ Assessment

1. HAP
2. COPD

3. HTN
4. S/P MI

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of an allergic drug reaction?
- 1.b. What additional information would be helpful to fully assess the patient's risk of hypersensitivity reactions to β -lactam antibiotics?
- 1.c. What additional information would be helpful to assess whether the patient experiences true hypersensitivity versus pseudo allergy to codeine?

Assess the Information

- 2.a. Based on the patient's allergy history, how should his allergies to ampicillin-sulbactam and ceftazidime be categorized—as minor, moderate, or severe?
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals for treating pneumonia in this case?

■ CLINICAL COURSE

The patient is started on standing DuoNeb (albuterol 3 mg/3 mL and ipratropium 0.5 mg/3 mL) by nebulizer 3 mL Q 2 H, guaifenesin with codeine (100 mg/10 mg/5 mL) PO Q 4 H PRN, and acetaminophen 325–650 mg PO Q 4 H PRN. While cultures are pending, review of the hospital course to date, the C&S obtained 3 weeks ago, and the hospital's guidelines for treating HAP, consideration is given to initiating empiric therapy with meropenem 1 g IV Q 8 H, ciprofloxacin 400 mg IV Q 8 H, and vancomycin 1 g IV Q 24 H. The medical team discusses the appropriateness of starting meropenem in this patient.

- 3.b. The initial empiric regimens recommended for hospital-acquired pneumonia (HAP) are summarized in Table 101-1. Both cefepime and aztreonam are alternatives to meropenem in these multidrug regimens. Based on this patient's history, are cefepime and aztreonam safe alternatives to meropenem for empiric therapy of HAP? (See Fig. 101-1 for the chemical structures of cefepime and ceftazidime.)
- 3.c. If a multidrug regimen including cefepime was chosen for empiric therapy, would this patient require another course of desensitization prior to initiating full-dose cefepime therapy?
- 3.d. Assess the risk of a hypersensitivity cross-reaction to meropenem in this patient. Based on your review of the literature, determine which of the following courses of action is best: (a) initiation of full-dose meropenem therapy; (b) desensitization to meropenem prior to initiating full treatment doses; or (c) graded challenge dosing of meropenem prior to initiating full treatment doses. Substantiate your position on the most appropriate course of action based on evidence from the literature.

TABLE 101-1 Initial Empiric Treatment for HAP in Patients With Risk Factors for Drug-Resistant Pathogens and Receipt of Intravenous Antibiotics During the Previous 90 Days^a**Two of the following, avoiding two β -lactams:** *β -Lactam/ β -lactamase inhibitor*

Piperacillin-tazobactam 4.5 g IV Q 6 H

Or antipseudomonal cephalosporin

Cefepime 2 g IV Q 8 H

Ceftazidime 2 g IV Q 8 H

Or antipseudomonal fluoroquinolone

Levofloxacin 750 mg IV daily

Ciprofloxacin 400 mg IV Q 8 H

Or antipseudomonal carbapenem

Imipenem 500 mg IV Q 6 H

Meropenem 1 g IV Q 8 H

Or aminoglycoside

Amikacin 15–20 mg/kg IV daily

Gentamicin 5–7 mg/kg IV daily

Tobramycin 5–7 mg/kg IV daily

*Or monocyclic β -lactam (monobactam)*Aztreonam 2 g Q 8 H^b**PLUS**

Vancomycin 15 mg/kg IV Q 8–12 H with target trough level of 15–20 mcg/mL

Or

Linezolid 600 mg IV Q 12 H

HAP, hospital-acquired pneumonia.

^aKalil AC, Metersky ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of American and the American Thoracic Society. *Clin Infect Dis* 2016;63(5):e61–e111.^bIf patient has severe penicillin allergy and aztreonam will be used instead of any β -lactam antibiotic, include coverage for methicillin-sensitive *Staphylococcus aureus* (MSSA).**Implement the Care Plan**

- 4.a. What information should be provided to the patient about his drug allergies to minimize allergic events in the future?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. In patients who undergo desensitization and/or graded challenge dosing, what clinical and laboratory parameters should be

evaluated during and after these procedures to detect or prevent allergic events?

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

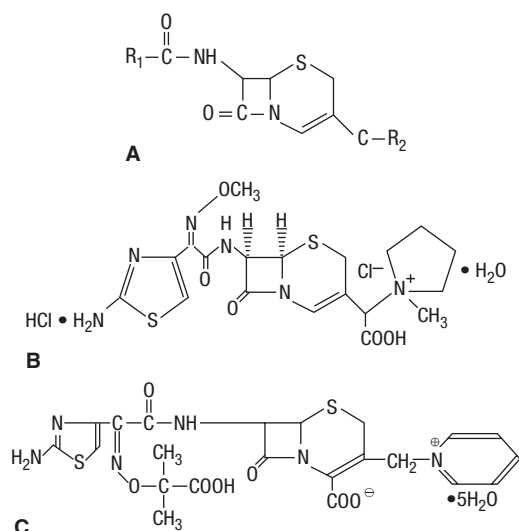
1. Define the following terms: CAP, HAP, HCAP, and VAP. Differentiate the initial empiric regimens for each of these types of pneumonia.
2. Develop a care map for patients allergic to penicillin for whom a carbapenem is ordered. Outline the process by which the clinician would determine the most appropriate course of action for these patients. Be specific as to the type of allergy to the penicillin (ie, maculopapular rash vs Stevens–Johnson syndrome vs anaphylactic reaction).
3. Apply the concepts of graded challenge dosing and desensitization (see the section “Clinical Pearl”) to the issue of β -lactam hypersensitivity. Develop criteria describing those patients with history of β -lactam hypersensitivity who would be appropriate candidates for graded challenge dosing versus desensitization to structurally related antibiotics.

CLINICAL PEARL

A graded challenge dose (test dosing) involves the cautious administration of a medication to a patient. Graded challenge doses of a medication are often recommended for patients who have history of hypersensitivity to a structurally related medication and the risk of a cross-reaction is deemed unlikely. Unlike desensitization, graded challenge dosing does not alter the body’s immune response to an antigenic medication.

REFERENCES

1. Solensky R, Khan DA. Drug allergy: an updated practice parameter. *Ann Allergy Asthma Immunol* 2010;105:273.e1–e78.
2. Romano A, Di Fonso M, Viola M, Adesi FB, Venuti A. Selective hypersensitivity to piperacillin. *Allergy* 2000;55(8):787.
3. Pichichero ME. Cephalosporins can be prescribed safely for penicillin-allergic patients. *J Fam Pract* 2006;55:106–112.
4. Romano A, Gaeta F, Arribas Poves MF, et al. Cross-reactivity among beta-lactams. *Curr Allergy Asthma Rep* 2016;16:24.
5. Lieberman P, Nicklas RA, Randolph C, et al. Anaphylaxis—a practice parameter update 2015. *Ann Allergy Asthma Immunol* 2015;115:341–384.
6. Prescott WA, Kusmierski KA. Clinical importance of carbapenem hypersensitivity in patients with self-reported and documented penicillin allergy. *Pharmacotherapy* 2007;27(1):137–142.
7. Romano A, Viola M, Gueant-Rodriguez RM, et al. Brief communication: tolerability of meropenem in patients with IgE-mediated hypersensitivity to penicillins. *Ann Intern Med* 2007;146:266–269.
8. Atanaskovic-Markovic M, Gaeta F, Medjo B, et al. Tolerability of meropenem in children with IgE-mediated hypersensitivity to penicillins. *Allergy* 2008;63:237–240.
9. Gaeta F, Valluzzi RL, Alonzi C, et al. Tolerability of aztreonam and carbapenems in patients with IgE-mediated hypersensitivity to penicillins. *J Allergy Clin Immunol* 2015;135:972–976.
10. Wilson DL, Owens RC, Zuckerman JB. Successful meropenem desensitization in a patient with cystic fibrosis. *Ann Pharmacother* 2003;37:1424–1428.

**FIGURE 101-1.** Chemical structures of cefepime and ceftazidime. A. Basic cephalosporin structure. B. Cefepime. C. Ceftazidime.

102

SOLID ORGAN TRANSPLANTATION

Kidney—Don't Fail Me Now! Level III

Kristine S. Schonder, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Develop a patient-specific care plan for acute cellular rejection following solid organ transplantation.
- Assess a transplant medication regimen for potential drug interactions and develop a plan to resolve any identified interactions.
- Describe possible adverse effects of immunosuppressive medications and prophylactic medications for solid organ transplant recipients and develop a plan to resolve these effects.
- Counsel a transplant recipient on the importance of medication adherence and implement strategies to enhance adherence.

PATIENT PRESENTATION

■ Chief Complaint

"I have pain over my kidney transplant, my legs are swollen, and my urine output is decreased."

■ HPI

Brent Salston is a 42-year-old man who presents to the renal transplant clinic for evaluation of the above complaints. He states the symptoms began about 1 week ago and have gotten progressively worse.

■ PMH

5 months S/P living kidney transplant from his wife. He is CMV seronegative; his wife (the donor) was CMV seropositive.

ESRD secondary to IgA nephropathy

HTN

Gout

Peripheral neuropathy, diagnosed 2 weeks ago by PCP

■ FH

Mother is alive with hypertension; father deceased from kidney disease. Two aunts and sister also have kidney disease. He is married with two children, Sarah and Justin, who are alive and well.

■ SH

He drinks beer occasionally with friends, but not since his transplant. He has no history of smoking or IVDA.

■ Meds

Tacrolimus 4 mg PO BID (last dose taken last night at 8:00 PM)

Mycophenolate mofetil 1000 mg PO BID

Dapsone 100 mg PO daily

Valganciclovir 900 mg PO daily

Aspirin 81 mg PO once daily

Metoprolol XL 100 mg PO daily

Amlodipine 10 mg PO daily

Magnesium chloride 64 mg PO BID

Allopurinol 100 mg PO daily

Carbamazepine 200 mg PO BID, started 2 weeks ago by PCP for neuropathy

■ All

Sulfa (rash)

■ ROS

He has pain in the left lower quadrant of his abdomen (at the site of his kidney transplant) and bilateral lower extremity edema. He reports mild pain and tingling in both legs, primarily in his feet. He also notes that his total daily urine output has decreased over the past week; he estimates that he is now producing about 1.5 L of urine/day, compared to more than 2 L/day 2 weeks ago, despite drinking the same amount of liquid every day.

■ Physical Examination

Gen

WDWN man in NAD

VS

BP 169/92 mm Hg, P 66 reg, RR 14, T 37.4°C; Wt 87 kg (previous Wt 85 kg 2 weeks ago), Ht 5'10"

Skin

Warm and dry

HEENT

PERRLA; EOMI

Chest

CTA & P

CV

Normal S₁ and S₂; no MRG

Abd

Tenderness in LLQ (over kidney allograft); incisional wound healed; liver size normal

Ext

3+ pitting edema in ankles, extending to the knee; 2+ DP pulses bilaterally. No cyanosis.

Neuro

A&O × 3; CN II–XII intact; DTRs 2+ throughout; decreased sensation to filament test

■ Labs

At 8:00 AM today (fasting):

Na 141 mEq/L	Hgb 12.2 g/dL	Ca 8.9 mg/dL
K 5.4 mEq/L	Hct 36.6%	Phos 2.3 mg/dL
Cl 104 mEq/L	RBC $5.1 \times 10^6/\text{mm}^3$	Mg 1.1 mg/dL
CO ₂ 23 mEq/L	Plt $289 \times 10^3/\text{mm}^3$	Uric acid 6.8 mg/dL
FBG 78 mg/dL	WBC $1.9 \times 10^3/\text{mm}^3$	TAC <2 ng/mL ^a
BUN 39 mg/dL	Polys 68%	
SCr 2.5 mg/dL	Lymphs 27%	
	Monos 2%	
	Eos 1%	
	Basos 2%	

^aTacrolimus (TAC) whole blood concentration (therapeutic range, 5–20 ng/mL).

■ Renal Biopsy

Moderate acute cellular rejection (Banff 2A); mild tubular atrophy with minimal interstitial fibrosis.

■ Assessment

1. Acute rejection of kidney allograft (last BUN 20 mg/dL, SCr 1.1 mg/dL 4 weeks ago)
2. Hyperkalemia (serum potassium 4.9 mEq/L 4 weeks ago)
3. Leukopenia

QUESTIONS

Collect Information

1. What subjective and objective information indicates rejection of the kidney allograft?

Assess the Information

- 2.a. Assess the severity of kidney transplant rejection based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating kidney allograft rejection?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial therapy for acute rejection fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The patient received the treatment you recommended for acute cellular rejection. Carbamazepine treatment for peripheral neuropathy was discontinued and replaced with gabapentin, starting at 100 mg PO TID and titrating gradually upward. Valganciclovir was discontinued 6 months post-transplant as per the usual protocol.

The rejection episode resolved, and renal function returned to baseline levels. He now presents to the transplant clinic 7 months post-transplant for a routine follow-up appointment.

Meds

Tacrolimus 4 mg PO BID (last dose taken last night at 8:00 PM)
 Prednisone 5 mg PO once daily
 Mycophenolate mofetil 1000 mg PO BID
 Dapsone 100 mg PO daily
 Aspirin 81 mg PO daily
 Metoprolol XL 100 mg PO daily
 Amlodipine 10 mg PO daily
 Gabapentin 300 mg PO TID
 Magnesium chloride 128 mg PO BID
 Allopurinol 100 mg PO daily

Labs (at 8:00 AM Today)

Na 139 mEq/L	Hgb 12.1 g/dL	Ca 9.1 mg/dL
K 4.8 mEq/L	Hct 36.3%	Phos 3.5 mg/dL
Cl 109 mEq/L	RBC $5.2 \times 10^6/\text{mm}^3$	Mg 1.8 mg/dL
CO ₂ 25 mEq/L	Plt $278 \times 10^3/\text{mm}^3$	TAC 8.4 ng/mL
FBG 82 mg/dL	WBC $1.9 \times 10^3/\text{mm}^3$	CMV PCR 659,831 IU/mL
BUN 19 mg/dL		
SCr 1.1 mg/dL		

■ FOLLOW-UP QUESTION

1. What changes, if any, should be made to the patient's drug regimen?

■ SELF-STUDY ASSIGNMENTS

1. Develop a pharmacotherapeutic plan for the different strategies to treat acute cellular rejection of the allograft in solid organ transplant recipients.
2. Design a systematic approach for patient education for a new solid organ transplant recipient focusing on immunosuppressive therapies, adverse effects and drug interactions, and strategies to manage patient compliance with a complicated regimen.
3. Formulate a pharmacotherapeutic plan for managing hyperkalemia that includes different strategies based on the onset and magnitude of hyperkalemia.

CLINICAL PEARL

Acute rejection can occur in up to 20% of kidney transplant recipients within the first 6 months after transplant. Although an abrupt rise in serum creatinine $\geq 30\%$ over baseline can signal an acute rejection episode, a renal biopsy must be performed for a definitive diagnosis. The greatest risk factor for acute cellular rejection is a decrease in the level of immunosuppression. Treatment of acute rejection is typically based on the severity of the rejection episode.

REFERENCES

1. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: executive summary. *J Am Coll Cardiol* (2017). doi: 10.1016/j.jacc.2017.11.005.
2. Weir MR, Burgess ED, Cooper JE, et al. Assessment and management of hypertension in transplant patients. *J Am Soc Nephrol* 2015;26(6):1248–1260.

3. Kidney Disease: Improving Global Outcomes (KDIGO) Transplant Work Group. KDIGO clinical practice guideline for the care of kidney transplant recipients. *Am J Transplant* 2009;9(Suppl 3):S1–S157.
4. van der Zwan M, Clahsen-Van Groningen MC, Roodnat JJ, et al. The efficacy of rabbit anti-thymocyte globulin for acute kidney transplant rejection in patients using calcineurin inhibitor and mycophenolate-based immunosuppressive therapy. *Ann Transplant* 2018;23:577–590.
5. Baia LC, Heilberg IP, Navi G, de Borst MH. Phosphate and FGF-23 homeostasis after kidney transplantation. *Nat Rev Nephrol* 2015; 11:656–666.
6. Kotton CN, Kumar D, Caliendo AM, et al. Updated international consensus guidelines on the management of cytomegalovirus in solid-organ transplantation. *Transplantation* 2013;96(4):333–360.

SECTION 12

BONE AND JOINT DISORDERS

103

OSTEOARTHRITIS

Ease His Pain Level II

Christopher M. Degenkolb, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the most common signs and symptoms of osteoarthritis (OA).
- Design an appropriate pharmacotherapeutic regimen for treating OA, taking into account the patient's other medical problems and drug therapy.
- Incorporate potential adjunctive therapies (pharmacologic, non-pharmacologic, and alternative) into the regimen of a patient with OA.
- Assess and evaluate the efficacy of an analgesic regimen for a patient with OA, and formulate an alternative plan if the regimen is inadequate or causes unacceptable toxicity.

PATIENT PRESENTATION

■ Chief Complaint

"What can I take to help this pain? This new medication has only made me feel worse!"

■ HPI

Ray Kansella is a 74-year-old man who comes in to see his PCP today complaining of right knee and right hip pain for the past 10 years since he retired from an assembly plant. He often did very heavy lifting in his job and put a lot of strain on his back and legs; now the patient feels he is paying the price for all of his hard work. Mr Kansella wakes up every morning very stiff, and his right knee cracks when he gets up out of bed. The cracking in the joint goes away after he finishes his breakfast, but the aching in his knee and hip persists and chronically bothers him. For several months the patient has been taking scheduled doses of Tylenol Extra Strength. He visited his PCP 3 weeks ago with similar complaints and was prescribed Norco for additional pain management. He reports being given a month supply and taking this new medication three to four times per day. He reports good adherence to prescribed medications; however, he is not sure what medications he has tried in the past; all he knows is that whatever he is taking is not helping. He reports some vague abdominal cramping and intermittent nausea.

Additionally, patient complains of lack of energy due to sleepiness during the day and has been unable to do any exercise. He states he is very depressed because he can't enjoy time with family and his two grandchildren. His PCP wants more aggressive pain management and asking for your dosing recommendation on converting his Norco to a long-acting opioid given his past medical history and limited treatment options.

■ PMH

OA × 10 years
HTN × 20 years
Obesity × 15 years
Seizure disorder × 12 years (last seizure was 5 years ago)
CKD × 5 years

■ PSH

Appendectomy 35 years ago

■ FH

Father died at age 68 due to myocardial infarction
Mother died at age 81 of CVA
Lives at home with wife and two grandchildren

■ SH

Retired and has good insurance plan and a steady pension from his company
Denies tobacco use
Occasional EtOH (two to three beers on weekends)

■ Meds

Amlodipine 10 mg PO daily in AM
Lisinopril 10 mg PO daily in AM
Metoprolol 50 mg PO BID
Hydrocodone/acetaminophen 5 mg/325 mg two tablets PO Q 6 H PRN pain
Acetaminophen 500 mg one tablet PO Q 6 H PRN pain
Levetiracetam 1000 mg PO BID

■ All

NKDA; reports allergy to egg products

■ ROS

Positive for pain and stiffness in the right knee and right hip; has low back pain with occasional shooting and aching pains radiating to the buttocks and groin area; negative for headache, neck stiffness, joint swelling, or erythema; no SOB or palpitations; reports some vague abdominal cramping, intermittent nausea; and no bowel movement in the past 5 days

■ PE

Gen

Well-developed, obese, Caucasian man with moderate pain, otherwise in NAD

VS

BP 148/89 mm Hg, P 68 bpm, RR 18, T 37.1°C; Ht 5'9", Wt 225 lb (102.1 kg), pain 6/10. No orthostatic changes.

Skin

Warm, dry, intact

HEENT

NC/AT; PERRLA; fundoscopic exam reveals sharp disks; mild AV nicking, but no hemorrhages or exudates; no scleral icterus; TMs intact; mucous membranes moist; poor dentition with gingival erythema; no lateral deviation of tongue; no pharyngeal edema or erythema

Neck/Lymph Nodes

Supple; no thyromegaly or lymphadenopathy; no carotid bruits

Lungs

CTA

CV

Distant heart sounds, normal S₁ and S₂; PMI at fifth ICS/MCL; RRR; no MRG; no JVD or HJR

Abd

Obese, soft, mild tenderness on palpation; no guarding; diminished BS; unable to assess liver size on palpation

Genit/Rect

Prostate gland normal; normal sphincter tone; guaiac (–) stool in rectal vault

MS/Ext

Back pain radiating to right buttock with straight leg raising at 60°; right hip pain with flexion >90° and with internal and external rotation >45°; right hip tender to palpation; right knee (+) crepitus; no swelling or edema; good pedal pulses

Neuro

Oriented × 3; normal affect; appears at times to alternate between apathy and anger/frustration; CN II–XII intact; DTRs equal bilaterally except for slightly diminished Achilles reflexes bilaterally; no focal deficits; gait impaired secondary to hip and knee pain; Babinski downgoing

Labs

Na 135 mEq/L	Hgb 11.8 g/dL	AST 38 IU/L
K 4.7 mEq/L	Hct 34.5%	Alk phos 96 IU/L
Cl 98 mEq/L	WBC $6.5 \times 10^3/\text{mm}^3$	T. prot 7.4 g/dL
CO ₂ 26 mEq/L	Plt $286 \times 10^3/\text{mm}^3$	Alb 4.2 g/dL
BUN 18 mg/dL	MCV 85.3 μm^3	Phos 4.5 mg/dL
SCr 1.8 mg/dL	MCH 28.4 pg	ESR 18 mm/hour
Glu 99 mg/dL	MCHC 34.5 g/dL	Ca 11.2 mg/dL

UA

SG 1.011; pH 6.5; WBC (–), RBC (–), leukocyte esterase (–), nitrite (–), 2+ protein; microscopic examination reveals two to five epithelial cells/hpf and no bacteria.

X-Rays

Lumbar spine: advanced degenerative changes at L3–4 and at L4–5
 Right hip: moderate degenerative changes with some spurring of the femoral head and slight decrease in joint space
 Right knee: moderate degenerative changes; no effusion

Assessment

1. Pain secondary to OA
2. Hypertension
3. Obesity
4. Seizure disorder
5. CKD

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of osteoarthritis?
- 1.b. What additional information is needed to fully assess this patient's osteoarthritis?

Assess the Information

- 2.a. Assess the severity of OA based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for osteoarthritis might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's OA?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's osteoarthritis and other drug therapy problems. Include specific drugs, dosing forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE: ALTERNATIVE THERAPY

While discussing multiple treatment options with Mr Kansella, he says, "This may seem silly, but I have a neighbor a couple years older than me who was getting some pretty bad arthritis in both knees a few years ago. He says he hardly has any pain anymore because he's taking these glucosamine and chondroitin pills. He even started back to golfing! Is there any way those could help me with my pain?"

See Section 19 in this Casebook for questions about the use of glucosamine and chondroitin for osteoarthritis.

SELF-STUDY ASSIGNMENTS

1. While discussing multiple treatment options with Mr Kansella, he says, “This may seem silly, but I have a neighbor who has pretty bad arthritis in both knees. He says he hardly has any pain anymore because he’s taking cannabidiol (CBD) oil. Is there any way it could help me with my pain?” Create a response for his request utilizing current status of this medication.
2. Many patients who deal with pain and osteoarthritis often turn to unproven methods to control their pain. Research some of these unproven methods online and try to find active ingredients to determine if these are unsafe to recommend for patients with complex medication regimens.
3. Evaluate this patient’s CKD. What stage of CRI does this patient have, and what is the most likely etiology of his renal disease? Prepare a paper describing some of the complications of long-standing kidney disease and how such complications should be managed.

CLINICAL PEARLS

Current treatment guidelines for OA have variable recommendations published by different organizations. Medical therapy can provide some benefit in pain reduction and functional improvement, but some therapies bear significant harms when used long term. A patient-centric approach is required in prioritizing selection of safe and effective adjunctive methods of OA pain management as there are many unproven and unsubstantiated pharmacologic and non-pharmacologic treatment modalities.

REFERENCES

1. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology. American College of Rheumatology 2012 recommendations for the use of non-pharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. *Arthritis Care Res (Hoboken)* 2012;64:465–474.
2. American Academy of Orthopaedic Surgeons (AAOS). American Academy of Orthopaedic Surgeons clinical practice guideline on treatment of osteoarthritis of the knee. 2nd ed. <https://www.aaos.org/research/guidelines/TreatmentofOsteoarthritisoftheKneeGuideline.pdf>. Accessed November 30, 2019.
3. McAlindon TE, Bannuru RR, Sullivan MC, et al. OA Research Society International (OARSI) guidelines for the non-surgical management of knee osteoarthritis. *Osteoarthritis Cartilage* 2014;22:363–388.
4. Ebell MH. Osteoarthritis: rapid evidence review. *Am Fam Physician*. 2018;97(8):523–526.
5. Dowell D, Haegerich TM, Chou R. CDC guideline for prescribing opioids for chronic pain—United States, 2016. *MMWR Recomm Rep* 2016; 65:1. <https://www.cdc.gov/mmwr/volumes/65/rr/rr6501e1.htm>. Accessed November 30, 2019.
6. Machado GC, Maher CG, Ferreira PH, et al. Efficacy and safety of paracetamol for spinal pain and osteoarthritis: systematic review and meta-analysis of randomized placebo controlled trials. *BMJ* 2015;350:h1225. doi:10.1136/bmj.h1225.
7. Krebs EE, Gravelly A, Nugent S, et al. Effect of opioid vs nonopioid medications on pain-related function in patients with chronic back pain or hip or knee osteoarthritis pain: the SPACE randomized clinical trial. *JAMA* 2018; 319:872–882.
8. Wang ZY, Shi SY, Li SJ, et al. Efficacy and safety of duloxetine on osteoarthritis knee pain: a meta-analysis of randomized controlled trials. *Pain Med* 2015;16(7):1373–1385.

104

RHEUMATOID ARTHRITIS

Joint Project Level II

Amie D. Brooks, PharmD, FCCP, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify signs and symptoms of rheumatoid arthritis (RA) and assess disease severity.
- Recommend appropriate nonpharmacologic therapy for adjunctive management of RA.
- Recommend evidence-based, patient-specific analgesic, anti-inflammatory, and disease-modifying drug therapy for patients with RA.
- Develop an evidence-based, patient-specific monitoring plan to assess disease progress and evaluate the safety and efficacy of medication therapy.
- Educate patients and their families about the medications used to treat RA.

PATIENT PRESENTATION

Chief Complaint

“Lately I am very achy, I feel exhausted, and I am having a hard time getting going in the morning.”

HPI

Analise Schaefer is a 54-year-old African-American woman who presents to rheumatology clinic with complaints of generalized arthralgias, fatigue, and morning stiffness. She has a 13-year history of RA currently treated with methotrexate. She reports worsening in her symptoms over the past 6 months.

PMH

RA × 13 years
Heart failure with reduced ejection fraction (currently NYHA class III)

FH

Father is alive and being treated for hypertension and osteoarthritis. Mother is alive and being treated for severe RA. Two siblings with no major health concerns.

SH

Tax accountant; married for 25 years; heterosexual, sexually active, monogamous. Denies tobacco or illicit drug use. Drinks one to two glasses of wine per week.

Meds

Methotrexate 2.5 mg, six tablets (15 mg) PO once a week
Folic acid 1 mg PO once daily

Lisinopril 40 mg PO once daily
 Metoprolol succinate 100 mg PO once daily
 Spironolactone 25 mg PO once daily
 Furosemide 40 mg PO once daily
 Patient receives medications at a local community pharmacy. Medication profile indicates that she refills her medications on time on the first of each month.

■ All

Sulfonamides (hives)

■ ROS

Complains of swelling and pain in both hands; reports decreased ROM in hands and wrists; has morning stiffness every day for about 2 hours and fatigue daily during the afternoon hours; denies HA, chest pain, bleeding episodes, or syncope; no nausea, vomiting, diarrhea, loss of appetite, or weight loss.

■ PE

Gen

African-American woman in moderate distress because of pain, swelling, and fatigue related to arthritis

VS

BP 118/76 mm Hg, P 62 bpm, RR 14, T 37.1°C; Wt 65 kg, Ht 5'6"

Skin

No rashes; normal turgor; no breakdown or ulcers; no subcutaneous nodules

HEENT

Normocephalic, atraumatic; moist mucous membranes; PERRLA; EOMI; pale conjunctiva bilaterally; TMs intact; no oral mucositis

Neck/Lymph Nodes

Neck supple, no JVD or thyromegaly; no thyroid bruit; no lymphadenopathy

Chest

CTA

Breasts

Deferred

CV

RRR; normal S₁, S₂; no MRG

Abd

Soft, NT/ND; (+) BS

Genit/Rect

Deferred

MS/Ext

Total of 16 tender and 16 swollen joints bilaterally
 Hands: swelling and tenderness on palpation of second, third, fourth, and fifth PIP and MTP joints bilaterally; decreased grip strength, L > R (patient is left-handed)
 Wrists: decreased ROM

Elbows: good ROM

Shoulders: decreased ROM (especially abduction) bilaterally

Hips: good ROM

Knees: good ROM, no pain bilaterally

Feet: no obvious swelling of MTP joints; full plantar flexion; reduced dorsiflexion; 2+ pedal pulses

Neuro

CN II–XII intact; muscle strength 4/5 UE, 4/5 LE, DTRs 2+ throughout

Labs

Na 135 mEq/L	Hgb 10.8 g/dL	AST 15 IU/L	CK <20 IU/L
K 4.1 mEq/L	Hct 31%	ALT 12 IU/L	ANA negative
Cl 101 mEq/L	WBC 6.2 × 10 ³ /mm ³	Alk phos 56 IU/L	Wes ESR
CO ₂ 22 mEq/L		T. bili 0.8 mg/dL	60 mm/hr
BUN 12 mg/dL	Plt 356 × 10 ³ /mm ³	Alb 4.2 g/dL	RF (+) 50 U/mL
SCr 0.8 mg/dL	Ca 9.1 mg/dL	HbsAg (–)	Anti-CCP 70 EU
Glu 103 mg/dL	Urate 5.1 mg/dL	Anti-HCV (–)	aPTT 31 seconds
	TSH 0.74 mIU/L		INR 1.0

■ UA

Normal

■ Chest X-Ray

No fluid, masses, or infection; no cardiomegaly

■ Hand X-Ray

Multiple erosions of MCP and PIP joints bilaterally; measurable joint space narrowing from previous x-ray 1 year ago

■ DAS 28

6.2 today; 3.0 one year ago

■ Assessment

1. RA
2. Heart failure

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of rheumatoid arthritis?
- 1.b. What additional information is needed to fully assess this patient's rheumatoid arthritis?

Assess the Information

- 2.a. Assess the severity of rheumatoid arthritis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for rheumatoid arthritis might be useful for this patient?

- 3.c. What feasible pharmacotherapeutic alternatives are available for treating rheumatoid arthritis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's rheumatoid arthritis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial therapy for rheumatoid arthritis fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Create a list of clinically significant drug interactions for NSAIDs and DMARDs, including methotrexate.
2. Compare the biologic agents used to treat RA with respect to drug class, route of administration, efficacy, contraindications, and side effects.

CLINICAL PEARL

Patients with RA are at increased risk for TB infection due to underlying immune dysfunction.⁸ In most cases, TB infection in patients receiving immunosuppressant therapy has been attributed to reactivation of latent disease.^{9,10} Reactivation of latent tuberculosis infection is a concern with all immunosuppressant therapy but has been specifically associated with corticosteroid use, all biologic agents (TNF- α antagonists, IL-1 and IL-6 receptor inhibitors, B-cell-depleting agents, T-cell costimulation inhibitors), and some nonbiological agents (tofacitinib and leflunomide).^{9,10}

REFERENCES

1. Niewold TB, Harrison MJ, Paget SA. Anti-CCP antibody testing as a diagnostic and prognostic tool in rheumatoid arthritis. *QJM* 2007;100(4):193–201.
2. Aletaha D, Neogi T, Silman A, et al. 2010 Rheumatoid arthritis classification criteria. *Arthritis Rheum* 2012;62:2569–2581.
3. Fransen J, van Riel PLCM. The disease activity score and the EULAR response criteria. *Rheum Dis Clin North Am* 2009;35:745–757.
4. Singh JA, Saag KG, Bridges SL, et al. 2015 American College of Rheumatology guideline for the treatment of rheumatoid arthritis. *Arthritis Rheumatol* 2016;68:1–26.
5. U.S. Food and Drug Administration. Safety trial finds risk of blood clots in the lungs and death with higher dose of tofacitinib (Xeljanz, Xeljanz XR) in rheumatoid arthritis patients; FDA to investigate. <https://www.fda.gov/Drugs/DrugSafety/ucm631871.htm>. Accessed March 18, 2019.

6. Carmona L, Hernández-García C, Vadillo C, et al. Increased risk of tuberculosis in patients with rheumatoid arthritis. *J Rheumatol* 2003;30:1436–1439.
7. Keane J, Gershon S, Wise RP, et al. Tuberculosis associated with infliximab, a tumor necrosis factor alpha-neutralizing agent. *N Engl J Med* 2001;345:1098–1104.
8. Singh JA, Christensen R, Wells GA, et al. Biologics for rheumatoid arthritis: an overview of Cochrane reviews (Protocol). *Cochrane Database Syst Rev* 2009, Issue 2. Art. No.: CD007848. doi:10.1002/14651858.CD007848.
9. Curtis JR, Patkar N, Xie A, et al. Risk of serious bacterial infections among rheumatoid arthritis patients exposed to tumor necrosis factor alpha antagonists. *Arthritis Rheum* 2007;56:1125–1133.
10. Saag KG, Teng GG, Patkar NM, et al. American College of Rheumatology 2008 recommendations for the use of nonbiologic and biologic disease-modifying antirheumatic drugs in rheumatoid arthritis. *Arthritis Care Res* 2008;59:762–784.

105

OSTEOPOROSIS

No Bones About It: Osteoporotic Fractures Warrant Treatment Level II

Mollie Ashe Scott, PharmD, BCACP, CPP, FASHP

Lisa LaVallee, MD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the risk factors for the development of osteoporosis and use the Fracture Risk Assessment Tool (FRAX) to assess risk of an osteoporotic fracture.
- Recommend appropriate nonpharmacologic measures for the prevention and treatment of osteoporosis.
- Recommend appropriate calcium and vitamin D supplementation required for the prevention and treatment of osteoporosis.
- Design an appropriate pharmacologic treatment regimen for the treatment of osteoporosis in postmenopausal women.
- Provide patient education regarding osteoporosis and its therapy.
- Discuss the role that the fracture liaison service plays in coordinating care and preventing additional fractures.

PATIENT PRESENTATION

Chief Complaint

“I recently fell while walking my dog Ruby, and my lower back is sore. I would also like to get the results of my DXA scan. My mother is still undergoing rehabilitation in the nursing home after her hip fracture three weeks ago. I’ve heard osteoporosis can run in families, and I don’t want to experience what she is going through.”

HPI

Betsy Fritsch is a 65-year-old Caucasian woman with a history of hypertension, hypothyroidism, and GERD. She presents to the

family medicine clinic for her yearly physical and to discuss the results of her recent labs and DXA scan.

In an effort to become more active, she recently started walking around her neighborhood every day but fell 3 days ago and injured her back. She admits that she has a hard time remembering to take her medications faithfully. She states she takes her medicines “most of the time.” She states that she was prescribed alendronate 2 years ago but that she is “afraid of its side effects” and did not start it.

■ PMH

Hypothyroidism × 5 years

Hypertension

Breast cancer with mastectomy of left breast and radiation therapy at age 45

Menopause at age 51

GERD with history of esophageal stricture

■ FH

Paternal history (+) for hypertension; father died in his sleep at age 80

Maternal history (+) for stroke and vascular disorders; hip fracture

■ SH

Married; G₂P₂; drinks occasionally, retired real estate agent, lives independently with her husband and dog, manages her own medicines, completed college, does not have a Medicare Part D plan

■ Meds

Omeprazole 20 mg PO once daily × 1 year

Levothyroxine sodium (Synthroid) 75 mcg PO once daily × 5 years

Hydrochlorothiazide 25 mg PO once daily

■ All

NKDA

■ ROS

Reports vaginal dryness; has noticed that her height has decreased by 2” since she was “in her prime;” denies headache, chest pain, GI pain, or heartburn

■ PE

Gen

WDWN Caucasian woman in NAD, ambulating with a cane

VS

Today

BP initially 133/88 mm Hg sitting, repeated at end of office visit 100/64 mm Hg standing, P 70 bpm sitting 90 standing, RR 18, T 37°C; Wt 53.5 kg, Ht 5’3”

Timed Up and Go (TUG) test: 15 seconds

1 month ago

BP 130/82 mm Hg, P 66 bpm, RR 20, T 37°C; Wt 53.5 kg, Ht 5’3”

Skin

Fair complexion, no lesions

HEENT

PERRLA; EOMI; eyes and throat clear; normal dentition

Neck/Lymph Nodes

Supple, without obvious nodes; no JVD, no thyromegaly

Chest

Clear to auscultation; no rales or rhonchi

Breasts

Mastectomy scar left breast; right breast normal

CV

RRR; no MRG

Abd

Soft, NT/ND, (+) BS, no mass, no hepatosplenomegaly

Genit/Rect

Deferred

MS/Ext

Good pulses bilaterally, spine straight without scoliosis, moderate kyphosis, tender midthoracic tenderness to palpation, no stigmata of Cushing disease

Neuro

CN II–XII intact; DTRs 2+; sensory and motor levels intact

■ Labs

Na 145 mEq/L	SCr 1.1 mg/dL	25-OH vitamin D 15 ng/mL
K 4.0 mEq/L	Glu 97 mg/dL	PTH 200 ng/L
Cl 104 mEq/L	AST 32 IU/L	Hbg 13 g/dL
CO ₂ 25 mEq/L	ALT 27 IU/L	HCT 39%
BUN 18 mg/dL	Corrected Ca 9.1 mg/dL	TSH 3.492 mIU/L

■ Other

DXA scan results from Hologic machine 2 weeks prior:

Lumbar spine 2 weeks ago reveals: L2–4 = 0.780 g/cm² (T score: –3.2 SD);
right femoral neck = 0.52 g/cm² (T score: –2.8 SD)

X-ray of the spine today shows a compression fracture in T10

Patient is referred to fracture liaison service for coordination of care

■ Assessment

1. Osteoporosis
2. Hypertension with orthostasis
3. Hypothyroidism
4. GERD with esophageal stricture history
5. History of breast cancer 10 years ago

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of osteoporosis?
- 1.b. What additional information is needed to fully assess this patient’s osteoporosis?

Assess the Information

- 2.a. Assess the severity of osteoporosis based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating osteoporosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's osteoporosis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Create a list of medications and disease states that associated with an increased risk for developing osteoporosis.
2. Investigate the sclerostin inhibitor, romosuzumab, and its role in the treatment of osteoporosis.
3. Discuss the role of the fracture liaison service and the different responsibilities of the members of the interprofessional team in the clinical care of patients with fracture.

CLINICAL PEARL

Patients with osteoporosis with a history of fracture are not considered candidates for a bisphosphonate holiday due to the high risk of additional fractures.

REFERENCES

1. Cosman F, de Beur SJ, LeBoff MS, et al. Clinician's guide to prevention and treatment of osteoporosis. *Osteoporosis Int* 2014;25:2359–2381.
2. Camacho P, Petak SM, Binkley N, et al. American Association of Clinical Endocrinologists and American College of Endocrinology clinical practice guidelines for the diagnosis and treatment of postmenopausal osteoporosis. *Endocrine Pract* 2016;22(Suppl 4):1–42.
3. The North American Menopause Society. Management of osteoporosis in postmenopausal women: 2010 position statement of The North American Menopause Society. *Menopause* 2010;17(1):25–54.

4. Wu CH, Tu ST, Chang YF, Chan DC, Chien, JT et al. Fracture liaison services improve outcomes for patients with osteoporosis-related fracture: a systematic literature review and meta-analysis. *Bone* 2018;111:92–100.
5. American Geriatrics Society. 2019 updated AGS Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 2019;67(4):674–694.
6. Centers for Disease Control and Prevention. STEADI: Stopping elderly accidents, deaths, and injuries. <https://www.cdc.gov/steady/index.html>. Accessed November 15, 2018.
7. Zhou B, Huang Y, Li H, Sun W, Liu J. Proton pump inhibitors and risk of fractures: an update meta-analysis. *Osteopor Int* 2016;27:339–347.
8. Holick MF, Binkley NC, Heike A, et al. Evaluation, treatment, and prevention of vitamin D deficiency: an Endocrine Society Clinical Practice Guideline. *J Clin Endocrinol Metab* 2011;96:1911–1930.
9. Kopecky SL, Bauer DC, Gulati M, et al. Lack of evidence linking calcium with or without vitamin D supplementation to cardiovascular disease in generally health adults: a clinical guideline from the National Osteoporosis Foundation and American Society for Preventive Cardiology. *Ann Intern Med* 2016;165:867–868.
10. Miller PD, Hattersly G, Riis, JR, et al. Effect of abaloparatide vs placebo on new vertebral fractures on postmenopausal women with osteoporosis. A randomized clinical trial. *JAMA* 2016;316:722–733.

106

GOUT AND HYPERURICEMIA

The King of Oktoberfest Level II

Erik D. Maki, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify major risk factors for developing gout in a given patient, including drugs that may contribute to or cause this disorder.
- Develop a pharmacotherapeutic plan for a patient with acute gouty arthritis that includes individualized drug selection and assessment of the treatment for efficacy or toxicity.
- Identify patients in whom maintenance therapy for gout and hyperuricemia is warranted.
- Identify medications not used primarily for gout that may have a beneficial effect on serum uric acid (SUA) levels.

PATIENT PRESENTATION

■ Chief Complaint

“My toe is on fire.”

■ HPI

Roy Huff is a 78-year-old man who presents to the ED complaining of significant toe pain. Mr Huff states, “I think I’m paying the price for my fun at Oktoberfest.” He reports having spent the weekend indulging on beer and sausage at the local Oktoberfest festival. In the early hours of Monday morning (approximately 3 hours ago), he awoke to sudden excruciating pain in his right big toe. Over the past

hour, this toe has become red, swollen, and so painful that he cannot walk. He has not experienced any trauma or injuries. He also denies having experienced these symptoms previously.

■ PMH

HTN × 28 years
PUD × 15 years
Obesity × 40 years

■ SH

The patient typically drinks “a can of beer or two” daily but drank significantly on Friday, Saturday, and Sunday. He does not smoke or use illicit drugs.

■ Meds

Chlorthalidone 25 mg PO daily, started 1 month ago
Pantoprazole 20 mg PO daily

■ All

NKDA

■ ROS

Other than feeling somewhat dehydrated from all of his drinking, the patient has no major complaints prior to this ED visit. No chest pain, nausea/vomiting, or respiratory symptoms. Bowel habits are normal. He has no prior history of arthritic symptoms or joint problems.

■ PE

Gen

A healthy-appearing, obese, white man in acute distress

VS

BP 135/70 mm Hg, P 105 bpm, RR 17, T 37.5°C; Wt 88 kg, Ht 5'6"

Skin

Poor skin turgor. No rashes or other dermatologic abnormalities.

HEENT

PERRLA, dry mucous membranes, throat/ears clear of redness or inflammation

Neck/Lymph Nodes

Negative for lymph node swelling or masses

Lungs/Thorax

Clear to auscultation bilaterally, symmetric movement with inspiration

CV

Tachycardic, normal rhythm, normal S₁ and S₂

Abd

Obese, but soft, nontender; positive bowel sounds in all quadrants.

Genit/Rect

Deferred

MS/Ext

Erythematous, edematous right first metatarsophalangeal joint, which is very warm to touch; joint is exquisitely painful with patient relating the pain as currently a 10/10 (on a 1–10 scale with 0 being

no pain and 10 being the worse pain the patient has ever suffered); no swelling of any other joints. No signs of tophi present.

Neuro

A&O × 3; CN II–XII grossly intact, no focal neurologic deficits

■ Labs

Ankle and foot radiographs: negative for break or damage

Aspirated fluid from first metatarsophalangeal joint tap: >50 WBC/hpf, containing negatively birefringent monosodium urate crystals

Na 143 mEq/L	Hgb 15 g/dL	WBC 12.9 × 10 ³ /mm ³	Fasting lipid panel
K 3.7 mEq/L	Hct 44%		HDL 55 mg/dL
Cl 99 mEq/L	RBC 4.9 × 10 ⁶ /mm ³	Neutros 88%	Trig 188 mg/dL
CO ₂ 22 mEq/L		Bands 0%	LDL 97 mg/dL
BUN 39 mg/dL	Plt 225 × 10 ³ /mm ³	Eos 1%	T. chol
SCr 3.0 mg/dL	MCV 84 μm ³	Lymphs 10%	179 mg/dL
Glu 101 mg/dL	MCHC 37 g/dL	Monos 1%	
SUA 11.6 mg/dL	ESR 47 mm/hr	RF negative	

■ Assessment

1. Primary presentation of acute gouty arthritis
2. ARF
3. Hypertension
4. PUD

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of gout?
- 1.b. What additional information is needed to fully assess this patient's gout?

Assess the Information

- 2.a. Assess the severity of gout based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for gout might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating gout?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's gout and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient responded to the therapy you recommended, and within 96 hours his pain has subsided significantly. Toe redness and swelling have decreased to near normal. Additionally, with fluids, his SCr has returned to baseline (0.8 mg/dL). After consultation with you, the patient's physician decides against maintenance therapy to decrease SUA levels. The patient, remembering the severe pain this episode caused, follows your recommended lifestyle changes and is adherent to the new medication you recommended for his hypertension. At his 6-month follow-up appointment, he reports no more attacks of gout. He has lost 20 lb and no longer drinks ethanol. His SUA level has decreased to 6.9 mg/dL, and his BP is 130/80 mm Hg.

ADDITIONAL CASE QUESTIONS

1. Should chronic treatment to decrease the patient's SUA level be initiated at this time? Why or why not?
2. If at some point maintenance therapy to decrease SUA is begun, what additional therapy is needed to prevent acute flares?

SELF-STUDY ASSIGNMENTS

1. List antihyperuricemic agents that are available in the United States and their relative advantages and disadvantages. Describe new agents that are being studied for this indication and what clinical data support their use.
2. List medications that can either increase or decrease serum uric acid concentrations.

CLINICAL PEARL

Historically, colchicine was used for treating acute gout flares at doses of 0.6 mg Q 1–2 H until symptoms resolved or adverse GI symptoms developed (6 mg maximum). GI side effects were

employed as a clinical endpoint for discontinuing the drug because these side effects tended to occur prior to the more severe adverse effects of colchicine-induced myopathy and myelosuppression. However, current recommendations are to use low-dose colchicine at a dose of 1.2 mg, followed in 1 hour with a single dose of 0.6 mg. For patients receiving prophylactic colchicine prior to the flare, it is recommended to wait 12 hours after treatment dosing before resuming prophylactic dosing.

REFERENCES

1. Khanna D, Fitzgerald JD, Khanna PP, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 1: systematic nonpharmacologic and pharmacologic therapeutic approaches to hyperuricemia. *Arthritis Care Res (Hoboken)* 2012;64:1431–1446.
2. Richette P, Doherty M, Pascual E, et al. 2016 updated EULAR evidence-based recommendations for the management of gout. *Ann Rheum Dis* 2017;76(1):29–42.
3. Hui M, Carr A, Cameron S, et al. The British Society for Rheumatology guideline for the management of gout. *Rheumatology* 2017; 56(7):e1–e20.
4. Khanna D, Khanna PP, Fitzgerald JD, et al. 2012 American College of Rheumatology guidelines for management of gout. Part 2: therapy and antiinflammatory prophylaxis of acute gouty arthritis. *Arthritis Care Res (Hoboken)* 2012;64:1447–1461.
5. Abhishek A, Doherty M. Education and non-pharmacological approaches for gout. *Rheumatology* 2018;57:i51–i58.
6. James PA, Oparil S, Carter BL, et al. 2014 Evidence-based guideline for the management of high blood pressure in adults: report from the panel members appointed to the Eighth Joint National Committee (JNC 8). *JAMA* 2014;311:507–520.
7. Wilson L, Nair KV, Saseen JJ. Comparison of new-onset gout in adults prescribed chlorthalidone vs hydrochlorothiazide for hypertension. *J Clin Hypertens (Greenwich)* 2014;16:864–868.
8. Wolff ML, Cruz JL, Vanderman AJ, Brown JN. The effect of angiotensin II receptor blockers on hyperuricemia. *Ther Adv Chronic Dis* 2015;6:339–346.
9. Choi H, Soriano, L, Zhang Y, et al. Antihypertensive drugs and risk of incident gout among patients with hypertension: population based case-control study. *BMJ* 2012;344:d8190.
10. Dalbeth N, Merriman TR, Stamp LK. Gout. *Lancet* 2016;388:2039–2052.

This page intentionally left blank

SECTION 13

EYES, EARS, NOSE, AND THROAT DISORDERS

107

GLAUCOMA

Silent Blindness Level III

Brian McMillan, MD

Ashlee McMillan, PharmD, BCACP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the importance of regular eye examinations and the early diagnosis of glaucoma.
- List the risk factors for developing open-angle glaucoma.
- Select and recommend agents from different pharmacologic classes when indicated and provide the rationale for drug selection, including combination products to increase adherence.
- Recommend conventional glaucoma therapy as well as other options in glaucoma management when indicated.
- Formulate basic ophthalmologic monitoring parameters used in glaucoma therapy.
- Counsel patients on medication regimens and proper ophthalmic administration technique.
- Discuss potential adverse drug reactions with patients to increase therapy adherence.

PATIENT PRESENTATION

■ Chief Complaint

“My vision is closing down and I am having difficulty seeing cars at intersections while driving.”

■ HPI

Macy Connor is a 75-year-old woman who presents for follow-up of advanced primary open-angle glaucoma (POAG). She reports adherence with latanoprost nightly and timolol/brimonidine (Combigan) two times daily in the right eye and dorzolamide three times daily in the left eye. She feels that her vision in the left eye is beginning to blur, and she is having more difficulty seeing objects in the top part of her vision. She finds that she has to move her head more to see objects in her periphery. She denies eye pain, flashes, or floaters. She is feeling more tired recently.

Mrs Connor was first diagnosed with POAG 20 years ago during a routine eye exam to update her eyeglass prescription. She had no visual disturbances at that time, and her best corrected vision was

20/20 OU. She was started on pilocarpine 1% three times daily in both eyes and developed brow ache and blurred vision. This was discontinued and she was started on timolol 0.5% twice daily in both eyes. Her highest IOP prior to treatment was 30 mm Hg, which improved to 25 mm Hg on timolol. Her eye pressure gradually increased requiring the addition of brimonidine three times daily and latanoprost nightly in both eyes. She underwent cataract surgery 2 years ago and experienced an IOP spike to 55 mm Hg and was given acetazolamide 250 mg PO four times daily for 5 days after surgery until her pressure improved. Three months after surgery, her IOP control had improved, and therapy in her left eye was changed to dorzolamide three times daily only.

■ PMH

Hypertension, well controlled on lisinopril for 6 years
Kidney stones (occurred while taking acetazolamide)
Migraine headaches; well controlled on sumatriptan with one to two migraines per year
Depression; controlled with exercise and counseling only; has never taken medications for depression
Myopia; corrected with glasses
Astigmatism; corrected with glasses
Pseudophakia; cataract surgery 3 years ago

■ FH

Parents are both deceased; father had POAG requiring surgery and was blind in right eye; mother died of breast cancer; has one brother who is alive with myopia

■ SH

Nonsmoker; drinks one to two glasses of wine per week

■ ROS

Decreased energy with two falls in the last month at home. All other systems negative.

■ Meds

Latanoprost 0.005% one drop nightly OD
Combigan 0.2%/0.5% one drop twice daily OD
Dorzolamide 2% one drop three times daily OS
Sumatriptan 25 mg PO as needed for headache
Lisinopril 20 mg PO once daily

■ All

Penicillin—rash

■ Physical Examination

VS

BP 112/72, P 82, R 18, T 36.4°C

Eyes

Visual acuity: ODcc: 20/25; OSc: 20/60 (cc = with glasses)
Intraocular pressure: OD: 23; OS: 24 (normal range: 10–21 mm Hg)
Central corneal thickness (CCT): OD: 515; OS: 510 (normal 540 µm)
Gonioscopy: Iridocorneal angle is open with ciliary body band visible OU (open angle).

Pupils: Equal round and reactive OU; no relative afferent pupillary defect (rAPD)

Extraocular movements: Full OU

Slit lamp exam

Lids: Normal

Conjunctiva: 1+ injection OU

Cornea: Clear OU

Anterior chamber: Deep and quiet OU

Iris: Round and reactive OU

Lens: Posterior chamber intraocular lens OU

Vitreous: Normal

Optic nerve

OD: Superior and inferior rim thinning with focal notch superiorly; cup-to-disk (C/D) ratio 0.85

OS: Superior rim loss, inferior rim thinning; disk hemorrhage inferotemporal disk; C/D ratio 0.95 (normal C/D 0.25)

CN II–XII grossly intact

Humphrey visual fields

OD: Good reliability, inferior arcuate depression; stable

OS: Good reliability, denser superior altitudinal defect splitting fixation, decreased foveal threshold

Assessment

1. Advanced POAG

OD: Stable visual field, IOP slightly higher today

OS: Dense visual field loss now affecting central vision. IOP improved from baseline; however, it remains elevated and patient continues to progress.

2. Pseudophakia: Excellent result of cataract surgery

3. Myopia/Astigmatism

4. Decline in energy

5. Recent falls

6. Depression well controlled on lifestyle modifications

7. Hypertension well controlled on lisinopril

8. Migraines well controlled on sumatriptan

Plan

1. *Right eye:* Continue latanoprost nightly and Combigan 0.2%/0.5% twice daily.

2. *Left eye:* Discontinue dorzolamide. Add latanoprost nightly and Combigan 0.2%/0.5% twice daily.

3. Follow-up in 1 month for IOP check of both eyes. If pressure remains elevated OU, schedule for glaucoma laser surgery.

4. *Decline in energy and falls:* Refer to PCP for systemic evaluation including depression and falls. May need to consider side effects of β -blocker if workup is negative.

5. Hypertension and migraine well controlled. Continue current medications.

QUESTIONS

Collect Information

1.a. What subjective and objective evidence indicates that this patient has primary open-angle glaucoma (POAG)? See Figs. 107-1 to 107-3.

1.b. What additional information is needed to fully assess this patient?

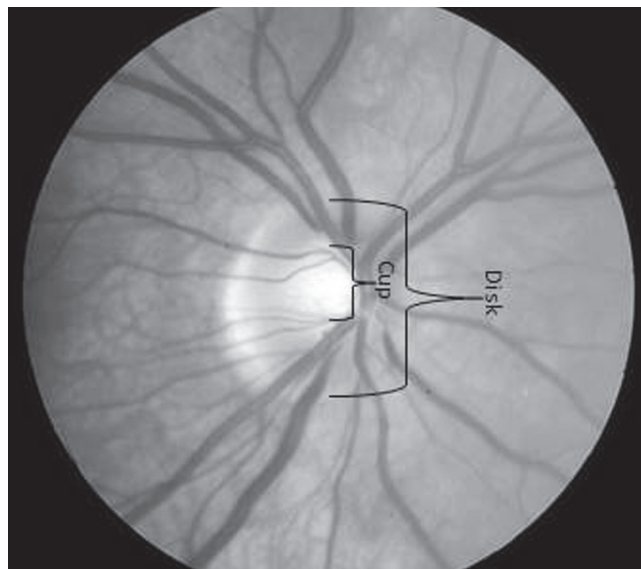


FIGURE 107-1. Normal optic nerve with cup-to-disk ratio (C/D) = 0.3.

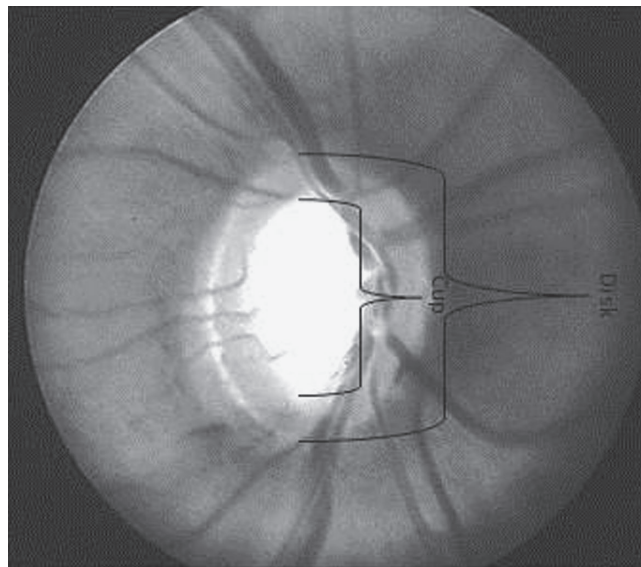


FIGURE 107-2. Abnormal, glaucomatous optic nerve with increased cup-to-disk ratio (C/D) = 0.8.



FIGURE 107-3. Simulated vision of patient with glaucoma. (Source: National Eye Institute, National Institutes of Health.)

Assess the Information

- 2.a. What are this patient's risk factors for POAG?
- 2.b. Assess the severity of POAG based on the subjective and objective information available.
- 2.c. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What pharmacologic classes and individual agents are available to treat glaucoma?
- 3.c. How can glaucoma medications be combined to improve patient adherence?
- 3.d. If this patient were diagnosed today, what would be the optimal first-line pharmacologic therapy?
- 3.e. What surgical treatments might be useful for this patient?
- 3.f. During what phase of this patient's disease case are surgical treatments indicated?
- 3.g. Create an individualized, patient-centered, team-based care plan for this patient's glaucoma. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.h. Which medications should be avoided in this patient?

Implement the Care Plan

- 4.a. What information should the patient receive about the disease of glaucoma, proper medication administration technique, and possible side effects of treatment?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Perform a literature search on the reason why antimetabolites such as mitomycin C and 5-fluorouracil (5-FU) are used in glaucoma surgery. What is the mechanism of action of these antimetabolites in trabeculectomy pressure-lowering surgery?
2. Discuss the mechanism of action of latanoprostene bunod (Vyzulta) and netarsudil (Rhopressa). How does their efficacy compare to timolol?

CLINICAL PEARL

Glaucoma is a silent and generally slowly progressive optic neuropathy. Optimizing pharmacotherapy of glaucoma must consider systemic medical conditions, social situations, and environmental factors that may limit adherence. Patients should be monitored regularly for disease progression because many continue to progress on treatment despite "normal pressures."

REFERENCES

1. Heijl A, Leske MC, Bengtsson B, et al. Reduction of intraocular pressure and glaucoma progression: results from the Early Manifest Glaucoma Trial. *Arch Ophthalmol* 2002;120:1268–1279.
2. Gordon MO, Beiser JA, Brandt JA, et al. The Ocular Hypertension Treatment Study: baseline factors that predict the onset of primary open-angle glaucoma. *Arch Ophthalmol* 2002;120:714–720.
3. Drance S, Anderson DR, Schulzer M. Collaborative Normal-Tension Glaucoma Study. Risk factors for progression of visual field abnormalities in normal-tension glaucoma. *Am J Ophthalmol* 2001;131:699–708.
4. Tielsch JM, Katz J, Sommer A, Quigley HA, Javitt JC. Family history and risk of primary open angle glaucoma. The Baltimore Eye Survey. *Arch Ophthalmol* 1994;112(1):69–73.
5. Newman-Casey PA, Blachley T, Lee PP, et al. Patterns of glaucoma medication adherence over four years of follow up. *Ophthalmology* 2015;122:2010–2021.
6. Weinreb RN, Scassellati Sforzolini B, Vittitow J, Leibmann J. Latanoprostene bunod 0.024% versus timolol maleate 0.5% in subjects with open-angle glaucoma or ocular hypertension: the APOLLO study. *Ophthalmology* 2016;123(5):965–973.
7. Serle JB, Katz LJ, McLaurin E, et al; Rocket-1 and Rocket-2 Study Groups. Two phase 3 clinical trials comparing the safety and efficacy of netarsudil to timolol in patients with elevated intraocular pressure: Rho Kinase Elevated IOP Treatment Trial 1 and 2 (ROCKET 1 and ROCKET-2). *Am J Ophthalmol* 2018;186:116–127.
8. Higginbotham EJ. Considerations in glaucoma therapy: fixed combination versus their component medications. *Clin Ophthalmol* 2010;4:1–9.
9. Gross RL. Current medical management of glaucoma. In: Yanoff M, Duker J, et al, eds. *Ophthalmology*. 3rd ed. Oxford, UK: Mosby-Elsevier; 2009:1220–1225.
10. Katz LJ, Steinmann WC, Kabir A, et al. Selective laser trabeculectomy versus medical therapy as initial treatment of glaucoma: a prospective randomized trial. *J Glaucoma* 2012;21:460–468.

108

ALLERGIC RHINITIS

Breathe In, Breathe Out Level I

Jon P. Wietholter, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize common signs and symptoms associated with allergic rhinitis.
- Educate patients on appropriate measures to limit or avoid exposure to specific antigens.
- Select an appropriate pharmacotherapeutic regimen for managing allergic rhinitis, focusing on specific symptoms.
- Educate patients with allergic rhinitis on appropriate medication use, including instillation technique for intranasal medications.

PATIENT PRESENTATION

■ Chief Complaint

"I can't breathe!"

■ HPI

Aidan Evans is a 17-year-old African-American boy presenting to his outpatient internal medicine clinic with complaints of severe congestion, intermittent bilateral rhinorrhea, and persistent sneezing. He states that symptoms are at their worst when he is outdoors, particularly after it rains. Because he spends time outdoors daily, the symptoms have been bothering him consistently over the past 1–2 months, and he is having trouble sleeping due to nasal congestion. He has struggled with these types of symptoms since he was a child, but they have significantly worsened over the past 2 years after his family moved to West Virginia from Arizona. He hasn't noticed a fever or a sore throat, but the symptoms are becoming unbearable. He is seeking advice on how to cope with and manage these symptoms.

■ PMH

Moderate-persistent asthma (diagnosed when he was age 13)

■ FH

Father, age 44, with a history of asthma and allergic rhinitis. Mother, age 38, with a history of migraines. One younger sibling with no significant medical history.

■ SH

Is a high school junior; (–) tobacco, (–) illicit drugs, (+) social alcohol use (primarily on weekends when partying with friends); family has two cats and two dogs.

■ Meds

Diphenhydramine 25 mg PO Q 8 H PRN for allergy symptoms
Albuterol MDI two puffs Q 6 H PRN (uses roughly one inhaler per year for asthma symptoms)
Ciclesonide (Alvesco MDI, 80 mcg/puff) one puff twice daily for asthma

■ All

Penicillin (hives); cephalexin (trouble breathing)

■ ROS

Denies headaches; no shortness of breath, wheezing, chest pain, or abdominal discomfort

■ Physical Examination

Gen

Young African-American boy who appears tired and sounds congested. Although sneezing and rhinorrhea are complaints, they are not ongoing during this evaluation.

VS

BP 112/74 mm Hg, P 68 bpm, RR 18, T 36.9°C; Wt 155 lb (70.5 kg), Ht 5'8" (173 cm)

Skin

Turgor normal, no rashes or lesions

HEENT

NC/AT; PERRLA; EOMI; (–) periorbital edema or discoloration; TMs are intact; (+) swollen nasal mucous membranes and nasal turbinates with a pale, bluish hue and discharge down the posterior pharynx; (–) tenderness over frontal and maxillary sinuses; (–) oropharyngeal lesions; throat is nonerythematous.

Neck/Lymph Nodes

No lymphadenopathy or thyromegaly

Chest

CTA bilaterally; no noticeable wheezing

CV

RRR without murmur or rub

Abd

Soft, nontender, (+) BS

Genit/Rect

Deferred

MS/Ext

No erythema, pain, or edema; pulses 2+

Neuro

A&O × 3; CN: visual fields and hearing intact; 5/5 strength throughout

■ Labs

Na 140 mEq/L	Hgb 15.4 g/dL
K 3.9 mEq/L	Hct 45.3%
Cl 108 mEq/L	Plt $391 \times 10^3/\text{mm}^3$
CO ₂ 28 mEq/L	WBC $9.6 \times 10^3/\text{mm}^3$
BUN 10 mg/dL	
SCr 0.7 mg/dL	
Glu 88 mg/dL	

■ Other

Peak expiratory flow (PEF): Patient states that readings are always >80% of personal best.

■ Assessment

This is a 17-year-old boy complaining of signs and symptoms consistent with moderate–severe persistent allergic rhinitis.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of allergic rhinitis?
- What additional information is needed to fully assess this patient's allergic rhinitis?

Assess the Information

- Assess the severity of allergic rhinitis based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for allergic rhinitis in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's allergic rhinitis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's allergic rhinitis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to a patient receiving an intranasal corticosteroid to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE: ALTERNATIVE THERAPY

Aidan's mother is quite concerned about drowsiness associated with treatments for his symptoms because he has a tendency to nap when he is supposed to be doing homework. Mrs Patrick uses butterbur extract for migraine prophylaxis and has heard that it is effective for allergy symptoms; she asks about using the same product for James. See Section 19 of this Casebook for questions regarding the use of butterbur extract for allergy symptoms.

SELF-STUDY ASSIGNMENTS

1. Describe how the recommended treatment plan might differ if this was instead a 78-year-old person or a 5-year-old child.

2. Describe a situation where monotherapy with an antihistamine, a leukotriene receptor antagonist, or an oral decongestant would be appropriate or preferred for managing allergic rhinitis. Support your recommendations with efficacy and safety data.
3. Evaluate the utility of herbal medications that have been recommended for managing allergic rhinitis. Develop a list of positives and negatives regarding their potential use.

CLINICAL PEARL

For patients interested in only nonpharmacologic therapy, some studies have suggested that acupuncture can improve allergic rhinitis symptom scores and quality of life. Although the exact mechanism is unknown, there is some evidence that acupuncture may inhibit cytokine production.

REFERENCES

1. Seidman MD, Gurgel RK, Lin SY, et al. Clinical practice guideline: allergic rhinitis. *Otolaryngol Head Neck Surg* 2015;152(IS):S1–S43.
2. Blaiss MS, Hammerby E, Robinson S, Kennedy-Martin T, Buchs S. The burden of allergic rhinitis and allergic rhinoconjunctivitis on adolescents: a literature review. *Ann Allergy Asthma Immunol* 2018; 121:43–52.
3. Dykewicz MS, Wallace DV, Baroody F, et al. Treatment of seasonal allergic rhinitis: an evidence-based focused 2017 guideline update. *Ann Allergy Asthma Immunol* 2017;119(6):489–511.
4. Wheatley LM, Togias A. Clinical practice. Allergic rhinitis. *N Engl J Med* 2015;372:456–463.
5. Brozek JL, Bousquet J, Agache I, et al. Allergic rhinitis and its impact on asthma (ARIA) guidelines: 2016 revision. *J Allergy Clin Immunol* 2017;140:950–958.
6. Sur DKC, Plesa ML. Treatment of allergic rhinitis. *Am Fam Physician* 2015;92(11):985–992.
7. Bousquet J, Schunemann HJ, Hellings PW, et al. MACVIA clinical decision algorithm in adolescents and adults with allergic rhinitis. *J Allergy Clin Immunol* 2016;138(2):367–374.

This page intentionally left blank

SECTION 14

DERMATOLOGIC DISORDERS

109

ACNE VULGARIS

The Graduate Level II

Rebecca M. Law, BS Pharm, PharmD

Wayne P. Gulliver, MD, FRCPC

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Understand risk factors and aggravating factors in the pathogenesis of acne vulgaris.
- Understand the treatment strategies for acne, including appropriate situations for using nonprescription and prescription medications and use of topical and systemic therapies.
- Educate patients with acne on systemic therapies.
- Monitor the safety and efficacy of selected systemic therapies.

PATIENT PRESENTATION

■ Chief Complaint

"I can't stand this acne!"

■ HPI

Elaine Morgan is an 18-year-old woman with a history of facial acne since age 15. One month ago, she completed a 3-month course of minocycline in combination with Differin (adapalene). Her acne has flared up again, and she presents again to her family physician for treatment.

■ PMH

Has irregular menses as a result of polycystic ovary syndrome diagnosed 3 years ago, which has not required medical treatment. However, it has resulted in an acne condition that was initially quite mild; she responded well to nonprescription topical products. In the past 2 years, the number of facial lesions has increased despite OTC and, later, prescription drug treatments. Initially her physician prescribed Benzamycin Gel (benzoyl peroxide 5%/erythromycin 3%), which was beneficial, but this had to be discontinued because of excessive drying. Differin XP (adapalene 0.3% gel) was used next, and it controlled her condition for about 6 months; then the acne worsened and oral antibiotics were added.

Most recently, she has received two 3-month courses of minocycline over the past year. She has also noted some scarring and cysts in the past few months.

■ FH

Parents alive and well; two older brothers (ages 21 and 25). Father had acne with residual scarring.

■ SH

The patient is under some stress because she is graduating from high school in a few weeks. She wants to do well in school so she will qualify for the best colleges. Both of her brothers graduated with honors. She has been sexually active for the past 2 months, and her boyfriend uses condoms.

■ Meds

None currently

■ All

NKDA

■ ROS

In addition to the complaints noted above, the patient has irregular menstrual periods and mild hirsutism

■ Physical Examination

Gen

Alert, moderately anxious teenager in NAD

VS

BP 110/70 mm Hg, RR 15, T 37°C; Wt 45 kg, Ht 5'2"

Skin

Ten to fifteen comedones on forehead, nose, and chin; four to five papules and pustules on the nose and malar area. A few healing cysts on the chin. Superficial scars on malar area. Increased facial hair.

HEENT

PERRLA, EOMI, fundi benign, TMs intact

Chest

CTA bilaterally

Cor

RRR without MRG, S₁ and S₂ normal

Abd

(+) BS, soft, nontender, no masses

MS/Ext

No joint aches or pains; peripheral pulses present

Neuro

CN II–XII intact

Labs

Na 140 mEq/L	Hgb 13.0 g/dL	AST 21 IU/L	T. chol 170 mg/dL
K 3.7 mEq/L	Hct 38%	ALT 39 IU/L	LDL-C 90 mg/dL
Cl 100 mEq/L	Plt $300 \times 10^3/\text{mm}^3$	LDH 105 IU/L	Trig 90 mg/dL
CO ₂ 25 mEq/L	WBC $7.0 \times 10^3/\text{mm}^3$	Alk phos 89 IU/L	HDL 45 mg/dL
BUN 12 mg/dL		T. bili 1.0 mg/dL	FSH 30 mIU/mL
SCr 1.0 mg/dL		Alb 3.9 g/dL	LH 150 mIU/mL
Glu 100 mg/dL			DHEAS 221 mcg/dL (6 $\mu\text{mol/L}$)
			Testosterone (free) 2.3 ng/mL
			Prolactin 15 ng/mL

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of acne vulgaris?
- 1.b. What additional information is needed to fully assess this patient's acne?

Assess the Information

- 2.a. Assess the severity of acne vulgaris based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. How does polycystic ovary syndrome contribute to this patient's acne and other physical findings?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating acne vulgaris?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's acne and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Two months later, the patient's acne is improving, but she has developed bloating, weight gain, and increased appetite, likely related to the therapy prescribed. She also reveals that her maternal grandmother and aunt both died of melanoma, and a friend told her that she should not be using her new therapy.

FOLLOW-UP QUESTION

1. Based on this new information, what is the most appropriate course of action?

SELF-STUDY ASSIGNMENTS

1. Review the dysmorphic syndrome associated with acne.
2. Review the nonpharmacologic management of acne, including stress reduction and dietary changes.

CLINICAL PEARL

In females with acne, scarring + cysts + two courses of oral antibiotics means hormonal therapy and "consider isotretinoin."

REFERENCES

1. Dreno B, Pecastaings S, Corvec S, et al. *Cutibacterium acnes* (*Propionibacterium acnes*) and acne vulgaris: a brief look at the latest updates. *J Eur Acad Dermatol Venereol* 2018; 32(Suppl 2):5–14.
2. Eichenfield LF, Krakowski AC, Piggott C, et al. Evidence-based recommendations for the diagnosis and treatment of pediatric acne. *Pediatrics* 2013;131:S163–S186. Available at: https://pediatrics.aappublications.org/content/pediatrics/131/Supplement_3/S163.full.pdf. Accessed February 22, 2019.
3. Nast A, Dreno B, Bettoli V, et al. European evidence-based (S3) guidelines for the treatment of acne—update 2016—short version. *J Eur Acad Dermatol Venereol* 2016;30(8):1261–1268.
4. Asai Y, Baibergenova A, Dutil M, et al. Management of acne: Canadian clinical practice guideline. *CMAJ* 2016;188(2):118–126.
5. Thiboutot D, Dreno B, Abanmi A, et al. Practical management of acne for clinicians: an international consensus from the Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol* 2018;78:S1–S23.
6. Polycystic Ovary Syndrome. Office of Women's Health, US Department of Health & Human Services. October 22, 2018. Available at: <https://www.womenshealth.gov/a-z-topics/polycystic-ovary-syndrome>. Accessed March 7, 2019.
7. Gollnick H, Cunliffe W, Berson D, et al. Management of acne: a report from a Global Alliance to Improve Outcomes in Acne. *J Am Acad Dermatol* 2003;49(1 Suppl):S1–S37.
8. Law RM. The pharmacist's role in the treatment of acne. *America's Pharmacist* 2003;125:35–42.
9. Zaenglein AL, Pathy AL, Schlosser BJ, et al. Guidelines of care for the management of acne vulgaris. *J Am Acad Dermatol* 2016 74(5):945–973.
10. Tan J. Dapsone 5% gel: a new option in topical therapy for acne. *Skin Therapy Lett* 2012;17(8):1–3.
11. Chung JP, Yiu AK, Chung TK, et al. A randomized crossover study of medroxyprogesterone acetate and Diane-35 in adolescent girls with polycystic ovarian syndrome. *J Pediatr Adolesc Gynecol* 2014;27:166–171.
12. Karagas MR, Stukel TA, Dykes J, et al. A pooled analysis of 10 case-control studies of melanoma and oral contraceptive use. *Br J Cancer* 2002;86:1085–1092.

110

PSORIASIS

The Harried School Teacher Level II

Rebecca M. Law, BS Pharm, PharmD

Wayne P. Gulliver, MD, FRCPC

LEARNING OBJECTIVES

After completing this case study, students should be able to:

- Describe the pathophysiology and clinical presentation of plaque psoriasis.
- Discuss the appropriate use of topical, photochemical, and systemic treatment modalities including biologic agents for psoriasis, based on disease severity.
- Compare the efficacy and adverse effects of systemic therapies for psoriasis, including first-line standard therapies (methotrexate, acitretin, cyclosporine), second-line therapies (azathioprine, hydroxyurea, sulfasalazine), and the biologic agents (TNF-alpha inhibitors, ustekinumab, IL-17 inhibitors, and IL-23 inhibitors).
- Select appropriate therapeutic regimens for patients with plaque psoriasis based on disease severity and patient-specific considerations such as organ dysfunction.
- Educate patients with psoriasis about proper use of pharmacotherapy, potential adverse effects, and necessary precautions.

PATIENT PRESENTATION

■ Chief Complaint

“Nothing is helping my psoriasis.”

■ HPI

Gerald Kent is a 50-year-old man with a 27-year history of psoriasis who presented to the outpatient dermatology clinic 2 days ago with another flare-up of his psoriasis. He was admitted to the inpatient dermatology service for a severe flare of plaque psoriasis involving his arms, legs, elbows, knees, palms, abdomen, back, and scalp (Fig. 110-1).

The patient was diagnosed with plaque psoriasis at age 23. He initially responded to topical therapy with medium-potency topical corticosteroids, later to calcipotriol. He subsequently required photo-chemotherapy using psoralens with UVA phototherapy (PUVA) to control the condition. PUVA eventually became ineffective, and about 10 years ago he was started on oral methotrexate 5 mg once weekly. Dosage escalations kept the condition under fairly good control for about 5 years. Flare-ups during that period were initially managed with SCAT (short-contact anthralin therapy), but they eventually became more frequent and lesions were more widespread despite increasing the methotrexate dose. A liver biopsy performed about 5 years ago showed no evidence of fibrosis, hepatitis, or cirrhosis.

After requiring two SCAT treatments in a 4-month period, along with methotrexate 25 mg once weekly orally (given as two doses of 12.5 mg 12 hours apart), a change in therapy was considered

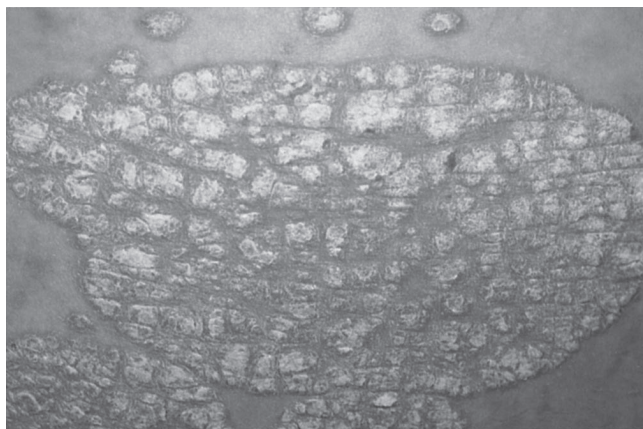


FIGURE 110-1. Plaque psoriasis. This papulosquamous skin disease is characterized by small and large erythematous papules and plaques with overlying adherent silvery scale. (Adapted with permission from: Yancey KB, Lawley TJ. Approach to the patient with a skin disorder. In: Jameson J, Fauci AS, Kasper DL, et al, eds. *Harrison's Principles of Internal Medicine*. 20th ed. 2018. New York, NY: McGraw-Hill Education; 2018. <https://accesspharmacy.com>. Accessed April 12, 2019.)

necessary at that time. Because he was receiving the maximum recommended methotrexate dose and had already reached a lifetime cumulative methotrexate dose of 2.2 grams, he was changed to a cyclic regimen of cyclosporine microemulsion (Neoral) 75 mg orally twice daily for 3 months, followed by acitretin (Soriatane) 25 mg orally once daily with dinner for 3 months, and repeat. He found the acitretin drying, so after 6 months he was changed to the current regimen of only cyclosporine microemulsion 75 mg orally twice daily. Flare-ups had become infrequent and were again successfully managed by SCAT for over 1 year. However, in the past 6 months, he has already required two SCAT treatments for flare-ups, and this is his third flare-up.

■ PMH

One episode of major depressive illness triggered by the death of his first wife, which occurred 16 years ago (age 34). He was treated by his family physician who prescribed fluoxetine for 6 months. He has had no recurrences. He has no other chronic medical conditions and no other acute or recent illnesses.

■ FH

Parents alive and well. Father has HTN and type 2 diabetes. Has two older sisters and a younger brother. Younger brother was diagnosed with psoriasis about 5 years ago. No history of other immune disorders or malignancy.

■ SH

Patient is an elementary school teacher. He is currently a nonsmoker but used to be a heavy smoker in his younger years (20s and 30s); social use of alcohol (glass of wine with dinner). He is married and has two children ages 10 and 12 with his second wife. There has been an increased workload for the past year because of teacher layoffs at his school.

■ Meds

Neoral 75 mg PO twice daily
Acetaminophen for occasional headaches

■ All

NKDA

■ **ROS**

Skin feels very itchy despite using a nonmedicated moisturizer TID. No joint aches or pains. No complaints of shortness of breath. Occasional nausea associated with a cyclosporine dose. Has been feeling stressed because of tensions at work but does not feel depressed.

■ **Physical Examination****Gen**

Alert, mildly anxious 50-year-old Caucasian man in NAD

VS

BP 129/83 mm Hg, P 88 bpm, T 37°C; Wt 75 kg, Ht 5'9"

Skin

Confluent plaque psoriasis with extensive lesions on abdomen, arms, legs, back, and scalp. Thick crusted lesions on elbows, knees, palms, and soles. Lesions are red to violet in color, with sharply demarcated borders except where confluent, and are loosely covered with silvery-white scales. There are no pustules or vesicles. There are excoriations on trunk and extremities consistent with scratching.

HEENT

PERRLA, EOMI, fundi benign, TMs intact; extensive scaly lesions on scalp as noted

Neck/Lymph Nodes

No lymphadenopathy; thyroid nonpalpable

Chest

CTA bilaterally

CV

RRR without MRG; S₁ and S₂ normal

Abd

(+) BS, soft, nontender, no masses; extensive scaly lesions and excoriations on skin as noted above

Genit/Rect

Deferred

MS/Ext

No joint swelling, warmth, or tenderness; skin lesions as noted above; no nail involvement; peripheral pulses 2+ throughout

Neuro

A&O × 3; CN II–XII intact; DTRs 2+ toes downgoing

■ **Labs**

Na 139 mEq/L	Hgb 13.5 g/dL	AST 22 IU/L
K 4.0 mEq/L	Hct 35.0%	ALT 38 IU/L
Cl 102 mEq/L	Plt 255 × 10 ³ /mm ³	LDH 107 IU/L
CO ₂ 25 mEq/L	WBC 6.0 × 10 ³ /mm ³	Alk phos 98 IU/L
BUN 14 mg/dL		T. bili 1.0 mg/dL
SCr 1.0 mg/dL		Alb 3.7 g/dL
Glu 98 mg/dL		Uric acid 4 mg/dL
		T. chol 180 mg/dL

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of plaque psoriasis?
- What comorbidities does this patient have that are associated with psoriasis?
- What additional information is needed to fully assess this patient?
- What risk factors for developing psoriasis or experiencing a disease flare-up are present in this patient?

Assess the Information

- Assess the severity of psoriasis based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy for this patient's plaque psoriasis and other drug therapy problems?
- What nondrug therapies might be useful for managing this patient's psoriasis and related drug therapy problems?
- What feasible pharmacotherapeutic alternatives are available for managing this patient's psoriasis and related drug therapy problems?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's plaque psoriasis and related drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ **SELF-STUDY ASSIGNMENTS**

- Perform a literature search to identify potential future therapies for psoriasis: topical therapies such as NSAIDs, protein kinase C inhibitors, methotrexate gel, an implantable 5-fluorouracil formulation; systemic therapies such as glucosamine, monoclonal antibodies, and cytokines.
- Perform a literature search to review the current guidelines, opinions, and evidence regarding liver biopsies and long-term methotrexate use for patients with psoriasis.

CLINICAL PEARL

Provide patient-specific therapies and always consider any psychosocial effects, debilities, and comorbidities related to the patient's psoriasis.

REFERENCES

- Kim WB, Jerome D, Yeung J. Diagnosis and management of psoriasis. *Can Fam Physician* 2017;63(4):278–285.
- Papp KA, Gulliver W, Lynde CW, Poulin Y (Steering Committee). Canadian Guidelines for the Management of Plaque Psoriasis. 1st ed. June 2009. Available at: <https://dermatology.ca/dermatologists/guidelines/psoriasis>. Also see: Canadian Psoriasis Guidelines Addendum Committee. Addendum to the Canadian Guidelines for the Management of Plaque Psoriasis, May 2016. *J Cutan Med Surg* 2016;20(5):375–431. Available at: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5014087/>. Accessed March 26, 2019.
- Menter A, Korman NJ, Elmets CA, et al. 2009 guidelines of care for the management of psoriasis and psoriatic arthritis—Section 3. Guidelines of care for the management and treatment of psoriasis with topical therapies. *J Am Acad Dermatol* 2009;60:643–659.
- Smith N, Weymann A, Tausk FA, et al. Complementary and alternative medicine for psoriasis: a qualitative review of the clinical trial literature. *J Am Acad Dermatol* 2009;61:841–856.
- Menter A, Korman NJ, Elmets CA, et al. 2009 guidelines of care for the management of psoriasis and psoriatic arthritis—Section 4. Guidelines of care for the management and treatment of psoriasis with traditional systemic agents. *J Am Acad Dermatol* 2009;61:451–485.
- Menter A, Korman NJ, Elmets CA, et al. 2009 guidelines of care for the management of psoriasis and psoriatic arthritis—Section 5. Guidelines of care for the treatment of psoriasis with phototherapy and photochemotherapy. *J Am Acad Dermatol* 2010;62:114–135.
- Rosmarin DM, Lebwohl M, Elewski BE, et al. Cyclosporine and psoriasis: 2008 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol* 2010;62:838–853.
- Kalb RE, Strober B, Weinstein G, Lebwohl M. Methotrexate and psoriasis: 2009 National Psoriasis Foundation Consensus Conference. *J Am Acad Dermatol* 2009;60:824–837.
- European S3-Guidelines on the systemic treatment of psoriasis vulgaris. Updated 2015. EDF in cooperation with EADV and IPC. *J Eur Acad Dermatol Venereol* 2015;29(12):e1–22. Available at: [https://www.edf.one/dam/jcr:d0c615a6-0631-4bf7-9f87-c8f95c21ab9b/European%20S3-Guidelines%20on%20the%20systemic%20treatment%20of%20psoriasis%20\(2\).pdf](https://www.edf.one/dam/jcr:d0c615a6-0631-4bf7-9f87-c8f95c21ab9b/European%20S3-Guidelines%20on%20the%20systemic%20treatment%20of%20psoriasis%20(2).pdf). Accessed March 31, 2019.
- Smith CH, Jabbar-Lopez ZK, Yiu ZZ, et al. British Association of Dermatologists guidelines for biologic therapy for psoriasis 2017. *Br J Dermatol* 2017;177(3):628–636.
- Menter A, Strober BE, Kaplan DH, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with biologics. *J Am Acad Dermatol* 2019;80(4):1029–1072.
- Elmets CA, Leonardi CL, Davis DMR, et al. Joint AAD-NPF guidelines of care for the management and treatment of psoriasis with awareness and attention to comorbidities. *J Am Acad Dermatol* 2019;80(4):1073–1113.
- Armstrong AW, Siegel MP, Bagel J, et al. From the Medical Board of the National Psoriasis Foundation: treatment targets for plaque psoriasis. *J Am Acad Dermatol* 2017;76(2):290–298.

111

ATOPIC DERMATITIS

The Itch That Erupts When Scratched Level I

Rebecca M. Law, BS Pharm, PharmD

Poh Gin Kwa, MD, FRCPC

Howard I. Maibach, MD

LEARNING OBJECTIVES

After completing this case study, students should be able to:

- Understand risk factors and aggravating factors in the pathophysiology of atopic dermatitis.
- Understand treatment strategies for atopic dermatitis, including nonpharmacologic management.
- Educate patients and their caregivers about management of atopic dermatitis.
- Monitor the safety and efficacy of selected pharmacologic therapies.

PATIENT PRESENTATION

■ Chief Complaint

As stated by the patient's mother, "My child constantly wants to scratch her skin, and she can't sleep well during the night."

■ HPI

Julia Chan is a 3½-year-old girl who just started attending daycare about 1 month ago. She did not want to go and still exhibits a lot of clinging behavior when her mother tries to leave; she still cries when her mother eventually does manage to leave. Her mother says that Julia's atopic dermatitis has flared up again. Julia has had atopic dermatitis since she was about 6 months old. It had been well controlled by topical corticosteroids and liberal use of moisturizers. Her recent flare-up began about 2–3 weeks ago. She has not been sleeping well and is constantly trying to scratch her skin at night. Her mother has been using 100% cotton sheets for her bed since she was an infant. She has sewn mittens on Julia's 100% cotton pajamas to prevent her from scratching because she had previously caused excoriations from scratching, which then became infected. During the day, Julia constantly wants to scratch her skin but has been told to just "pat" the itchy area. The caregivers at the daycare center keep an eye on her scratching behavior as well but are not always able to prevent her from scratching herself. They also inform her mother that Julia likes to eat food shared by other children.

■ PMH

Julia was breast-fed from birth for a total of 8 weeks, when her mother decided to return to work. Julia was then cared for at home by a babysitter and fed cow's milk, with oatmeal cereal being introduced as the first solid food. She was fed lemon meringue pie (made with egg white) once, and developed generalized hives, which led to the recognition that Julia has an egg allergy. This was confirmed by prick testing. The parents recently became aware that the babysitter

left Julia alone a lot (sitting on the floor/carpet to play by herself). That was the major reason for sending Julia to a daycare center.

■ SH

Julia is the only child of a professional couple. Her father is an engineer, and her mother is a litigation lawyer who often works long hours. The couple has a stressful lifestyle, and it appears that the stress is reflected in Julia's care. Sometimes Julia would be driven to one or another babysitter's homes at the last minute, when something urgent arises that the couple must attend to. There is little family time. Unfortunately, their relatives do not live in the same city, and there is little social support for Julia on a day-to-day basis. The parents were hoping that the daycare center would be helpful, but so far that has proven to be another issue for Julia. She does not want to participate in activities there and has lots of temper tantrums. She does not play well with other children. She had been toilet-trained but has now lost her toilet training and is using diapers again. Julia's mother started smoking again due to the recent stress; Julia keeps her up at night, and her mother is having difficulty dealing with Julia's multiple issues at home and at the daycare center.

■ FH

There is a strong family history of atopy. Julia's father has a severe allergy to shellfish, and her mother has a history of hay fever. Her father's sister has multiple food allergies. Her maternal grandmother had asthma. Her paternal first cousin had infantile eczema. Her maternal first cousin has a severe peanut allergy (generalized hives).

■ Meds

Hydrocortisone 1% cream applied to affected areas two to four times a day; although twice daily is her usual maintenance dose, she is currently using it three to four times a day.

Vaseline ad lib

Diphenhydramine 0.5 teaspoonful PO at bedtime as needed (when skin is excessively itchy, to allow Julia to sleep)

■ Allergies

NKDA. Multiple food allergies: egg (hives, developed allergy as an infant), strawberries, raspberries, and tomatoes.

■ ROS

Not obtained

■ Physical Examination

Gen

Unhappy, cranky, thin, clinging girl who keeps sucking her thumb

VS

BP 98/50, HR 96, RR 18, T 37°C; Wt 12.2 kg (10th percentile), Ht 98 cm (38.6"; 50th percentile), head circumference 49.5 cm (19.5"; 50th percentile)

Skin

Generally dry over entire body. Eczematous skin lesions on her cheeks and in flexure areas (behind ears, wrist joints, elbows, knees). Numerous pruritic papules in flexure areas with mild excoriations seen from scratching. Some spots of bleeding seen, but there is no crusting and the skin does not appear infected. Some cracking skin lesions seen behind the ears and knees. No lichenification. There are no lesions on the extensor parts of her body, the top of her nose, or in the diaper area.

The remainder of the physical exam was normal.

■ Labs

Na 135 mEq/L	Hgb 12.0 g/dL	WBC differential	AST 20 IU/L
K 4.0 mEq/L	Hct 35%	Neutros 50%	ALT 7 IU/L
Cl 102 mEq/L	Plt $230 \times 10^3/\text{mm}^3$	Bands 3%	IgE 300 IU/mL
CO ₂ 26 mEq/L	WBC $5.0 \times 10^3/\text{mm}^3$	Eosinophils 18%	D-dimer 90 ng/mL
BUN 8 mg/dL		Lymphs 27%	INR 1.1
SCr 0.2 mg/dL		Basophils 1%	aPTT 30 seconds
		Monos 1%	

Allergen-specific serum IgE tests: Elevated for egg, strawberries, raspberries

Note: Reference ranges at age 3.5—BUN 8–20 mg/dL, SCr 0.2–0.8 mg/dL, AST 20–60 IU/L, ALT 0–37 IU/L, and IgE 0–25 IU/mL; WBC differential—neutros 20–65%, eos 0–15%, basos 0–2%, lymphs 20–60%, and monos 0–10%.

Swab of skin lesion where there is bleeding: No growth

■ Assessment

This is a 3½-year-old child with an exacerbation of atopic dermatitis, likely stress induced.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of atopic dermatitis?
- What additional information is needed to fully assess this patient's atopic dermatitis?

Assess the Information

- Assess the severity of atopic dermatitis based on the subjective and objective information available.
- What risk factors or aggravating factors may have contributed to the patient's atopic dermatitis flare?
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy for atopic dermatitis and related concerns (behavior issues, caregiver stress) in this case?
- What nondrug therapies might be useful to manage this patient's pruritus, atopic dermatitis, behavioral issues, and her caregivers' stress?
- What feasible pharmacotherapeutic alternatives are available to manage this patient's pruritus, atopic dermatitis, behavioral issues, and caregiver stress?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's atopic dermatitis and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- How would you inform the patient's caregiver about the atopic dermatitis treatment regimen to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Review the use of phototherapy for atopic dermatitis.
2. Discuss how the clinical presentation and treatment strategies for an 8-month-old infant with atopic dermatitis might differ from those of a 3½-year-old child.

CLINICAL PEARL

In atopic dermatitis, minimizing preventable risk factors such as stress, eliminating triggers, providing appropriate skin care, and controlling the itch are as important as pharmacologic treatment.

REFERENCES

1. Wollenberg A, Barbarot S, Bieber T, et al. Consensus-based European guidelines for treatment of atopic eczema (atopic dermatitis) in adults and children: part I & part II. *J Eur Acad Dermatol Venereol* 2018;32(5):657–682, 850–878.
2. Wong ITY, Tsuyuki RT, Cresswell-Melville A, et al. Guidelines for the management of atopic dermatitis (eczema) for pharmacists. *Can Pharm J (Ott)* 2017;150(5):285–297.
3. Kim BS. Atopic Dermatitis. Medscape eMedicine updated Oct 30, 2018. Available at: <http://emedicine.medscape.com/article/1049085-overview>. Accessed November 19, 2018.
4. Eichenfield LE, Tom WL, Chamlin SI, et al. Guidelines of care for the management of atopic dermatitis. Section 1. Diagnosis and assessment of atopic dermatitis. *J Am Acad Dermatol* 2014;70:338–351.
5. Sidbury R, Tom WL, Bergman JN, et al. Guidelines of care for the management of atopic dermatitis. Section 4. Prevention of disease flares and use of adjunctive therapies and approaches. *J Am Acad Dermatol* 2014;71(6):1218–1233.
6. DaVeiga SP. Epidemiology of atopic dermatitis: a review. *Allergy Asthma Proc* 2012;23:227–234.
7. Koblenzer CS. Itching and the atopic skin. *J Allergy Clin Immunol* 1999;104(3 Pt 2):S109–S113.
8. Eichenfield LE, Tom WL, Berger TG, et al. Guidelines of care for the management of atopic dermatitis. Section 2. Management and treatment of atopic dermatitis with topical therapies. *J Am Acad Dermatol* 2014;71(1):116–132.
9. Eichenfield LE, Boguniewicz M, Simpson EL, et al. Translating atopic dermatitis management guidelines into practice for primary care providers. *Pediatrics* 2015;136(3):554–565.
10. Sidbury R, Davis DM, Cohen DE, et al. Guidelines of care for the management of atopic dermatitis. Section 3. Management and treatment with phototherapy and systemic agents. *J Am Acad Dermatol* 2014;71:327–349.
11. Gooderham M, Lynde CW, Papp K, et al. Review of systemic treatment options for adult atopic dermatitis. *J Cutan Med Surg* 2017;21(1):31–39.
12. Patel R, DuPont HL. New approaches for bacteriotherapy: prebiotics, new-generation probiotics, and synbiotics. *Clin Infect Dis* 2015; 60(Suppl 2):S108–S121.

112

DERMATOLOGIC DRUG REACTION

A Case of TEN Level III

Rebecca M. Law, BS Pharm, PharmD

Howard I. Maibach, MD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the approach to identifying or ruling out a suspected drug-induced skin reaction.
- Recognize the signs and symptoms of drug-induced Stevens–Johnson syndrome (SJS) and toxic epidermal necrolysis (TEN).
- Name the drugs most commonly implicated in causing SJS and TEN.
- Determine an appropriate course of action for a patient with a suspected drug-induced skin reaction.
- Discuss the treatment approach for a patient with TEN, including nonpharmacologic and pharmacologic therapies.
- Participate in a collaborative interprofessional team approach when managing a patient with TEN.
- Counsel patients with suspected drug-induced SJS or TEN about the nature of the reaction and necessary precautions, including which medications to avoid in the future.
- Identify patients with potentially serious skin reactions who should be referred for further medical evaluation and treatment.

PATIENT PRESENTATION

Chief Complaint

“My child has a blistering rash all over her body and is really sick!”

HPI

April Rayne is a 14-year-old girl who presents to the ED with a high fever, vomiting, diarrhea, and a 3-day history of a skin rash. The rash is maculopapular with blisters and has spread to involve 75% of her body surface area. She had a UTI about 1.5 weeks ago and was prescribed a 7-day course of TMP/SMX. She adhered to the regimen; her urinary tract symptoms of dysuria and frequency and her abdominal discomfort resolved within 2–3 days. This was her first UTI. She continued to take the TMP/SMX as directed. Seven days after starting therapy, she noticed red spots on her arms and legs that began to spread over the whole body. The rash began to blister. She became febrile, and last night she began vomiting and had two bouts of diarrhea. This morning her mother brought her to the ED where she was assessed (physical exam) and quickly transferred to the ICU. Upon arrival in the ICU, she was immediately intubated to protect her airway patency. The rash was continuing to spread with additional blisters observed.

PMH

Unremarkable

FH

Parents A&W, no siblings

SH

April is a student who just began taking jazz classes about 2 months ago, which she really enjoys. She is not sexually active, does not smoke, and does not use alcohol. There have been no recent changes in diet or in her living environment.

Meds

Just completed a 7-day course of TMP/SMX. No additional drugs taken including OTCs, vitamins, herbals, or drugs of abuse. Not on oral contraceptives.

Meds in Hospital

For intubation: Ketamine 40 mg IV $\times$ 1, midazolam 1 mg IV $\times$ 1, propofol 120 mg IV $\times$ 1
For BP support: Dopamine IV infusion at 12 mcg/kg/min

All

NKDA

ROS

Skin is tender to the touch, with rash and blisters. Continues to have loose BM. Vomited $\times$ 1 in ED. Otherwise negative except for complaints noted above.

Physical Examination (in ICU)**Gen**

Fairly anxious 14-year-old Caucasian girl looking acutely ill

VS

BP 90/50 mm Hg, HR 90, RR 25, T 40.1°C

Skin

Extensive maculopapular rash over 75% of BSA. Blisters involve over 30% of BSA and are still spreading—additional blisters have appeared since her initial arrival to the ED. Some blisters have become confluent, and there is detachment of the epidermis. Small blisters on discrete dark red purpuric macules symmetrically over face, hands, feet, limbs, and trunk with widespread erythema. Blisters and intensely red oozing erosions over lips (especially vermilion border), oral mucosa, and vaginal area. Some ruptured blisters on skin and some with necrotic centers. Positive Nikolsky's sign. Skin is tender to the touch.

HEENT

PERRLA, EOMI, fundi benign, TMs intact. Corneal abrasions but no blisters. Conjunctivitis with some debris collecting under eyelids. External nares clear. Blisters in oral cavity and ulceration on lower lip. Pharynx erythematous and blistering.

Chest

Upper airway congestion; debris and ulceration in mouth, throat, and epiglottis

Cor

RRR without murmurs, rubs, or gallops; S₁ and S₂ normal

Abd

(+) BS, soft, nontender, no masses

Genitourinary

Blistering in vaginal area. Foley catheter inserted—urine output approximately 40–50 mL/hr

Rectal

Deferred

MS/Ext

Maculopapular rash and some blisters on arms and legs. Bilateral arthralgias and myalgias. Peripheral pulses present.

Neuro

Oriented $\times$ 3. No signs of confusion.

Labs

Na 140 mEq/L	Glucose	WBC $11 \times 10^3/\text{mm}^3$	Hgb 12 g/dL
K 4.0 mEq/L	95 mg/dL	PMNs 65%	Hct 31%
Cl 101 mEq/L	BUN 9 mg/dL	Bands 5%	Plt $239 \times 10^3/\text{mm}^3$
CO ₂ 32 mEq/L	SCr 0.7 mg/dL	Eos 8%	INR 1.24
PO ₄ 2.2 mg/dL	AST 15 IU/L	Monos 1%	aPTT 32.4 seconds
T. protein 6.5 g/dL	ALT 22 IU/L	Basos 1%	ESR 35 mm/hr
Albumin 3.1 g/dL	LDH 120 IU/L	Lymphs 20%	RF negative

Urinalysis: No protein, ketones, blood, WBC, or bacteria.

Chest X-Ray

WNL

Clinical Course**Day 2 of Admission**

Urine output still 40–50 mL/hr; 1050 mL/previous 24 hr.

Day 3 of Admission

Histopathology of biopsy specimen from lesion on lip: Epidermal degeneration with intraepidermal vesiculation and subepidermal bullae. Mild perivascular lymphocytic infiltrate.

Direct immunofluorescence of biopsy specimen from lip lesion: Negative.

Swab from blisters on arm: Coagulase-negative *Staphylococcus*, *Pseudomonas aeruginosa*.

Blood cultures: (+) Coagulase-negative *Staphylococcus*, sensitive to vancomycin.

Urine culture (midstream urine): No growth.

Assessment

This is a 14-year-old girl with TEN, likely drug induced, who has developed secondary *Staphylococcus epidermidis* bacteremia.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of TEN?
- What additional information is needed to fully assess this patient's skin disorder?

Assess the Information

- 2.a. What subjective and objective information correlates with TEN disease severity and a worse prognosis?
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for managing TEN in this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating TEN?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Differentiate among the various types, terminology, and manifestations of cutaneous drug reactions, including irritant drug reactions, fixed drug reactions, maculopapular skin reactions, photoallergic and phototoxic reactions, bullous reactions, morbilliform and urticarial reactions, pigmentation, lichenoid eruptions, SJS, TEN, drug hypersensitivity syndrome, and vasculitis.
2. If this patient had SJS, how would the clinical presentation, disease course, and treatment differ from those of TEN?

3. Obtain information on the anticonvulsants and NSAIDs that have been most commonly implicated in causing SJS/TEN.
4. Investigate the genetics of drug hypersensitivity, including associations with specific genetic markers (eg, HLA-B*5701 and HLA-B*1502 alleles).

CLINICAL PEARL

Aggressive and vigilant nondrug supportive therapies are vital to the effective management of TEN.

REFERENCES

1. Schwartz RA, McDonough PH, Lee BW. CME: toxic epidermal necrolysis. Part I. Introduction, history, classification, clinical features, systemic manifestations, etiology, and immunopathogenesis. Part II. Prognosis, sequelae, diagnosis, differential diagnosis, prevention, and treatment. *J Am Acad Dermatol* 2013;69:173.e1–11 (part 1), 187.e1–16 (part 2).
2. Cohen V. Toxic epidermal necrolysis. eMedicine, updated Dec. 1, 2017. Available at: <http://emedicine.medscape.com/article/229698-overview>. Accessed September 13, 2018.
3. Roujeau J-C, Bricard G, Nicolas J-F. Drug-induced epidermal necrolysis: important new piece to end the puzzle. *J Allergy Clin Immunol* 2011; 128:1277–1278.
4. Gerull R, Nelle M, Schaible T. Toxic epidermal necrolysis and Stevens-Johnson syndrome: a review. *Crit Care Med* 2011;39(6):1521–1532.
5. Mockenhaupt M, Viboud C, Dunant A, et al. Stevens-Johnson syndrome and toxic epidermal necrolysis: assessment of medication risks with emphasis on recently marketed drugs. The EuroSCAR-Study. *J Invest Dermatol* 2008;128:35–44.
6. Schnyder B, Pichler WJ. Allergy to sulfonamides. *J Allergy Clin Immunol* 2013;131(1):256–257.e1–e5. <http://dx.doi.org/10.1016/j.jaci.2012.10.003>.
7. deShazo RD, Kemp SF. Allergic reactions to drugs and biologic agents. *JAMA* 1997;278:1895–1906.
8. Schnyder B. Approach to the patient with drug allergy. *Med Clin N Am* 2010;94(4):665–679.
9. Creamer D, Walsh SA, Dziewulski P, Exton LS. Guidelines for the management of Stevens-Johnson syndrome/toxic epidermal necrosis in adults. *Br J Dermatol* 2016;174(6):1194–1227.
10. Wang C-W, Yang L-Y, Chen CB, et al. Randomized, controlled trial of TNF-alpha antagonist in CTL-mediated severe cutaneous adverse reactions. *J Clin Invest* 2018;128(3):985–996.
11. Lee HY, Walsh SA, Creamer D. Long-term complications of Stevens-Johnson syndrome/toxic epidermal necrolysis (SJS/TEN): the spectrum of chronic problems in patients who survive an episode of SJS/TEN necessitates multidisciplinary follow-up. *Br J Dermatol* 2017;177(4):924–935.

This page intentionally left blank

SECTION 15

HEMATOLOGIC DISORDERS

113

IRON DEFICIENCY ANEMIA

Iron It Out Level I

Matthew A. Cantrell, PharmD, BCPS

Elizabeth M. Bald, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize that certain drugs such as NSAIDs can cause chronic blood loss and iron deficiency anemia (IDA).
- Identify the signs, symptoms, and laboratory manifestations of IDA.
- Select appropriate iron therapies for the treatment of IDA.
- Understand the monitoring parameters for both short- and long-term treatment of IDA.
- Inform patients of the potential adverse effects of iron therapy.
- Educate patients about the importance of adherence to their iron therapy regimen.

PATIENT PRESENTATION

■ Chief Complaint

"I feel tired all the time."

■ HPI

Anita Williamson is a 68-year-old woman who presents to her primary care provider with the above complaint. With further questioning, she reveals that she first noticed these symptoms approximately 2 months ago. She initially believed they were age-related changes; however, the symptoms have worsened in the past two weeks leading her to believe that something else could be the cause. She denies any recent diet changes or signs of bleeding. She states that she has taken a few doses of ibuprofen to help manage occasional headaches.

■ PMH

COPD × 8 years

Depression × 2 years

HTN × 10 years

Obesity s/p Roux-en-Y gastric bypass surgery 7 years ago

■ FH

Mother alive age 93 with HTN, type 2 DM, and depression; father died of colon cancer at age 62

■ SH

Former smoker with a 15 pack-year history—quit in 1995. Drinks a glass of wine with dinner two nights per week; married with two children.

■ ROS

No fever or chills; (–) burning pain in stomach after meals; (–) heartburn; (–) melena; good appetite; has one BM daily; no significant weight changes over past 5 years; (+) dry mouth; (+) fatigue, tires easily; (–) paralysis, fainting, numbness, paresthesia, or tremor; (+) headache; has myopic vision; (–) tinnitus or vertigo; has hay fever in spring; (+) wheezing; denies chest pain, edema; (+) dyspnea and orthopnea; denies nocturia, hematuria, dysuria, or history of stones.

■ Meds

Albuterol HFA two puffs 4–6 H PRN shortness of breath

Hydrochlorothiazide 25 mg PO daily

Lisinopril 10 mg PO daily

Pantoprazole 40 mg PO daily

Potassium chloride 20 mEq PO daily

Sertraline 50 mg PO daily

Ibuprofen 200 mg PO daily PRN for headaches

Tiotropium 18 mcg one inhalation once daily

Fluticasone/salmeterol DPI 100 mcg/50 mcg one inhalation twice daily

■ Allergies

Codeine (upset stomach)

Sulfa antibiotics (rash)

■ Physical Examination

Gen

WF in no acute distress who appears her stated age

VS

BP 134/88 mm Hg, P 92 bpm, RR 18, T 36.2°C, pulse oximetry 96% in room air; Wt 84 kg, Ht 5'5"

Skin

Age- and sun-related lentigines and seborrheic keratoses noted

HEENT

PERRL; EOMI; conjunctivae are pale; mucous membranes pale and dry; normal funduscopic examination with no retinopathy noted; deviated nasal septum; no sinus tenderness; oropharynx clear

Neck/Lymph Nodes

Neck supple without masses; trachea midline; no thyromegaly, no JVD

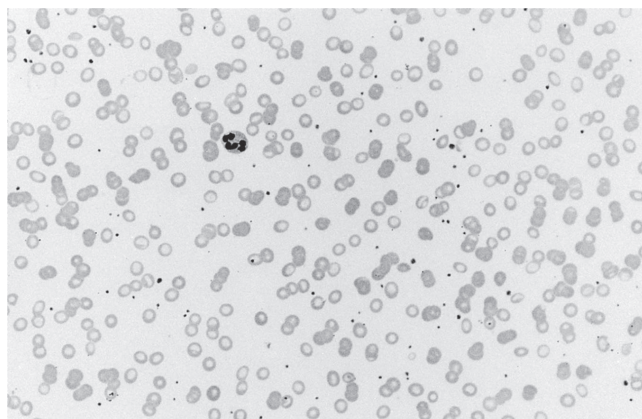


FIGURE 113-1. Blood smear with hypochromic, microcytic red blood cells (Wright–Giemsa $\times 330$). (Photo courtesy of Lydia C. Contis, MD.)

Thorax

Breath sounds decreased bilaterally, increased anterior–posterior diameter, (+) rhonchi, pursed-lip breathing

CV

RRR

Abd

Soft, tender to palpation; no masses or organomegaly; (+) BS

Genit/Rect

Rectal examination (–)

MS/Ext

Spoon-shaped nails (koilonychia) on the second and fourth fingers

Neuro

A&O $\times 3$; DTR 2+; normal gait

Other

Peripheral blood smear: hypochromic, microcytic red blood cells (Fig. 113-1)

Labs

See Table 113-1.

Colonoscopy Report Summary

Indication for procedure: Anemia, rule out blood loss.

Preparation: ECG, pulse, pulse oximetry, and blood pressure were monitored throughout.

Medications administered during procedure: fentanyl 50 mcg IV, midazolam 2.5 mg IV.

Procedure: The colonoscope was passed through the anus and advanced to the ileocecal valve. The scope was removed and the surrounding mucosa was examined.

Rectal Exam: Normal rectal exam.

Findings: No evidence of diverticulosis, polyps, or ulcerations, no evidence of blood loss. Negative for acute bleed.

Assessment

1. Severe IDA possibly secondary to poor dietary intake following gastric bypass surgery
2. Depression
3. COPD
4. HTN
5. Obesity

Plan

1. Initiate ferrous sulfate 325 mg once orally with a meal. After 1 week, increase dose to one tablet twice daily with meals. After 2 weeks, increase dose to one tablet three times daily with meals.
2. Initiate docusate 100 mg twice daily.
3. Return to clinic for follow-up with labs in 1 month.

Clinical Course

One month later the patient returns to the provider's office for a follow-up appointment. She reports that her dizziness and fatigue have improved; however, she has been experiencing significant nausea, abdominal pain, and constipation every day since starting the ferrous sulfate. She asks if there are any additional options for treating her IDA because she does not want to continue taking the iron.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of iron deficiency anemia (IDA)?
- 1.b. What additional information is needed to fully assess this patient's IDA?

Assess the Information

- 2.a. Assess the severity of IDA based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

TABLE 113-1 Lab Values

Na 138 mEq/L	Hgb 9.8 g/dL	WBC $10.7 \times 10^3/\text{mm}^3$	AST 10 IU/L	Ca 8.7 mg/dL
K 3.7 mEq/L	Hct 30%	Segs 61%	ALT 23 IU/L	Iron 4 mcg/dL
Cl 104 mEq/L	RBC $3.77 \times 10^6/\text{mm}^3$	Bands 2%	T. bili 0.3 mg/dL	TIBC 465 mcg/dL
CO ₂ 27 mEq/L	MCV 66.2 μm^3	Lymphs 23%	LDH 85 IU/L	Transferrin sat 1%
BUN 12 mg/dL	MCH 19 pg	Monos 10%	T. prot 6.3 g/dL	Ferritin 5 ng/mL
SCr 0.8 mg/dL	MCHC 28.7 g/dL	Eos 3%	Alb 3.7 g/dL	B ₁₂ 680 pg/mL
Glucose 90 mg/dL	RDW 20.9%	Basos 1%	Folic acid 8.2 ng/mL	
	MPV 8.1 fL			
	Microcytosis 2+			
	Anisocytosis 1+			

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for this patient's anemia?
- 3.b. What nondrug therapy may be effective for managing this anemia?
- 3.c. What oral and parenteral pharmacotherapeutic alternatives could be used to treat this patient's anemia?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Make a list of oral medications that should not be taken close to the time of oral iron administration; note the medications for which ferrous salts may interfere with their absorption.
2. Perform a literature search to determine the evidence supporting use of various sustained-release iron preparations, and determine the incremental cost of such products.
3. Calculate the correct total dose of parenteral iron dextran (ie, total dose iron dextran) for this patient, and write a comprehensive order for its administration.

CLINICAL PEARL

Indications for parenteral iron therapy include failure or intolerance to oral iron therapy or when a quicker recovery is necessary.

ACKNOWLEDGMENT

This case is adapted from the case written for the 10th edition by Robin L. Southwood, PharmD, CDE.

REFERENCES

1. Parrott J, Frank L, Rabena R, Craggs-Dino L, Isom KA, Greiman L. American Society for Metabolic and Bariatric Surgery Integrated Health Nutritional Guidelines for the Surgical Weight Loss Patient 2016 Update: micronutrients. *Surg Obes Relat Dis* 2017;13(5):727–741.
2. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2013;129(25 Suppl 2):S1–S45.
3. Zhu A, Kaneshiro M, Kaunitz JD. Evaluation and treatment of iron deficiency anemia: a gastroenterological perspective. *Dig Dis Sci* 2010;55:548–559.

4. Hershko C, Skikne B. Pathogenesis and management of iron deficiency anemia: emerging role of celiac disease, *Helicobacter pylori*, and autoimmune disease. *Semin Hematol* 2009;46:339–350.
5. Camaschella C. Iron-deficiency anemia. *N Engl J Med* 2015;372:1832–1843.
6. Auerbach M, Rodgers GM. Intravenous iron. *N Engl J Med* 2007;357:93–94.
7. Alleyne M, Horne MK, Miller JL. Individualized treatment for iron-deficiency anemia in adults. *Am J Med* 2008;121:943–948.
8. Mechanick JL, Youdim A, Jones DB, et al. Clinical practice guidelines for the perioperative nutritional, metabolic, and nonsurgical support of the bariatric surgery patient 2013 update. Cosponsored by American Association of Clinical Endocrinologists, the Obesity Society, and the American Society for Metabolic and Bariatric Surgery. *Surg Obes Relat Dis* 2013;9(2):159–191.

114

VITAMIN B₁₂ DEFICIENCY

Like Hot Pizza to the Tongue Level II

Jon P. Wietholter, PharmD, BCPS

*Notice to the Reader: The case author provided suggested answers to the questions related to this case in **Appendix D** to give students an example of how case answers should be constructed.*

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize signs, symptoms, and laboratory abnormalities associated with vitamin B₁₂ deficiency anemia.
- Select an appropriate regimen for treatment of anemia resulting from vitamin B₁₂ deficiency.
- Describe monitoring parameters for the initial and subsequent evaluations of patients with anemia caused by vitamin B₁₂ deficiency.
- Educate patients about appropriate vitamin B₁₂ therapy.

PATIENT PRESENTATION

Chief Complaint

"I feel like I'm constantly tired and fatigued. Also, my tongue is always sore and swollen, almost like I burned it on a piece of hot pizza, making it really hard for me to eat or drink anything."

HPI

Julie Kindred is a 45-year-old woman who presents to your outpatient clinic with her husband. She claims that her fatigue and lethargy have been going on for 10+ years but have been worsening over the last 4–5 months to the point that she always feels tired. Additionally, she claims that over the past 2–3 weeks her tongue has become extremely painful and swollen and that she struggles to eat. Her appetite has diminished because she tries to avoid eating anything that could worsen her pain, and she feels "fuller" more quickly than usual. On questioning, she also mentions a slight tingling and

numbness in her feet that seems to worsen when finishing any physical activity. The patient has lost about 10 lb over the past 3 months and states that she feels like she is running a constant low-grade fever.

PMH

Type 2 diabetes mellitus
Asthma
GERD

FH

Father alive (65 years old) with CAD, HTN, glaucoma, and type 2 DM;
Mother alive (64 years old) with HTN and asthma

SH

Married for 12 years, lives with her husband; has two children (one son and one daughter) who are both healthy; (+) tobacco, 1 ppd since age 24; (–) alcohol, (–) illicit drugs; is an elementary school teacher with adequate health insurance

Meds

Albuterol (90 mcg/actuation) MDI two puffs Q 6 H PRN
Fluticasone/salmeterol 250/50 mcg one puff Q 12 H
Metformin 1000 mg PO Q 12 H
Omeprazole 20 mg PO daily

All

Penicillin (hives)
Levofloxacin (anaphylaxis)

ROS

Complains of tongue pain and tingling sensation in her toes; (–) SOB, headache, chest pain, polyuria, or polydipsia; denies any visual changes, constipation, diarrhea, or urinary retention

Physical Examination

Gen

African-American woman in no acute distress with normal affect and speech; appears fatigued

VS

BP 123/87 mm Hg, P 106 bpm, RR 16, T 37.8°C; O₂ sat 94% on room air; Wt 92 kg, Ht 5'9"

Skin

Pale, turgor normal, no rashes or lesions

HEENT

PERRLA; EOMI; (+) red, smooth, swollen, sore tongue with loss of papillae; TMs normal

Neck

Supple; no masses, lymphadenopathy, or thyromegaly

Chest

Bilateral breath sounds; minor wheezing present on auscultation; (–) rales

CV

No discernible rhythm abnormality by auscultation; no murmurs or gallops; (+) mild tachycardia

Abd

Soft, nontender; mild splenomegaly; no masses; normal bowel sounds present

Rect

Deferred

Ext

No erythema, pain, or edema; normal pulses; (+) paresthesias; no joint redness or swelling; no limb weakness; reflexes intact

Neuro

A&O × 3; CN: visual fields and hearing intact; coordination intact; decreased pinprick in both lower extremities; decreased vibratory sensation in both lower extremities; decreased temperature sensation in both lower extremities; (–) ataxia, lightheadedness

Labs (All Fasting)

Na 136 mEq/L	Hgb 8.4 g/dL	AST 30 IU/L	Iron 124 mcg/dL
K 3.5 mEq/L	Hct 25.3%	ALT 24 IU/L	Ferritin 100 ng/mL
Cl 108 mEq/L	RBC $2.09 \times 10^6/\text{mm}^3$	Alk phos 79 IU/L	Transferrin
CO ₂ 24 mEq/L	Plt $91 \times 10^3/\text{mm}^3$	T. bili 0.8 mg/dL	229 mg/dL
BUN 11 mg/dL	WBC $5.5 \times 10^3/\text{mm}^3$	D. bili 0.4 mg/dL	LDH 140 IU/L
SCr 0.7 mg/dL	MCV 121 μm^3		B ₁₂ 101 pg/mL
Glu 134 mg/dL	MCH 40 pg		Folate 12.3 ng/mL
A1C 6.8%	MCHC 33.2 g/dL		
TSH 3.4 mIU/L	Retic. (corr) 0.7%		

Peripheral Blood Smear Morphology

Macro-ovalocytosis, hypersegmented granulocytes, large platelets, macrocytic red blood cells with megaloblastic changes (Fig. 114-1)

Assessment

1. Macrocytic anemia consistent with vitamin B₁₂ deficiency of unknown origin
2. Atrophic glossitis and peripheral sensory neuropathy possibly associated with vitamin B₁₂ deficiency
3. Type 2 diabetes mellitus (controlled)
4. Asthma (controlled)
5. GERD (uncertain control)

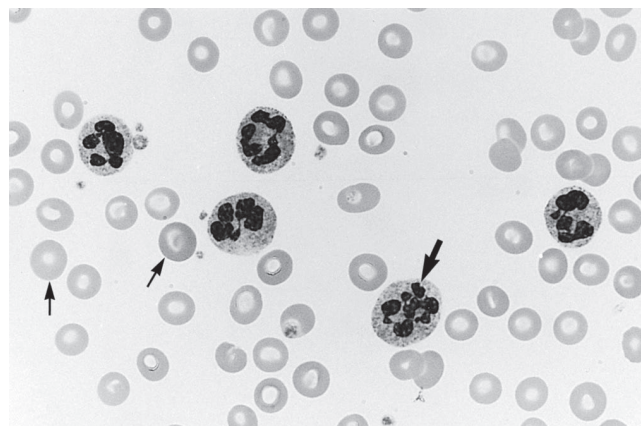


FIGURE 114-1. Blood smear with enlarged hypersegmented neutrophils, one with eight nuclear lobes (large arrow) and macrocytes (small arrows) (Wright-Giemsa × 1650). (Photo courtesy of Lydia C. Contis, MD.)

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of vitamin B₁₂ deficiency?
- 1.b. What additional information is needed to fully assess this patient's vitamin B₁₂ deficiency?

Assess the Information

- 2.a. Assess the severity of vitamin B₁₂ deficiency based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies for vitamin B₁₂ deficiency might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's vitamin B₁₂ deficiency?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's vitamin B₁₂ deficiency and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ FOLLOW-UP QUESTION

1. Mrs Kindred returns to your clinic 3 months later reporting that she is feeling much less fatigued and is able to eat a more consistent diet but still has tingling in her toes and a milder form of tongue soreness. What information can you give her regarding these remaining complaints?

■ SELF-STUDY ASSIGNMENTS

1. A serum vitamin B₁₂ level is no longer the most reliable laboratory test for evaluation of vitamin B₁₂ deficiency. Review the diagnostic tests that are more commonly used and provide a rationale for their increased use.
2. The anemia resulting from vitamin B₁₂ deficiency can be corrected by giving patients folic acid. Why then must we

differentiate between the two common causes of macrocytic anemia (folic acid deficiency or vitamin B₁₂ deficiency) instead of simply treating all patients with folic acid monotherapy?

CLINICAL PEARL

Pernicious anemia is a chronic illness arising from impaired absorption of vitamin B₁₂ due to a lack of intrinsic factor in gastric secretions. It garnered its name because it was universally fatal (pernicious is from the Latin word for violent death or destruction) due to a lack of available treatment options in the early stages of disease recognition. It can now be simply treated as any other vitamin B₁₂ deficiency and is a rather benign disease process if detected early.

REFERENCES

1. Green R. Vitamin B₁₂ deficiency from the perspective of a practicing hematologist. *Blood* 2017;129(19):2603–2611.
2. Briani C, Dalla Torre C, Citton V, et al. Cobalamin deficiency: clinical picture and radiological findings. *Nutrients* 2013;5:4521–4539.
3. Langan RC, Zawistoski KJ. Update on vitamin B₁₂ deficiency. *Am Fam Physician* 2011;83(12):1425–1430.
4. Chan CQ, Low LL, Lee KH. Oral vitamin B₁₂ replacement for the treatment of pernicious anemia. *Front Med (Lausanne)* 2016;3(38):1–6.
5. Oberley MJ, Yang DT. Laboratory testing for cobalamin deficiency in megaloblastic anemia. *Am J Hematol* 2013;88:522–526.
6. Aroda VR, Edelstein SL, Goldberg RB, et al. Long-term metformin use and vitamin B₁₂ deficiency in the Diabetes Prevention Program Outcomes Study. *J Clin Endocrinol Metab* 2016;101(4):1754–1761.
7. Maes ML, Fixen DR, Linnebur SA. Adverse effects of proton-pump inhibitor use in older adults: a review of the evidence. *Ther Adv Drug Saf* 2017;8(9):273–297.
8. Liu Q, Li S, Quan H, Li J. Vitamin B₁₂ status in metformin treated patients: systematic review. *PLoS One* 2014;9(6):e100379. doi: 10.1371/journal.pone.0100379.
9. Lewis JR, Barre D, Zhu K, et al. Long-term proton pump inhibitor therapy and falls and fractures in elderly women: a prospective cohort study. *J Bone Miner Res* 2014;29(11):2489–2497.

115

FOLIC ACID DEFICIENCY

More Wine, Anyone? Level I

Jonathan M. Kline, PharmD, CACP, BCPS, CDE

Amber Nicole Chiplinski, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs, symptoms, and laboratory abnormalities associated with folic acid deficiency.
- Identify the confounding factors that may contribute to the development of folic acid deficiency (eg, medications, concurrent disease states, and dietary habits).

- Recommend an appropriate treatment regimen to correct anemia resulting from folic acid deficiency.
- Educate patients with folic acid deficiency regarding pharmacologic and nonpharmacologic interventions used to correct folic acid deficiency.
- Describe appropriate monitoring parameters for initial and subsequent monitoring of folic acid deficiency.

PATIENT PRESENTATION

■ Chief Complaint

“My stomach hurts and I have been throwing up today.”

■ HPI

Laura Jones is a 43-year-old woman with a 1-day history of vomiting and mild abdominal pain. The pain radiates down to the lower abdominal quadrants bilaterally. She presents to the ED after experiencing some chest discomfort late in the day. She denies any fevers, chills, or similar pains in the past. She also complains of loose stools and chronic fatigue for the past 2–3 months.

■ PMH

Fibromyalgia
Celiac disease
Hypothyroidism
Osteopenia
History of endometriosis
Placenta previa—s/p TAH–BSO

■ FH

Mother positive for lupus; sister with Crohn disease; negative for DM, CAD, CVA, CA

■ SH

Married; (+) alcohol—three to four glasses of wine per day, increased recently from one to two glasses after her mother-in-law moved in; (+) smoking tobacco 0.5 ppd × 25 years, (–) recreational drug use; unemployed

■ Meds

Levothyroxine 100 mcg PO daily
Ortho Tri-Cyclen Lo 1 tab PO daily

■ All

Doxycycline—rash

■ ROS

(+) Generalized weakness; (–) dizziness; (–) weight gain or loss; (–) fever; (–) vision or hearing changes; (–) cough, chest pain, palpitations; (–) shortness of breath; (+) nausea/vomiting, abdominal pain, loose stools; (–) rectal bleeding; (–) nocturia or dysuria; (+) bilateral lower extremity weakness; (–) edema, rashes, or petechiae; (–) symptoms of depression or anxiety; (–) history of bleeding problems or VTE

■ Physical Examination

Gen

Caucasian female who appears generally ill, but nontoxic

VS

BP 135/90 mm Hg, P 82 bpm, RR 40, T 35.5°C; Ht 64", Wt 52 kg

Skin

No petechiae, rashes, ecchymoses, or active lesions; decreased skin turgor

HEENT

Atraumatic/normocephalic; PERRLA, EOMI; conjunctivae pink, sclera white; TMs intact and reactive; nares patent; tongue is large and erythematous; dry mucous membranes.

Neck/Lymph Nodes

Normal ROM; no JVD, adenopathy, thyromegaly, or bruits

Lung/Thorax

Lungs CTA bilaterally

CV

RRR; no murmurs, gallops, or rubs

Abd

Soft, nondistended, with midepigastria and right flank and right lower quadrant tenderness; (+) bowel sounds

Genit/Rect

Deferred

MS/Ext

Lower extremities warm with 2+ bipedal pulses; no clubbing, cyanosis, or edema

Neuro

CN II–XII grossly intact; decreased muscle strength 3/5 bilaterally in upper and lower extremities; DTRs 2+ throughout

■ Labs

Na 138 mEq/L	Hgb 12.6 g/dL	AST 128 IU/L	Folate 2.8 ng/mL
K 4.2 mEq/L	Hct 37.2%	ALT 52 IU/L	B ₁₂ 242 pg/mL
Cl 102 mEq/L	RBC 3.78 × 10 ⁶ /mm ³	Alk phos	
CO ₂ 21 mEq/L	Plt 217 × 10 ³ /mm ³	142 IU/L	
BUN 7 mg/dL	WBC 6.3 × 10 ³ /mm ³	GGT 288 IU/L	
SCr 0.52 mg/dL	MCV 120.4 μm ³	T. bili 2.1 mg/dL	
Glu 89 mg/dL	MCH 40.5 pg	Alb 3.4 g/dL	
Amylase	MCHC 33.6 g/dL	TSH 2.06 mIU/L	
404 IU/L	RDW 12.1%	T ₄ , free 1.2 ng/dL	
Lipase 679 IU/L			

■ Assessment

Acute pancreatitis secondary to alcohol use

Dehydration

Macrocytic anemia secondary to folate deficiency

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of anemia secondary to folate deficiency?
- What additional information is needed to fully assess this patient's anemia?

Assess the Information

- 2.a. Assess the severity of the anemia based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. Could the patient's folate deficiency have been caused by drug therapy or comorbidity?
- 2.d. Why is it important to differentiate folate deficiency from vitamin B₁₂ deficiency, and how is this accomplished?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for this patient's anemia?
- 3.b. What nondrug therapies may be used to correct this patient's folic acid deficiency?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's anemia?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the folic acid replacement therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. What are the advantages and disadvantages of folinic acid (leucovorin calcium) over standard folic acid, and why is this the preferred folate supplement in patients receiving high-dose methotrexate?
2. List and compare the mechanism for how the following drugs can lead to folic acid deficiency: azathioprine, trimethoprim, and phenytoin.
3. What is the role of folic acid in the management of methanol ingestion?

CLINICAL PEARL

Unlike dietary folate, supplemented folic acid (pteroylglutamic acid) is absorbed even with abnormal function of GI mucosal cells. Likewise, persistent alcohol ingestion or the use of drugs affecting folic acid absorption, folate transport, or dihydrofolate reductase will not prevent a sufficient therapeutic response to oral supplementation.

REFERENCES

1. Malouf R, Grimley Evans J. Folic acid with or without vitamin B₁₂ for the prevention and treatment of healthy elderly and demented people. *Cochrane Database Syst Rev* 2008;(4):CD004514. doi:10.1002/14651858.CD004514.pub2.
2. Snow CF. Laboratory diagnosis of vitamin B₁₂ and folate deficiency: a guide for the primary care physician. *Arch Intern Med* 1999;159:1289–1298.
3. Seppa K, Sillanaukee P, Saarni M. Blood count and hematologic morphology in nonanemic macrocytosis: differences between alcohol abuse and pernicious anemia. *Alcohol* 1993;10:343–347.
4. Medici V, Halstead CH. Folate, alcohol, and liver disease. *Mol Nutr Food Res* 2013;57(4):596–606.
5. Devalia V, Hamilton MS, Molloy AM. Guidelines for the diagnosis and treatment of cobalamin and folate disorders. *Br J Haematol* 2014;166(4):496–513.
6. Hesdorffer CS, Longo DL. Drug-induced megaloblastic anemia. *N Engl J Med* 2015;373(17):1649–1658.
7. Rampersaud GC, Kauwell GP, Bailey LB. Folate: a key to optimizing health and reducing disease risk in the elderly. *J Am Coll Nutr* 2003;22:1–8.
8. Theisen-Toupal J, Horowitz G, Breu A. Low yield of outpatient serum testing: eleven years of experience. *JAMA Intern Med* 2014;174(10):1696–1697.
9. Arafah BM. Increased need for thyroxine in women with hypothyroidism during estrogen therapy. *N Engl J Med* 2001;344:1743–1749.
10. Presutti RJ, Cangemi JR, Cassidy HD, Hill DA. Celiac disease. *Am Fam Physician* 2007;76:1795–1802.

116

SICKLE CELL ANEMIA

Engineering a Crisis Level I

Jamal Brown, PharmD, BCGP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the clinical characteristics associated with an acute sickle cell crisis.
- Discuss the presentation of acute chest syndrome and treatment options.
- Recommend optimal analgesic therapy based on patient-specific information.
- Identify optimal endpoints of pharmacotherapy in sickle cell anemia patients.
- Recommend treatment to reduce the frequency of sickle cell crises.

PATIENT PRESENTATION

Chief Complaint

"I'm in pain all over and no one believes me! I can't breathe ... and I don't like being considered an addict!"

HPI

Danny Johnson is a 21-year-old African-American man with a history of sickle cell anemia who presents to the local community hospital ED frustrated and in pain. On waking up three days prior to admission, he experienced a sudden onset of pain in his hands, legs, and lower back. He began taking oxycodone 15 mg every 2 hours at that time with limited pain relief. When reaching out to his physician for additional pain medication, he was denied due to a disbelief of the patient's recently reported pain. His primary physician said that he was taking much larger doses of opioids than the physician's other patients. The ED physician questioned his level of pain and the opioid doses that he reported taking at home. This morning he had a temperature of 102°F, progressive shortness of breath, and priapism, which caused him to seek treatment at the ED. The patient acknowledged having sick contacts at his workplace.

PMH

Sickle cell anemia (hemoglobin SS disease) diagnosed before the age of 1 with approximately seven to eight crises per year requiring hospitalization

Acute chest syndrome 2 years ago that required intubation

Transfusion exchange with PRBC during the intubation admission

Several episodes of priapism, usually associated with sickle cell pain crisis

FH

Mother and father alive and well, both with sickle cell trait. Patient has one sister with sickle cell trait.

SH

College student who is struggling to pass courses due to frequent missing of school for hospitalizations; depressed because sickle cell is affecting his life including limitation in sports and social activities. Struggling financially to keep up with hospital bills due to lapses in insurance.

ROS

Denies nausea, vomiting, or diarrhea. Cannot remember his last bowel movement but believes he has not had one in the last 3 days. Has had fever with some chills and sweats; no cough, nasal discharge, rashes, or skin lesions. Reports stuttering priapism with recurring episodes each lasting approximately 1 hour, with no intervention.

Meds

Folic acid 1 mg PO daily

Hydroxyurea 500 mg PO daily

Oxycodone 15 mg PO Q 2 H PRN pain

All

Sulfa (reported rash when very young)

Codeine (nausea and dysphoria)

Physical Examination**Gen**

Thin, well-developed, diaphoretic African-American man in acute distress

V/S

BP 115/72 mm Hg, P 110 bpm, RR 20, T 101.3°F (38.5°C); 72 kg; O₂ sat is 84% in room air improving to 97% on 4 L O₂

HEENT

PERRL; EOMI; oral mucosa soft and moist; scleral icterus and funduscopic examination; no sinus tenderness

Skin

Normal turgor; no rashes or lesions

Neck

Supple; nontender, no lymphadenopathy or thyromegaly

CV

RRR; II/VI SEM; no rubs or gallops

Lungs

Crackles in both bases on auscultation; dullness to percussion

Abd

Voluntary guarding, mild distention, hypoactive bowel sounds, no palpable spleen; no hepatomegaly or masses

Genitourinary

Priapism evident

Ext

No edema; notable tenderness in right shoulder and elbow

Neuro

A&O × 3; normal strength, reflexes intact

Labs

Na 143 mEq/L	Hgb 7.7 g/dL	AST 40 IU/L	Ca 8.8 mg/dL
K 4.2 mEq/L	Hct 20.8%	ALT 28 IU/L	Mg 1.9 mEq/L
Cl 112 mEq/L	Plt 480 × 10 ³ /mm ³	Alk phos 77 IU/L	Phos 3.9 mg/dL
CO ₂ 28 mEq/L	MCV 88 μm ³	LDH 1215 IU/L	(+) Anti-E red cell antibody
BUN 50 mg/dL	Retic 18.2%	T. bili 5.0 mg/dL	
SCr 1.4 mg/dL	WBC 18.2 × 10 ³ /mm ³	D. bili 0.8 mg/dL	
Glu 92 mg/dL	Segs 74%	Alb 3.4 g/dL	
	Bands 7.5%		
	Eos 1.5%		
	Lymphs 14%		
	Monos 3%		

Other

Arterial blood gas: pH 7.49, PaCO₂ 38 mm Hg, PaO₂ 72 mm Hg, bicarb 30 mEq/L, O₂ sat 96% on oxygen

Sputum culture: Mixed flora

Hgb electrophoresis: Hgb A₂ 3%; Hgb F 8%; Hgb S 89%

Peripheral blood smear: Sick cells and target cells present (Fig. 116-1)

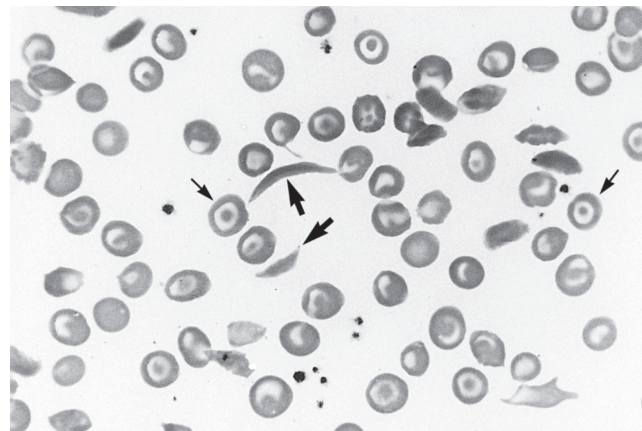


FIGURE 116-1. Peripheral blood with sickle cells (large arrows) and target cells (small arrows) (Wright–Giemsa ×1650). (Photo courtesy of Lydia C. Contis, MD.)



FIGURE 116-2. Lung radiograph of patient with acute chest syndrome secondary to sickle cell anemia. (Photo courtesy of Kenneth I. Ataga, MD.)

■ Chest X-Ray

This is a portable chest x-ray remarkable for diffuse interstitial infiltrates in both lung fields consistent with acute chest syndrome (Fig. 116-2). Cardiomegaly is also notable.

■ ECG

Normal sinus rhythm

■ Echocardiogram

Normal LV function

■ Assessment

A 21-year-old, African-American man in sickle cell crisis with probable acute chest syndrome, priapism, and constipation. Patient complains of severe pain but there are questions about the actual level of pain and the intensity of his home opioid regimen.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information is consistent with an acute sickle cell crisis in this patient?
- 1.b. What information supports a diagnosis of acute chest syndrome in this patient?
- 1.c. What additional information is needed to fully assess this patient's acute sickle cell crisis?

Assess the Information

- 2.a. Assess the severity of this patient's acute sickle cell crisis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. If healthcare providers incorrectly assume that a patient in sickle cell crisis who requests opioid analgesics is exhibiting drug-seeking behavior, how can that affect the provider's assessment and treatment of the patient's pain?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the patient's pain?
- 3.d. What feasible pharmacotherapeutic alternatives are available for treating opioid-induced constipation?
- 3.e. Create an individualized, patient-centered, team-based care plan to resolve this patient's medical problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

■ CLINICAL COURSE

The plans you recommended have been initiated, and on the fourth day of hospitalization the patient's pain is markedly improved, oxygen saturation improved to 98% on room air, he is afebrile, and his priapism has resolved. He has had two bowel movements but still feels his bowel habits have not yet returned to normal. He is only using two to three demands on his PCA per day and is asking to switch back to oral medication.

- 5.b. Considering this information, what changes (if any) in the pharmacotherapeutic plan are warranted while the patient is hospitalized?
- 5.c. What evidence exists to suggest that the patient is adherent with hydroxyurea therapy, and how should this therapy continue to be monitored?
- 5.d. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Determine the likelihood of the patient's offspring having sickle cell trait and/or disease if the father has:
 - a. Normal hemoglobin
 - b. Sickle cell trait
 - c. Sickle cell disease
2. Describe the complications associated with frequent crises in each organ system.
3. Discuss the differences between sickle cell anemia and β -thalassemia in terms of etiologies, laboratory abnormalities, and disease complications.
4. Discuss bias in sickle cell patients based on the article entitled, "Do Words Matter? Stigmatizing Language and the Transmission of Bias in the Medical Record."³ How can you avoid bias in treating these patients and educating providers on this issue?

CLINICAL PEARL

Vaccination with pneumococcal conjugate 13-valent (PCV13) vaccine is necessary in addition to the 23-valent pneumococcal polysaccharide vaccine (PPSV23) for all adult sickle cell anemia patients with functional or anatomic asplenia if they have not received it previously. The PCV13 should be given at least 1 year after the last PPSV23 dose. For patients who have not received any pneumococcal vaccine, they should receive the PCV13 first, then the PPSV23 at least 8 weeks after receiving the PCV13, and a second dose 5 years after the first dose.

ACKNOWLEDGMENT

This case is based on the patient case written for the 10th edition by Sheh-Li-Chen, PharmD, BCOP.

REFERENCES

1. Vichinsky EP, Neumayr LD, Earles AN, et al. Causes and outcomes of the acute chest syndrome in sickle cell disease. National Acute Chest Syndrome Study Group. *N Engl J Med* 2000;342:1855–1865.

2. Tassel C, Arnaud C, Kulpa M, et al. Leukocytosis is a risk factor for lung function deterioration in children with sickle cell disease. *Resp Med* 2011;105(5):788–795.
3. P Goddu A, O'Connor KJ, Lanzkron S, et al. Do words matter? Stigmatizing language and the transmission of bias in the medical record. *J Gen Intern Med*. 2018;33(5):685–691.
4. Ballas SK, Lieff S, Benjamin LJ, et al. Definitions of the phenotypic manifestations of sickle cell disease. *Am J Hematol* 2010;85(1):6–13.
5. Vichinsky E, Torres M, Minniti CP, et al. Efficacy and safety of deferasirox compared with deferoxamine in sickle cell disease: two-year results including pharmacokinetics and concomitant hydroxyurea. *Am J Hematol* 2013;88(12):1068–1073.
6. Yawn BP, Buchanan GR, Afenyi-Annan AN, et al. Management of sickle cell disease: summary of the 2014 evidence-based report by expert panel members. *JAMA* 2014;312(10):1033–1048.
7. Demerol® (meperidine hydrochloride) [Package insert]. Parsippany, NJ, Validus Pharmaceuticals, LLC, August 2017. Available at: https://www.accessdata.fda.gov/drugsatfda_docs/label/2017/005010s055lbl.pdf. Accessed November 27, 2018.
8. Baddam S, Aban I, Hilliard L, Howard T, Askenazi D, Lebensburger JD. Acute kidney injury during a pediatric sickle cell vaso-occlusive pain crisis. *Pediatr Nephrol* 2017;32(8):1451–1456.
9. Niihara Y, Miller ST, Kanter J, et al. A phase 3 trial of l-glutamine in sickle cell disease. *N Engl J Med* 2018;379(3):226–235.
10. Argoff CE, Brennan MJ, Camilleri M, et al. Consensus recommendations on initiating prescription therapies for opioid-induced constipation. *Pain Med* 2015;16(12):2324–2337.

SECTION 16

INFECTIOUS DISEASES

117

USING LABORATORY TESTS IN INFECTIOUS DISEASES

Chief of Staph Level III

Anthony J. Guarascio, PharmD, BCPS

Branden D. Nemecek, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Discuss the possible etiology of bacterial disease following a viral illness such as influenza.
- Discuss the use of rapid diagnostic testing methods that help differentiate bacterial species as well as determine organism-specific antibiotic resistance profiles.
- Evaluate culture and sensitivity results, and determine the clinical significance of the minimum inhibitory concentration.
- Design an evidence-based care plan to treat a bloodstream infection based on laboratory information.
- Recommend a plan for monitoring efficacy and adverse effects of an antimicrobial therapy regimen.

PATIENT PRESENTATION

■ Chief Complaint

Patient's wife states of her husband, "Lately he has not been acting like himself. He has been very dizzy, tired, and has not been eating or drinking well."

■ HPI

Jordan Zimmerman is a 68-year-old man who came to the ED via ambulance. The patient's history is obtained from his wife. She describes a change in mental status, lethargy, and shortness of breath, along with a significant decrease in activity and nutritional intake. Over the past 24 hours he has become very nauseated and developed a fever (39°C). The symptoms started 3 days ago and have progressively worsened. He was seen by his primary care physician 6 days ago (last week) and determined to have a positive influenza-A nasal swab. He was prescribed oseltamivir and recently completed his 5-day treatment course.

■ PMH

Gout
Diabetes mellitus
Resistant hypertension
Influenza pneumonia

■ FH

Both parents are deceased (mother age 88 of PE; father age 71 of stroke). He is married without any children.

■ SH

Retired steel mill worker and union chief, distant history of tobacco and alcohol use with no current use

■ Meds

Metformin 1000 mg PO BID
Glyburide 5 mg PO daily
Spironolactone 25 mg PO daily
Lisinopril 40 mg PO Q HS
Amlodipine 10 mg PO daily
Allopurinol 300 mg PO daily

■ All

Penicillin: hives when he was a child
Morphine: itching

■ ROS

Patient's primary complaint is of nausea and dizziness, but due to current status, unable to review further.

■ Physical Examination

Gen

The patient is clearly fatigued and appearing in respiratory distress.

VS

BP 108/58, P 108, RR 36, T 39°C; Wt 64.2 kg, Ht 68"

Skin

Warm and diaphoretic

HEENT

PERRLA; EOM intact; dry mucous membranes, teeth clean and intact, pharynx negative

Neck/Lymph Nodes

No nodules, negative lymphadenopathy

Chest

Respiratory distress with marked effort and use of accessory muscles; generalized bilateral wheezing

CV

Tachycardic; normal S₁ and S₂; no heaves, thrills, or bruits

Abd

Soft, nondistended; nontender, no splenomegaly

Genit/Rect

Deferred

MS/Ext

Deferred

Neuro

Decreased responses; delayed recognition; responds to painful stimuli

■ Labs**From PCP visit 6 days ago**

Na 140 mEq/L	Hgb 11.2 g/dL	INR 1.1
K 4.5 mEq/L	Hct 32.1%	Influenza A/B PCR: positive A
Cl 100 mEq/L	RBC $3.68 \times 10^6/\text{mm}^3$	
CO ₂ 22 mEq/L	Plt $360 \times 10^3/\text{mm}^3$	
BUN 22 mg/dL	WBC $14.8 \times 10^3/\text{mm}^3$	
SCr 1.2 mg/dL	MCV $84.6 \mu\text{m}^3$	
Glu 168 mg/dL		

Today's values

Na 148 mEq/L	Hgb 10.6 g/dL	WBC $16.3 \times 10^3/\text{mm}^3$	INR 1.2
K 5.4 mEq/L	Hct 29.8%	Segs 70%	Influenza A/B PCR: negative
Cl 102 mEq/L	RBC $3.34 \times 10^6/\text{mm}^3$	Bands 22%	D-dimer
CO ₂ 18 mEq/L	Plt $280 \times 10^3/\text{mm}^3$	Lymphs 6%	0.2 mcg/mL
BUN 68 mg/dL	MCV $86.1 \mu\text{m}^3$	Monos 2%	Nares MRSA swab: positive
SCr 2.9 mg/dL			O ₂ saturation 92%
Glu 58 mg/dL			

■ Urinalysis

Color, yellow; specific gravity, 1.170; pH 5; +2 protein; negative nitrites; negative LE; 15–20 RBC; few bacteria; 0–3/HPF WBC; moderate uric acid crystals

■ Chest X-Ray

Patchy infiltrates with left lower lobe consolidation

■ Electrocardiogram

Normal sinus rhythm, heart rate 108 bpm, no axis deviation, no peaked T waves or T-wave inversion. No prior ECG for comparison.

■ Assessment

1. Respiratory distress with differential diagnosis pneumonia versus pulmonary embolus
2. Acute kidney injury of unknown cause
3. Lab abnormalities (hyperkalemia, hypoglycemia)

■ Plan

1. Collect two sets of blood cultures and a sputum specimen. Collect urine sample for urinalysis and culture.
2. Start empiric vancomycin and piperacillin/tazobactam per pharmacy to dose protocol.
3. Begin fluid resuscitation for acute kidney injury, hypotension, hypoglycemia, and hyperkalemia.

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates both the presence and absence of infection?
- 1.b. What additional information is needed to fully assess this patient's infection?

Assess the Information

- 2.a. Assess the severity of infection based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating infection in this patient?

■ CLINICAL COURSE

In the ED, the patient responds well to IV fluids with normalization of potassium and improvement in blood pressure and blood glucose. Shortly after the patient arrived on the medical floor, the microbiology lab calls the physician and reports that Mr Zimmerman's Gram stain from both blood cultures reveal gram-positive cocci in clusters. Bruker matrix-assisted laser desorption/ionization time-of-flight (MALDI-TOF) Biotyper indicated positive identification of *Staphylococcus aureus*, while the Alere rapid immunochromatographic assay and culture colony PBP2a test has returned as presumptive positive for MRSA. Sputum culture also reveals preliminary results of gram-positive cocci in clusters. Final culture and susceptibility results are pending. The following day, blood and sputum culture and susceptibility results become available. Table 117-1 depicts the final culture susceptibility report that is identical for both sputum and blood isolates.

Develop a Care Plan (continued)

- 3.d. Based on this new information, create an individualized, patient-centered care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

TABLE 117-1 *S. aureus* Susceptibility Report

Antibiotic	MIC/Interpretation
Clindamycin	≤0.25/susceptible ^a
Erythromycin	≥8/resistant
Gentamicin	≤0.5/susceptible
Levofloxacin	0.25/susceptible
Oxacillin	≥4/resistant
Penicillin	≥0.5/resistant
Rifampin	≤0.5/susceptible
Trimethoprim/sulfamethoxazole	≤10/susceptible
Vancomycin	1/susceptible
Tetracycline	≤1/susceptible

^aPositive for inducible clindamycin resistance.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers within the hospital setting.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy. This should include a discussion about the timing of serum vancomycin concentrations to determine the appropriateness of drug dosing, appropriate frequency of serum vancomycin concentration assessments, and goal trough serum concentration in this patient.

FOLLOW-UP CASE QUESTIONS

1. How can laboratory data be used to assess acute kidney injury for this patient?
2. When should the patient's blood cultures have been drawn in relation to antibiotic administration?
3. What is the clinical advantage of using a rapid identification test, such as rapid culture colony PBP2a test and MALDI-TOF, to help determine the staphylococcal species?
4. What effect does the organism's MIC have on the current treatment plan?

SELF-STUDY ASSIGNMENTS

1. Identify the organisms that most frequently represent contaminants in blood cultures.
2. Define the role of rapid diagnostic testing in the treatment of bloodstream infections.
3. Explain how a clinician interprets MRSA nasal swab surveillance results.
4. Describe how the management of this patient would change if kidney injury progressed to necessitate hemodialysis.

CLINICAL PEARL

Use of rapid diagnostic testing methods can decrease time to pathogen identification from approximately 48–72 hours using conventional culture methods to a few hours using rapid diagnostic testing. Rapid identification, combined with timely follow-up and intervention, can reduce time to appropriate antimicrobial therapy resulting in improved patient outcomes.

REFERENCES

1. Sobel JD, Kaye D. Chapter 74 Urinary tract infections. In: Bennett JE, Dolin R, Blaser MJ, eds. *Mandell, Douglas, and Bennett's Principles and Practice of Infectious Diseases*. 8th ed. Philadelphia, PA, Saunders Elsevier; 2014:886–913.
2. Metersky ML, Masterson RG, Lode H, File TM Jr, Babinchak T. Epidemiology, microbiology, and treatment considerations for

bacterial pneumonia complicating influenza. *Int J Infect Dis* 2012;16(5):e321–e331.

3. Polenakovik HM, Pleiman CM. Ceftriaxone for methicillin-resistant *Staphylococcus aureus* bacteraemia: case series and review of the literature. *Int J Antimicrob Agents* 2013;42(5):450–455.
4. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:1–38.
5. Gilbert JS, Weiner DE, Bombardieri AS, Perazella MA, Tonelli M, eds. *National Kidney Foundation's Primer on Kidney Diseases*. 7th ed. Philadelphia, PA Saunders Elsevier; 2018:300–310, 345–354.
6. Prybylski JP. Vancomycin trough concentration as a predictor of clinical outcomes in patients with *Staphylococcus aureus* bacteremia: a meta-analysis of observational studies. *Pharmacotherapy* 2015;35(10):889–898.
7. Rybak M, Lomaestro B, Rotschafer JC, et al. Therapeutic monitoring of vancomycin in adult patients: a consensus review of the American Society of Health-System Pharmacists, the Infectious Diseases Society of America, and the Society of Infectious Diseases Pharmacists. *Am J Health Syst Pharm* 2009;66:82–98.
8. Trienski TL, Barrett HL, Pasquale TR, DiPersio JR, File TM Jr. Evaluation and use of a rapid *Staphylococcus aureus* assay by an antimicrobial stewardship program. *Am J Health Syst Pharm* 2013;70(21):1908–1912.
9. Goff DA, Jankowski C, Tenover FC. Using rapid diagnostic tests to optimize antimicrobial selection in antimicrobial stewardship programs. *Pharmacotherapy* 2012;32(8):677–687.
10. CLSI. Performance Standards for Antimicrobial Susceptibility Testing; Twenty-Ninth Informational Supplement. CLSI Document M100-S25. Wayne, PA, Clinical and Laboratory Standards Institute; 2019.

118

BACTERIAL MENINGITIS

This Is Spinal Tap Level II

S. Travis King, PharmD, BCPS

Elizabeth A. Cady, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- List risk factors and common presenting signs and symptoms of bacterial meningitis in infants and children.
- Differentiate common bacterial pathogens associated with meningitis in children of different ages.
- Recommend appropriate empiric and definitive antimicrobial and adjunctive therapy for bacterial meningitis.
- Identify appropriate monitoring parameters for antimicrobial therapy of bacterial meningitis.

PATIENT PRESENTATION

Chief Complaint

From mom: “Why is my baby so sleepy? And what is this purple rash?”

HPI

David St. Hubbins is a 2-year-old, 13.6 kg male toddler who presented to the emergency department with his mother. Mom reports that she noticed him sleeping longer than normal since yesterday evening after returning from daycare, as well as this morning. She also reports that he had a poorer than normal appetite at dinner and breakfast. She also notes the rapid appearance of a purplish rash on his extremities, trunk, and back. At 08:00 she checked his temperature, which was of 39.1°C. At that point, the mother called her sister who is a nurse, who told her to go straight to the emergency room. When aroused prior to transport, David was irritable and crying frequently. During transport, David was in and out of sleep and did not respond well to normal stimuli. There was one episode of slight vomiting during transit.

PMH

David was born via an uncomplicated vaginal delivery at 39 weeks. Mother reports one episode of otitis media at 13 months of age, treated with amoxicillin.

FH

Mother is in good health; father has hypercholesterolemia; maternal grandparents both with metabolic syndrome; paternal grandfather in good health; maternal grandmother alive, history of breast cancer.

SH

Lives with mother and father. Father is a rock musician, and mother is a teacher. David began attending daycare 3 months ago. Father is a smoker. No pets in the home.

Meds

None; immunizations up to date per the US CDC Advisory Committee for Immunization Practices (ACIP)

All

NKDA

Review of Systems

Refer to HPI

Physical Examination**Gen**

Lethargic toddler with generalized rash in mild–moderate distress

VS

SBP 75, HR 152, RR 48, T 39.4°C; Wt 13.6 kg, SatO₂ (RA): 98%

HEENT

PERRLA, tympanic membranes erythematous bilaterally

Chest

Lungs clear bilaterally

CV

Sinus tachycardia, regular rhythm, no murmurs, rubs, gallops

Abd

Soft, distended, (+) BS, (+) purpuric rash

Extremities

Capillary refill 4 seconds, extremities mottled and cool to the touch; (+) mildly blanching, purpuric rash is present; petechial lesions noted.

Neuro

Listless; arousable to strong stimuli only, (–) Brudzinski's, (–) Kernig's, (+) Babinski

Labs

Na 135 mEq/L	Hgb 13.2 g/dL	Ca 9.2 mg/dL	Arterial blood gases
K 3.9 mEq/L	Hct 39.6%	Mg 1.4 mEq/L	pH 7.32
Cl 110 mEq/L	Plt 160 × 10 ³ /mm ³	PO ₄ 4.2 mg/dL	PaO ₂ 80 mm Hg
CO ₂ 14 mEq/L	WBC 25 × 10 ³ /mm ³	T. prot 6.6 g/dL	PaCO ₂ 40 mm Hg
SCr 0.9 mg/dL	Neutros 70%	Alb 4.1 g/dL	HCO ₃ 15 mEq/L
BUN 19 mg/dL	Bands 16%	Bili 0.7 mg/dL	Base excess
Glucose	Lymphs 10%	AST 86 IU/L	5.3 mEq/L
130 mg/dL	Monos 2%	ALT 20 IU/L	Procalcitonin:
	Eos 1%	ALP 285 IU/L	20.2 ng/mL
	Basos 1%		

CSF Serology/Urine Antigen Testing

Haemophilus influenzae type B (–); *Streptococcus pneumoniae* (–); group B *Streptococcus* (–)

CSF Analysis

Color/appearance: straw/cloudy, glucose 38 mg/dL, protein 315 mg/dL, WBC 420/mm³ (2% lymphs, 2% monos, 96% neutros), RBC 500/mm³

CSF Gram stain: Gram-negative diplococci

Cultures

Blood, urine, and CSF cultures: Pending

Chest X-Ray

No acute cardiopulmonary process noted

Assessment

1. Acute bacterial meningitis, suspected meningococcal
2. Hypotension/metabolic acidosis

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of meningitis?
- 1.b. What additional information is needed to fully assess this patient's meningitis?

Assess the Information

- 2.a. Assess the severity of meningitis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for managing this patient's meningitis?

- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this case of meningitis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial therapy fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient received fluids, supportive care, and empiric antibiotics according to the hospital sepsis protocol. The patient was begun on vancomycin and ceftriaxone empirically. He also received dexamethasone (0.15 mg/kg every 6 hours starting with the first dose of antibiotics). Blood cultures returned positive for *Neisseria meningitidis*. CSF cultures return positive for *N. meningitidis*. Urine cultures remain negative.

Susceptibility testing of *N. meningitidis* from CSF culture demonstrates the following profile:

penicillin MIC: 0.1 mcg/mL
 ceftriaxone MIC: 0.06 mcg/mL
 rifampin MIC: 0.25 mcg/mL
 ciprofloxacin MIC: 0.03 mcg/mL

Repeat procalcitonin on day 3 of admission is 6.3 ng/mL.

Repeat CBC at that time revealed: Hgb 13.5 g/dL, Hct 40.5%, platelets $225 \times 10^3/\text{mm}^3$, and WBC $12 \times 10^3/\text{mm}^3$ (66% Neutros, 32% Lymphs, 1% Basos, 1% Eos).

FOLLOW-UP CASE QUESTION

1. Given the culture report, what changes, if any, should be made to the patient's antimicrobial or adjunctive regimen?

SELF-STUDY ASSIGNMENTS

1. Discuss the impact of vaccination on reducing the rates of meningitis and other invasive diseases in pediatric patients. What impact may be anticipated after FDA approval of the *N. meningitidis*, serotype B vaccine?
2. Describe the pharmacokinetic properties that influence the ability of antimicrobials to penetrate the blood–brain barrier.
3. Discuss the role of procalcitonin in the evaluation of bacterial versus aseptic meningitis.
4. Discuss the management alternatives when treating meningitis caused by drug-resistant meningococcal and pneumococcal pathogens.

CLINICAL PEARL

The *N. meningitidis*, serotype B vaccine may be administered in addition to the quadrivalent vaccine to patients between the ages of 16 and 23 years. If patients age ≥ 10 years are deemed to be at risk for meningococcal disease (asplenia, complement deficiency, microbiology lab personnel), they should receive the serotype B vaccine.

REFERENCES

1. Tunkel AR, Hartman BJ, Kaplan SL, et al. Practice guidelines for the management of bacterial meningitis. Clin Infect Dis 2004;39:1267–1284.
2. Chavez-Bueno S, McCracken GH. Bacterial meningitis in children. Pediatr Clin North Am 2005;52:795–810.
3. Brouwer MC, Tunkel AR, van de Beek D. Epidemiology, diagnosis, and antimicrobial treatment of acute bacterial meningitis. Clin Microbiol Rev 2010;23(3):467–492.
4. Bonadio W. Pediatric lumbar puncture and cerebrospinal fluid analysis. J Emerg Med 2014;46(1):141–150.
5. Alkholi UM, Abd Al-Monem N, Abd El-Azim AA, Sultan MH. Serum procalcitonin in viral and bacterial meningitis. J Glob Infect Dis 2011;3(1):14–18.
6. Centers for Disease Control and Prevention. Prevention and Control of Meningococcal Disease Recommendations of the Advisory Committee on Immunization Practices (ACIP). MMWR 2013;62(No. RR02):1–22.
7. Cohn A, MacNeil J. The changing epidemiology of meningococcal disease. Infect Dis Clin North Am 2015;29(4):667–677.
8. World Health Organization. Antimicrobial susceptibility testing of *Neisseria meningitidis*, *Haemophilus influenzae*, and *Streptococcus pneumoniae*. Laboratory Methods for the Diagnosis of Meningitis Caused by *Neisseria meningitidis*, *Streptococcus pneumoniae*, and *Haemophilus influenzae*. 2011. Available: <https://www.cdc.gov/meningitis/lab-manual/chpt11-antimicrobial-suscept-testing.html>. Accessed February 26, 2019.
9. Brouwer MC, McIntyre P, Prasad K, van de Beek D. Corticosteroids for acute bacterial meningitis. Cochrane Database Syst Rev 2015;(9):CD004405.
10. Wall EC, Ajdukiewicz KM, Heyderman RS, Garner P. Osmotic therapies added to antibiotics for acute bacterial meningitis. Cochrane Database Syst Rev 2013;(3):CD008806.

119

COMMUNITY-ACQUIRED PNEUMONIA

The Coughing Conundrum Level II

Trent G. Towne, PharmD, BCPS

Sharon M. Erdman, PharmD, FIDP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the common signs, symptoms, physical examination, laboratory, and radiographic findings in a patient with community-acquired pneumonia (CAP).

- Describe the most common causative pathogens of CAP, including their frequency of occurrence and susceptibility to frequently used antimicrobials.
- Discuss the risk stratification strategies that can be employed to determine whether a patient with CAP should be treated as an inpatient or outpatient.
- Provide recommendations for initial empiric antibiotic therapy for an inpatient or outpatient with CAP based on clinical presentation, severity of infection, age, allergies, and comorbidities.
- Define the goals of antimicrobial therapy for a patient with CAP, as well as the monitoring parameters that should be used to assess the response to therapy, conversion from IV to PO therapy (where warranted), and the occurrence of adverse effects.

PATIENT PRESENTATION

■ Chief Complaint

“I have been short of breath and have been coughing up rust-colored phlegm for the past 3 days.”

■ HPI

James Thompson is a 55-year-old African-American man with a 3-day history of worsening shortness of breath, subjective fevers, chills, right-sided chest pain, and a productive cough. The patient states that his initial symptom of shortness of breath began approximately 1 week ago after delivering mail on an extremely cold winter day. He has been taking ibuprofen and an over-the-counter cough and cold preparation but feels that his symptoms are getting “much worse.” The patient began experiencing right-sided pleuritic chest pain and a productive cough with rust-colored sputum over the past 3 days and feels that he has been feverish with chills, although he did not take his temperature. On presentation to the ED, he is febrile and visibly short of breath.

■ PMH

Hypertension × 15 years
Dyslipidemia × 15 years
Type 2 diabetes mellitus × 10 years

■ FH

Adopted; unknown birth parents

■ SH

Lives with wife and four children
Employed as a mail carrier for the US Postal Service
Denies alcohol, tobacco, or intravenous drug use

■ Medications

Prescription

Lisinopril 10 mg orally once daily
Hydrochlorothiazide 25 mg orally once daily
Atorvastatin 20 mg orally once daily
Metformin 1000 mg orally twice daily

Over-the-Counter

Ibuprofen 200 mg PO Q 6 H as needed for pain and fever
Guaiifenesin/dextromethorphan (100 mg/10 mg/5 mL) two teaspoonfuls every 4 hours as needed for cough

■ All

NKDA

■ ROS

Patient is a good historian. He has been experiencing shortness of breath, a productive cough with rust-colored sputum, subjective fevers, chills, and pleuritic chest pain that is “on the right side of my chest.” He denies any nausea, vomiting, constipation, or problems urinating.

■ Physical Examination

Gen

Patient is a well-developed, well-nourished, African-American man in moderate respiratory distress appearing somewhat anxious and uncomfortable.

■ VS

BP 155/85, P 127, RR 30, T 39.5°C; Wt 110 kg, Ht 5'11"

Skin

Warm to the touch; poor skin turgor

HEENT

PERRLA; EOMI; dry mucous membranes

Neck/Lymph Nodes

No JVD; full range of motion; no neck stiffness; no masses or thyromegaly; no cervical lymphadenopathy

Lungs/Thorax

Tachypneic, labored breathing; coarse rhonchi throughout right lung fields; decreased breath sounds in right middle and right lower lung fields

CV

Audible S₁ and S₂; tachycardic with regular rate and rhythm; no MRG

Abd

NTND; (+) bowel sounds

Genit/Rect

Deferred

Extremities

No CCE; 5/5 grip strength; 2+ pulses bilaterally

Neuro

A&O × 3; CN II–XII intact

■ Labs on Admission

Na 140 mEq/L	Hgb 12.1 g/dL	WBC 23.1 × 10 ³ /mm ³
K 4.3 mEq/L	Hct 35%	Neutrophils 67%
Cl 102 mEq/L	RBC 3.8 × 10 ⁶ /mm ³	Bands 15%
CO ₂ 22 mEq/L	Plt 220 × 10 ³ /mm ³	Lymphs 12%
BUN 42 mg/dL	MCV 91 μm ³	Monos 6%
SCr 1.4 mg/dL	MCHC 35 g/dL	Procalcitonin 1.9 ng/mL
Glu 295 mg/dL		Lactic Acid 2.3 mmol/L

■ ABG

pH 7.38; PaCO₂ 29; PaO₂ 70 with 87% O₂ saturation on room air

■ Chest X-Ray

Right middle and right lower lobe consolidative airspace disease, likely pneumonia. Left lung is clear. Heart size is normal.

■ Chest CT Scan Without Contrast

No axillary, mediastinal, or hilar lymphadenopathy. The heart size is normal. There is consolidation of the right lower lobe and lateral segment of the middle lobe, with air bronchograms. No significant pleural effusions. The left lung is clear.

■ Sputum Gram Stain

>25 WBCs/hpf, <10 epithelial cells/hpf, many gram (+) cocci in pairs

■ Sputum Culture

Pending

■ Blood Cultures × Two Sets

Pending

■ Other Lab Tests

Streptococcus pneumoniae urine antigen—Pending

Legionella pneumophila urine antigen—Pending

■ Assessment

Probable multilobar CAP involving the RML and RLL

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of CAP in this patient?
- 1.b. What additional information is needed to fully assess this patient's CAP?

Assess the Information

- 2.a. Assess the severity of this patient's CAP based on subjective and objective information available and use this information to decide on the site of care (inpatient or outpatient).
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating CAP?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient including specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

While in the ED, the patient was placed on 4 L NC of O₂, and his oxygen saturation improved to 98%. The patient was initiated on ceftriaxone 1 g IV daily and azithromycin 500 mg IV daily and admitted to the hospital. Over the next 48 hours, the patient's clinical status improved with decreasing fever, tachypnea, tachycardia, and shortness of breath. On hospital day 2, the *S. pneumoniae* urine antigen was positive, and the sputum culture demonstrated the growth of *S. pneumoniae*, resistant to erythromycin (MIC ≥1 mcg/mL), but susceptible to penicillin (MIC ≤2 mcg/mL), ceftriaxone (MIC ≤1 mcg/mL), levofloxacin (MIC ≤0.5 mcg/mL), and vancomycin (MIC ≤1 mcg/mL).

■ FOLLOW-UP QUESTIONS

1. Given this new information, what changes in the antimicrobial therapy would you recommend?
2. What oral antibiotic would be suitable to complete the course of therapy for CAP in this patient? When is it appropriate to convert a patient from IV to oral therapy for the treatment of CAP?
3. By hospital day 4, the patient's clinical symptoms of pneumonia had almost completely resolved, and the patient was discharged home on oral antibiotics to complete a 7-day course of treatment. What information should be provided to the patient about his oral outpatient antibiotic therapy to enhance adherence, ensure successful therapy, and minimize adverse effects?

■ SELF-STUDY ASSIGNMENTS

1. Describe the role of molecular diagnostic testing and microbiology in the diagnosis and treatment of patient's with CAP?
2. Describe the role of procalcitonin testing in the decision to initiate and de-escalation of antibiotics in patients with CAP.
2. Review national, regional, and local patterns of *S. pneumoniae* susceptibility and compare the data with what is seen at your institution or clinic.
3. Describe the role of short-course (5-day) antibiotic therapy in the management of CAP.

CLINICAL PEARL

Influenza and pneumococcal vaccines for appropriate patient types are important components for preventing CAP as well as for reducing the morbidity and mortality associated with CAP.

REFERENCES

1. Mandell LA, Wunderink RG, Anzueto A, et al. Infectious Diseases Society of America/American Thoracic Society consensus guidelines on the management of community-acquired pneumonia in adults. Clin Infect Dis 2007;44(Suppl 2):S27–S72.
2. Prina E, Ranzani OT, Torres A. Community-acquired pneumonia. Lancet 2015;386:1097–1108.

3. Infections of the lower respiratory tract. In: Tile PM, ed. Bailey and Scott's Diagnostic Microbiology. 13th ed. St Louis, MO: Mosby; 2014:878–891.
4. Segreti J, House HR, Siegel RE. Principles of antibiotic treatment of community-acquired pneumonia in the outpatient setting. *Am J Med* 2005;118(7A):21S–28S.
5. Bochud PY, Moser F, Erard P, et al. Community-acquired pneumonia: a prospective outpatient study. *Medicine* 2001;80(2):75–87.
6. Fine MJ, Auble TE, Yealy DM, et al. A prediction rule to identify low-risk patients with community-acquired pneumonia. *N Engl J Med* 1997;336:243–250.
7. Lim WS, van der Eerden MM, Laing R, et al. Defining community-acquired pneumonia severity on presentation to hospital: an international derivation and validation study. *Thorax* 2003;58:377–382.
8. File TM. Community-acquired pneumonia. *Lancet* 2003;362:1991–2001.
9. Pfaller MA, Farrell DL, Sader HS, Jones RN. AWARE-Ceftaroline Surveillance Program (2008–2010): trends in resistance patterns among *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Moraxella catarrhalis* in the United States. *Clin Infect Dis* 2012;55(Suppl 3):S187–S193.
10. Fine MJ, Stone RA, Singer DE, et al. Process and outcomes of care for patients with community-acquired pneumonia: results from the Pneumonia Patients Outcomes Research Team (PORT) cohort study. *Arch Intern Med* 1999;159:970–980.

120

HOSPITAL-ACQUIRED PNEUMONIA

The HAPpening Level II

Kendra M. Damer, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of hospital-acquired pneumonia (HAP).
- Identify the most common causative organisms associated with HAP, and recognize the impact of bacterial resistance on the etiology and treatment of HAP.
- Design an appropriate empiric antimicrobial therapy regimen for a patient with suspected HAP.
- Formulate a list of alternative antimicrobial therapy options for treating HAP based on the most common causative organisms.
- Recommend a directed/targeted antimicrobial therapy regimen for a patient with HAP based on patient-specific data and final microbiology culture and susceptibility results.

PATIENT PRESENTATION

■ Chief Complaint

“I can’t catch my breath, and this cough is getting worse.”

■ HPI

Justin Case is a 60-year-old man with a past medical history significant for MI who was admitted to the hospital 5 days ago to undergo a scheduled surgical procedure following a recent diagnosis of colorectal adenocarcinoma with metastatic lesions to the liver. The patient was taken to the OR on hospital day 2 and underwent an exploratory laparotomy, diverting ileostomy, and Hickman catheter placement in preparation for chemotherapy. Postoperatively, the patient was transferred to the progressive ICU for recovery without complication. The patient had no new complaints until hospital day 5 when he complained of shortness of breath, and a worsening cough with sputum production. He was noted to be in respiratory distress with an RR of 43 breaths/min, HR 147 bpm, BP 162/103 mm Hg, and O₂ saturation of 87%. He was transferred to the medical ICU and underwent endotracheal intubation due to worsening respiratory status. Imaging studies along with blood and sputum cultures were obtained after transfer.

■ PMH

CAD, S/P MI 3 years ago for which he did not undergo any surgical intervention

Colorectal carcinoma metastatic to liver (newly diagnosed)

■ SH

Lives with his wife; smokes one ppd × 40 years; denies alcohol or illicit drug use

■ Meds

Patient states that he did not take any medications at home. Hospital medications include (ICU medication list):

Aspirin 81 mg PO daily
 Enoxaparin 40 mg subcutaneously every 24 hours
 Esomeprazole 40 mg PO daily
 Fentanyl 25 mcg/hr IV continuous infusion
 Lorazepam 2 mg/hr IV continuous infusion
 Metoprolol 25 mg PO every 12 hours
 Nicotine patch 21 mg per day applied daily

■ All

NKDA

■ ROS

Patient experiencing significant shortness of breath and a cough with sputum production. He denies nausea, vomiting, or difficulty urinating. He complains of mild abdominal pain near his ostomy and incision sites.

■ Physical Examination

Gen

WDWN Caucasian man, initially anxious, ill-appearing, and in moderate respiratory distress; now, S/P endotracheal intubation and in NAD

VS

BP 162/103 mm Hg, P 147 bpm, RR 42 breaths/min, T 38.5°C; Wt 70 kg, Ht 5’6”

Skin

Warm; no rash; no skin breakdown

HEENT

PERRLA; moist mucous membranes

Neck/Lymph Nodes

Supple; no lymphadenopathy

Lungs/Thorax

Scattered rhonchi with expiratory wheezing; diffuse bilateral crackles; decreased breath sounds in bilateral bases; right IJ Hickman catheter intact without erythema

CV

Tachycardic with regular rhythm; no MRG

Abd

Soft; mildly distended; hypoactive BS; large liver palpated in RUQ; ileostomy in RLQ is pink and functioning; surgical incision is C/D/I.

Genit/Rect

Deferred

MS/Ext

1+ pitting edema; 2+ pulses bilaterally; good peripheral perfusion

Neuro

Prior to intubation, A&O × 3; CN II–XII intact; patient is now intubated and sedated.

■ Labs

Lab Parameter	Admission	Hospital Day 5
Na (mEq/L)	130	141
K (mEq/L)	4.1	5.1
Cl (mEq/L)	92	110
CO ₂ (mEq/L)	24	19
BUN (mg/dL)	22	34
SCr (mg/dL)	1	1.1
Glu (mg/dL)	113	148
Ca (mg/dL)	9.4	9.2
WBC (cells/mm ³)	9.5 × 10 ³	17 × 10 ³
Neutros (%)	89	88
Bands (%)	0	5
Lymphs (%)	5	4
Monos (%)	6	3
Eos (%)	0	0
Hgb (g/dL)	11.9	12.4
Hct (%)	35	37
Plts (cells/mm ³)	448 × 10 ³	584 × 10 ³

■ ABG

Preintubation: pH 7.39; PaCO₂ 30; PaO₂ 51 make HCO₃ 25 mEq/L with 87% O₂ saturation on room air

Postintubation: pH 7.44; PaCO₂ 29; PaO₂ 89 make HCO₃ 23 mEq/L with 100% O₂ saturation on 40% inspired oxygen

■ Chest X-Ray

New bilateral opacities in the left upper lobe and right middle lobe; likely infectious process. Some increased alveolar infiltrates in the perihilar location and involving the lower lobes.

■ Chest CT Scan With IV Contrast

No evidence of pulmonary embolism. The heart size is normal. There are small mediastinal and axillary lymph nodes; none are pathologically enlarged. There are small bilateral pleural effusions with adjacent atelectasis. There are pleural-based airspace opacities within the left upper lobe and right middle lobe; this is most consistent with an acute infectious process.

■ Sputum Gram Stain

Greater than 25 WBC/hpf, <10 epithelial cells/hpf, 1+ (few) gram-positive cocci, 3+ (many) gram-negative rods

■ Sputum Culture

Pending

■ Blood Cultures × Two Sets

Pending

■ Assessment

Presumed bilobar HAP involving the LUL and RML

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of HAP in this patient?
- What additional information is needed to fully assess this patient's pneumonia?

Assess the Information

- Assess the severity of the patient's HAP infection based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include an assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in treating this patient's HAP?
- What nondrug therapies might be useful for this patient's HAP?
- What feasible pharmacotherapeutic alternatives are available for treating this patient's HAP?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare professionals.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

Following endotracheal intubation, the patient experienced improved oxygen saturation and a normalization of his respiratory and heart rates. He was started on appropriate empiric antimicrobial

therapy while awaiting the results of sputum and blood cultures. The blood and sputum cultures revealed *Klebsiella pneumoniae*. The organism's susceptibility profile is provided below. Over the next 72 hours, the patient's clinical status improved with decreased sputum production, oxygen requirement, temperature, and WBC count; improvement in chest x-ray findings was also noted, resulting in extubation on hospital day 8. The patient was transferred to the progressive ICU for his continued recovery.

Susceptibility Report for *Klebsiella pneumoniae*

Antimicrobial Agent	MIC (mg/L)	Interpretation
Ampicillin	≥32	Resistant
Ampicillin/sulbactam	≥32	Resistant
Piperacillin/tazobactam	≤4	Susceptible
Cefazolin	32	Resistant
Ceftriaxone	≤1	Susceptible
Cefepime	≤1	Susceptible
Meropenem	≤0.25	Susceptible
Gentamicin	≤1	Susceptible
Tobramycin	≤1	Susceptible
Ciprofloxacin	≤0.25	Susceptible
Levofloxacin	≤0.12	Susceptible
Trimethoprim/sulfamethoxazole	≥320	Resistant

FOLLOW-UP CASE QUESTION

- Based on this new information, provide a recommendation for de-escalation of antimicrobial therapy from empiric to directed/targeted therapy. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

SELF-STUDY ASSIGNMENTS

- Review national, regional, and local patterns of bacterial susceptibility for the most common causative organisms associated with HAP to determine appropriate empiric antimicrobial therapy choices for your geographic location.
- Evaluate the literature to determine the most appropriate duration of therapy for HAP according to the causative microorganism.
- Review the published literature to determine the role and utility of biomarkers (eg, procalcitonin [PCT]) and severity scoring (eg, acute physiologic assessment and chronic health evaluation II [APACHE II] and clinical pulmonary infection score [CPIS]) for the diagnosis, and treatment of HAP.
- Given the patient's past history of MI, evaluate the literature to determine the most appropriate recommendations for the medical management of CAD both as an inpatient and upon hospital discharge.

CLINICAL PEARL

Delays in initiation of appropriate empiric antimicrobial therapy have been associated with significant increases in hospital lengths of stay, healthcare costs, and mortality among patients with HAP.

REFERENCES

- Kalil AC, Meterski ML, Klompas M, et al. Management of adults with hospital-acquired and ventilator-associated pneumonia: 2016 clinical practice guidelines by the Infectious Diseases Society of America and the American Thoracic Society. *Clin Infect Dis* 2016;63(5):e61–e111.
- Cilloniz C, Martin-Loeches I, Garcia-Vidal C, et al. Microbial etiology of pneumonia: epidemiology, diagnosis and resistance patterns. *Int J Mol Sci* 2016;17:1–18.

- ATS/IDSA Therapeutics Work Group. Guidelines for the management of adults with hospital-acquired, ventilator-associated, and healthcare-associated pneumonia. *Am J Respir Crit Care Med* 2005;171:388–416.
- Martin-Loeches I, Deja M, Koulenti D, et al. Potentially resistant microorganisms in intubated patients with hospital-acquired pneumonia: the interaction of ecology, shock and risk factors. *Intensive Care Med* 2013;39:672–681.
- Maruyama T, Fujisawa T, Ishida T, et al. A therapeutic strategy for all pneumonia patients: a 3-year prospective multicenter cohort study using risk factors for multidrug-resistant pathogens to select initial empiric therapy. *Clin Infect Dis* 2018;68(7):1080–1088.
- Niederman MS. Antibiotic treatment of hospital-acquired pneumonia: is it different from ventilator-associated pneumonia? *Curr Opin Crit Care* 2018;24:353–360.
- Napolitano LM. Use of severity scoring and stratification factors in clinical trials of hospital-acquired and ventilator-associated pneumonia. *Clin Infect Dis* 2010;51(S1):S67–S80.
- Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:1–38.
- Purrello SM, garau J, Giamarellos E, et al. Methicillin-resistant *Staphylococcus aureus* infections: a review of the currently available treatment options. *J Glob Antimicrob Resist* 2016;7:178–186.
- Pugh R, Grant C, Cooke RPD, Dempsey G. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. *Cochrane Database Syst Rev* 2015;8:CD007577.

121

ACUTE BRONCHITIS

The Collegiate Cough Level II

Jessica Helmer Brady, PharmD, BCPS

Sherry Peveto, DNP, WHNP-BC

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify signs and symptoms of acute bronchitis and their duration, and evaluate relevant laboratory values to rule out more serious illness such as pneumonia.
- Discuss why obtaining sputum cultures and Gram stains is not relevant in evaluation and treatment of patients with uncomplicated acute bronchitis.
- Discuss why antibiotic treatment is not indicated for uncomplicated acute bronchitis.
- Select nonpharmacologic and pharmacologic treatment alternatives for supportive care, incorporating data regarding efficacy.

PATIENT PRESENTATION

Chief Complaint

"I can't seem to stop coughing! It's keeping me and my roommate awake at night, not to mention totally disrupting my classes. And now my throat is also really sore. I even tried my roommate's

asthma inhaler hoping that my cough would stop, but it didn't. I just want an antibiotic to make this all go away!"

HPI

Allie Comeaux, a 21-year-old college student, is being seen at her university's Student Health Center for complaints of a productive, purulent cough and sore throat for the past 8 days. On questioning, Allie denies that she has had any fever, chills, or myalgias. She expresses concern that a dorm mate was recently hospitalized with pneumonia. She admits to using her roommate's albuterol asthma inhaler with no relief. While her throat is still sore, she is most concerned with her disruptive cough. "My history professor even asked me to leave the class when I couldn't stop coughing!"

PMH

Mild acne $\times$ 5 years

Irregular menstrual cycle, ranging from 25 to 40 days in length

Current with age-appropriate vaccinations, with the exception of influenza and HPV

FH

Father, 51, has been diagnosed with hypertension and hyperlipidemia and has a distant history of alcohol abuse. Mother, 50, is menopausal. The patient also has two younger brothers, ages 16 and 18, with no health issues.

SH

Allie lives at university dorm with a suitemate. She smokes "socially" when out with friends but denies alcohol use due to her father's history of alcohol abuse. She also denies any illicit drug use. She is currently a junior kinesiology major and hopes to attend physical therapy school on completion of her degree. She is also on the university dance line. Allie states that she is sexually active with her boyfriend of 8 months. They use condoms as a method of birth control, although inconsistently.

Meds

Acetaminophen 650 mg PO PRN headache or menstrual cramps
Benzoyl peroxide 2.5% cream topically daily PRN acne

All

Penicillin—"all-over body rash"

ROS

No fever, chills, myalgia, chest pain, or shortness of breath; no nausea, vomiting, or diarrhea

Physical Examination

Gen

Well-developed, thin woman in NAD

VS

BP 104/68 mm Hg, P 64, RR 14, T 37°C; Wt 52 kg, Ht 5'6"

HEENT

PERRLA, conjunctivae clear, TMs intact. No epistaxis or nasal discharge. No sinus swelling or tenderness, and mucous membranes are moist. There are no oropharyngeal lesions.

Neck/Lymph Nodes

Supple without adenopathy or thyromegaly

Chest

(—) Rhonchi, rales, increased fremitus, wheezing, or egophony; negative bronchophony

CV

RRR without MRG

Abd

Soft, nontender, (+) BS

Genit/Rect

Deferred

MS/Ext

Pulses 2+ throughout

Neuro

A&O $\times$ 3; 2+ reflexes throughout, 5/5 strength; CN II–XII intact

Labs

Na 140 mEq/L	Hgb 14 g/dL	WBC $6 \times 10^3/\text{mm}^3$
K 4.5 mEq/L	Hct 38%	Segs 55%
Cl 102 mEq/L	RBC $5.0 \times 10^6/\text{mm}^3$	Bands 3%
HCO ₃ 24 mEq/L	Plt $250 \times 10^3/\text{mm}^3$	Lymphs 33%
BUN 14 mg/dL		Monos 6%
SCr 0.7 mg/dL		Eos 2%
FPG 88 mg/dL		Basos 1%

Sputum Culture

No pathogens isolated

Assessment

1. Presumed acute bronchitis.
2. Sexual/reproductive health issues should be further explored and addressed.
3. (+) Smoking history, although patient states, "I only smoke when I'm out, so I can stop at any time."
4. Need for updated immunizations.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of acute bronchitis?
- 1.b. What additional information is needed to fully assess this patient's acute bronchitis?

Assess the Information

- 2.a. Assess the severity of acute bronchitis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What psychosocial considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for acute bronchitis in this case?
- 3.b. What nondrug therapies might be useful for this patient's acute bronchitis?

- 3.c. What feasible pharmacotherapeutic alternatives are available for treating uncomplicated acute bronchitis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Outline a treatment plan for a patient with chronic bronchitis presenting with an acute exacerbation, and contrast how this treatment would differ from treatment for a patient with a new diagnosis of acute bronchitis.
2. Prepare a patient education pamphlet on acute bronchitis. Be sure to address why antibiotics are not usually first-line therapy for uncomplicated acute bronchitis.
3. Discuss the differences in presentation and treatment of uncomplicated acute bronchitis for a child versus an adult versus an elderly patient.

CLINICAL PEARL

Many patients who present with symptoms of acute bronchitis expect to receive an antibiotic. Therefore, time should be spent with the patient explaining the decision to not prescribe an antibiotic, and why excessive use of unnecessary antibiotics could harm the community at large.

REFERENCES

1. Woodhead M, Blasi F, Ewig S, et al. Joint Taskforce of the European Respiratory Society and European Society for Clinical Microbiology and Infectious Diseases. Guidelines for the management of adult lower respiratory tract infections-full version. *Clin Microbiol Infect* 2011;17(Suppl 6):E1–E59.
2. Kinkade S, Long NA. Acute bronchitis. *Am Fam Physician* 2016;94(7):560–565.
3. Albert RH. Diagnosis and treatment of acute bronchitis. *Am Fam Physician* 2010;82(11):1345–1350.
4. Harris AM, Hicks LA, Qaseem A. Appropriate antibiotic use for acute respiratory tract infection in adults: advice for high-value care from the American College of Physicians and the Centers for Disease Control and Prevention. *Ann Intern Med* 2016;164:425–434.
5. Tackett KL, Atkins A. Evidence-based acute bronchitis therapy. *J Pharm Pract* 2012;25(6):586–590.
6. Smith SM, Fahey T, Smucny J, Becker LA. Antibiotics for acute bronchitis. *Cochrane Database Syst Rev* 2017;(6):CD000245.
7. Becker LA, Hom J, Villasis-Keever M, van der Wouden JC. Beta2-agonists for acute bronchitis. *Cochrane Database Syst Rev* 2011;(7):CD001726.
8. Smith SM, Schroeder K, Fahey T. Over-the-counter (OTC) medications for acute cough in children and adults in community settings. *Cochrane Database Syst Rev* 2014;(11):CD001831.
9. Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination—updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep* 2016;65(49):405–1408.

122

OTITIS MEDIA

Up to My Ears With Ear Infections Level II

Rochelle Rubin, PharmD, BCPS, CDE

Lauren Camaione, PharmD, BCPPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the signs and symptoms of acute otitis media (AOM).
- Identify risk factors associated with an increased incidence of AOM.
- Identify the pathogens most commonly causing AOM.
- Recommend an effective and economical treatment regimen, including specific agent(s), route of administration, and dose(s) of antibiotics and analgesic medications.
- Recognize the role of delaying antibiotic therapy for AOM.
- Educate parents about recommended drug therapy using appropriate nontechnical terminology.

PATIENT PRESENTATION

Chief Complaint

Per patient's mom: "I've had it up to my ears with his ear infections!"

HPI

Seth Jacobs is a 16-month-old boy who is brought to his pediatrician by his distraught mother on a Monday morning in early March. Mom describes a 2-day history of tugging at his right ear and crying, decreased appetite, decreased playfulness, and difficulty sleeping. Mom states that his temperature last night was elevated by electronic axillary thermometer (39.5°C), so she gave him 5 mL of ibuprofen every 12 hours × 2 doses. Mom requests all recommendations be written as prescriptions (even ibuprofen) for day care administration. She also notes that it is tax season, and she needs Seth to be able to return to day care immediately so she can return to work as an accountant.

■ PMH

Former full-term, NSVD, 4-kg healthy infant at birth, breast-fed for 6 months.

Immunizations are up-to-date, including four doses of 13-valent pneumococcal conjugate vaccination (Prevnar-13).

First episode of AOM at age 4 months treated with amoxicillin without adverse effects. Recurrent AOM $\times$ 3 over the past year; most recent episode 2 weeks ago treated with high-dose amoxicillin for 10 days without adverse effects.

Seth was seen approximately 1 month ago for persistent nonproductive cough of 5-day duration. A diagnosis of acute bronchiolitis was made, and symptoms improved with ibuprofen, fluids, and rest.

■ FH

Both parents in good health. Two siblings, 3 and 6 years old, in good health.

■ SH

Seth lives at home with his parents and two sisters. Both parents are employed and work out of the house. Seth and his 3-year-old sister attend day care. His elder sister attends elementary school. There is a pet dog in the home. Seth uses a pacifier regularly throughout the day. There is no smoking in the house.

■ Meds

Ibuprofen suspension 100 mg/5 mL, 100 mg (5 mL) Q 12 H $\times$ 2 doses in the past 24 hours

■ All

NKDA

■ ROS

Head: Otorrhea noted; ears tender to the touch

Respiratory: (per mom) denies wheezing. Lingering, mild cough still present, no sputum production.

■ Physical Examination**Gen**

WDWN Caucasian male teen, now crying

VS

BP 104/60, HR 130, RR 26, T 39.1°C; Wt 10 kg, Ht 30"

Skin

Warm and dry; no rashes

HEENT

Both TMs erythematous (with R > L); right TM with moderate bulging and limited mobility; copious cerumen and purulent fluid behind TM; otorrhea noted; left TM landmarks appear normal including the pars flaccida, the malleus, and the light reflex below the umbo. However, the right TM landmarks are difficult to visualize, and fluid is obstructing visualization of the umbo. Throat is erythematous; nares patent.

Neck/Lymph nodes

Supple; no lymphadenopathy

Chest

Mild crackles at bases bilaterally, improved since bronchiolitis visit 1 month ago

CV

RRR, no murmurs

Abd

Soft, nontender

Genit/Rect

Tanner stage I; rectal exam not performed

MS/Ext

No CCE; moves all extremities well; warm, pink, no rashes; normal range of motion

Neuro

Responsive to stimulation, DTR 2+ no clonus, CN intact

■ Labs

None obtained

■ Assessment

Right ear AOM

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the diagnosis of AOM?
- 1.b. What additional information is needed to fully assess this patient's AOM?

Assess the Information

- 2.a. Assess the severity of AOM based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for AOM in this child?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating AOM?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include the specific drugs, dose, schedule, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Describe a scenario in which it would be appropriate to use azithromycin to treat AOM.

CLINICAL PEARL

Streptococcus pneumoniae has been shown to cause 40–50% of childhood AOM cases. First-line treatment remains high-dose amoxicillin despite significant resistance because the high dose used is generally effective against susceptible, intermediate, and often resistant pneumococci, and it is a low-cost, safe, and acceptable-tasting option with a narrow microbiologic spectrum.

REFERENCES

1. Lieberthal AS, Carroll AE, Chonmaitree T, et al. Clinical practice guideline: diagnosis and management of acute otitis media. *Pediatrics* 2013;131:e964–e999.
2. American Academy of Pediatrics, American Academy of Otolaryngology-Head and Neck Surgery, American Academy of Pediatrics Subcommittee on Otitis Media with Effusion. Otitis media with effusion. *Pediatrics* 2004; 113:1412–1429.
3. Neto JFL, Hemb L, Silva DB. Systematic literature review of modifiable risk factors for recurrent otitis media in childhood. *J Pediatr* 2006;82:87–96.
4. Kaur R, Morris M, Pichichero M. Epidemiology of acute otitis media in the post pneumococcal conjugate vaccine era. *Pediatrics* 2017;140(3):1–11.
5. Bertin L, Pons G, d'Athys P, et al. A randomized, double-blind, multicentre controlled trial of ibuprofen versus acetaminophen and placebo for symptoms of acute otitis media in children. *Fundam Clin Pharmacol* 1996;10:387–392.
6. Centers for Disease Control and Prevention. Active Bacterial Core Surveillance Report, Emerging Infections Program Network, *Streptococcus pneumoniae*, 2010. Atlanta, GA: Centers for Disease Control and Prevention; 2012. Available at: <http://www.cdc.gov/abcs/reports-findings/survreports/spneu12.pdf>. Accessed January 15, 2019.
7. Venekamp RP, Sanders S, Glasziou PP, et al. Antibiotics for acute otitis media in children. *Cochrane Database Syst Rev* 2013;(1): CD000219.
8. Spiro DM, Tay KY, Arnold DH, Dziura JD, Baker MD, Shapiro ED. Wait-and-see prescription for the treatment of acute otitis media. *JAMA* 2006;196:1235–1241.
9. Centers for Disease Control and Prevention. Advisory committee on immunization practices (ACIP) recommended immunization schedule for children and adolescents aged 18 years and younger—United States, 2018. *MMWR* 2018;67(5):156–157.
10. Suaya J, Gessner B, Fung S, et al. Acute otitis media, antimicrobial prescriptions, and medical expenses among children in the United States during 2011–2016. *Vaccine* 2018;36:7479–7486.

123

RHINOSINUSITIS

Sick Sinus. Level II

Michael B. Kays, PharmD, FCCP, BCIDP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Compare and contrast the signs and symptoms of acute viral and bacterial rhinosinusitis in a given patient, noting the cardinal symptoms of acute rhinosinusitis.
- Differentiate viral from bacterial etiology in rhinosinusitis based on a patient's symptoms.
- Identify the most common pathogens causing acute bacterial rhinosinusitis.
- Identify adult patients with a diagnosis of acute bacterial rhinosinusitis who may be candidates for observation without use of antibiotics.
- Formulate a treatment plan for a patient with acute bacterial rhinosinusitis based on duration of symptoms, severity of symptoms, and history of previous antibiotic use.
- Revise the treatment plan for a patient who fails the initially prescribed therapy.

PATIENT PRESENTATION

Chief Complaint

"I feel awful and congested, and my head hurts. I was starting to feel better, but now I think my sinus infection is back."

HPI

Kyle Rheinhardt is a 54-year-old man who presents to his primary care physician with fever, purulent nasal discharge from the left naris, facial pain (L > R), nasal congestion, headache, and fatigue. He states that his symptoms of runny nose, congestion, fever, and malaise began 8 days ago, and the symptoms initially improved over the first 4–5 days. However, the symptoms have become progressively worse over the past few days. He also complains of intense facial pressure when he bends forward to tie his shoes or to pick up something. He has noticed a decreased ability to smell and states that foods do not taste the same as before. He has experienced occasional episodes of nausea, dizziness, tremors, and palpitations for the past week, and states that he has difficulty sleeping the past few nights. He has been taking ibuprofen as needed and loratadine 5 mg/pseudoephedrine sulfate 120 mg every 12 hours but has received little relief from his symptoms. Mr Rheinhardt states that he was treated for a sinus infection about 4 weeks ago. When questioned further, he states that he presented to an urgent care clinic complaining of a runny nose, congestion, sneezing, cough, and a mild sore throat for 2–3 days. He was leaving the following day for a business trip and asked the physician for an antibiotic prescription. He told the physician that azithromycin has always worked for him, so he was prescribed azithromycin 500 mg PO daily for 3 days.

His symptoms slowly improved over 7–10 days, and he was symptom-free for a several days before his current symptoms began 8 days ago. He states that he only gets sick occasionally and has not had an infection in the past year prior to these episodes.

■ PMH

Sinus infection 4 weeks ago
Hypertension (well controlled with medication)
Hypercholesterolemia

■ FH

Father died of MI at 64 years of age.
Mother with hypertension and diabetes mellitus.

■ SH

Smokes cigars on occasion (one to two per week). Denies cigarette smoking and illicit drug use. Drinks socially (three to four beers and one bottle of red wine per week). He is divorced with two children (27-year-old son, 24-year-old daughter).

■ Meds

Lisinopril 20 mg PO daily
Hydrochlorothiazide 25 mg PO daily
Simvastatin 40 mg PO daily
Ibuprofen 200–400 mg PO as needed
Claritin-D 12 hours (loratadine 5 mg/pseudoephedrine sulfate 120 mg) PO Q 12 H

■ All

None

■ ROS

Patient with an 8-day history of runny nose, congestion, fever, and malaise now with fever, purulent nasal drainage, congestion, facial pain, headache, fatigue, hyposmia, and occasional nausea, dizziness, and palpitations. The symptoms improved initially but have progressively worsened over the past few days. In addition, the patient complains of insomnia, which may be contributing to the fatigue. He denies vomiting, diarrhea, chills, diaphoresis, dyspnea, productive cough, or allergies.

■ Physical Examination

Gen

Tired-looking, overweight white man in mild distress; appears uncomfortable

VS

BP 158/102, P 95, RR 16, T 39.3°C; Wt 118 kg, Ht 73"

Skin

Warm to touch; good skin turgor; no other abnormalities

HEENT

NC/AT; PERLLA; EOMI; funduscopic exam normal; injected conjunctivae; anicteric sclerae. Thick, purulent, yellow-green nasal discharge; mucosal hypertrophy (L > R) without evidence of nasal polyps. Facial pain over left maxillary and frontal sinuses. No oral lesions; no periorbital swelling. Tympanic membranes intact, non-erythematous, nonbulging. Throat erythematous.

Neck/Lymph Nodes

Supple, no JVD, mild lymphadenopathy

Lungs/Thorax

CTA; no crackles or wheezing

CV

Slightly tachycardic; normal S₁ and S₂, no MRG

Abd

Soft, nontender; bowel sounds present; no masses

Genit/Rect

Deferred

MS/Ext

No CCE

Neuro

A&O × 3; CN II–XII intact

■ Labs

None obtained

■ Assessment

1. Recurrent rhinosinusitis—patient is able to afford medications and states that he took all of his previous antibiotic prescription as directed.
2. Dizziness, tremors, palpitations
3. Hypertension
4. Hypercholesterolemia

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of acute bacterial rhinosinusitis versus viral rhinosinusitis?
- 1.b. What additional information is needed to fully assess this patient's rhinosinusitis?

Assess the Information

- 2.a. Assess the severity of acute bacterial rhinosinusitis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for acute bacterial rhinosinusitis in this case?
- 3.b. What nondrug therapies might be useful for this patient's acute bacterial rhinosinusitis?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating acute bacterial rhinosinusitis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy?
- 3.e. What alternatives would be appropriate if the initial plan for acute bacterial rhinosinusitis fails?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Determine if a change in mucus color from clear to yellow or green is an indication of a bacterial infection or if it is the natural course of a viral infection.
2. If the patient had a reported penicillin allergy, review appropriate questions for assessing the severity of the patient's allergy and the likelihood of an allergic reaction if he had received a cephalosporin.
3. Review the pharmacokinetic and pharmacodynamic properties of antibacterial agents commonly used in the treatment of acute bacterial rhinosinusitis.
4. Review the most common mechanisms of bacterial resistance in pathogens frequently encountered in acute bacterial rhinosinusitis.

CLINICAL PEARL

The etiology of most cases of acute rhinosinusitis is viral; however, an antibiotic is prescribed in approximately 80% of cases. In patients with a clinical diagnosis of acute bacterial rhinosinusitis, the spontaneous resolution rate is 50–60%. This information is important to consider when evaluating antimicrobial efficacy from comparative clinical studies.

REFERENCES

1. Chow AW, Benninger MS, Brook I, et al. IDSA clinical practice guideline for acute bacterial rhinosinusitis in children and adults. *Clin Infect Dis* 2012;54:e72–e112.
2. Rosenfeld RM, Piccirillo JF, Chandrasekhar SS, et al. Clinical practice guideline (update): adult sinusitis. *Otolaryngol Head Neck Surg* 2015;152 (2 Suppl):S1–S39.
3. Aring AM, Chan MM. Current concepts in adult acute rhinosinusitis. *Am Fam Physician* 2016;94:97–105.
4. Benninger MS, Payne SC, Ferguson BJ, Hadley JA, Ahmad N. Endoscopically directed middle meatal cultures versus maxillary sinus taps in acute bacterial maxillary rhinosinusitis: a meta-analysis. *Otolaryngol Head Neck Surg* 2006;134:3–9.
5. Fleming-Dutra KE, Hersh AL, Shapiro DJ, et al. Prevalence of inappropriate antibiotic prescriptions among US ambulatory care visits, 2010–2011. *JAMA* 2016;315:1864–1873.
6. Benninger MS, Holy CE, Trask DK. Acute rhinosinusitis: prescription patterns in a real-world setting. *Otolaryngol Head Neck Surg* 2016;154:957–962.
7. Benninger M, Brook I, Farrell DJ. Disease severity in acute bacterial rhinosinusitis is greater in patients infected with *Streptococcus*

pneumoniae than in those infected with *Haemophilus influenzae*. *Otolaryngol Head Neck Surg* 2006;135:523–528.

8. Matho A, Mulqueen M, Tanina M, et al. High-dose versus standard-dose amoxicillin/clavulanate for clinically-diagnosed acute bacterial sinusitis: a randomized clinical trial. *PLoS One* 2018;13(5):e0196734.
9. FDA Drug Safety Communication: FDA advises restricting fluoroquinolone antibiotic use for certain uncomplicated infections; warns about disabling side effects that can occur together. Available at: <https://www.fda.gov/Drugs/DrugSafety/ucm500143.htm>. Accessed March 9, 2019.
10. Flamm RK, Mendes RE, Hogan PA, Ross JE, Farrell DJ, Jones RN. In vitro activity of linezolid as assessed through the 2013 LEADER surveillance program. *Diagn Microbiol Infect Dis* 2015;81:283–289.

124

ACUTE PHARYNGITIS

A Hard Pill to Swallow Level II

Anthony J. Guarascio, PharmD, BCPS

Autumn Stewart-Lynch, PharmD, BCACP, CTTS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- List the subjective and objective information that a healthcare professional must gather from a patient with pharyngitis.
- Assess the need for antibiotic therapy in a patient with pharyngitis based on signs and symptoms and the results from microbiological and immunologic diagnostic studies.
- Prepare an evidence-based care plan for a patient with acute pharyngitis that is individualized to the patient's current presentation, past medical history and concurrent medications.
- Identify the key educational and counseling points needed by the patient and/or caregivers to safely and effectively implement the therapeutic plan and to prevent disease transmission.
- List the parameters monitored by the healthcare professional to ensure clinical resolution and the prevention of suppurative and nonsuppurative complications of acute pharyngitis.

PATIENT PRESENTATION

Chief Complaint

"It hurts to swallow."

HPI

Elizabeth Grant is a 14-year-old girl who presents to her family medicine provider complaining of sore throat. Her mother measured a fever of 102°F (38.9°C) on and off for the past 24 hours that was treated with acetaminophen. She has been more tired in school than usual over the past 2 days and has been drinking only liquids since this time. She denies cough, shortness of breath, or difficulty breathing. The patient complains of nausea and headaches but denies vomiting. Mother notes no recent illness in the family.

PMH

The patient has had prior cases of otitis media as a young child. Six months ago she was diagnosed with primary dysmenorrhea. Otherwise she is healthy. Immunization records indicate receipt of the following immunizations:

HepB: four doses (last dose age 12 months)
 DTaP: five doses (last dose age 4 years)
 Tdap: one dose given at age 11
 Hib: four doses (last dose age 12 months)
 PCV: four doses (last dose age 12 months)
 IPV: four doses (last dose age 4 years)
 MMR: two doses (last dose age 12 months)
 Varicella two doses (last dose age 12 months)
 HPV: one dose given at age 11
 MenACWY-D: one dose given at age 11
 Influenza IIV/LAIV: last received at age 11

FH

Noncontributory

SH

Elizabeth lives with her parents and 5-year old twin brothers. She started high school 2 months ago and is on the junior varsity soccer team. She denies the use of tobacco, alcohol, marijuana, or other substances.

Meds

Ethinyl estradiol 20 mcg/levonorgestrel 0.1 mg (21 days active-7 days placebo): one tablet by mouth daily
 Naproxen 500 mg by mouth twice daily for 5 days (begin 2 days before menses)

All

Amoxicillin: rash, hives

ROS

Negative except for complaints noted in the HPI

Physical Examination**Gen**

WDWN 14-year-old girl, clearly fatigued

VS

BP 104/70, P 92, RR 22, T 38.8°C, Wt 50 kg, Ht 63"

Skin

Pale, warm, faint scarlatiniform rash on arms and trunk

HEENT

PERRLA; tonsils erythematous with associated white exudates; uvula edematous; soft palate with notable petechiae, TM normal

Neck/Lymph Nodes

Multiple enlarged anterior cervical lymph nodes, greater than 2 cm in diameter

Lungs/Thorax

CTA bilaterally, (–) shortness of breath, (–) cough

CV

RRR, normal S₁ and S₂

Abd

Soft, nontender, nondistended, (+) BS

Genit/Rect

Deferred; LMP 3 weeks ago; not sexually active

Neuro

CN I–XII intact

Labs

RADT: negative
 Throat culture: results pending

Assessment

A 14-year-old girl presents with suspected group A *Streptococcus* (GAS) pharyngitis.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of GAS infection versus viral pharyngitis?
- What additional information is needed to fully assess this patient's acute pharyngitis?

Assess the Information

- Assess the severity of acute pharyngitis based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case if the throat culture returns positive for GAS?
- What nondrug therapies might be useful for this patient's acute pharyngitis?
- What feasible pharmacotherapeutic alternatives are available for treating GAS acute pharyngitis?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- What alternatives would be appropriate if the initial care plan for acute pharyngitis fails or cannot be used?

Implement the Care Plan

- What information should be provided to the patient and caregivers to enhance compliance, ensure successful therapy, minimize adverse effects, and prevent disease transmission to others?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTIONS

1. What is the clinical significance of potential drug interactions between the patient's new and current medications?
2. The patient's mother is concerned about transmission to household contacts and requests antibiotic prescriptions for her siblings. Explain whether or not this would be necessary.

■ SELF-STUDY ASSIGNMENTS

1. Create a table that lists the preferred and alternative therapeutic options for GAS pharyngitis and includes the following comparative data: Drug name, dose, frequency, duration, available dosage forms, adverse effects, and cost.
2. Prepare a one-page paper that describes the incidence, risk factors, signs/symptoms, onset and possible complications of scarlet fever, rheumatic fever, and poststreptococcal glomerulonephritis.

CLINICAL PEARL

While early initiation of antibiotic therapy can reduce the duration of GAS symptoms, withholding antibiotics until laboratory confirmation of GAS bacterial disease in the majority of clinical circumstances can reduce the potential for inappropriate antibiotic therapy while still preventing the spread of GAS to others and prevent development of complications.

REFERENCES

1. Gerber MA, Baltimore RS, Eaton CB, et al. Prevention of rheumatic fever and diagnosis and treatment of acute streptococcal pharyngitis. *Circulation* 2009;119:1541–1551.
2. Shulman ST, Bisno AL, Clegg HW, et al. Practice guidelines for the diagnosis and management of group A streptococcal pharyngitis: 2012 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2012;55:1279–1282.
3. Wessels MR. Streptococcal pharyngitis. *N Engl J Med* 2011;364:648–655.
4. Cohen JF, Bertille N, Cohen R, Chalumeau M. Rapid antigen detection test for group A *Streptococcus* in children with pharyngitis. *Cochrane Database Syst Rev* 2016;7:CD010502. doi: 10.1002/14651858.CD010502.pub2.
5. McIsaac WJ, Kellner JD, Aufricht P, Vanjaka A, Low DE. Empirical validation of guidelines for the management of pharyngitis in children and adults. *JAMA* 2004;291:1587–1595.
6. Center for Medicare and Medicaid Services. Core quality measures: pediatric measures. Available at: <https://www.cms.gov/Medicare/Quality-Initiatives-Patient-Assessment-Instruments/QualityMeasures/Downloads/Pediatric-Measures.pdf>. Accessed January 30, 2019.
7. Centers for Disease Control and Prevention. Is it strep throat? Available at: <http://www.cdc.gov/Features/strepthroat/>. Accessed January 30, 2019.
8. Centers for Disease Control and Prevention. Pharyngitis (strep throat): information for Clinicians. Available at: <https://www.cdc.gov/groupastrep/diseases-hcp/strep-throat.html>. Accessed January 30, 2019.
9. ACOG Committee on Practice Bulletins-Gynecology. ACOG Practice Bulletin No. 73: use of hormonal contraception in women with coexisting medical conditions. *Obstet Gynecol* 2006 Jun;107:1453.
10. Curtis KM, Tepper NK, Jatlaoui TC, et al. U.S. Medical Eligibility Criteria for Contraceptive Use, 2016. *MMWR Recomm Rep* 2016; 65(No. RR-3):1–104. doi: <http://dx.doi.org/10.15585/mmwr.rr6503a1>.

125

INFLUENZA

Run Over by the Flu Level II

Christo L. Cimino, PharmD, BCPS, AAHIVP

Douglas Slain, PharmD, BCPS, FCCP, FASHP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the clinical presentation of influenza.
- Discuss influenza-related complications.
- Develop a patient-specific treatment plan for influenza.
- Identify appropriate target populations for vaccination against influenza.
- Compare and contrast available options for preventing influenza.
- Discuss strategies to control influenza outbreaks.

PATIENT PRESENTATION

■ Chief Complaint

"I feel like a truck ran over me. Every muscle and bone hurts, and I am burning up."

■ HPI

Vladimir Kharitonov is a 67-year-old Russian man who presents in mid-December to an urgent care clinic with complaints of 1-day history of fever, up to 39°C (102.2°F), muscle and bone aches, feeling tired, and headache. He has not had anything to eat in the past 12 hours due to loss of appetite and has not taken his glyburide this morning. He has been in his usual state of health previously and reports that some of his coworkers have been sick with the "flu." He decided to come to the clinic in hopes that an antibiotic can allow him to recover sooner since his son is getting married next weekend. He missed his regular appointment 1 month ago because he was "too busy."

■ PMH

Type 2 DM for 14 years
Hyperlipidemia
HTN

■ FH

Father and sister with type 2 DM

■ SH

Lives at home with his wife; works full time; quit smoking 10 years ago, but smokes occasionally when really stressed or in a social setting; drinks alcohol in a social setting—mostly vodka

■ Meds

Aspirin 81 mg PO daily
Hydrochlorothiazide 25 mg PO daily

Glyburide 5 mg PO every morning
 Metformin 1 g PO twice daily
 Lantus 35 units SC at bedtime
 Atorvastatin 10 mg PO daily
 Centrum Silver one tablet PO daily

■ All

NKDA

■ ROS

Complains of severe fatigue, body aches, alternating between being too cold and sweating, sore throat, nonproductive cough, and a headache. He denies nasal congestion, nausea, vomiting, or diarrhea.

■ Physical Examination

Gen

WDWN overweight man in NAD

VS

BP 150/90 (patient reports similar readings at home), P 95, RR 18, T 38.5°C; Wt 95.5 kg, Ht 5'10"

Skin

Warm and moist secondary to diaphoresis, no lesions

HEENT

PERRLA; EOMI; TMs intact; wears dentures; mild pharyngeal erythema with no exudates

Neck/Lymph Nodes

Neck is supple and without adenopathy; no JVD

Lungs/Thorax

CTA; no crackles or wheezing

CV

RRR; normal S₁, S₂; no murmurs

Abd

Soft, obese; NT/ND; normal BS

Genit/Rect

Not performed

MS/Ext

Muscle strength and tone 4–5/5; no CCE

Neuro

A&O × 3; CN II–XII intact; decreased sensation to light touch of the lower extremities (both feet)

■ Labs

Na 138 mEq/L	Hgb 13.2 g/dL	WBC $10 \times 10^3/\text{mm}^3$	Fasting lipid profile
K 3.8 mEq/L	Hct 41%	Neutros 50%	T. chol
Cl 98 mEq/L	Plt $275 \times 10^3/\text{mm}^3$	Bands 4%	177 mg/dL
CO ₂ 24 mEq/L		Eos 0%	LDL 110 mg/dL
BUN 26 mg/dL		Lymphs 39%	HDL 35 mg/dL
SCr 1.3 mg/dL		Monos 7%	Trig 160 mg/dL
Glu 135 mg/dL			
A1C 7.1%			

■ Diagnostic Tests

QuickVue rapid influenza test—positive

■ Assessment

A 67-year-old man with diabetes, HTN, and hyperlipidemia presents with influenza.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of influenza?
- What additional information is needed to fully assess this patient's influenza?

Assess the Information

- Assess the severity of influenza infection based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful for this patient's influenza?
- What feasible pharmacotherapeutic alternatives are available for treating influenza infection? Include the drug name, dose, dosage form, route, frequency, and treatment duration. Are these options affected by the type of influenza that this patient is experiencing and the time since onset of illness?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- What clinical and laboratory parameters are necessary to evaluate the therapy for achievement of the desired therapeutic outcome and detect or prevent adverse effects?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

In October of the following year, Mr Kharitonov presents for his routine physical exam. He has been doing very well. His diabetes, hypertension, and hyperlipidemia are well controlled.

FOLLOW-UP QUESTIONS

1. What indications does this patient have for administration of the seasonal influenza vaccine?
2. If the vaccine is desirable, what is the optimal time frame for this patient to receive vaccination(s)?
3. What are all available options for vaccination against seasonal influenza?
4. Provide your individualized recommendations for protecting this patient against influenza virus infections.
5. Should all patients with confirmed influenza receive treatment with antiviral medications?

CLINICAL COURSE: ALTERNATIVE THERAPY

As Mr Kharitonov is leaving, he thanks you and promises to follow your recommendations. He states that he is worried about making anyone else sick, because of his son's upcoming wedding. "My cousins back in Russia keep telling me they use elderberry syrup to keep from getting sick during flu season. Could that help keep my wife from getting this flu?" See Section 19 in this Casebook for information regarding the use of elderberry for influenza treatment and prevention.

SELF-STUDY ASSIGNMENTS

1. Prepare an educational pamphlet on influenza prevention and treatment directed at both patients and general practice physicians. Include recommendations for controlling influenza outbreaks.
2. Investigate the role of pharmacists as immunization providers.
3. Investigate the threat of human infection with avian influenza viruses. Are currently available influenza prevention strategies effective against avian flu?

CLINICAL PEARL

Development of antibodies takes approximately 2 weeks after influenza vaccination in adults, during which time they remain at high risk for influenza infection. If the immunization occurs during an influenza outbreak, chemoprophylaxis with antiviral agents can be administered for 2 weeks immediately after vaccination to minimize the risk of infection. The live attenuated influenza vaccine (LAIV) can cause a false-positive result for up to 7 days on a rapid influenza diagnostic test since these tests cannot differentiate between live attenuated and wild-type influenza viruses.

REFERENCES

1. Harper SA, Bradley JS, Englund JA, et al. Seasonal influenza in adults and children—diagnosis, treatment, chemoprophylaxis and institutional outbreak management: clinical practice guidelines of the Infectious Diseases Society of America for seasonal influenza in adults and children. *Clin Infect Dis* 2009;48:1003–1032.
2. Fiore AE, Fry A, Shay D, et al. Antiviral agents for the treatment and chemoprophylaxis of influenza—recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2011;60(1):1–24.
3. United States Centers for Disease Control and Prevention. Guidance for clinicians on the use of rapid influenza diagnostic tests. Available at: http://www.cdc.gov/flu/professionals/diagnosis/clinician_guidance_ridt.htm. Accessed December 30, 2018.
4. United States Centers for Disease Control and Prevention. FDA-cleared RT-PCR assays and other molecular assays for influenza viruses. Available at: <http://www.cdc.gov/flu/pdf/professionals/diagnosis/table1-molecular-assays.pdf>. Accessed December 30, 2018.
5. Center for Disease Control and Prevention. Influenza antiviral medications: summary for clinicians. Available at: <http://www.cdc.gov/flu/professionals/antivirals/>. Accessed December 30, 2018.
6. Louie JK, Yang S, Acosta M, et al. Treatment with neuraminidase inhibitors for critically ill patients with influenza A (H1N1) pdm09. *Clin Infect Dis* 2012;55(9):1198–1204.
7. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018–2019 influenza season. *MMWR Morb Mortal Wkly Rep* 2018;67(3):1–20.
8. Whelton PK, Carey RM, Aronow WS, et al. 2017 ACC/AHA/AAPA/ABC/ACPM/AGS/APhA/ASH/ASPC/NMA/PCNA guideline for the prevention, detection, evaluation, and management of high blood pressure in adults: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines. *Circulation* 2018 Oct 23;138(17):e484–e594.
9. Stone NJ, Robinson JG, Lichtenstein AH, et al. 2013 ACC/AHA guideline on the treatment of blood cholesterol to reduce atherosclerotic cardiovascular risk in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014;129(25 Suppl 2):S1–S45.
10. Black S, Nicolay U, Del Giudice G, Rappuoli R. Influence of statins on influenza vaccine response in elderly individuals. *J Infect Dis* 2015; 213(8):1224–1228.

126

SKIN AND SOFT TISSUE INFECTION

A Pain in the Butt Level II

Jarrett R. Arnsden, PharmD, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Evaluate the signs and symptoms of skin and soft tissue infections (SSTIs).
- Recommend appropriate empiric nonpharmacologic and pharmacologic treatment options for patients presenting with SSTIs.
- Differentiate between the definition and clinical manifestations of mild, moderate, and severe SSTI.
- Compare and contrast the clinical characteristics and presentation of a purulent vs nonpurulent SSTI.
- Design an antimicrobial treatment regimen for purulent and nonpurulent SSTIs that are mild, moderate, or severe.
- Develop monitoring parameters for nondrug and pharmacologic treatment of SSTIs.
- Identify treatment modalities for decolonizing a patient with recurrent purulent SSTIs.

PATIENT PRESENTATION

■ Chief Complaint

"I have a boil on my butt, and I cannot sit down for class."

■ HPI

Jimmie Chipwood is a 19-year-old college student who presents to the ED with a new-onset "boil" on his right buttock. He noticed some pain and irritation in the right buttock area over the past week but thought it was due to having slid into second base during a baseball game. The pain gradually increased over the next few days, and he went to the student health center, where they cleaned the wound and gave him a prescription for clindamycin 300 mg QID for 7 days. They recommended he try to keep the area covered until the antibiotic began to work. Today (7 days later), Jimmie returned to the student health center for further evaluation and was referred to the ED for further care for his continued SSTI. At the ED, Jimmie says the area on his buttock is worse, and he cannot sit down for class. He reports only partial adherence to the clindamycin regimen, because he often forgets to take it and says it makes him nauseated.

■ PMH

Noncontributory

■ Surgical History

Appendectomy 4 years ago

Repair of left ACL tear 2 years ago

■ SH

Denies any alcohol or illicit drug use.

■ Meds

Clindamycin 300 mg PO QID $\times$ 7 days (prescribed at student health center visit 1 week ago; patient did not complete full course).

■ All

Penicillin (hives as a child)

■ Immunizations

Up-to-date per student health center records

■ ROS

Negative except for complaints noted in HPI

■ Physical Examination

Gen

WDWN Caucasian man in no acute distress, but with noticeable pain when he walks and tries to sit

VS

BP 129/74, P 81, RR 16, T 37.5°C; Wt 77.5 kg, Ht 6'0"

Skin

Lateral right gluteal area: red, erythematous, warm, and tender to touch; localized fluid collection that appears fluctuant, consistent with a carbuncle and surrounding erythema

HEENT

PERRLA; EOMI, oropharynx clear

Neck/Lymph Nodes

Supple, no lymphadenopathy

Lungs/Thorax

CTA, no rales or wheezing

CV

RRR, no MRG

Abd

Soft, NT/ND; (+) BS

Genit/Rect

Large 2 cm $\times$ 4 cm red swollen area over the lateral right buttock, with a localized fluid collection and surrounding erythema

MS/Ext

Upper extremities: WNL

Lower extremities: could not be adequately assessed due to patient's inability to sit; 2+ pulses bilaterally

Neuro

A&O $\times$ 3

■ Labs

Na 138 mEq/L	Hgb 15.5 g/dL	WBC $11.3 \times 10^3/\text{mm}^3$
K 3.7 mEq/L	Hct 44%	Neutros 89%
Cl 98 mEq/L	Plt $279 \times 10^3/\text{mm}^3$	Lymphs 10%
CO ₂ 23 mEq/L		Monos 1%
BUN 23 mg/dL		
SCr 0.9 mg/dL		
Glu 95 mg/dL		
Ca 9.4 mg/dL		

■ Urine Drug Screen

(-) Alcohol, (-) marijuana, (-) cocaine, and other substances

■ Assessment

Progressive lateral right gluteal SSTI with focal area of fluctuance/fluid

QUESTIONS

Collect Information

- What subjective and objective clinical data are consistent with the diagnosis of an SSTI?
- What additional information is needed to fully assess this patient's SSTI?

Assess the Information

- Assess the severity (mild, moderate, or severe) of this patient's SSTI based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- What economic or psychosocial considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating his SSTI?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. List the therapeutic alternatives, in order of preference, for this patient if the initial care plan fails or cannot be used and justify your selections.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient was treated in the ED with I&D alone and was given wound care instructions. The fluid was not sent for culture and susceptibility. He returns to the ED 8 days later with a recurrent boil in the same right buttock area. On physical exam, the patient is found to have a new area of fluid collection (1 cm × 3 cm) and surrounding erythema. An MRI of the gluteal area was negative for deep tissue involvement and extension to other adjacent areas. Two sets of blood cultures were drawn and are pending, and a second I&D of the area was performed and sent for culture and susceptibility. The patient did have his nares and groin area swabbed for MRSA detection, and the results are pending. The patient reported mild fevers without chills, but he has not taken his temperature at home. His current temperature is 37.7°C, and all other vital signs are stable. Given the current information, the ED physician does not think Jimmie needs to be admitted.

Microbiology

Blood cultures × two sets: pending
 Culture of abscess fluid from right buttock: pending
 Nares swab: pending
 Groin swab: pending

Imaging Studies

Negative for deep tissue involvement; localized area of inflammation and fluid consistent with an abscess.

FOLLOW-UP CASE QUESTIONS

1. Was I&D alone an appropriate management strategy for the initial patient presentation (ED visit 1)?
2. How does the lack of culture data limit your pharmacotherapy treatment options?
3. Based on the Clinical Course information, has your assessment of the patient's wound (purulent vs nonpurulent and severity) changed since his first ED visit?
4. Have your goals of pharmacotherapy for treating this patient's SSTI changed? If so, then list the new goals.
5. What pharmacologic decolonization measures could be considered for Jimmie if his nares and/or groin culture(s) is/are positive for MRSA? Discuss the relative options for both, if you would treat them differently.
6. What nonpharmacologic (hygiene or environmental) measures (other than proper local/wound care) could you recommend for Jimmie to ensure successful therapy and minimize possible recurrences?
7. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
8. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects for this patient's SSTI?
9. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Compare the therapeutic alternatives for treatment of mild, moderate, and severe SSTIs with purulence versus SSTIs without purulence.
2. Prepare a table that differentiates the presentation, signs, and symptoms of the patient in this case with those of a patient presenting with erysipelas, diabetic foot infection, and necrotizing fasciitis and also the organisms involved in each respective infection.

CLINICAL PEARL

Necrotizing fasciitis is a severe, progressing form of cellulitis that affects the subcutaneous tissues and moves along the superficial fascia. The infection may encompass all tissues from the skin to the muscle. The most commonly implicated organisms are *Streptococcus pyogenes* or *Clostridium perfringens*; however, in patients with exposures to fresh water *Aeromonas hydrophila* should be suspected, and for those with exposures to salt water, *Vibrio vulnificus* should be considered. The empiric treatment is doxycycline plus ciprofloxacin or doxycycline plus ceftazidime for *A. hydrophila* and *V. vulnificus*, respectively.^{1,2}

REFERENCES

1. Stevens DL, Bisno AL, Chambers HF, et al. Practice guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. Clin Infect Dis 2014;59(2):e10–e52.
2. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. Clin Infect Dis. 2011;52(3):e18–e55.
3. Raff AB, Kroshinsky D. Cellulitis a review. JAMA 2016;316(3):325–337.
4. Talan DA, Mower WR, Krishnadasan A, et al. Trimethoprim-sulfamethoxazole versus placebo for uncomplicated skin abscess. N Engl J Med 2016;374(9):823–832.

5. Creech CB, Al-Zubeidi DN, Fritz SA. Prevention of recurrent staphylococcal skin infections. *Infect Dis Clin North Am* 2015;29(3):429–464.
6. Miller LG, Daum RS, Creech CB, et al. Clindamycin versus trimethoprim-sulfamethoxazole for uncomplicated skin infections. *N Engl J Med* 2015;372(12):1093–1103.
7. Stein GE, Throckmorton JK, Scharmen AE, et al. Tissue penetration and antimicrobial activity of standard- and high-dose trimethoprim/sulfamethoxazole and linezolid in patients with diabetic foot infection. *J Antimicrob Chemother* 2013;68(12):2852–2858.
8. McConeghy KW, Mikolich DJ, Laplante KL. Agents for the decolonization of methicillin-resistant *Staphylococcus aureus*. *Pharmacotherapy* 2009;29(3):263–280.
9. Miller LG, Diep BA. Clinical practice: colonization, fomites, and virulence: rethinking the pathogenesis of community-associated methicillin-resistant *Staphylococcus aureus* infection. *Clin Infect Dis* 2008;46(5):752–760.
10. Barrett TW, Moran GJ. Update on emerging infections: news from the Centers for Disease Control and Prevention. Methicillin-resistant *Staphylococcus aureus* infections among competitive sports participants—Colorado, Indiana, Pennsylvania, and Los Angeles County, 2000–2003. *Ann Emerg Med* 2004;43(1):43–47.

127

DIABETIC FOOT INFECTION

Let's Nail That Infection Level II

Renee-Claude Mercier, PharmD, BCPS-AQ ID, PhC, FCCP

Paulina Deming, PharmD, PhC

Notice to the Reader: The case author provided suggested answers to the questions related to this case in Appendix D to give students an example of how case answers should be constructed.

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of diabetic foot infections and identify the risk factors and the most likely pathogens associated with these infections.
- Recommend appropriate antimicrobial regimens for diabetic foot infections, including for patients with drug allergies or renal insufficiency.
- Recommend appropriate home IV therapy and proper counseling to patients.
- Outline monitoring parameters for achievement of the desired pharmacotherapeutic outcomes and prevention of adverse effects.
- Counsel diabetic patients about adequate blood glucose control as part of an overall plan for good foot health.

PATIENT PRESENTATION

■ Chief Complaint

As per the Spanish interpreter: “He had an ingrown toe nail that became infected several weeks ago, and now the whole foot is swollen.”

■ HPI

Jesus Chavez is a 67-year-old Hispanic man, Spanish-speaking only, who presents to the ED complaining of a sore and swollen foot. Three weeks ago he noticed that his right great toe became swollen and red due to an ingrown toenail. The patient tried to fix the nail with scissors and tweezers, but the swelling got worse, and thick, foul-smelling drainage became noticeable approximately 2 weeks ago. The patient was visiting family in Mexico at the time and now has just returned home to New Mexico. History is per translation by a hospital interpreter. His wife, who also speaks only Spanish, accompanies the patient. The primary care physician is Dr Martinez at First Choice Clinic in Albuquerque.

■ PMH

Type 2 DM × 18 years

Hospitalized 2 months ago for HHS

Left second toe amputation 1 year ago secondary to diabetic foot infection

Hyperlipidemia

Hypertension

Chronic renal insufficiency

■ FH

Father is deceased (56-year-old) secondary to MI, type 2 DM, HTN. Mother is deceased secondary to breast cancer (41-year-old).

One daughter, alive and well, 42-year-old

■ SH

The patient lives with his wife in Albuquerque, New Mexico. He denies tobacco and illicit drug use; however, he admits to a long history of drinking four to five beers per day. He admits to nonadherence with his medications and glucometer.

■ Meds

Lantus SoloStar 40 units once daily

Humalog KwikPen 12 units with each meal

Metformin 1000 mg PO twice daily

Aspirin 81 mg PO once daily

Lisinopril 20 mg PO once daily

Atorvastatin 40 mg PO daily

■ All

Sulfa—severe rash

■ ROS

Negative except as noted in the HPI

■ Physical Examination

Gen

Patient is a thin Hispanic man who appears very concerned about losing his foot.

VS

BP 126/79, P 92, RR 20, T 38.4°C; Wt 60 kg, Ht 5'10"

Skin

Warm, coarse, and very dry

HEENT

PERRLA; EOMI; funduscopic exam is normal with absence of hemorrhages or exudates. TMs are clouded bilaterally but with no

erythema or bulging. Oropharynx shows poor dentition but is otherwise unremarkable.

Neck/Lymph Nodes

Neck is supple; normal thyroid; no JVD; no lymphadenopathy

Chest

CTA

CV

RRR, normal S_1 and S_2

Abd

Distended, (+) BS, no guarding, no hepatosplenomegaly or masses felt

Ext

2+ edema with markedly diminished sensation of the right foot. Significant swelling and induration extend from first metatarsal to midfoot (4 cm × 5 cm) consistent with cellulitis. Purulent foul-smelling drainage expressed from great toe wound. Wound probe 2 cm deep. Pedal pulses present but diminished. Normal range of motion. Poor nail care with some fungus and overgrown toenails.

Neuro

A&O × 3; CN II–XII intact. Motor system intact (overall muscle strength 4–5/5). Sensory system exam showed a decreased sensation to light touch of the lower extremities (both feet); intact upper body sensation.

Labs

Na 136 mEq/L	Hgb 14.1 g/dL
K 3.6 mEq/L	Hct 42.3%
Cl 98 mEq/L	Plt $390 \times 10^3/\text{mm}^3$
CO ₂ 24 mEq/L	WBC $17.3 \times 10^3/\text{mm}^3$
BUN 30 mg/dL	PMNs 78%
SCr 2.4 mg/dL	Lymphs 17%
Glu 323 mg/dL	Monos 5%
A1C 11.8%	
ESR 73 mm/h	

X-Ray

Right foot: There is soft tissue swelling from first metatarsal to mid-foot consistent with cellulitis. No fluid collection noted. No evidence of adjacent periosteal reactions or erosions to suggest radiographic evidence of osteomyelitis. No definite subcutaneous air is evident. Presence of vascular calcifications.

Assessment

Diabetic foot infection with significant cellulitis in a patient with poorly controlled diabetes mellitus.

Clinical Course

On the day of admission, the patient went to surgery for I&D. Blood and tissue specimens were sent for culture and sensitivity testing.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of a diabetic foot infection?
- 1.b. What additional information is needed to fully assess this patient's diabetic foot infection?

Assess the Information

- 2.a. Assess the severity of the diabetic foot infection based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic and psychosocial considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient's diabetic foot infection?
- 3.c. What feasible pharmacotherapeutic alternatives are available for the treatment of diabetic foot infection?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan for the infection fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Mr Chavez received the empiric therapy you recommended until the tissue cultures were reported positive for *Bacteroides fragilis* and *Staphylococcus aureus*, and reported sensitive to vancomycin, linezolid, quinupristin/dalfopristin, and daptomycin and resistant to oxacillin (and other β -lactams), tetracycline, erythromycin, clindamycin, and sulfamethoxazole/trimethoprim. Susceptibilities are not available for *B. fragilis*. The blood cultures were all found to have no growth. The patient remained hospitalized for an additional 10 days and received a more directed antimicrobial regimen and multiple surgical debridements of the wound. The cellulitis slowly improved over this time, and multiple x-rays did not suggest osteomyelitis. He was then discharged to complete the antimicrobial regimen on an outpatient basis. Over the next 2 weeks, he received wound care at home and showed significant but slow progress in healing of the wound.

FOLLOW-UP CASE QUESTIONS

1. What therapeutic options are available for treating this patient after results of cultures are known to contain MRSA and *B. fragilis*?

2. Design an optimal drug treatment plan for treating the mixed infection while he remains hospitalized.
3. Design an optimal pharmacotherapeutic plan for completion of treatment after he is discharged from the hospital.

■ SELF-STUDY ASSIGNMENTS

1. Review in more detail different therapeutic options available for home IV therapy, including the antimicrobial agents suitable for use, types of IV lines available, and contraindications to home IV therapy.
2. Outline the patient counseling you would provide for successful home IV therapy.
3. Describe how you would educate this diabetic patient about proper foot care to prevent further skin or tissue breakdown.

CLINICAL PEARL

Treatment of diabetic foot infections with antimicrobial agents alone is often inadequate; local wound care (incision, drainage, debridement, and amputation), good glycemic control, and immobilization of the limb are often required.

REFERENCES

1. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;54:132–173.
2. Levin ME. Management of the diabetic foot: preventing amputation. *South Med J* 2002;95:10–20.
3. Echániz-Aviles G, Velazquez-Meza ME, Vazquez-Larios Mdel R, Soto-Noguerón A, Hernández-Dueñas AM. Diabetic foot infection caused by community-associated methicillin-resistant *Staphylococcus aureus* (USA300). *J Diabetes* 2015 Nov;7(6):891–892.
4. Lipsky BA, Cannon CM, Ramani A, et al. Ceftaroline fosamil for treatment of diabetic foot infections: the CAPTURE study experience. *Diabetes Metab Res Rev* 2015;31(4):395–401.
5. Lipsky BA, Tabak YP, Johannes RS, Vo L, Hyde L, Weigelt JA. Skin and soft tissue infections in hospitalised patients with diabetes: culture isolates and risk factors associated with mortality, length of stay and cost. *Diabetologia* 2010;53:914–923.
6. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:1–38.
7. Martí-Carvajal AJ, Gluud C, Nicola S, et al. Growth factors for treating diabetic foot ulcers. *Cochrane Database Syst Rev* 2015 Oct 28;10:1–144.
8. Guillet CV, Kollef MH. How to stratify patients at risk for resistant bugs in skin and soft tissue infections? *Curr Opin Infect Dis* 2016;29(2):116–123.
9. Weigelt J, Itani K, Stevens D, Lau W, Dryden M, Knirsch C. Linezolid versus vancomycin in the treatment of complicated skin and soft tissue infections. *Antimicrob Agents Chemother* 2005;46:2260–2266.
10. Nicolau DP, Stein GE. Therapeutic options for diabetic foot infections: a review with an emphasis on tissue penetration characteristics. *J Am Podiatr Med Assoc* 2010;100:52–63.

128

INFECTIVE ENDOCARDITIS

A Symptom of the Larger Disease Level II

Ryan L. Crass, PharmD, BCIDP

Manjunath (Amit) P. Pai, PharmD, FCP

Keith A. Rodvold, PharmD, FCCP, FIDSA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify major and minor diagnostic criteria for infective endocarditis.
- Select an appropriate empiric antibiotic regimen for presumed infective endocarditis.
- Design a pharmacotherapy regimen for endocarditis that takes into account patient-specific factors such as medication allergies, comorbidities, and social history.
- Recognize the psychosocial and ethical issues related to the treatment of infective endocarditis among intravenous drug users.
- Establish monitoring parameters for a selected drug therapy in the treatment of a patient with infective endocarditis.

PATIENT PRESENTATION

■ Chief Complaint

“Let me go home! I was just tired, nothing is wrong with me! Why am I here?”

■ HPI

Christina Meyer is a 27-year-old woman who presents in police custody after being found unconscious outside the local gas station. She was only minimally responsive upon arrival of EMS but became combative in the field following a dose of naloxone. Upon arrival to the emergency department, Ms Meyer remains altered but is able to relay symptoms of cough, chest pain, and shaking chills. She vehemently denies any illicit drug use.

■ PMH

Generalized anxiety disorder (diagnosed 5 years ago)
Chronic back pain (diagnosed 6 years ago, due to workplace-related injury)
Migraine headache (diagnosed 8 years ago)
Genital herpes (diagnosed 2 years ago)

■ FH

Mother: Depression, committed suicide 12 years ago

■ SH

Tobacco use, 1/2 ppd; “social” EtOH use; denies illicit drugs

■ **Meds**

Amitriptyline 100 mg PO QHS
 Ibuprofen 200 mg, two tablets PO Q 6 H PRN back pain
 Sertraline 100 mg PO QD
 Valacyclovir 500 mg QD

■ **All**

Amoxicillin (unknown reaction as a child)

■ **ROS**

Constitutional: Chills. Uncertain about fevers. No weight loss or appetite change.

HEENT: No visual disturbances, nose bleeds, recent cold symptoms, or voice changes.

Respiratory: No shortness of breath, cough. No hemoptysis or wheezing.

Cardiovascular: Diffuse chest pain. No palpitations, orthopnea, or leg swelling.

GI: No diarrhea, stomach pain, nausea, vomiting, or blood in stools.

GU: No dysuria, hematuria, or frequent urination.

MS: No joint pain or swelling. No extremity weakness. (+) back pain.

Integumentary: No rash or jaundice.

Neuro: Headache, questionable syncope, mild confusion. No dizziness or seizures.

Psych: Anxious. No depression, hallucinations, or insomnia.

Endo: No menstrual irregularities or intolerance to heat or cold.

Heme: No swollen glands or easy bruising.

■ **PE****Gen**

Patient is a woman in some distress; clothing is dirty and poorly maintained.

VS

BP 85/60, HR 120, RR 24, T 39.5°C; Wt 55 kg, Ht 5'2"

Skin

Skin is clean, dry, and intact. No evidence of rash or petechiae. Track marks noted on the anterior arm bilaterally.

HEENT

PERRLA, EOMI, anicteric sclerae, no Roth spots, poor dentition

Neck/Lymph Nodes

No lymphadenopathy, JVD, or thyromegaly

Lungs

Trachea midline. Lungs clear to auscultation bilaterally; no wheezing, rales, or rhonchi.

CV

No tenderness with palpation of chest wall. HRRR, normal S₁ and S₂, III/VI holosystolic murmur located over left sternal border.

Abd

Bowel sounds present in all four quadrants. Abdomen soft, non-tender, nondistended.

MS/Ext

Reflexes 2/4 in upper and lower extremities bilaterally; 5/5 muscle strength in all four extremities. No edema.

Neuro

Nonfocal; alert and oriented × 2; negative asterixis. CN II–XII intact.

■ **Labs**

Na 136 mEq/L	Hgb 9.8 g/dL	WBC 17.6 × 10 ³ /mm ³
K 4.1 mEq/L	Hct 19.4%	Neutros 78%
Cl 102 mEq/L	Plt 200 × 10 ³ /mm ³	Bands 8%
CO ₂ 25 mEq/L	RDW 14.2%	Lymphs 12%
BUN 15 mg/dL	MCV 81.1 mm ³	Monos 2%
SCr 0.8 mg/dL	MCH 26.3 pg/cell	Alb 2.1 g/dL
Glu 98 mg/dL	MCHC 34 g/dL	INR 1.0
ESR 140 mm/hr	CRP 12 mg/L	Lactate 2.0 mmol/L

■ **Urine Drug Screen**

Positive for opiates, benzodiazepines, and cannabinoids.

■ **Urine Culture**

Urinalysis: Trace leukocyte esterase, trace nitrite, bacteria present,

WBC <5/hpf, RBC, <5/hpf, epithelial cells 10/hpf

Urine culture: 10–100,000 gram-negative rods

■ **ECG**

Sinus tachycardia. Nonspecific T-wave changes.

■ **Chest X-Ray**

Normal heart size. Small lower lobe infiltrates. Correlate clinically.

■ **CT Chest**

Multiple small nodular lesions consistent with septic pulmonary emboli

■ **Blood Cultures**

Two sets from right hand, collected and pending (drawn @ 0100)

Two sets from left antecubital, collected and pending (drawn @ 1400)

■ **Assessment**

A 27-year-old woman with recent intravenous drug use presenting s/p naloxone in the field with sepsis and probable infective endocarditis.

QUESTIONS

Collect Information

- What subjective and objective criteria indicate the presence of infective endocarditis in this patient?
- What additional information is needed to fully assess this patient?

■ **CLINICAL COURSE (PART 1)**

Ms Meyer is initiated on vancomycin, aztreonam, and tobramycin. Review of the electronic medical record reveals that she has received ceftriaxone in the past without a documented reaction. The transthoracic echocardiogram demonstrates a 5-mm vegetation on the tricuspid valve with no evidence of valvular dysfunction or perivalvular abscess. Magnetic resonance imaging of the spine shows only chronic changes and no evidence of vertebral osteomyelitis. Four out of four blood culture sets result positive with Gram stain demonstrating gram-positive cocci in clusters. The rapid diagnostic panel identifies the organism as *Staphylococcus aureus* and does not

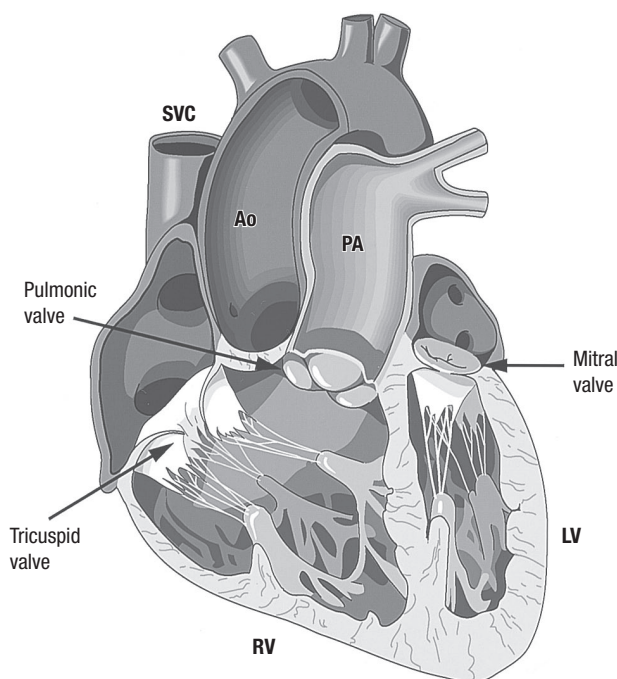


FIGURE 128-1. Diagram illustrating the location of the tricuspid, pulmonic, and mitral valves. Ao, aorta; LV, left ventricle; PA, pulmonary artery; RV, right ventricle; SVC, superior vena cava.

detect any resistance genes (*mecA*, *VanA*, *VanB*). The hepatitis C antibody test is positive and the fourth-generation HIV immunoassay is negative.

Assess the Information

- 2.a. Assess the location and severity of infective endocarditis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. Is it ethical to discharge this patient with an indwelling central venous catheter for outpatient parenteral antimicrobial therapy (OPAT)?
- 2.d. What ethical considerations are there regarding surgical management of this patient's infective endocarditis?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for infective endocarditis?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating *Staphylococcus aureus* native valve infective endocarditis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, schedules, and durations of therapy.

CLINICAL COURSE (PART 2)

On hospital day 3, the patient's vital signs have stabilized and she is transferred out of the intensive care unit to a floor bed. Ms Meyer refuses to engage in any discussions regarding her substance abuse

and is adamant that she will leave against medical advice if she is not discharged soon. Additionally, she is refusing to take a penicillin or a cephalosporin due to concern regarding her allergy, which occurred during childhood. Cardiothoracic surgery has evaluated the patient and deemed her to not be a good surgical candidate at this time point due to a lack of functional impairment in the valve and high risk for reinfection of any implanted prosthesis.

- 3.e. What alternatives would be appropriate due to Ms Meyer's refusal of all penicillins and cephalosporins? What are the options if she refuses to remain in the hospital or another monitored setting?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

CLINICAL COURSE (PART 3)

Ms Meyer has not been accepted by any skilled nursing facilities due to her low acuity, substance abuse history, and lack of medical insurance. She has agreed to remain in the hospital for the remainder of her antibiotic therapy.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Evaluate the clinical literature to identify studies assessing intravenous-to-oral antibiotic switch therapy for intravenous drug users with right-sided infective endocarditis due to methicillin-susceptible *S. aureus*.
2. Review the clinical literature assessing intravenous-to-oral antibiotic switch therapy for patients with left-sided infective endocarditis.
3. Assess the clinical literature evaluating two-week courses of antistaphylococcal penicillins with or without a concurrent aminoglycoside for left-sided infective endocarditis due to methicillin-susceptible *S. aureus* in intravenous drug users.
4. Interpret existing data on daptomycin as an alternative treatment for infective endocarditis due to methicillin-susceptible *S. aureus* in patients with suspected or confirmed type I allergy to β -lactams.

CLINICAL PEARL

The incidence of hospitalization for injection drug user-associated infective endocarditis increased approximately 12-fold between 2010 and 2015 in parallel with the opioid epidemic. These hospitalizations occur disproportionately among younger persons aged 18–25 years compared to those over 40 years of age. Hepatitis C co-infection occurs in roughly a third of these patients. There is an option to use 2 weeks of an antistaphylococcal β -lactam or

daptomycin for treatment of intravenous drug users with uncomplicated, right-sided infective endocarditis due to methicillin-susceptible *S. aureus*. Although not commonly employed in clinical practice, this regimen may help reduce the treatment burden in this challenging patient population.

REFERENCES

1. Baddour LM, Wilson WR, Bayer AS, et al. Infective endocarditis in adults: diagnosis, antimicrobial therapy, and management of complications. A scientific statement for healthcare professionals from The American Heart Association. *Circulation* 2015;132:1435–1486.
2. Habib G, Lancellotti P, Antunes MJ, et al. 2015 ESC guidelines for the management of infective endocarditis: the Task Force for the Management of Infective Endocarditis of the European Society of Cardiology (ESC). Endorsed by: European Association for Cardio-Thoracic Surgery (EACTS), the European Association of Nuclear Medicine (EANM). *Eur Heart J* 2015;36(44):3075–3128.
3. Fleischauer AT, Ruhl L, Rhea S, Barnes E. Hospitalizations for endocarditis and associated health care costs among persons with diagnosed drug dependence. *MMWR Morb Mortal Wkly Rep* 2017;66(22):569–673.
4. Hull SC, Jadbabaie F. When is enough enough? The dilemma of valve replacement in a recidivist intravenous drug user. *Ann Thorac Surg* 2014;97(5):1486–1487.
5. Eljaaly K, Alshehri S, Erstad BL. Systematic review and meta-analysis of the safety of antistaphylococcal penicillins compared to cefazolin. *Antimicrob Agents Chemother* 2018;62(4). pii: e01816–17.
6. Gudiol C, Cuervo G, Shaw E, Pujol M, Carratala J. Pharmacotherapeutic options for treating *Staphylococcus aureus* bacteremia. *Expert Opin Pharmacother* 2017;18(18):1947–1963.
7. McDanel JS, Perencevich EN, Diekema DJ, et al. Comparative effectiveness of beta-lactams versus vancomycin for treatment of methicillin-susceptible *Staphylococcus aureus* bloodstream infections among 122 hospitals. *Clin Infect Dis* 2015;61(3):361–367.
8. Schweizer ML, Furuno JP, Harris AD, et al. Comparative effectiveness of nafcillin or cefazolin versus vancomycin in methicillin-susceptible *Staphylococcus aureus* bacteremia. *BMC Infect Dis* 2011;11:279.
9. Crass RL, Powell KL, Huang AM. Daptomycin for the treatment of *Staphylococcus aureus* infections complicated by pulmonary septic emboli. *Diag Microbiol Infect Dis* 2019;93(2):131–135.

129

TUBERCULOSIS

Close Encounters Level II

Sharon M. Erdman, PharmD, FIDP

Kendra M. Damer, PharmD, FIDP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the common signs and symptoms, physical examination, laboratory, and radiographic findings in a patient with active pulmonary tuberculosis.
- Design a therapeutic regimen for treatment of a patient with newly diagnosed active pulmonary tuberculosis based on clinical presentation, patient-specific history and physical characteristics,

subjective and objective findings, comorbidities, and desired clinical response.

- Define the goals of therapy for a patient with active pulmonary tuberculosis, as well as the monitoring parameters that should be used to assess the response to therapy and to prevent/minimize the occurrence of adverse effects.
- Provide patient education on the proper administration of drug therapy for active pulmonary tuberculosis including directions for use, administration of therapy in relation to meals, the importance of adherence, and potential side effects of the medications.
- Recognize potential drug interactions that may occur with anti-tuberculosis medication.

PATIENT PRESENTATION

Chief Complaint

“I have been coughing up blood for the past 3 days.”

HPI

José Rodriguez is a 35-year-old Hispanic man who presents to the ED at the county hospital in Indianapolis, Indiana with a 3- to 4-week history of a productive cough, which was originally productive of yellow sputum but is now accompanied by the presence of blood streaks in the sputum for the past 3 days. He also complains of subjective fevers, chills, night sweats, dyspnea that worsens on exertion, fatigue, and an unintentional 20-lb weight loss over the past several weeks.

PMH

None

FH

Mother has DM and HTN.

Father died of MI 6 months ago.

SH

The patient moved to the United States from Mexico 4 years ago but has not recently traveled. Patient has a 10-pack-year history of smoking but quit several weeks ago when the current illness started. The patient denies illicit drug use but does report drinking alcohol socially on weekends. He is a laborer and is currently working for cash on a new home construction project in close contact with other workers. Several of his coworkers have recently moved to the United States from Mexico and have similar respiratory symptoms. The patient does not have any medical insurance. He lives with several adult friends in an apartment.

Meds

Over-the-counter antitussives, which have not provided any relief

All

No known drug allergies

ROS

Negative except for the complaints noted above

Physical Examination

Gen

Somewhat thin-appearing Hispanic man in mild respiratory distress

VS

BP 131/70, P 100, RR 24, T 38.8°C, 93% O₂ saturation on room air; Wt 65 kg, Ht 5'9"

Skin

No lesions

HEENT

PERRLA, EOMI, no scleral icterus

Neck

Supple

Chest

Rhonchi and dullness to percussion in RUL

CV

Slightly tachycardic, no MRG

Abd

Soft NTND; (+) bowel sounds; no hepatosplenomegaly

Ext

No CCE, pulses 2+ throughout; full ROM

Neuro

A&O × 3; CN II–XII intact; reflexes 2+, sensory and motor levels intact

■ Labs

Na 143 mEq/L	Hgb 11.6 g/dL	WBC $12.3 \times 10^3/\text{mm}^3$	Bili 0.6 mg/dL
K 3.7 mEq/L	Hct 34.8%	Neutros 74%	Alk phos 120 IU/L
Cl 106 mEq/L	RBC $3.8 \times 10^6/\text{mm}^3$	Bands 8%	ALT 45 IU/L
CO ₂ 22 mEq/L	Plt $269 \times 10^3/\text{mm}^3$	Lymphs 10%	AST 34 IU/L
BUN 21 mg/dL	MCV 92 μm^3	Monos 8%	
SCr 0.9 mg/dL	MCHC 33 g/dL		
Glu 101 mg/dL			

Tuberculin skin test (TST) result: Pending

Interferon gamma release assay (IGRA): Pending

Sputum AFB smear: Numerous AFB (Fig. 129-1)

XPert® MTB/RIF real-time PCR: Pending

Sputum AFB culture: Pending

HIV antibody test (fourth-generation HIV antibody/antigen ELISA + supplemental antibody differentiation immunoassay): Pending

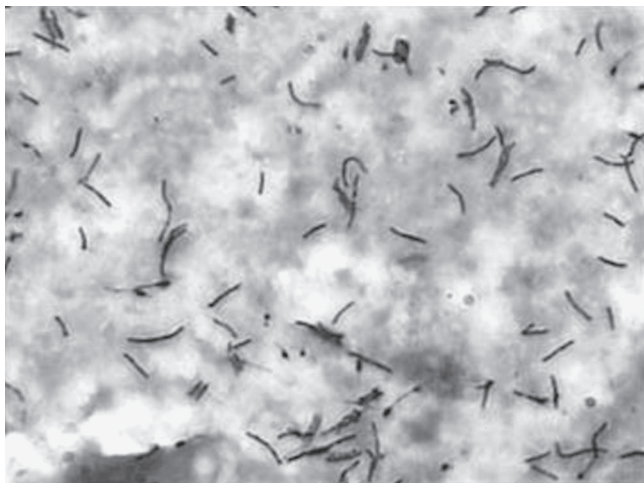


FIGURE 129-1. AFB smear. AFB (shown as thin rods) are tubercle bacilli.

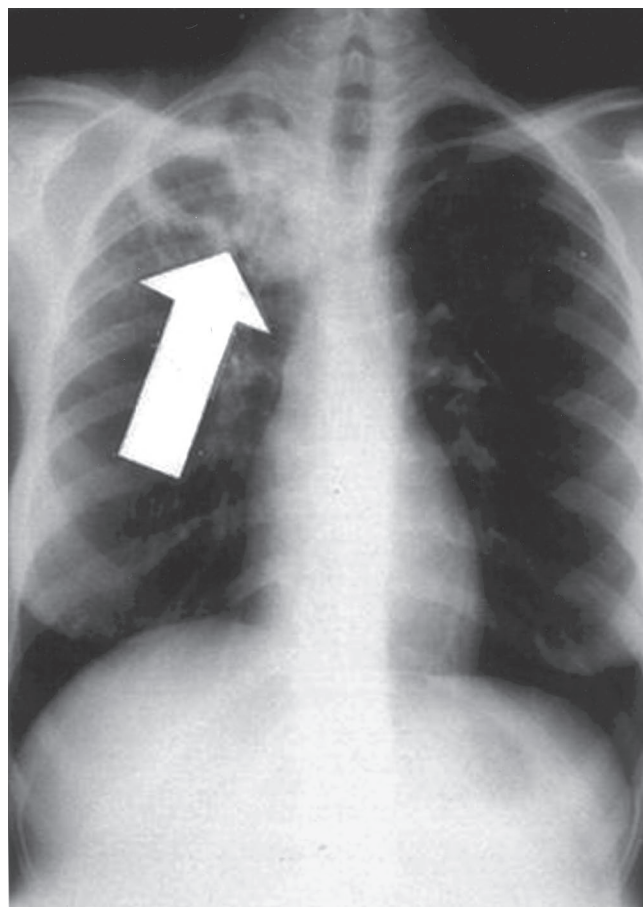


FIGURE 129-2. Chest radiograph. Arrow points to cavitation in patient's upper right lobe.

■ Radiology

CXR: RUL cavitory lesion with surrounding consolidation/air space disease (Fig. 129-2)

Chest CT: Focal airspace disease with tree-in-bud pattern in the RUL, including a cavitory lesion measuring 3.5 cm × 3.5 cm. Right hilar lymphadenopathy with scattered mediastinal lymphadenopathy. There is no pleural effusion or pneumothorax. Findings are consistent with active tuberculosis infection.

■ Assessment

Active pulmonary tuberculosis

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence of active pulmonary tuberculosis in this patient?
- 1.b. What additional information is needed to fully assess this patient's tuberculosis?

Assess the Information

- 2.a. Assess the severity of this patient's active pulmonary tuberculosis based on the subjective and objective information available.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic and social considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in the treatment of active pulmonary tuberculosis?
- 3.b. What nondrug therapies should be considered in managing patients with active pulmonary tuberculosis?
- 3.c. What feasible pharmacologic therapies and dosing strategies are available for the treatment of active pulmonary tuberculosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drug regimen(s) with specific drugs, dosage forms, doses, schedules for administration, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, minimize adverse effects, and avoid drug interactions?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient was admitted to the hospital and placed into respiratory isolation in a negative-pressure hospital room. Because the initial sputum sample demonstrated the presence of numerous AFB, the patient was started on the antituberculosis therapy you recommended while waiting for the results of culture and susceptibility tests. Later that day, the XPert® MTB/RIF real-time PCR result performed on the sputum smear sample revealed the presence of *Mycobacterium tuberculosis* complex, and rifampin (RIF) resistance was not detected.

On hospital day 2, his TST was measured as 20 mm, the IGRA was positive, and his HIV test result was negative. The patient tolerated the antituberculosis regimen during the initial weeks of therapy, and subsequent sputum AFB smears became negative 2 weeks after initiation of therapy. The sputum AFB culture eventually grew *M. tuberculosis*, which was susceptible to isoniazid, rifampin, pyrazinamide, ethambutol, and streptomycin. During the third week of antituberculosis therapy, an increase in the patient's AST (140 IU/L) and ALT (120 IU/L) was noted, although the patient remained asymptomatic. The total bilirubin and alkaline phosphatase remained within normal limits. Follow-up mycobacterial sputum cultures obtained after 2 months of antituberculosis therapy were negative.

FOLLOW-UP CASE QUESTIONS

1. What factors place this patient at increased risk for acquiring TB?
2. How should other close contacts of the patient be evaluated and treated?
3. How should the results of the susceptibility report of this patient's *M. tuberculosis* isolate influence his drug therapy?
4. How should the increase in AST and ALT in this patient be managed? What changes should be made to the current antituberculosis regimen and/or monitoring plan?
5. How should AST and ALT elevations greater than five times the upper limit of normal be managed in a patient on antituberculosis therapy?

SELF-STUDY ASSIGNMENTS

1. Review the differences (eg, methodology, turnaround time, advantages, disadvantages, cost) between the TST and IGRAs in the diagnosis of active pulmonary and latent tuberculosis. Discuss the populations or scenarios where the IGRA may be preferred over the TST.
2. Review the safety and efficacy of rifapentine in managing active pulmonary tuberculosis and latent tuberculosis.
3. Perform a literature search to determine the national and regional rates of isoniazid resistance in clinical isolates of *M. tuberculosis*. How do these rates compare with those reported in other areas of the world where tuberculosis is endemic?
4. Review the management strategies of active pulmonary tuberculosis in an HIV-infected patient on antiretroviral therapy, with special attention to potential drug interactions between first-line antituberculosis agents and the non-nucleoside reverse transcriptase inhibitors or protease inhibitors.

CLINICAL PEARL

The treatment of tuberculosis in patients with HIV infection is often modified based on the many drug interactions that can occur among the rifamycins and antiretroviral agents.

REFERENCES

1. Sia IG, Wieland ML. Current concepts in the management of tuberculosis. *Mayo Clin Proceed* 2011;86(4):348–361.
2. American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America Clinical Practice Guidelines. Treatment of drug-susceptible tuberculosis. *Clin Infect Dis* 2016; 63(7):e147–e195.
3. American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America Clinical Practice Guidelines. Treatment of tuberculosis. *Am J Respir Crit Care Med* 2003;167:603–662.
4. American Thoracic Society, Centers for Disease Control and Prevention, Infectious Diseases Society of America. Controlling tuberculosis in the United States. *Am J Respir Crit Care Med* 2005;172: 1169–1227.
5. Official American Thoracic Society/Infectious Diseases Society of America/Centers for Disease Control and Prevention Clinical Practice Guidelines: Diagnosis of tuberculosis in adults and children. *Clin Infect Dis* 2017;64:e1–e33.
6. Hass MK, Belknap RW. A review of rifapentine for the treating active and latent tuberculosis. *Clin Invest (Land)* 2015;5:1–10.

7. CDC. Reported Tuberculosis in the United States, 2016. Atlanta, GA: U.S. Department of Health and Human Services, CDC; November 2017.
8. Gilpin C, Korobitsyn A, Weyer K. Current tools available for the diagnosis of drug-resistant tuberculosis. *Ther Adv Infectious Dis* 2016;3:145–151.
9. Chang KC, Leung CC, Yew WW, Chan SL, Tam CM. Dosing schedules of 6-month regimens and relapse for pulmonary tuberculosis. *Am J Respir Crit Care Med* 2006;174:1153–1158.
10. Saukkonen JJ, Cohn DL, Jasmer RM, et al. An official ATS statement: hepatotoxicity of antituberculosis therapy. *Am J Respir Crit Care Med* 2006;174:935–952.

130

CLOSTRIDIoidES DIFFICILE INFECTION

You Want to Transplant What?? Level II

Michael J. Gonyeau, BS, MEd, PharmD, FCCP, BCPS

Brandon Dionne, PharmD, BCPS-AQ ID, BCIDP, AAHIVP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify signs and symptoms of *Clostridioides difficile* infection (CDI).
- Discuss CDI complications and prevention strategies.
- Evaluate treatment options and develop an optimal patient-specific treatment plan for initial and recurrent CDI, including drug, dose, frequency, route of administration, and duration of therapy.
- Develop a pertinent monitoring plan for a CDI regimen from a therapeutic and toxic standpoint.

PATIENT PRESENTATION

■ Chief Complaint

“I have been having to go to the bathroom a lot more frequently, and my stomach hurts a lot.”

■ HPI

Bernice Cooper, a 68-year-old woman, is transferred to your medical team from the MICU after being admitted for sepsis secondary to a urinary tract infection and hypotension requiring pressor support. Over the past 2 days, she has been complaining of frequent foul-smelling stools. One week prior to being transferred to your team, she was admitted to the hospital complaining of urinary frequency and urgency for 3 days, nausea, vomiting, and left-sided flank pain, as well as light-headedness and dizziness. In the ED, the patient was hypotensive (BP 92/63 mm Hg) and tachycardic (HR 112–124 bpm), with an elevated lactate level and leukocytosis. She was transferred to the MICU for pressor support and started on an empiric regimen of cefepime and vancomycin 1 g IV Q 12 H for suspected urosepsis. Urine (×2) and blood (×3) cultures were

subsequently found to be growing *Escherichia coli* and enteric gram-negative rods, respectively, and antibiotic coverage was narrowed to ceftriaxone 2 g IV daily on day 5. The patient’s blood pressure was stabilized, no ileus was detected, and she was transferred to the internal medicine service on day 7 of hospitalization. She is now complaining of new-onset diarrhea and abdominal pain.

■ PMH

CDI 2 months ago
Hyperlipidemia
HTN
s/p MI 2003

■ SH

Lives at home alone, lifetime smoker (half pack per day for 54 years), drinks alcohol socially

■ Medications

Metoprolol XL 100 mg PO once daily
Lisinopril 10 mg PO once daily
Atorvastatin 10 mg PO once daily
Pantoprazole 40 mg PO once daily

■ All

NKDA

■ Physical Examination

Gen

Patient is overweight and complains of abdominal discomfort.

VS

BP 149/85, P 98, RR 20, T 38.8°C; Ht 5’8”, Wt 87.2 kg

Skin

Warm and moist secondary to diaphoresis, no lesions

HEENT

PERRLA; EOMI; TMs intact; clear oropharynx, moist oral mucosa

Neck/Lymph Nodes

Neck is supple and without adenopathy; no JVD.

Lungs/Thorax

CTA

CV

RRR; normal S₁, S₂; no murmurs

Abd

Abdomen is soft and nondistended, diffusely tender to palpation. Slight rebound and guarding. Positive bowel sounds.

Genit/Rect

Not performed

MS/Ext

Muscle strength and tone 5/5 in upper and lower; no C/C/E

Neuro

A&O × 3; CN II–XII intact

■ Labs

Na 138 mEq/L	Hgb 16.1 g/dL	WBC $16.9 \times 10^3/\text{mm}^3$	T. chol 205 mg/dL
K 3.5 mEq/L	Hct 49.8%	Neutros 50%	LDL 137 mg/dL
Cl 102 mEq/L	Plt $375 \times 10^3/\text{mm}^3$	Bands 9%	HDL 29 mg/dL
CO ₂ 22 mEq/L	A1C 7.9%	Eos 0%	Trig 197 mg/dL
BUN 36 mg/dL		Lymphs 34%	
SCr 1.8 mg/dL		Monos 7%	
(baseline 0.9 mg/dL)			
Glu 101 mg/dL			
Alb 1.9 mg/dL			

■ CXR

Clear

■ ECG

NSR, unchanged from previous

■ *Clostridioides difficile* GDH/toxin EIA test

GDH antigen and A/B toxin assay both positive

■ Assessment

A 68-year-old woman presents with frequent, foul-smelling stools for 2 days with recent history of receiving broad-spectrum antibiotics and currently receiving ceftriaxone for pyelonephritis and a bloodstream infection (day 9); *C. difficile* antigen/toxin positive.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of CDI?
- 1.b. What additional information is needed to fully assess this patient's CDI?

Assess the Information

- 2.a. Assess the severity of CDI based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating CDI?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTIONS

1. What changes would you make to the care plan if the patient does not respond to initial therapy?
2. What should be done if the patient develops similar signs and symptoms 3 weeks after successful CDI treatment?
3. Your medical team wants to start the patient on loperamide 2 mg PO after each bowel movement to control diarrhea. Do you agree with this course of action? Why or why not?

■ SELF-STUDY ASSIGNMENTS

1. Evaluate the relationship between PPI use and CDI recurrence and develop a plan to assess patient need for PPI use on discharge.
2. Conduct a literature search and develop a policy regarding infection control procedures to reduce the risk of CDI.
3. Assess the potential use of probiotics as an adjunct in the treatment and prevention of recurrent CDI.
4. Conduct a literature search to assess the cost-effectiveness and/or cost utility of fecal microbiota transplant in the treatment of recurrent CDI.

CLINICAL PEARL

While fidaxomicin has a higher drug cost than oral vancomycin, the higher rate of global cure may make it more cost-effective in patients at higher risk for recurrence due to decreased hospital readmissions. It is important to consider transitions of care (ie, ensuring that the patient will be able to afford the fidaxomicin) before initiating it.

REFERENCES

1. Bagdasarian N, Rao K, Malani PN. Diagnosis and treatment of *Clostridium difficile* in adults: a systematic review. *JAMA* 2015;313:398–408.
2. McDonald LC, Gerding DN, Johnson S, et al. Clinical practice guidelines for *Clostridium difficile* infection in adults and children: 2017 update by the Infectious Diseases Society of America (IDSA) and Society for Healthcare Epidemiology of America (SHEA). *Clin Infect Dis* 2018;66:987–994.
3. Magill SS, Edwards JR, Bamberg W, et al. Multistate point-prevalence survey of health care-associated infections. *N Engl J Med* 2014;370:1198–1208.
4. Brown KA, Khanafer N, Daneman N, Fisman DN. Meta-analysis of antibiotics and the risk of community-associated *Clostridium difficile* infection. *Antimicrob Agents Chemother* 2013;57:2326–2332.
5. Azab M, Doo L, Doo DH, et al. Comparison of the hospital-acquired *Clostridium difficile* infection risk of using proton pump inhibitors versus histamine-2 receptor antagonists for prophylaxis and treatment of stress ulcers: a systematic review and meta-analysis. *Gut Liver* 2017;11:781–788.
6. Gallagher JC, Reilly JP, Navalkele B, et al. Clinical and economic benefits of fidaxomicin compared to vancomycin for *Clostridium difficile* infection. *Antimicrob Agents Chemother* 2015;59:7007–10.

7. Wilcox MH, Gerding DN, Poxton IR, et al. Bezlotoxumab for prevention of recurrent *Clostridium difficile* infection. *N Engl J Med* 2017;376:305–317.
8. Flack JM, Calhoun D, Schiffrin EL. The new ACC/AHA hypertension guidelines for the prevention, detection, evaluation, and management of high blood pressure in adults. *Am J Hypertension* 2018;31(2):133–135.
9. Grundy SM, Stone NJ, Bailey AL, et al. 2018 AHA/ACC/AACVPR/AAPA/ABC/ACPM/ADA/AGS/APhA/ASPC/NLA/PCNA guideline on the management of blood cholesterol: a report of the American College of Cardiology/American Heart Association task force on clinical practice guidelines. *J Am Coll Cardiol* 2018;25709. doi: 10.1016/j.jacc.2018.11.003.

131

INTRA-ABDOMINAL INFECTION

Like Mother, Like Son Level II

Paulina Deming, PharmD, PhC

Renee-Claude Mercier, PharmD, BCPS, PhC

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the clinical manifestations of spontaneous bacterial peritonitis (SBP; also known as primary bacterial peritonitis).
- List the goals of antimicrobial therapy for SBP.
- Recommend appropriate therapy for SBP.
- Monitor therapy for SBP for safety and efficacy.
- Recommend secondary prophylaxis for SBP.

PATIENT PRESENTATION

■ Chief Complaint

“My belly hurts so bad I can barely move.”

■ HPI

John Chavez is a 47-year-old Hispanic man who was brought to the ED by his wife. She stated that he has been suffering from nausea, vomiting, and severe abdominal pain for the past 2–3 days. His intake of food and fluids has been minimal over the past several days.

■ PMH

Cirrhosis, diagnosed last year with onset of ascites
Cholecystectomy 15 years ago

■ FH

Mother was alcoholic; died 10 years ago in car accident. Father’s history unknown.

■ SH

Retired construction worker; EtOH abuse with 10–12 cans of beer per day × 25 years and occasional heavier use on weekends; denies use of tobacco or illicit drugs; inconsistent adherence to medications; per patient’s wife he avoids salt but confirms he eats fast food two to three times per week

■ Meds

Furosemide 40 mg PO once daily
Acetaminophen 325 mg PO PRN for pain

■ All

NKDA

■ ROS

As noted in the HPI. Denies any hematemesis or melena.

■ Physical Examination

Gen

Thin man who appears older than his stated age, with a distended abdomen and in severe pain

VS

BP 154/82, P 102, RR 32, T 38.2°C; current Wt 92 kg, (IBW 68 kg)

Skin

Jaundiced, warm, coarse, and very dry. Spider angiomas present on chest, back and arms.

HEENT

Yellow sclera; PERRLA; Oropharynxes show poor dentition but are otherwise unremarkable.

Neck/Lymph Nodes

Supple; normal-size thyroid; no JVD or palpable lymph nodes

Chest

Lungs are CTA; shallow and frequent breathing

Heart

Tachycardia, normal S₁ and S₂ with no S₃ or S₄

Abd

Distended; pain on pressure or movements; pain is sharp and diffuses throughout abdomen; (+) guarding. (+) HSM. Decreased bowel sounds.

Genit/Rect

Prostate normal size; guaiac (–) stool

Ext

No clubbing or cyanosis; bilateral pitting pedal edema 1+

Neuro

Oriented to person and place; lethargic and apathetic, slumped posture, slowed movements

■ Labs

Na 142 mEq/L	Hgb 13.1 g/dL	AST 90 IU/L
K 3.9 mEq/L	Hct 40.6%	ALT 60 IU/L
Cl 96 mEq/L	Plt $65 \times 10^3/\text{mm}^3$	Alk phos 350 IU/L
CO ₂ 20 mEq/L	WBC $12.25 \times 10^3/\text{mm}^3$	T. bili 2.2 mg/dL
BUN 44 mg/dL	Neutros 73%	D. bili 1.8 mg/dL
SCr 1.2 mg/dL	Bands 9%	Albumin 2.8 g/dL
Glu 101 mg/dL	Lymphs 13%	INR 1.34
	Monos 5%	

■ Abdominal Ultrasound

Nodular liver consistent with cirrhosis; ascites; splenomegaly

■ Blood Cultures

Pending $\times 2$

■ Paracentesis

Ascitic fluid: leukocytes $720/\text{mm}^3$, protein 2.8 g/dL, albumin 1.1 g/dL, pH 7.28, lactate 30 mg/dL. Gram stain: numerous PMNs, no organisms.

■ Assessment

SBP

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of spontaneous bacterial peritonitis (SBP)?
- 1.b. What additional information is needed to fully assess this patient's SBP?

Assess the Information

- 2.a. Assess the severity of SBP based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating SBP?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan for SBP fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The blood cultures were reported positive for *Klebsiella pneumoniae*; resistant to ampicillin and ampicillin/sulbactam; and sensitive to aztreonam, ceftriaxone, levofloxacin, gentamicin, and piperacillin/tazobactam. The ascitic fluid culture grew *K. pneumoniae* as well. The patient received cefotaxime 2 g IV Q 8 H for a total of 7 days. After 3 days of antimicrobial treatment, repeat blood cultures were negative. He rapidly improved, and on discharge, his mental status had returned to baseline.

■ SELF-STUDY ASSIGNMENTS

1. Develop a table that illustrates the primary differences (clinical manifestations, pathogens involved, diagnosis methods, and treatment) between primary and secondary bacterial peritonitis.
2. Describe the pathophysiologic changes that occur in cirrhosis that contribute to the development of ascites and SBP.
3. Develop a table that compares the pharmacotherapeutic options for patients to assist in reducing alcohol cravings and consumption.
4. Develop a plan for nonpharmacologic management of patients with cirrhosis.

CLINICAL PEARL

Bacteremia is present in up to 75% of patients with primary peritonitis caused by aerobic bacteria but is rarely found in those with peritonitis caused by anaerobes. Ascitic fluid cultures are often negative, and a diagnosis of SBP is frequently made based on ascitic fluid PMN counts and the patient's clinical presentation.

REFERENCES

1. Garcia-Tsao G, Lim J; Veterans Affairs Hepatitis C Resource Center Program. Management and treatment of patients with cirrhosis and portal hypertension: recommendations from the department of Veterans Affairs Hepatitis C Resource Center Program and the National Hepatitis C Program. *Am J Gastroenterol* 2009;104:1802–1829.
2. Angeli P, Gines P, Wong F, et al. Diagnosis and management of acute kidney injury in patients with cirrhosis: revised consensus recommendations of the International Club of Ascites. *Gut* 2015;64:531–537.
3. Runyon BA, McHutchison JG, Antillon MR, Akriviadis EA, Montano AA. Short-course versus long-course antibiotic treatment of spontaneous bacterial peritonitis: a randomized controlled study of 100 patients. *Gastroenterology* 1991;100:1737–1742.
4. Runyon BA. American Association for the Study of Liver Diseases (AASLD) practice guideline: management of adult patients with ascites due to cirrhosis: update 2012. Available at: <https://www.aasld.org/publications/practice-guidelines-0>. Accessed December 30, 2018.
5. Fernandez J, Tandon P, Mensa J, Garcia-Tsao G. Antibiotic prophylaxis in cirrhosis: good and bad. *Hepatology* 2016;63:2019–2031.
6. Wiest R, Krag A, Gerbes A. Spontaneous bacterial peritonitis: recent guidelines and beyond. *Gut* 2012;61:297–310.

132

LOWER URINARY TRACT INFECTION

Where Is the Bathroom? Level I

Melissa E. Badowski, PharmD, MPH, FCCP, BCIDP, BCPS, AAHIVP

Sharon M. Erdman, PharmD, FIDP

Keith A. Rodvold, PharmD, FCCP, FIDSA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize common signs and symptoms of acute uncomplicated cystitis/urinary tract infections (UTIs) in females.
- Design a therapeutic regimen for the treatment of acute uncomplicated cystitis after consideration of symptoms, medical history, allergies, objective findings, drug–drug interactions, and desired clinical response.
- Describe parameters that should be monitored during the treatment of acute uncomplicated cystitis to ensure efficacy and minimize toxicity.
- Provide patient education on the proper administration of antibiotic therapy for acute uncomplicated cystitis, including directions for use, administration of therapy in relation to meals, importance of medication adherence (including the need to complete the entire prescribed course), proper storage, and potential side effects of the medication.

PATIENT PRESENTATION

■ Chief Complaint

“It burns when I urinate. I am urinating all the time.”

■ HPI

A 26-year-old woman presents to a family medicine clinic in Seattle with complaints of dysuria, urinary frequency and urgency, and suprapubic tenderness for the past 2 days.

■ PMH

Patient has been previously diagnosed with three UTIs over the past 8 months based on symptoms. Each episode was treated with oral TMP/SMX.

■ FH

Mother has DM; remainder of FH is noncontributory.

■ SH

Denies smoking but admits to occasional marijuana and social EtOH use. Patient has been sexually active with one partner for the past 9 months and typically uses spermicide-coated condoms for contraception.

■ Meds

None

■ All

No known allergies

■ ROS

Patient reports urethral pain and burning with urination, as well as mild suprapubic tenderness. She denies systemic symptoms such as fever, chills, vomiting, or back pain, and does not report any urethral or vaginal discharge. Upon further questioning, she notes that the UTIs started soon after she met her boyfriend, and she does not always completely empty her bladder after sexual intercourse.

■ Physical Examination

Gen

Cooperative woman in no acute distress

VS

BP 110/60, P 68, RR 16, T 36.8°C; Wt 57 kg, Ht 5'5"

Skin

No skin lesions

HEENT

PERRLA; EOMI; TMs intact

Neck/Lymph Nodes

Supple without lymphadenopathy

Chest

CTA

CV

RRR, no MRG

Back

No CVA tenderness

Abd

Soft; (+) bowel sounds; no organomegaly or tenderness

Pelvic

No vaginal discharge or lesions; LMP 2 weeks ago; mild suprapubic tenderness

Ext

Pulses 2+ throughout; full ROM

Neuro

A&O × 3; CN II–XII intact; reflexes 2+; sensory and motor levels intact

■ Labs

Urinalysis

Yellow, cloudy; pH 5.0; WBC 50 cells/hpf; RBC 1–5 cells/hpf; protein (–); trace blood; glucose (–); leukocyte esterase (+); nitrite (+); many bacteria (Fig. 132-1)

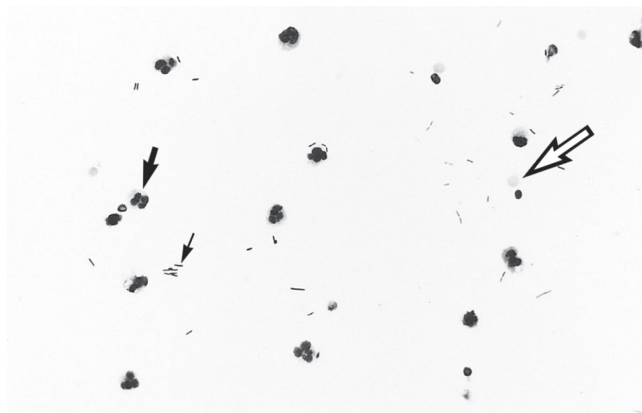


FIGURE 132-1. Urine sediment with neutrophils (solid arrow), bacteria (small arrow), and occasional red blood cells (open arrow) (Wright–Giemsa $\times 1650$). (Photo courtesy of Lydia C. Contis, MD.)

Urine Culture

Not performed

■ Assessment

Acute uncomplicated cystitis (Fig. 132-2)

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of acute uncomplicated cystitis in this patient?
- 1.b. What additional information is needed to fully assess this patient's acute uncomplicated cystitis?

Assess the Information

- 2.a. Assess the severity of this episode of acute uncomplicated cystitis based on the subjective and objective information available.

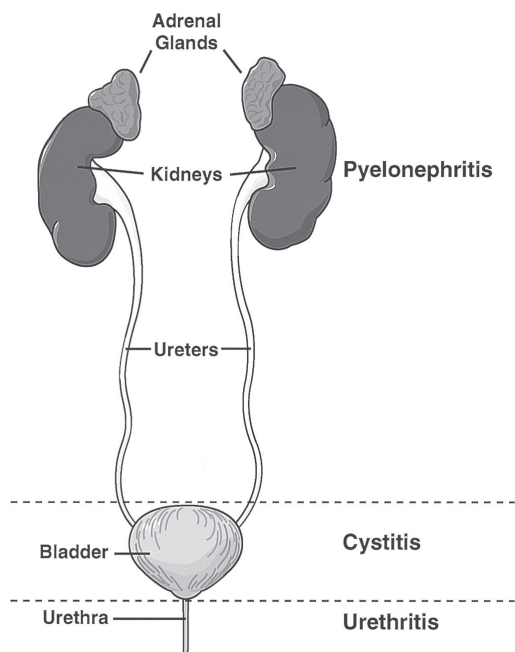


FIGURE 132-2. Anatomy and associated infections of the urinary tract.

- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient's acute uncomplicated cystitis?
- 3.c. What feasible pharmacotherapeutic alternatives are available for empiric first- and second-line treatment of acute uncomplicated cystitis?
- 3.d. Create a patient-centered care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan for acute uncomplicated cystitis fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTION

1. What long-term treatment strategies could be employed for this patient to prevent further episodes of acute uncomplicated cystitis?

■ SELF-STUDY ASSIGNMENTS

1. Review the safety and efficacy of single-dose, 3-, 5-, and 7-day antimicrobial therapy for the treatment of acute uncomplicated cystitis.
2. Perform a literature search to obtain current data on the national and regional rates of resistance of outpatient urinary tract isolates of *Escherichia coli* to TMP/SMX and fluoroquinolone antibiotics. How do these rates compare with those reported at your institution, your clinic, or your geographic area?
3. If this patient were pregnant, what antibiotics would be appropriate for treatment?
4. Differentiate between reinfection and relapse infection.

CLINICAL PEARL

UTIs occur rarely in young males, unless there is an underlying structural abnormality or instrumentation of the urinary tract.

REFERENCES

1. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52:e103–e120.
2. Hooton TM. Clinical practice. Uncomplicated urinary tract infection. *N Engl J Med* 2012;366:1028–1037.
3. Dielubanza EJ, Schaeffer AJ. Urinary tract infections in women. *Med Clin North Am* 2011;95:27–41.
4. Walker E, Lyman A, Gupta K, Mahoney MV, Snyder GM, Hirsch EB. Clinical management of an increasing threat: outpatient urinary tract infections due to multidrug-resistant uropathogens. *Clin Infect Dis* 2016;63:960–965.
5. Gupta K, Grigoryan L, Trautner B. Urinary tract infection. *Ann Intern Med* 2017;167:ITC49–64.
6. Etienne M, Lefebvre E, Frebourg N, et al. Antibiotic treatment of acute uncomplicated cystitis based on rapid urine test and local epidemiology: lessons from a primary care series. *BMC Infect Dis* 2014;14:137–144.
7. Stapleton AE, Dziura J, Hooton TM, et al. Recurrent urinary tract infection and urinary *Escherichia coli* in women ingesting cranberry juice daily: a randomized controlled trial. *Mayo Clin Proc* 2012;87:143–150.
8. Cunha BA, Cunha CB, Lam B, et al. Nitrofurantoin safety and effectiveness in treating acute uncomplicated cystitis (AUC) in hospitalized adults with renal insufficiency: antibiotic stewardship implications. *Eur J Clin Microbiol Infect Dis* 2017;36:1213–1216.
9. Sanchez GV, Babiker A, Master RN, Luu T, Mathur A, Bordon J. Antibiotic resistance among urinary isolates from female outpatients in the United States in 2003 and 2012. *Antimicrob Agents Chemother* 2016;60:2680–2683.
10. Gupta K. Emerging antibiotic resistance in urinary tract pathogens. *Infect Dis Clin North Am* 2003;17:243–259.

133

PYELONEPHRITIS

Resistant Rod Level II

Elizabeth A. Coyle, PharmD, FCCM, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Differentiate the signs, symptoms, and laboratory findings associated with pyelonephritis from those seen in lower urinary tract infections.
- Recommend appropriate empiric antimicrobial and symptomatic pharmacotherapy for a patient with suspected pyelonephritis.
- Make appropriate adjustments in pharmacotherapy based on patient response and culture results, recognizing the prevalence of *Escherichia coli* and the risk of resistance.
- Design a monitoring plan for a patient with pyelonephritis that allows objective assessment of the response to therapy.

PATIENT PRESENTATION

■ Chief Complaint

“I can’t get warm and my back is killing me.”

■ HPI

Isabella Toms is a 24-year-old college student with type 1 diabetes, who presents to the ED complaining that she has had pain in her right flank region over the last 24 hours, as well as pain in her abdomen. She complains of some nausea and reports that she woke up this morning with severe stomach and back pain, but has not vomited. The patient states she has not eaten for 24 hours, but has been able to drink water and non-diet soda, and has continued to keep her insulin pump on, but has not given any additional regular insulin. The patient reports she recently started treatment for a urinary tract infection about 2 days ago with trimethoprim/sulfamethoxazole. She states that she has been feeling feverish and has chills. She reports no substernal chest pain, shortness of breath, cough, or sputum production. She denies any diarrhea or rash.

■ PMH

Type 1 diabetes, diagnosed at age 11; has an insulin pump

■ FH

Mother and father are in their 40s and healthy; one sister with asthma, and an older brother with Crohn disease

■ SH

Nonsmoker, no IVDA, drinks alcohol socially. Single, but has a steady boyfriend and is sexually active. Currently is a first-year law student at the local university.

■ Meds

Ortho-Novum 7/7/7 one tablet daily
 Insulin pump; regular insulin basal rate of 28 units per day
 Regular insulin 2 units with breakfast, lunch, and supper
 Trimethoprim/sulfamethoxazole one double strength tablet twice daily for 3 days (she has completed 2 days of therapy)

■ All

No known drug allergies

■ ROS

She has a history of UTIs and has had two UTIs in the past year, the most recent 2 days ago.

■ Physical Examination

Gen

Conscious, alert, and oriented young Caucasian woman in mild distress

VS

BP 120/72, P 68, RR 16, T 39.0°C, O₂ sat 98% room air; Wt 65 kg (IBW 61.1 kg), Ht 5’7”

Skin

No tenting; dry skin; no signs of redness or rash

HEENT

EOMI; fundoscopic examination WNL; pharynx clear and dry

Neck

Supple, no JVD

Chest

CTA

CV

RRR

Abd

Soft with suprapubic tenderness to deep palpation; no rebound or guarding; active bowel sounds. There is no hepatosplenomegaly or masses.

Back

No paraspinal or spinal tenderness

Genit/Rect

Normal female genitalia; no abnormal vaginal discharge; normal sphincter tone; last menstrual period 1 week ago

Ext

No CCE; pulses 2+ bilaterally

Neuro

A&O × 3; CN II–XII intact; sensory and perception intact

Labs and UA on Admission

See Table 133-1.

TABLE 133-1 Laboratory Tests and Urinalyses on Days 1–3 of Hospitalization

Parameter (Units)	Day 1	Day 2	Day 3
Serum chemistry			
Na (mEq/L)	141	139	141
K (mEq/L)	3.9	4.0	4.1
Cl (mEq/L)	99	101	102
CO ₂ (mEq/L)	27	28	28
BUN (mg/dL)	25	18	12
SCr (mg/dL)	1.2	1.0	1.0
Glucose (mg/dL)	60	80	85
Hematology			
Hgb (g/dL)	13.9	13.8	13.6
Hct (%)	40.6	40.3	40.5
Plt (×10 ³ /mm ³)	275	276	276
WBC (×10 ³ /mm ³)	22.3	18.5	11.9
PMN/B/L/M (%)	80/13/7/0	85/10/5/0	86/6/7/1
Urinalysis			
Appearance	Hazy		
Color	Amber		
pH	5.0		
Specific gravity	1.017		
Blood	2+		
Ketones	Negative		
Leukocyte esterase	3+		
Nitrites	2+		
Urine protein, qualitative	Trace		
Urine glucose, qualitative	Trace		
WBC/hpf	625		
RBC/hpf	102		
Bacteria	Many		
WBC casts	2+		

B, bands; L, lymphocytes; M, monocytes; PMN, polymorphonuclear leukocytes.

Chest X-Ray

No infiltrates, no consolidation seen

CT Abdomen With Contrast

Findings: Liver, gallbladder, pancreas, spleen, and adrenals are unremarkable. No evidence of ascites or focal areas of fluid collection. The left kidney is unremarkable. A hypoattenuating lesion is seen involving the right kidney from mid- to lower pole.

Impression: Hypoattenuating lesion in right kidney consistent with pyelonephritis; correlate with clinical picture.

Abdominal Ultrasound

Findings: There is a hypoechoic region within the lateral cortex of the right kidney, which does not display through transmission.

Impression: Focal cortical thickening with decreased echogenicity involving the mid right renal cortex, similar to the recent CT scan, most likely representing focal pyelonephritis. No renal abscess identified. No hydronephrosis.

Urine Gram Stain

Many gram-negative rods

Blood Culture

Many gram-negative rods

Vaginal Swab

Negative

Assessment

1. Pyelonephritis
2. Bacteremia
3. Type 1 diabetes

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of pyelonephritis?
- 1.b. What additional information is needed to fully assess this patient's pyelonephritis?

Assess the Information

- 2.a. Assess the severity of the pyelonephritis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this patient?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating pyelonephritis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of goals of therapy.

CLINICAL COURSE

The patient was admitted to the hospital and started on the empiric antimicrobial regimen you recommended. She was given acetaminophen Q 6 H for pain. Her fevers subsided with the initiation of acetaminophen and antibiotics. On day 3 of hospitalization, she was much improved and was ready for discharge. Laboratory tests for days 2 and 3 are included in Table 133-1. Culture results from admission were finalized on day 3 (late in the day) and are shown in Table 133-2.

TABLE 133-2 Results of Urine and Blood Cultures Taken on Day 1 and Reported on Day 3

Urine Culture	
Result: >100,000 cfu/mL <i>Escherichia coli</i>	
Antibiotic	Kirby–Bauer Interpretation
Ampicillin/sulbactam	Resistant
Ampicillin	Resistant
Cefazolin	Resistant
Cefuroxime	Sensitive
Ceftriaxone	Sensitive
Levofloxacin	Sensitive
Piperacillin/tazobactam	Sensitive
Imipenem	Sensitive
Tobramycin	Sensitive
Fosfomycin	Sensitive
Nitrofurantoin	Sensitive
TMP/SMX	Resistant
Day 1 blood cultures × 2 sets	
Result: Many <i>E. coli</i>	
Antibiotic	Kirby–Bauer Interpretation
Ampicillin/sulbactam	Resistant
Ampicillin	Resistant
Cefazolin	Resistant
Cefuroxime	Sensitive
Ceftriaxone	Sensitive
Levofloxacin	Sensitive
Piperacillin/tazobactam	Sensitive
Imipenem	Sensitive
Tobramycin	Sensitive
TMP/SMX	Resistant
Vaginal swab	
No growth × 3 days	
Day 2 blood cultures	
Results: No growth to date	
Day 3 blood cultures	
Results: No growth to date	

FOLLOW-UP CASE QUESTION

1. Given this new information, what recommendations, if any, do you have for changes in the initial drug regimen?

SELF-STUDY ASSIGNMENTS

1. Develop a protocol for switching patients from IV to oral therapy when treating pyelonephritis.
2. Perform a literature search to find clinical trials comparing drug therapy in pyelonephritis, and compare inclusion criteria, drug regimens, outcomes, and costs of therapy.
3. Develop a clinical pathway that could be used for managing suspected pyelonephritis.

CLINICAL PEARL

Pyelonephritis can be managed with many different drugs; choose drugs that are bactericidal and cleared in the active form by the kidney. Drugs suitable for once-daily therapy help to reduce treatment costs.

REFERENCES

1. Sader HS, Castanheira M, Flamm RK, Jones RN. Antimicrobial activities of ceftazidime-avibactam and comparator agents against gram-negative organisms isolated from patients with urinary tract infections in U.S. medical centers, 2012 to 2014. *Antimicrob Agents Chemother* 2016;60(7):4355–4360.
2. Keepers TR, Gomez M, Celeri C, et al. Fosfomycin and comparator activity against select Enterobacteriaceae, *Pseudomonas*, and *Enterococcus* urinary tract infection isolates from the United States in 2012. *Infect Dis Ther* 2017;6(2):233–243.
3. Gupta K, Hooton TM, Naber KG, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52(5):e103–e120.
4. Colgan R, Williams M. Diagnosis and treatment of acute pyelonephritis in women. *Am Fam Physician* 2011;84(5):519–526.
5. Eliakim-Raz N, Yahar D, Paul M, Leibovici L. Duration of antibiotic treatment for acute pyelonephritis and septic urinary tract infection—7 days versus longer treatment: systematic review and meta-analysis of randomized controlled trials. *J Antimicrob Chemother* 2013;68:2183–2191.
6. Sandberg T, Skoog G, Hermansson AB, et al. Ciprofloxacin for 7 days versus 12 days in women with acute pyelonephritis: a randomized, open-label and double-blind, placebo-controlled, non-inferiority trial. *Lancet* 2012;380(9840):484–490.
7. Abbo LM, Hooton TM. Antimicrobial stewardship and urinary tract infections. *Antibiotics* 2014;3:174–192.
8. Wagenlehner F, Umeh O, Steenbergen J, Yuan G, Darouiche RO. Ceftolozane-tazobactam compared with levofloxacin in the treatment of complicated urinary-tract infections, including pyelonephritis: a randomized, double-blind, phase 3 trial (ASPECT-cUTI). *Lancet* 2015; 385:1949–1956.
9. Zasowski EJ, Rybak JM, Rybak MJ. The β -lactams strike back: ceftazidime-avibactam. *Pharmacotherapy* 2015;35(8):755–770.

134

PELVIC INFLAMMATORY DISEASE AND OTHER SEXUALLY TRANSMITTED INFECTIONS

Frankie and Jenny Were Lovers Level II

Neha Sheth Pandit, PharmD, AAHVP, BCPS

Christopher Roberson, MS, AGNP-BC, AAHIVS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify relevant information from patient history, physical examination, and laboratory data suggestive of the diagnosis of a sexually transmitted infection (STI).
- List major complications of STIs and appropriate strategies for prevention and/or treatment.
- Discuss other health issues that may be present in patients referred for treatment of STIs, including immunization needs and risk reduction.
- Provide appropriate treatment plans for patients with STIs, including drug(s), dosage form, doses, route of administration, frequency, duration, and monitoring.
- Compare and contrast criteria and options for ambulatory and inpatient treatment of women with pelvic inflammatory disease (PID).
- Recognize opportunities and provide appropriate recommendations for immunizations, including human papillomavirus (HPV) vaccine.
- Develop patient counseling strategies regarding drug treatment and possible adverse effects.

PATIENT PRESENTATION 1

Chief Complaint

“My lady and I don’t feel good.”

HPI

Frankie Mason is a 20-year-old man who presents to a health clinic with complaints of 5 days of painful urination and increasing amounts of discolored urethral discharge. Today he noted four painful blisters on the penis. He is heterosexual, sexually active with two to three concurrent partners, and admits to unprotected sex “at least once” in the past 2 weeks. He does not know the sexual histories of his current or past sexual partners or their sexual partners, and he admits to over 15 lifetime sexual partners. He denies oral or rectal intercourse.

PMH

History of genital herpes 2 years ago. He has not undergone testing for HIV. He has been immunized against hepatitis B but not against

HPV because “it’s only for women.” He is unaware of hepatitis A or C as infectious diseases, asking “Do you get that from sex or restaurant food?” No active medical problems.

FH

Noncontributory

SH

Denies IV drug and cigarette use; has two to four beers “on weekends”; may be unreliable in keeping follow-up appointments because he states, “I don’t like doctors.”

Meds

None

All

Ciprofloxacin (“makes me dizzy”)

ROS

Occasional headaches; denies stomach pain, constipation, vision problems, night sweats, weight loss, or fatigue

Physical Examination

Gen

Patient is a well-developed man in NAD, very talkative

VS

BP 104/80 mm Hg, HR 72 bpm, RR 12 breaths/min, T 37.6°C; Wt 78 kg

Skin

No rashes or other lesions

HEENT

No erythema of pharynx or oral ulcers

Neck/Lymph Nodes

No lymphadenopathy; neck supple

Chest

Normal breath sounds; good air entry

CV

RRR; no murmurs

Abd

No tenderness or rebound; no HSM

Genit/Rect

Tanner stage V; testes descended, nontender, without erythema. Thick yellow urethral discharge; four small erupting vesicles on penile tip and glans; negative rectal examination; no scrotal tenderness or swelling. No genital growths visualized.

MS/Ext

No inguinal or other lymphadenopathy; no lesions or rashes; muscle strength and tone normal

Neuro

CN II–XII intact; DTRs 2+ bilaterally and symmetric

■ Urethral Smear

15 WBC/hpf; Gram stain (+) for intracellular gram-negative diplococci

■ Other Tests

A urine specimen was sent for NAAT for gonococcus and *Chlamydia*.

■ Assessment

1. Urethritis caused by gonococcal infections, r/o chlamydial coinfection
2. Recurrent genital herpes

PATIENT PRESENTATION 2

■ Chief Complaint

"I have bad stomach pain."

■ HPI

Jenny Klein is a 20-year-old female sexual partner of Frankie who reports a 1-day history of increasingly severe dysuria, lower abdominal pain, and vaginal discharge. She is sexually active with "only Frankie," has no previous history of urinary or genital infections, and denies IV drug use. She is unaware of Frankie's multiple sexual partners. Her last menses started 10 days ago, and last intercourse was 7 days ago without the use of a condom. She noted the vaginal discharge yesterday, which she describes as thick and yellow. She denies oral or rectal intercourse. She admits to three lifetime sexual partners.

■ PMH

No previous pregnancies and current negative pregnancy test. She has received a complete hepatitis B series. She has not been immunized against hepatitis A and has not received the HPV vaccine series, because her mother did not consent to the vaccine. She believes she is "low risk" for HPV.

■ FH

HTN in maternal grandmother

■ SH

Denies nicotine or recreational drug use; occasional one to two glasses of wine; does not use hormonal or other contraception; reports occasional use of condoms; no routine medical care

■ Meds

None

■ All

NKDA

■ ROS

Occasional painful menses self-treated with brand name menstrual treatment (Pamprin or Midol—she does not recall exactly)

■ Physical Examination

Gen

Well-developed woman in moderate to severe abdominal discomfort

VS

BP 110/76 mm Hg, HR 100 bpm, RR 16 breaths/min, T 39.2°C; Wt 62 kg

Skin

No rashes

HEENT

No erythema of pharynx or oral ulcers

Neck/Lymph Nodes

No lymphadenopathy; neck supple

Chest

Normal breath sounds; good air entry; breasts Tanner stage V

CV

Regular rate and rhythm; no murmurs

Abd

Guarding of right and mid-lower quadrants with palpation

Genit/Rect

Pubic hair Tanner stage V; vulva with no ulcers, erythema, or excoriations. Vaginal area with large amount of thick yellow-white discharge. Cervix shows erythema and extensive yellow-white discharge; no masses on bimanual examination; cervical motion tenderness; adnexal tenderness and fullness on right. No genital growths visualized.

■ Vaginal Saline Wet Preparation and KOH

Examination of vaginal discharge: Increased WBCs (too numerous to count), pH 5.0, no yeast or hyphae seen; "whiff" test positive with KOH preparation; many clue cells present.

MS/Ext

No adenopathy, lesions, or rashes; no arthritis or tenosynovitis

Neuro

CN II–XII intact, DTRs 2+ and symmetric bilaterally

■ Labs

Na 138 mEq/L	Hgb 12.2 g/dL	WBC $12.75 \times 10^3/\text{mm}^3$
K 4.2 mEq/L	Hct 37%	Neutros 66%
Cl 102 mEq/L	Plt $250 \times 10^3/\text{mm}^3$	Bands 12%
BUN 22 mg/dL	SCr 0.9 mg/dL	Lymphs 10%
Glu 106 mg/dL		Monos 12%

■ Urine Dipstick

Small leukocytes, nitrites neg; protein 100 mg/dL; otherwise unremarkable

■ Other Tests

Vaginal specimen sent for NAAT for gonococcus and *Chlamydia*

■ Assessment

PID (infection of the upper genital tract and cervicitis)

Bacterial vaginosis

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of STIs in Frankie and pelvic inflammatory disease (PID) in Jenny?

- 1.b. What additional information is needed to fully assess Frankie's and Jenny's STIs and PID?

Assess the Information

- 2.a. Assess the severity of STIs in Frankie and PID in Jenny based on the subjective and objective information available.
- 2.b. Create a list of the Frankie's and Jenny's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in Frankie's and Jenny's cases?
- 3.b. What nondrug therapies might be useful for Frankie and Jenny?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating STIs in Frankie and PID in Jenny?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for these patients. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to Frankie and Jenny to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects for Frankie's and Jenny's therapeutic plan?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy for Frankie and Jenny.

CLINICAL COURSE

One day later, *Chlamydia* and gonorrhea NAAT-positive test results received on samples from both patients.

FOLLOW-UP CASE QUESTION

1. What changes, if any, in antibacterial therapy are required?

SELF-STUDY ASSIGNMENTS

- Review the legal status of expedited partner therapy (EPT) in your area of practice. Discuss the ethical implications of this practice (see www.cdc.gov/std/ept).
- Survey 10 local community pharmacists to assess their knowledge of EPT. Would they dispense the ordered medications?
- Review nonprescription brand name products for management of dysmenorrhea and accompanying pain for ingredients, effectiveness, and cost. Develop recommendations for the most cost-effective therapy.
- Review the current preexposure prophylaxis (PrEP) guidelines for HIV to see if either patient would be a good candidate for prophylaxis medication. If so, develop recommendations for PrEP with an appropriate monitoring plan.

CLINICAL PEARLS

- Although partner notification and treatment may be enhanced through EPT strategies, misconceptions regarding legality and ethics of this practice limit implementation of this public health initiative.
- Healthcare providers should view a diagnosis of STI as an immunization opportunity to enhance care of the individual while furthering public health initiatives for disease prevention.

REFERENCES

- Workowski KA, Bolan GA. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Recomm Rep* 2015;64(RR-03):1–137.
- Papp JR, Schachter J, Gaydos CA, Van Der Pol B. Recommendations for the laboratory-based detection of *Chlamydia trachomatis* and *Neisseria gonorrhoeae*—2014. *MMWR Recomm Rep* 2014;63:1–24.
- Lyss SB, Kamb ML, Peterman TA, et al. Chlamydia trachomatis among patients infected with and treated for *Neisseria gonorrhoeae* in sexually transmitted disease clinics in the United States. *Ann Intern Med* 2003;139:178–185.
- Trent M. Pelvic inflammatory disease. *Pediatr Rev* 2013;34:163–171.
- Brunham RC, Gottlieb SL, Paavonen J. Pelvic inflammatory disease. *N Engl J Med* 2015;372:2039–2048.
- Llata E, Bernstein KT, Kerani RP, et al. Management of pelvic inflammatory disease in selected US sexually transmitted disease clinics: sexually transmitted disease surveillance network, January 2010–December 2011. *Sex Transm Dis* 2015;42:429–433.
- Centers for Disease Control and Prevention. Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea. Available at: <http://www.cdc.gov/std/ept/GC-Guidance.htm>. Accessed January 30, 2019.
- Centers for Disease Control and Prevention. Expedited Partner Therapy in the Management of Sexually Transmitted Diseases. Atlanta, GA: US Department of Health and Human Services; 2006. <http://www.cdc.gov/std/treatment/eptfinalreport2006.pdf>. Accessed January 30, 2019.
- Gift TL, Kissiner P, Mohammed H, Leichter JS, Hogben M, Golden MR. The cost and cost-effectiveness of expedited partner therapy compared with standard partner referral for the treatment of chlamydia or gonorrhea. *Sex Transm Dis* 2011;38:1067–1073.
- Meites E, Kempe A, Markowitz LE. Use of a 2-dose schedule for human papillomavirus vaccination—updated recommendations of the Advisory Committee on Immunization Practices. *MMWR Morb Mortal Wkly Rep* 2016;65:1405–1408.

135

SYPHILIS

Here Today ... Gone Tomorrow? Level I

Craig Martin, PharmD, BCPS, MBA

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Discuss the diagnosis of syphilis and differentiate among the temporal stages of the disease.
- Develop a treatment plan individualized for the patient's stage of syphilis.

- Recommend alternative treatment regimens when the primary therapeutic option is contraindicated.
- Describe appropriate monitoring, follow-up, and counseling of patients with a syphilitic infection to ensure success of treatment.

PATIENT PRESENTATION

■ Chief Complaint

“This rash started 3–4 days ago on my back and stomach. My whole left side has been hurting, and I’ve also been feeling weaker than usual lately.”

■ HPI

John Rutherford, a 27-year-old man with a past medical history of HIV on HAART, presents with left upper quadrant/left back/left side pain and a diffuse rash. He states the rash started 3–4 days ago, and is mostly on his chest, abdomen, and arms. He also has seven macules on his scalp. The rash is nonpainful and nonpruritic, except on his scalp where he has developed a few scabs from itching; no drainage from any lesions is noted. He also has been having some chest pain that is worse with breathing. He notes nausea, though no vomiting, and reports ongoing nonbloody diarrhea for months. He presents to the ED primarily because of pain in his upper left back that radiates around his left side. His urine is very dark, brownish-red; however, he has no dysuria. The patient also states he has felt weaker than usual for the past few days.

■ PMH

Hepatitis B, now immune
HIV diagnosed 6 months ago, on HAART

■ FH

Both parents with hypertension, still living

■ SH

Unemployed; cigarette smoking 1.5 ppd since early teens; social alcohol usage (average four drinks per week); occasional methamphetamine use—both smoked and injected (with clean needles); previous MSM Hx (four partners in last 6 months) with inconsistent use of condoms

■ Meds

Bictegravir/tenofovir alafenamide/emtricitabine 50/25/200 mg (coformulated tablet) PO once daily
Acetaminophen–hydrocodone 325/5 mg PO Q 6 H PRN

■ All

Codeine

■ ROS

Constitutional: reports weakness and malaise; denies fever

Eyes: denies vision changes

Ears, nose, and throat: denies sore throat, rhinorrhea, or sinus pressure

Lymphatic: denies lymph node swelling

Respiratory: denies shortness of breath, dyspnea on exertion, or cough

Cardiovascular: reports some chest pain on inspiration

Gastrointestinal: reports intermittent nausea, no vomiting, and consistent diarrhea

Neurologic: denies neuropathy symptoms

Musculoskeletal: reports arthralgias and myalgias

Skin: rash on scalp, abdomen, arms, and legs present

Pain: reports persistent abdominal and left-sided pain

■ Physical Examination

Gen

Awake and alert, NAD. Appropriate. Oriented to person, place, and year.

VS

T 98.4°F, BP 114/70, HR 92, RR 16, O₂ sat 98; Ht 61", Wt 59 kg

Skin

Numerous palpable, blanchable macules mostly ~5 mm with one area of confluence on the left lower abdomen. Macules present on both arms, chest, and back. Four to five scabs with surrounding erythema on scalp.

HEENT

Moist mucous membranes, neck supple. No cervical, postauricular, or supraclavicular lymphadenopathy. No obvious oral lesions. Mild icterus.

Neck/Lymph Nodes

Supple; no lymphadenopathy, bruits, JVD, or thyromegaly

Chest

CTA bilaterally. No crackles or wheezes.

CV

RRR; S₁, S₂; no m/r/g

Abd

Soft, nondistended. Diffuse tenderness with minimal localization to the RUQ and more prominent on the epigastrium, LUQ, and back. (+) BS. No rebound or guarding.

Extremities

Warm, well perfused, no edema. 2+ DP and PT pulses

GU

Rash extending to penis; no other lesions present. Moderate inguinal lymphadenopathy.

Rectal

Scar from recently healed ulcer noted

Musculoskeletal

No joint swelling, or effusions

Neuro

CN II–XII grossly intact. No dysmetria. Strength 5/5 on all four extremities.

■ Labs

Na 138 mEq/L	Hgb 12.3 g/dL	AST 95 IU/L	HIV viral load
K 3.9 mEq/L	Hct 36.9%	ALT 66 IU/L	<20 copies/mL
Cl 96 mEq/L	WBC $9.3 \times 10^3/\text{mm}^3$	Alk phos	HBsAb positive
CO ₂ 28 mEq/L	CD4 460 cells/mm ³	1271 IU/L	HBsAg negative
BUN 7 mg/dL	Plt $391 \times 10^3/\text{mm}^3$	T. bili	HCV RNA negative
SCr 0.7 mg/dL		5.0 mg/dL	RPR titer positive
Glu 100 mg/dL			at 1:256
			FTA-ABS positive

■ CT Abdomen and Pelvis

Mild hepatosplenomegaly with minimal intrahepatic biliary ductal dilatation and prominence of the common duct. There are multiple tortuous perirectal vessels that may represent varices secondary to portal hypertension. Proctitis is present with innumerable reactive perirectal and pelvic lymph nodes.

■ Assessment

HIV-infected patient with newly diagnosed syphilis (appears to be in a secondary stage).

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of syphilis?
- 1.b. What additional information is needed to fully assess this patient's syphilis?

Assess the Information

- 2.a. Assess the severity of syphilis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating syphilis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Describe the differences in syphilis presentation in relation to disease progression.
2. Discuss the tests or procedures that should be used to diagnose and monitor the progression/regression of syphilis over time.
3. Identify potential confounding factors that may impact test results in HIV-infected patients with syphilis.

CLINICAL PEARL

Patients undergoing penicillin therapy for syphilis frequently experience the Jarisch–Herxheimer reaction within the first 24 hours of treatment. This is an inflammatory response to the breakdown of spirochetes and subsequent release of endotoxins. Usually manifesting as fever, chills, myalgias, arthralgias, and headache, it is generally self-limiting and may be treated with analgesics and antipyretics as needed.

REFERENCES

1. Centers for Disease Control and Prevention. Sexually Transmitted Disease Surveillance, 2013. Atlanta, GA: U.S. Department of Health and Human Services; December 2014. Available at: <http://www.cdc.gov/std/stats13/syphilis.htm>. Accessed February 27, 2019.
2. Centers for Disease Control and Prevention. Sexually transmitted diseases treatment guidelines, 2015. MMWR Morb Mortal Wkly Rep 2015;64(RR-3):34–50. Available at: www.cdc.gov. Accessed February 27, 2019.
3. Tramont EC. *Treponema pallidum* (syphilis). In: Mandell GL, Bennett JE, Dolin R, eds. Principles and Practice of Infectious Diseases. 7th ed. Philadelphia, PA: Churchill Livingstone; 2010:3035–3053.
4. Panel on Opportunistic Infections in HIV-infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from CDC, the National Institutes of Health, and the HIV Medicine Association of the Infectious Diseases Society of America, May 2018. Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oip.pdf. Accessed February 27, 2019.
5. Bai ZG, Wang B, Yang K, et al. Azithromycin versus penicillin G benzathine for early syphilis. Cochrane Database Syst Rev 2012;6:CD007270.
6. Warwick Z, Dean G, Fisher M. Should syphilis be treated differently in HIV-positive and HIV-negative individuals? Treatment outcomes at a university hospital, Brighton, UK. Int J STD AIDS 2009;20(4):229–230.
7. See S, Scott EK, Levin MW. Penicillin-induced Jarisch–Herxheimer reaction. Ann Pharmacother 2005;39(12):2128–2130.

136

GENITAL HERPES, GONOCOCCAL, AND CHLAMYDIAL INFECTIONS

Triple Threat Level II

Jonathan C. Cho, PharmD, MBA, BCIDP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify subjective and objective data consistent with genital herpes, gonorrhea, and chlamydia.
- Recommend appropriate therapies for treating genital herpes, gonorrhea, and chlamydia.

- Provide effective and comprehensive counseling for patients with genital herpes, gonorrhea, and chlamydia.
- Identify drug interactions of clinical significance and provide recommendations for managing them.

PATIENT PRESENTATION

■ Chief Complaint

"I have painful sores in my genital area, and I have terrible headaches and muscle aches."

■ HPI

Megan Thompson is a 19-year-old nulligravida woman who presents to the county health STD clinic for evaluation of genital lesions that have been present for 3 days. She has also noticed a white non-odorous vaginal discharge that has lasted 14 days. She admits to anal and vaginal intercourse with two regular partners in the past 60 days. It has been 5 days since her last sexual encounter.

■ PMH

Recurrent UTIs; most recent 3 months ago
Vaginal candidiasis; most recent 6 months ago
Gonorrhea 5 years ago
Trichomonas vaginalis 2 years ago

■ FH

Mother with type 2 DM; father died at age 50 of an acute MI.

■ SH

Lives with her boyfriend and works at a local grocery store. She admits to occasional use of alcohol and marijuana.

■ Meds

Ethinyl estradiol and norethindrone (Junel) 21 1/20 one tablet PO daily
Multivitamin with iron one tablet PO daily
Ibuprofen 200 mg PO Q 6 H PRN headache
Ciprofloxacin 250 mg PO once daily (recurrent UTI prophylaxis)

■ All

Penicillin (hives and tongue swelling)

■ ROS

(-) Cough, night sweats, weight loss, dysuria, or urinary frequency;
(+) anorectal pain; last menstrual period 6 weeks ago

■ Physical Examination

Gen

Thin, young woman in NAD

VS

BP 136/71 mm Hg, P 78 bpm, RR 17 breaths/min, T 37.8°C;
Wt 51 kg, Ht 5'5"

Skin

Dry, no lesions, normal color and temperature

HEENT

PERRLA, EOMI without nystagmus

Neck

Supple; no adenopathy, JVD, or thyromegaly

Chest

Air entry equal; no crepitations or wheezing

CV

RRR, normal S₁ and S₂; no S₃ or S₄; no murmurs or rubs

Abd

Soft, mild tenderness to palpation in RLQ, (+) bowel sounds

Genit/Rect

Tender inguinal adenopathy. External exam clear for nits and lice, several extensive shallow small painful vesicular lesions over vulva and labia, swollen and red. Vagina red, rugated, moderate amounts of creamy white discharge. Cervix pink, covered with above discharge, nontender, ~3 cm. Corpus nontender, no palpable masses. Adnexa with no palpable masses or tenderness. Rectum with no external lesions; (+) diffuse inflammation and friability internally, no masses.

Ext

Peripheral pulses 2+ bilaterally, DTRs 2+, no joint swelling or tenderness

Neuro

Alert and oriented, CN II–XII intact

■ Labs

Na 135 mEq/L	Hgb 12.9 g/dL	WBC $6.3 \times 10^3/\text{mm}^3$	RPR nonreactive
K 4.0 mEq/L	Hct 37.3%	PMNs 64%	Preg test: hCG
Cl 102 mEq/L	Plt $255 \times 10^3/\text{mm}^3$	Bands 2%	pending
CO ₂ 27 mEq/L		Eos 1%	HIV serology:
BUN 11 mg/dL		Lymphs 24%	ELISA pending
SCr 0.9 mg/dL		Monos 9%	
Glu 72 mg/dL			

■ Other

Vaginal discharge: Whiff test (-); pH <4.5; wet mount *Trichomonas* (-), clue cells (-), yeast (+)

■ Clinical Course

The following results were reported 2 days later:

Vulval swab DFA monoclonal stain: HSV-2 isolated

Vaginal and rectal swab gonorrhea NAAT (PCR): *Neisseria gonorrhoeae* (+)

Vaginal and rectal swab chlamydia NAAT (PCR): *Chlamydia trachomatis* (+)

■ Assessment

A 19-year-old woman who may be pregnant and has primary genital HSV-2 infection, vaginal candidiasis, and gonococcal and chlamydial infections of the vagina, cervix, and rectum.

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of sexually transmitted infections (STIs)?
- What additional information is needed to fully assess this patient's STIs?

Assess the Information

- 2.a. Assess the classification of genital herpes infection based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treatment of genital herpes, chlamydia, and gonorrhea?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

FOLLOW-UP QUESTIONS

1. Six months later, Megan calls the STD clinic complaining of genital lesions that look and feel the same as the lesions she had 6 months earlier when seen and treated in the clinic. Should this episode of recurrent genital herpes be treated? If so, what therapies would be appropriate?
2. Is daily suppressive therapy indicated because she had a recurrent episode?
3. When is herpes treatment indicated for sexual partners?
4. When is chlamydia and gonorrhea treatment indicated for sexual partners?

SELF-STUDY ASSIGNMENTS

1. Research the potential role of vaccines in the future management of herpes simplex disease.
2. Recommend alternative agents for treating acyclovir-resistant herpes.
3. Explain the relationship between herpes simplex and HIV infections. Is there a role for herpes simplex virus-suppressive therapy in preventing HIV transmission?
4. Describe herpes simplex complications that may require hospitalization, and recommend an appropriate treatment regimen.

CLINICAL PEARL

Most genital herpes infections are transmitted by persons who have asymptomatic viral shedding and are unaware that they have the infection. Systemic antiviral drugs control the signs and symptoms of genital herpes infection, but they do not eradicate latent virus.

ACKNOWLEDGMENT

This case is an updated version of a case created by Suellen J. Sorensen, PharmD., BCPS, FASHP in the 10th Edition of this book.

REFERENCES

1. Centers for Disease Control and Prevention. 2015 STD treatment guidelines. *MMWR Morb Mortal Wkly Rep*. 2015;64(RR-135). Available at: <http://www.cdc.gov/mmwr/pdf/rr/rr6403.pdf>. Accessed February 27, 2019.
2. Valtrex caplets [package insert]. Research Triangle Park, NC, GlaxoSmithKline, January 2013.
3. Comparative drug prices. Available at: www.rxpricequotes.com. Accessed March 30, 2019.
4. Famvir tablets [package insert]. East Hanover, NJ, Novartis Pharmaceuticals Corporation, September 2016.
5. Centers for Disease Control and Prevention. Update to CDC's sexually transmitted diseases treatment guidelines, 2010: oral cephalosporins no longer recommended treatment for gonococcal infections. *MMWR Morb Mortal Wkly Rep* 2012;61(31):590–594. Available at: http://www.cdc.gov/mmwr/preview/mmwrhtml/mm6131a3.htm?s_cid=mm6131a3_w. Accessed February 27, 2019.
6. Corey L, Wald A, Patel R, et al. Once daily valacyclovir to reduce the risk of transmission of genital herpes. *N Engl J Med* 2004;350:11–20.
7. Centers for Disease Control and Prevention. Expedited Partner Therapy in the Management of Sexually Transmitted Diseases. Atlanta, GA: US Department of Health and Human Services, 2006. Available at: <http://www.cdc.gov/std/treatment/EPTFinalReport2006.pdf>. Accessed February 27, 2019.
8. Centers for Disease Control and Prevention. Guidance on the Use of Expedited Partner Therapy in the Treatment of Gonorrhea. Atlanta, GA: US Department of Health and Human Services; November 2012. Available at: <http://www.cdc.gov/std/treatment/EPTFinalReport2006.pdf>. Accessed February 27, 2019.

137

OSTEOMYELITIS AND SEPTIC ARTHRITIS

I Must Be Getting Old Level II

R. Brigg Turner, PharmD, BCPS-AQ ID

Gregory B. Tallman, PharmD, MS, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the most common presenting signs and symptoms of osteomyelitis and septic arthritis.
- Recommend an antimicrobial treatment plan with empiric and definitive therapy for osteomyelitis and septic arthritis.

- Develop alternative treatment approaches for osteomyelitis and septic arthritis when the preferred regimen cannot be used.
- Identify monitoring parameters to evaluate the efficacy and toxicity of antimicrobial therapy for osteomyelitis and septic arthritis.
- Provide patient education on the proper administration of home infusion antibiotics for osteomyelitis and septic arthritis.

PATIENT PRESENTATION

■ Chief Complaint

“Back spasms.”

■ HPI

Richard Frost is a 52-year-old man with a history of chronic back pain who presents with a 1-week history of back spasms localized in the thoracic region. He was doing relatively well until 1 week ago when he went bowling and also did some maintenance around his house, whereupon his back felt tight. There is radiation of pain to his upper right leg with movement. He had a similar episode 3 months ago that resolved after approximately 2 days with no treatment. He reports this episode to be more severe.

■ PMH

Patient reports chronic back pain starting approximately 10 years ago. He does not routinely seek medical care and does not report any other chronic conditions.

■ FH

Noncontributory

■ SH

The patient has smoked one pack of cigarettes per day for the past 20 years. He admits to IV heroin use for the past 3–4 years.

■ Meds

Acetaminophen and ibuprofen as needed for back pain; the patient has increased use of these medications over the past week.

■ All

No known allergies

■ ROS

The patient denies nausea, vomiting, fevers, chills, chest pain, shortness of breath, and bowel or bladder incontinence. He reports decreased oral intake over the past week due to pain and general malaise.

■ Physical Examination

Gen

The patient does not appear to be in any acute distress.

VS

BP 152/109, P 84 bpm, RR 18, T 36.4°C; 96% SpO₂ on room air, Ht 5'8", Wt 90 kg

Skin

Open left lateral leg ulcer 4 × 2 in in size with foul-smelling, purulent drainage. Patient reports this ulcer to be a result of burning his leg on a motorcycle approximately 1 year previously. He has not previously sought medical care for this condition.

HEENT

PERRL, conjunctivae clear. Poor dentition noted.

Neck/Lymph nodes

No lymphadenopathy

Lungs/Thorax

Clear to auscultation bilaterally, no wheezing, rhonchi, or rales

CV

Regular rate and rhythm; no appreciable murmurs, gallops, or rubs

Abd

Soft, nontender, nondistended; bowel sounds present

Genit/Rect

Genitalia normal

MS/Ext

Decreased dorsiflexion on the left foot, which the patient states is chronic. He has reproducible pain in the thoracic spine.

Neurologic

Cranial nerves II–XII are intact.

Psychiatric

Oriented to person, place, and time. Mood and affect are appropriate.

■ Labs

Na 136 mEq/L	Hgb 13.7 g/dL
K 4.0 mEq/L	Hct 41.1%
Cl 102 mEq/L	Plt 341 × 10 ³ /mm ³
CO ₂ 25 mEq/L	WBC 22.7 × 10 ³ /mm ³
BUN 18 mg/dL	Neutros 71%
SCr 0.87 mg/dL	Bands 17%
Glu 120 mg/dL	Lymphs 3%
Ca 9.4 mg/dL	Monos 9%
ESR 73 mm/hr	
CRP 84.2 mg/L	

■ Abdominal and Pelvic CT Scan

CT scan of abdomen and pelvis are unremarkable. Thoracic spine shows degenerative disk disease from T1 to T5.

■ MRI

MRI shows T2–T3 osteomyelitis and paravertebral abscess.

■ Blood Cultures × Two Sets

Pending

■ Other

HCV Ab positive; HIV nonreactive

■ Assessment

1. Paravertebral abscess and osteomyelitis in the presence of chronic back pain; soft-tissue infection on the left lateral leg
2. Substance use disorder—heroin
3. Chronic tobacco smoker
4. Infection with hepatitis C virus

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of osteomyelitis?
- 1.b. What additional information is needed to fully assess this patient's osteomyelitis?

Assess the Information

- 2.a. Assess the severity of osteomyelitis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What psychosocial and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this patient?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating osteomyelitis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

CLINICAL COURSE

The patient was taken to interventional radiology, and a culture from CT-guided aspiration of his paravertebral abscess was obtained. Blood cultures were drawn and the patient was treated initially with empiric vancomycin plus cefepime. After 2 days, paravertebral abscess culture and blood cultures (two out of four) revealed methicillin-susceptible *Staphylococcus aureus* with susceptibilities reported in Table 137-1. A transthoracic echocardiogram reported an ejection fraction of approximately 65%, trace aortic and mitral regurgitation, and no evidence of vegetation or perivalvular abscess. The patient has improvement of symptoms, he is clinically stable, and the physician determines that discharge is appropriate and orders placement of a peripherally inserted central catheter (PICC).

- 3.e. Given this new clinical information, update your care plan to include targeted antimicrobial therapy against the causative pathogen.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Devise alternative IV and oral treatment regimens if the patient was unable to tolerate the antibiotic initially used.
2. Discuss the considerations that need to be made when sending a patient home with a PICC line.

CLINICAL PEARL

Bacteria causing vertebral osteomyelitis most commonly access vertebrae hematogenously from other sources. *S. aureus* is the most common organism causing osteomyelitis, and concurrent bacteremia is common. *S. aureus* bacteremia is a serious condition requiring specialized care. Consultation with infectious diseases specialists results in better patient care and outcomes. All patients should have a thorough physical exam to identify metastatic foci and an echocardiogram to detect vegetation, intracardiac abscess, or valvular perforation to aid in the diagnosis of infective endocarditis.

REFERENCES

1. Berbari EF, Kanj SS, Kowalski TJ, et al. 2015 Infectious Diseases Society of America (IDSA) clinical practice guidelines for the diagnosis and treatment of native vertebral osteomyelitis in adults. *Clin Infect Dis* 2015;61(6):e26–e46.
2. McHenry MC, Easley KA, Locker GA. Vertebral osteomyelitis: long-term outcome for 253 patients from 7 Cleveland-area hospitals. *Clin Infect Dis* 2002;34(10):1342–1350.
3. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;54(12):132–173.
4. Butalia S, Palda VA, Sargeant RJ, Detsky AS, Mourad O. Does this patient with diabetes have osteomyelitis of the lower extremity? *JAMA* 2008;299(7):806–813.
5. Weissman S, Parker RD, Siddiqui W, Dykema S, Horvath J. Vertebral osteomyelitis: retrospective review of 11 years of experience. *Scand J Infect Dis* 2014;46(3):193–199.
6. Tice AD, Rehm SJ, Dalovisio JR, et al. Practice guidelines for outpatient parenteral antimicrobial therapy. *Clin Infect Dis* 2004;38(12):1651–1672.
7. Norris AH, Shrestha NK, Allison GM, et al. 2018 IDSA clinical practice guideline for the management of outpatient parenteral antimicrobial therapy. *Clin Infect Dis* 2019;68(1):e1–e35.
8. Ho J, Archuleta S, Tice A, Fisher D. International approaches to treating intravenous drug users in outpatient parenteral antibiotic services. *Infect Dis Clin Pract* 2012;20(3):192–195.
9. Bidell MR, Patel N, O'Donnell JN. Optimal treatment of MSSA bacteraemias: a meta-analysis of cefazolin versus antistaphylococcal penicillins. *J Antimicrob Chemother* 2018;73(10):2643–2651.
10. Babouee Flury B, Elzi L, Kolbe M, et al. Is switching to an oral antibiotic regimen safe after 2 weeks of intravenous treatment for primary bacterial vertebral osteomyelitis? *BMC Infect Dis* 2014;14(1):226.

TABLE 137-1 Blood Culture Susceptibilities of *Staphylococcus aureus*: Final Report

Cefazolin	Susceptible
Clindamycin	Susceptible
Oxacillin	Susceptible
Trimethoprim/sulfamethoxazole	Susceptible
Vancomycin	Susceptible, MIC = 0.5 mg/L

138

SEPSIS

Time Is of the Essence Level III

Trisha N. Branan, PharmD, BCCCP

Christopher M. Bland, PharmD, FCCP, FIDSA, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of sepsis and septic shock.
- State patient variables used to diagnose sepsis and septic shock.
- Identify the initial treatment goals for patients after the diagnosis of sepsis.
- Formulate a comprehensive treatment plan for the initial management of patients with sepsis.
- Recommend appropriate supportive care therapies for patients with sepsis.

PATIENT PRESENTATION

■ Chief Complaint

The patient presents from her nursing home with altered mental status and lethargy that has progressively worsened over the past 24 hours.

■ HPI

Ruth Carter is an 80-year-old woman who resides in a nursing home with a past medical history that includes hypertension, advanced dementia, chronic kidney disease, depression, and GERD. She was discharged last week from another hospital after being treated for 5 days for a urinary tract infection. She did well through the first 2 days after discharge but has become increasingly lethargic and drowsy in the past 24 hours. She is barely responsive at the time of assessment. She has had no reports of fever, nausea, vomiting, or pain.

■ PMH

HTN
Advanced dementia
CKD, stage II
Depression
GERD

■ PSH

Noncontributory

■ FH

No HTN, DM, CAD, cancer, or vascular disease

■ SH

Lives in a nursing home due to dementia
No tobacco, alcohol, or illicit drug use

■ Medications

Clonidine 0.2 mg/24 H transdermal patch every week
Acetaminophen 500 mg PO Q 6 H as needed for pain/fever
Lorazepam 0.5 mg PO Q HS
Hydralazine 50 mg PO TID
Omeprazole 20 mg PO QAM
Rivastigmine 4.6 mg/24 H transdermal patch Q HS
Levofloxacin 500 mg PO Q 24 H for 3 days (received 5 days of inpatient therapy; completed total course 2 days ago)

■ Allergies

NKDA

■ Review of Systems

Unable to obtain due to patient's mental status

■ Physical Exam

Gen

Unresponsive, thin appearing woman in acute distress

Vital Signs

BP 86/42 mm Hg, P 118–142 bpm, RR 14–35 breaths/min, T 35.6°C;
SpO₂: 94% on 8L NC, Ht 5'3", Wt 50.8 kg

Skin

Skin is warm, dry and pink, intact with no rashes or lesions

HEENT

Normocephalic, no scleral icterus, no sinus tenderness
Neck/Lymph Nodes: Supple, nontender, no carotid bruits, no JVD,
no lymphadenopathy

Lungs

Decreased air entry in the bases, otherwise clear, tachypnea

CV

Tachycardia, regular rhythm, no murmur, gallop, or edema

Abdomen

Soft, NT/ND, normal bowel sounds, no masses

Musculoskeletal

Normal range of motion and strength, no tenderness or swelling

Neuro

Responsive to painful stimuli at this time, unable to assess further

■ Labs

Na 135 mEq/L	Mg 2.2 mg/dL	WBC 19.3 × 10 ³ /mm ³	Arterial blood gases
K 4.4 mEq/L	Phos 3.1 mg/dL	PMNs 72%	pH 7.15
Cl 105 mEq/L	Alb 2.3 g/dL	Bands 18%	PaCO ₂ 28 mm Hg
CO ₂ 12 mEq/L	Alk Phos 55 IU/L	Lymphs 5%	PaO ₂ 165 mm Hg
BUN 42 mg/dL	T. bili 0.4 mg/dL	Monos 5%	HCO ₃ 9.8 mEq/L
SCr 2.3 mg/dL	AST 15 IU/L		Lactate 6.3 mmol/L
Glu 195 mg/dL	ALT 10 IU/L	Hgb 12.2 g/dL	
Ca 7.2 mg/dL		Hct 38%	
		Plt 205 × 10 ³ /mm ³	

Urinalysis

Color yellow, appearance cloudy, WBC 120/hpf, RBC 5/hpf, leukocyte esterase (+), nitrite (+), epithelial cells 3–5/hpf, pH 5, bacteria 15/hpf

■ Other

ECG: sinus tachycardia (HR 122), QRS 98/QT-QT_c 358/425

■ Clinical Course

After several hours in the ED, Ms Carter's blood pressure failed to improve despite receiving 2 L of normal saline. Her mental status did not improve, and her urinary output has been approximately 50 mL over past 3 hours (via foley catheter). She was intubated and placed on mechanical ventilation secondary to respiratory failure and concern for airway protection due to her mental status. The intensivist is called to evaluate the patient. The intravenous medications she received in the ED included:

Normal saline 2 L
Etomidate 20 mg
Succinylcholine 75 mg
Midazolam 2 mg
Norepinephrine 15 mcg/min continuous infusion begun
Ceftriaxone 2 g × 1 dose

■ Assessment

An 80-year-old woman is admitted to the ICU with concerns of septic shock, respiratory failure, and acute kidney injury secondary to a UTI.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of septic shock?
- 1.b. What additional information is needed to fully assess this patient's septic shock?

Assess the Information

- 2.a. Assess the severity of septic shock based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating septic shock?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Review the medical literature supporting use of regular insulin infusions to achieve glycemic control in patients with sepsis focusing on target blood glucose values.
2. Review the medical literature on use of corticosteroids in sepsis focusing on dosing, administration, and diagnosis of sepsis-induced adrenal insufficiency.

CLINICAL PEARL

Antibiograms are an important tool in antimicrobial selection in sepsis syndromes. Patients can present with sepsis from a variety of settings such as the community, nursing home, or in-hospital settings. By knowing the typical resistance patterns of the most common pathogens within a given setting, the most likely beneficial empiric regimen can be selected to ensure coverage of the infecting pathogen.

REFERENCES

1. Singer M, Deutschman C, Seymour CW, et al. The third international consensus definitions for sepsis and septic shock (sepsis-3). *JAMA* 2016;315(8):801–810.
2. Rhodes A, Evans LE, Alhazzani W, et al. Surviving sepsis campaign: international guidelines for management of sepsis and septic shock: 2016. *Crit Care Med* 2017;45:486–552.
3. Rivers E, Nguyen B, Havstad S, et al. Early goal-directed therapy in the treatment of severe sepsis and septic shock. *N Engl J Med* 2001;345:1368–1377.
4. Yealy D, Kellum J, Huang D, et al. The ProCESS Investigators. A randomized trial of protocol-based care for early septic shock. *N Engl J Med* 2014;370:1683–1693.
5. Peake S, Delaney A, Bailey M, et al. Goal-directed resuscitation for patients with early septic shock. *N Engl J Med* 2014;371:1496–1506.
6. Mouncey P, Osborn T, Power S, et al. Trial of early, goal-directed resuscitation for septic shock. *N Engl J Med* 2015;372:1301–1311.
7. Sprung CL, Annane D, Keh D, et al. Hydrocortisone therapy for patients with septic shock. *N Engl J Med* 2008;358:111–124.
8. Annane D, Renault A, Brun-Buisson C, et al. Hydrocortisone plus fludrocortisone for adults with septic shock. *N Engl J Med* 2018;378:809–881.
9. Finfer S, Chittock DR, Su SY, et al; NICE-SUGAR Study Investigators. Intensive versus conventional glucose control in critically ill patients. *N Engl J Med* 2009;360:1346–1349.
10. Gupta K, Hooton T, Naber K, et al. International clinical practice guidelines for the treatment of acute uncomplicated cystitis and pyelonephritis in women: a 2010 update by the Infectious Diseases Society of America and the European Society for Microbiology and Infectious Diseases. *Clin Infect Dis* 2011;52(5):e103–e120.

139

DERMATOPHYTOSIS

Toeing the Line Level I

Ilya Rybakov, PharmD

Natalie R. Tucker, PharmD, BCPS, BCIDP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of a dermatophyte infection.
- Describe nonpharmacologic options for managing dermatophyte infection.
- Recommend an appropriate treatment plan for a dermatophyte infection.
- Explain the best way for the patient to use a selected antifungal product.

PATIENT PRESENTATION

■ Chief Complaint

“My feet itch.”

■ HPI

Dave Harvester is a 41-year-old man who presents to a family medicine clinic because of recent itching on his feet. He is an assistant manager at a local retail store who plays basketball at the YMCA for exercise three times a week. He sweats profusely during games and always showers before going home. He has not changed laundry detergent recently, but he admits that he does not always wash his athletic clothes between workouts. He says his feet have always smelled bad, but he first started to notice the burning and itching about 6 weeks ago. He started applying some deodorizing spray to his feet a week ago, but thus far it has only made a slight improvement in itching. Now his groin is starting to itch as well.

■ PMH

Appendectomy 20 years ago
GERD diagnosed 5 years ago
Type 2 diabetes mellitus diagnosed 1 year ago
Dyslipidemia diagnosed 1 year ago

■ SH

Recent sexual activity (within past month); denies tobacco use; drinks beer on weekends and after games or practice

■ Meds

Pantoprazole 40 mg daily
Simvastatin 20 mg daily
Metformin 500 mg twice daily
Men's multivitamin daily

■ All

Penicillin (rash as a baby)

■ ROS

Denies fever and chills. Fatigued only after basketball practice. Reports frequent trauma to feet while playing in games. Complains of itching between his toes and groin area.

■ PE

Gen

An obese, but healthy-looking man wearing sandals, shorts, and a T-shirt. Oriented $\times 3$, normal mood and affect.

VS

BP 118/78 mm Hg, P 60 bpm, RR 18; Wt 105 kg, Ht 5'11"

Skin

Visible regions are soft and moist.

HEENT

Normocephalic, PERLA, EOMI, external auditory canals and tympanic membranes clear, hearing grossly; no nasal discharge; oral cavity and pharynx normal, no inflammation, swelling, or lesions

Neck/Lymph Nodes

Neck supple, nontender without lymphadenopathy

Lungs

Clear to auscultation and percussion

CV

Rhythm is regular. Extremities are warm and well perfused.

Abd

Fat rolls can be seen around his belly.

Genit/Rect

Not directly examined, but patient reports pruritus and burning of skin around groin, not on penis or scrotum. Redness can be seen on the medial aspects of the upper thighs.

MS/Ext

Foul-smelling, dry, scaling feet with white flaking between toes. Toenails on both feet appear to have yellow-brown discoloration. The nails of some of the toes are thicker than the rest, particularly on the right foot.

Neuro

CN II–XII normal. Sensation to pain, touch, and proprioception normal.

■ Labs

None available, but patient states his cholesterol and blood sugars are “good.”

■ Assessment

1. Athlete's foot (tinea pedis)
2. Jock itch (tinea cruris)
3. Possible onychomycosis
4. Unsanitary foot and body hygiene

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of dermatophytosis?
- 1.b. What additional information is needed to fully assess this patient's dermatophytosis?

Assess the Information

- 2.a. Assess the severity of dermatophytosis based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating dermatophytosis?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

You recommend an OTC product, and the patient returns to your pharmacy 2 months later. He tells you that his itching has stopped, but his toenails have grown thick and crusty. They are also darker yellow than before. He has an appointment with his physician next week.

FOLLOW-UP QUESTIONS

1. What is "pulse" therapy for onychomycosis, and what are its advantages and disadvantages?
2. What are the differences between appropriate treatment of onychomycosis and tinea pedis?
3. If itraconazole had been prescribed for this patient, what could be some possible reasons for lack of efficacy?

SELF-STUDY ASSIGNMENTS

1. Explain the situations where it is necessary to refer a patient to a physician for the treatment of tinea infections and when oral therapy is preferred over topical agents.
2. Compare the mechanisms of action for the azole and allylamine antifungals.
3. Review the rates and precipitating factors of oral terbinafine- and itraconazole-associated hepatotoxicity.

CLINICAL PEARL

Over 70% of the population will experience a mycotic infection of the skin, hair, or nail at some point in their lifetime.

REFERENCES

1. Sahoo AK, Mahajan R. Management of tinea corporis, tinea cruris, and tinea pedis: a comprehensive review. *Indian Dermatol Online J* 2016;7(2):77–86.
2. Westerberg DP, Voyack MJ. Onychomycosis: current trends in diagnosis and treatment. *Am Fam Physician* 2013;88(11):762–770.
3. Ely JW, Rosenfeld S, Seabury SM. Diagnosis and management of tinea infections. *Am Fam Physician* 2014;90(10):702–710.
4. Gupta AK, Cooper EA. Update in antifungal therapy of dermatophytosis. *Mycopathologia* 2008;166:353–367.
5. Gupta AK, Foley KA, Versteeg SG. New antifungal agents and new formulations against dermatophytes. *Mycopathologia* 2017;182:127–141.
6. Ameen M, Lear JT, Madan V, Mustapa M, Richardson M. British association of dermatologists' guidelines for the management of onychomycosis. *Br J Dermatol* 2014;171(5):937–958.
7. Saunders J, Maki K, Koski R, Nybo SE. Tavaborole, efinaconazole, and luliconazole: three new antimycotic agents for the treatment of dermatophytic fungi. *J Pharm Pract* 2017;30(6):621–630.

140

BACTERIAL VAGINOSIS

Competition Among Bacteria Level I

Charles D. Ponte, BPharm, PharmD, BC-ADM, BCPS, CDE, CPE, FAADE, FAPhA, FASHP, FCCP, FNAP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify predisposing factors associated with bacterial vaginosis.
- List the common clinical and diagnostic findings associated with bacterial vaginosis.
- Develop a therapeutic plan for the management of bacterial vaginosis.
- Describe the role of the pharmacist in the overall management of infectious vaginitis.

PATIENT PRESENTATION

■ Chief Complaint

"I think I might have a yeast infection."

■ HPI

Judy Heyman is a 30-year-old female graduate student who comes to the family practice center for an acute care visit. She states that 1 month ago she was seen at an urgent care center for severe facial pain and headache. She was diagnosed with an acute sinus infection and given a prescription for a 2-week course of doxycycline (100 mg PO BID). During treatment, she developed a vaginal yeast infection. She self-treated it with a nonprescription antifungal cream that alleviated her symptoms. She states that she completed her course of doxycycline despite some mild diarrhea attributed to the drug. Presently, she complains of some mild vaginal discomfort (worse with intercourse) and a "fishy" vaginal odor. Her last period was approximately 5 weeks ago. She admits to inconsistent use of a diaphragm and foam for contraception.

■ PMH

Venereal warts—2011
GERD

■ FH

Noncontributory

■ SH

Is a graduate student in the College of Business and Economics. Has multiple sexual partners (including women); male partners rarely use condoms. Has smoked one pack of cigarettes per day since age 16. Alcohol use consists of a glass of wine nightly and occasional beer. Smokes an occasional marijuana joint.

■ Meds

Prilosec 20 mg PO Q HS
Multivitamin one PO daily
Calcium supplement with vitamin D one PO daily

■ All

Cats → itchy eyes and sneezing; house dust → watery eyes, sneezing; penicillin → hive-like pruritic rash, some tightness in her chest; topical clindamycin → facial rash when used to treat acne 15 years ago.

■ ROS

Noncontributory except that she has noticed a small amount of thin, white mucus on her underclothing and her period is approximately 7 days late.

■ Physical Examination

Limited because of acute visit for specific gynecologic complaint

Gen

Patient is a healthy-appearing 30-year-old woman in NAD.

VS

BP 130/75 mm Hg, P 90 bpm, RR 16, T 37.4°C; Wt 51.5 kg, Ht 5'3"

Genit/Rect

External genitalia WNL; no discharge expressed from the urethra, vagina with a small amount of thin white mucus; positive "whiff" test; pH 5.0. Cervix—not completely visualized; appears clear with a small amount of mucoid discharge from the os. Uterus is slightly enlarged, nontender, retroflexed, no cervical motion tenderness. Adnexa without tenderness or masses.

■ Labs

Microscopic examination of vaginal secretions: 20–25 WBC/hpf; 10–15 clue cells/hpf; 0 lactobacilli/hpf; 15–20 squamous epithelial cells/hpf
Serum pregnancy test—negative

■ Assessment

Vaginal candidiasis—resolved
Bacterial vaginosis

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of bacterial vaginosis (Table 140-1)?
- What additional information is needed to fully assess this patient's bacterial vaginosis?
- What is the pathophysiologic basis for the development of bacterial vaginosis?

Assess the Information

- Assess the severity of bacterial vaginosis based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

TABLE 140-1 Characteristics of Different Types of Vaginitis

Characteristic	<i>Candida</i>	Bacterial	<i>Trichomonas</i>	Chemical
Pruritus	++	+/-	+/-	++
Erythema	+	+/-	+/-	+
Abnormal discharge	+	+	+/-	—
Viscosity	Thick	Thin	Thick/thin	—
Color	White	Gray	White, yellow, green-gray	—
Odor	None	Foul, "fishy"	Malodorous	—
Description	Curdlike	Homogeneous	Frothy	—
pH	3.8–5.0	>4.5	5.0–7.5	—
Diagnostic tests	Potassium hydroxide preparation shows long, threadlike fibers of mycelia microscopically	(+) "Whiff test," "clue cells"	Pear-shaped protozoa, cervical "strawberry" spots	—

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What feasible pharmacotherapeutic alternatives are available for treating this patient's bacterial vaginosis?
- 3.c. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.d. What alternatives would be appropriate if the initial care plan fails or cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

After completion of the treatment you recommended, the patient returns to the clinic in 10 days for follow-up. She voices no complaints except that she has been experiencing some vaginal itching, dysuria, and continued painful intercourse. Physical examination reveals a thick, whitish material adherent to the vaginal mucosa. The vulva appears erythematous with excoriations on the labia majora. Microscopic analysis of vaginal secretions revealed hyphae and budding yeast. No white cells are noted. Vaginal pH is normal. The patient is diagnosed with vaginal candidiasis.

FOLLOW-UP QUESTION

1. What is the most likely cause of this patient's vaginal candidiasis?

SELF-STUDY ASSIGNMENTS

1. Discuss management of a patient who fails a specific course of treatment for bacterial vaginosis.
2. Discuss the pros and cons of screening asymptomatic pregnant women for the presence of bacterial vaginosis.
3. Describe the best therapeutic approach for a woman diagnosed with bacterial vaginosis who is breast-feeding her infant.
4. Discuss the role of sexual transmission in the pathogenesis of bacterial vaginosis.

CLINICAL PEARL

Patients should be counseled that oral metronidazole may cause a mild disulfiram (Antabuse)-like reaction if alcohol is consumed during therapy. Symptoms may include flushing, GI distress, sweating, thirst, and blurred vision. Advise patients to abstain from

alcoholic beverages during therapy and for 72 hours following its completion.

REFERENCES

1. Heather LP, Desai UA. Vaginitis: diagnosis and treatment. *Am Fam Physician* 2018;97:321–329.
2. Allsworth JE, Peipert JE. Severity of bacterial vaginosis and the risk of sexually transmitted infection. *Am J Obstet Gynecol* 2011;113:e1–e6.
3. Nyirjesy P. Vulvovaginal candidiasis and bacterial vaginosis. *Infect Dis Clin North Am* 2008;22:637–652.
4. McCormack WM, Augenbraun MH. Vulvovaginitis and cervicitis. In: Bennett JE, Dolin R, Blasser MJ, eds. *Mandell, Douglas, and Bennett's: Principles and Practice of Infectious Diseases*. 8th ed. Philadelphia, PA, Elsevier; 2015:1358–1371.e2.
5. Centers for Disease Control and Prevention. Diseases characterized by vaginal discharge. Sexually transmitted diseases treatment guidelines, 2015. *MMWR Morb Mortal Wkly Rep* 2015;64:59(RR-123):1–14009. Available at: www.cdc.gov/std/tg2015/default.htm. www.cdc.gov. Accessed January 21, 2019.
6. Sobel JD. What's new in bacterial vaginosis and trichomoniasis? *Infect Dis Clin North Am* 2005;19:387–406.
7. Swidsinski A, Mendling W, Loening-Baucke V, et al. An adherent *Gardnerella vaginalis* biofilm persists on the vaginal epithelium after standard therapy with oral metronidazole. *Am J Obstet Gynecol* 2008;198:e1–e6.
8. Coleman JS, Gaydos CA. Molecular diagnosis of bacterial vaginosis: an update. *J Clin Microbiol* 2018;56:e00342–18.
9. Nygren P. Evidence on the benefits and harms of screening and treating pregnant women who are asymptomatic for bacterial vaginosis: an update review for the U.S. Preventive Services Task Force. *Ann Intern Med* 2008;148:220–233.
10. Lamont RE, Nhan-Chang CL, Sobel JD, et al. Treatment of abnormal vaginal flora in early pregnancy with clindamycin for the prevention of spontaneous pre-term birth: a systematic review and metaanalysis. *Am J Obstet Gynecol* 2011;205:177–190.

141

CANDIDA VAGINITIS

It's Back Level I

Rebecca M. Law, BS Pharm, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Distinguish *Candida* vaginitis (vulvovaginal candidiasis, VVC) from other types of vaginitis.
- Know when to refer a patient with symptoms of vaginitis to a physician for further evaluation and treatment.
- Choose an appropriate treatment regimen for a patient with VVC.
- Choose appropriate alternatives for a patient with recurrent VVC, while considering issues relating to non-*albicans* VVC.
- Educate patients with vaginitis about proper use of pharmacotherapeutic treatments and nonpharmacologic management strategies.

PATIENT PRESENTATION

■ Chief Complaint

"I'm having the same problem I had 2 weeks ago, and my doctor is away until next Monday. Can you give me some more of these suppositories?"

■ HPI

Sophie Kim is a 32-year-old woman who presents to your pharmacy with the above complaint. Upon further questioning, you find that she was diagnosed 3 weeks ago by her physician as having another vaginal *Candida* infection. She was prescribed nystatin suppositories 100,000 units intravaginally for 14 nights, which was the same as what she had been prescribed for her previous episode of vaginal candidiasis 2 months earlier. She stated that she finished the prescription 1 week ago and felt better then. However, 3 days ago she began to notice mild vaginal itching again. She thought it was her new control-top panty hose and stopped wearing them, but the itching got worse and became fairly severe with a burning sensation. There was also a white, dry, curd-like vaginal discharge that was nonodorous. This seemed to be identical to what she had experienced 3 weeks ago. Her physician is away until next week, and she wondered if the pharmacy can give her some more suppositories. Last month, she began using tights (with an adjustable waist) to help prevent varicose veins.

■ PMH

Diabetes type 1 since age 11. Her blood glucose is well controlled, and her physician is keeping a close eye due to her pregnancy. Recurrent leg ulcers and foot infections for which she has been prescribed antibiotics on a frequent basis. Currently, there are no ulcers or infections, and she is not on antibiotics.

■ SH

Nonsmoker; drinks alcohol in moderate amounts (one to two drinks maximum) at social functions. She is married and is 7½ months pregnant.

■ Meds

Insulin glargine 15 units SC Q AM for past year
Insulin lispro 6 units SC 15 minutes prior to breakfast, 8 units 15 minutes prior to lunch, and 10 units 15 minutes prior to dinner, for past 4 months
Materna 1 PO Q AM

■ All

NKDA

■ ROS

Not performed

■ Physical Examination

VS

BP 120/78 mm Hg; Wt 70 kg, Ht 5'5"

Note: No further assessments performed

■ Labs

Not available

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of vulvovaginal candidiasis (VVC, *Candida* vaginitis) (Table 141-1)?
- What additional information is needed to fully assess this patient's VVC?

Assess the Information

- Assess the severity of VVC based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy in this case?
- What nondrug therapies might be useful to manage this patient's VVC?
- What feasible pharmacotherapeutic alternatives are available for treating VVC in this patient?
- Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

TABLE 141-1 Characteristics of Different Types of Vaginitis

Characteristic	<i>Candida</i>	Bacterial	<i>Trichomonas</i>	Chemical
Pruritus	++	+/-	+/-	++
Erythema	+	+/-	+/-	+
Abnormal discharge	+	+	+/-	-
Viscosity	Thick	Thin	Thick/thin	-
Color	White	Gray	White, yellow, green-gray	-
Odor	None	Foul, "fishy"	Malodorous	-
Description	Curd-like	Homogeneous	Frothy	-
pH	3.8–5.0	>4.5	5–7.5	-
Diagnostic tests	Potassium hydroxide prep. shows long, thread-like fibers of mycelia microscopically	+ Whiff test, clue cells	Pear-shaped protozoa, cervical "strawberry" spots	-

For some discussion of above conditions and diagnostic considerations, see: Diseases characterized by vaginal discharge: vulvovaginal candidiasis. CDC 2015 sexually transmitted diseases treatment guidelines. Available at: <http://www.cdc.gov/std/tg2015/candidiasis.htm> and Section 4: Management and treatment of specific syndromes: vaginal discharge (bacterial vaginosis, vulvovaginal candidiasis, trichomoniasis). Canadian Guidelines on Sexually Transmitted Infections, 2010. Ottawa, ON: Public Health Agency of Canada. Available at: <http://www.phac-aspc.gc.ca/std-mts/sti-its/cgsti-lcits/section-4-8-eng.php>.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of goals of therapy.

CLINICAL COURSE

The recommended treatment was successful. Two months later, Sophie had another episode of VVC, which was again successfully treated. She delivered a healthy 7-lb baby boy born at term. A month after that, she had another episode of VVC, and she is now nursing.

FOLLOW-UP CASE QUESTION

1. What is the most appropriate course of action for managing this patient's recurrent VVC?

SELF-STUDY ASSIGNMENTS

1. Obtain information on tests used to diagnose different types of vaginitis.
2. Compare the retail cost of nonprescription vaginitis treatments in your area.
3. Outline your plans for communicating your treatment recommendations to the patient's physician.

CLINICAL PEARL

Patients with symptoms suggestive of bacterial vaginosis or sexually transmitted infection (eg, fever, abdominal or back pain, foul-smelling discharge) should be referred to a physician for further evaluation and treatment.

REFERENCES

1. Centers for Disease Control and Prevention (CDC); Workowski KA, Bolan GA. Diseases characterized by vaginal discharge: vulvovaginal candidiasis. 2015 Sexually transmitted diseases treatment guidelines. Available at: <https://www.cdc.gov/std/tg2015/candidiasis.htm>. Accessed January 11, 2019.
2. Public Health Agency of Canada (PHAC). Section 4: Management and treatment of specific syndromes: vaginal discharge (bacterial vaginosis, vulvovaginal candidiasis, trichomoniasis). In: Canadian Guidelines on Sexually Transmitted Infections—January 2010. Also see the 2016 Updates Summary, the 2014 Supplementary Statement, and the Laboratory Diagnosis of Sexually Transmitted Infections chapter (revised in 2016).
3. Falagas ME, Betsi GI, Athanasiou S. Probiotics for prevention of recurrent vulvovaginal candidiasis: a review. *J Antimicrob Chemother* 2006; 58:266–272.
4. Hilton E, Isenberg HD, Alperstein P, France K, Borenstein MT. Ingestion of yogurt containing *Lactobacillus acidophilus* as prophylaxis for *Candida* vaginitis. *Ann Intern Med* 1992;116:353–357.
5. Young G, Jewell D. Topical treatment for vaginal candidiasis (thrush) in pregnancy. *Cochrane Database Syst Rev* 2001;(4):CD000225. Abstract available at: <https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD000225/abstract>. Accessed January 26, 2019.
6. Sobel JD, Chaim W, Nagappan V, Leaman D. Treatment of vaginitis caused by *Candida glabrata*: use of topical boric acid and flucytosine. *Am J Obstet Gynecol* 2003;189:1297–1300.
7. Wooltorton E. Drug advisory: the interaction between warfarin and vaginal miconazole. *CMAJ* 2001;165(7):938. Available at: <http://www.cmaj.ca/content/165/7/938.3.full>. Accessed March 25, 2019.
8. Sanchez JM, Moya G. Fluconazole teratogenicity. *Prenat Diagn* 1998;18:862–863.
9. Jick SS. Pregnancy outcomes after maternal exposure to fluconazole. *Pharmacotherapy* 1999;19:221–222.
10. Ray D, Goswami R, Banerjee U, et al. Prevalence of *Candida glabrata* and its response to boric acid vaginal suppositories in comparison with oral fluconazole in patients with diabetes and vulvovaginal candidiasis. *Diabetes Care* 2007;30:312–317.

142

INVASIVE FUNGAL INFECTIONS

The Brewer's Yeast Level II

Douglas Slain, PharmD, BCPS, FCCP, FASHP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Construct a prudent empiric antifungal regimen for a patient with candidemia.
- Determine situations in which to use echinocandins for invasive *Candida* infections.
- Discuss how identification of non-albicans *Candida* species can influence antifungal selection.

PATIENT PRESENTATION

Chief Complaint

"I am burning up and feel like I have the flu."

HPI

August Hops is a 50-year-old man who has been experiencing fever and chills and has not been feeling well over the past 4 days. He was admitted to our hospital yesterday. He was at home receiving home therapy with daptomycin 700 mg IV once daily (day 12 of a 14-day course) via PICC line for MRSA bacteremia, which he developed after having an appendectomy at an outside community hospital about a month ago. During that hospitalization, he also received a course of piperacillin-tazobactam for appendicitis. His postoperative stay was complicated by a surgical site infection and MRSA bacteremia. He had the catheter removed at that time and was started on vancomycin until he developed a rash and possible neutropenia. He was then switched to (and eventually sent home on) daptomycin. Prior to being discharged from the outside hospital,

Mr Hops also received 7 days of fluconazole 200 mg PO daily for a urine sample from a Foley catheter that grew 100,000 colonies/mL of *Candida glabrata*. He never grew *Candida* from any other site.

A set of blood cultures was drawn on this admission to our hospital and is showing no growth at 24 hours. His surgical site does not look infected. His PICC line was removed, and blood and urine cultures were drawn. Piperacillin–tazobactam was added to the daptomycin empirically on admission.

■ PMH

GERD
Hyperlipidemia
HTN

■ PSH

S/P hernia repair 2 years ago
S/P appendectomy 1 month ago

■ FH

Father died of CHF; mother still alive with no major medical problems.

■ SH

He is the brewmaster at the local brewery. Married; has four adult children. Denies smoking or excessive ethanol use.

■ Home Meds

Omeprazole 40 mg PO once daily
Simvastatin 40 mg PO once daily
Metoprolol XL 50 mg PO once daily
Ibuprofen 600 mg PO TID PRN

■ All

Vancomycin—reaction: neutropenia and rash.

■ Physical Examination

Gen

Patient is a 50-year-old Caucasian man who is resting somewhat comfortably in bed. Weight: 125 kg; height: 5'11".

VS

BP 128/85 mm Hg, P 70 bpm, RR 20, T 38.5°C, O₂ sat 97

Skin

Mildly clammy, no Janeway lesions or Osler nodes

HEENT

PERRLA, EOMI, nares patent

Neck/Lymph Nodes

Neck supple; no lymphadenopathy

Lungs/Thorax

CTA

Heart

ECG: Regular rate and rhythm. No murmurs.

Abd

Bowel sounds present. Last BM yesterday.

GU

Grossly normal, UA pending

MS/Ext

No abnormalities

Neuro

Intact

■ Labs

Na 137 mEq/L	Hgb 12.9 g/dL	WBC $13.4 \times 10^3/\text{mm}^3$	AST 35 IU/L
K 4.3 mEq/L	Hct 40%	PMNs 70%	ALT 30 IU/L
Cl 99 mEq/L	Plt $332 \times 10^3/\text{mm}^3$	Bands 8%	Alk phos 140 IU/L
CO ₂ 27 mEq/L		Lymphs 16%	T. bili 1.1 mg/dL
BUN 7 mg/dL		Monos 5%	CK 56 IU/L
SCr 0.8 mg/dL		Eos 1%	Lipase 92 IU/L
Glu 98 mg/dL			Amylase 112 IU/L
Mg 2.2 mg/dL			

Serum (1-3)- β -d-glucan: 85 pg/mL (positive)

■ Blood Cultures

No growth at 24 hours

■ Chest X-Ray

No infiltrates

■ Assessment

1. Possible bacterial infection (new source vs nonresponding MRSA bacteremia)
2. Possible fungal infection

■ Plan

1. Continue daptomycin 700 mg IV daily and piperacillin–tazobactam 3.375 mg IV Q 8 H.
2. Start fluconazole 800 mg IV loading dose, then 400 mg IV daily.
3. Order abdominal CT scan.
4. Draw additional blood cultures.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of invasive fungal infection?
- 1.b. What additional information is needed to fully assess this patient's fungal infection?

Assess the Information

- 2.a. Assess the severity of the possible fungal infection based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?

- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the fungal infection?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The abdominal CT scan showed no signs of intra-abdominal infection. Despite two more days of continued daptomycin therapy, the patient continues to be febrile with leukocytosis, but WBC is slightly improved.

Culture and sensitivity data are now available:

- Blood cultures positive at 72 hours (drawn on admission):
 - ✓ PICC line catheter: Rare budding yeast and rare coagulase-negative staphylococci
 - ✓ Left peripheral: Rare budding yeast

The team continued fluconazole and discontinued daptomycin and piperacillin-tazobactam. They also ordered a fundoscopic eye exam to check for *Candida* endophthalmitis. A transesophageal echocardiogram (TEE) was ordered and showed no signs of vegetation.

FOLLOW-UP QUESTIONS

1. Given the microbiology results at 72 hours, what changes (if any) would you recommend?
2. If the fundoscopic eye exam were to suggest endophthalmitis, what therapies would be best for treating the eye infection?

SELF-STUDY ASSIGNMENTS

1. Explain how the T2-*Candida* rapid diagnostic test works.
2. Search the medical literature to determine whether any antifungal agents have displayed useful activity against *Candida* in biofilm.

CLINICAL PEARL

Despite the general enhanced in vitro *Candida* activity of voriconazole over fluconazole, therapy with voriconazole may be affected by azole-class resistance mechanisms.

REFERENCES

1. Pappas PG, Kauffman CA, Andes D, et al. Clinical practice guidelines for the management of candidiasis: 2016 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2016 Feb 15;62(4):e1–e50.
2. Parkins MD, Sabuda DM, Elsayed S, Laupland KB. Adequacy of empirical antifungal therapy and effect on outcome among patients with invasive *Candida* species infections. *J Antimicrob Chemother* 2007;60:613–618.
3. Gubbins PO, Heldenbrand S. Clinically relevant drug interactions of current antifungal agents. *Mycoses* 2010;53:95–113.
4. Cauda R. Candidemia in patients with an inserted medical device. *Drugs* 2009;69(Suppl 1):33–38.
5. Chiotos K, Vendetti N, Zaoutis TE, et al. Comparative effectiveness of echinocandins versus fluconazole therapy for the treatment of adult candidaemia due to *Candida parapsilosis*: a retrospective observational cohort study of the Mycoses Study Group (MSG-12). *J Antimicrob Chemother* 2016;71(12):3536–3539.
6. Chen SC, Sorrell TC. Antifungal agents. *Med J Aust* 2007;187:404–409.
7. Andes DR, Safdar N, Baddley JW, et al. Impact of treatment strategy on outcomes in patients with candidemia and other forms of invasive candidiasis: a patient-level quantitative review of randomized trials. *Clin Infect Dis* 2012;54:1110–1122.
8. Cleary JD, Schwartz M, Rogers PD, de Mestral J, Chapman SW. Effects of amphotericin B and caspofungin on histamine expression. *Pharmacotherapy* 2003;23:966–973.
9. Riddell J, Comer GM, Kauffman CA. Treatment of endogenous fungal endophthalmitis: focus on new antifungal agents. *Clin Infect Dis* 2011;52(5):648–653.

143

INFECTION IN AN IMMUNOCOMPROMISED PATIENT

Making a Rash Decision Level II

Aaron Cumpston, PharmD, BCOP

Douglas Slain, PharmD, BCPS, FCCP, FASHP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Construct a prudent empiric antibiotic regimen for a febrile neutropenic patient.
- Determine appropriate situations to use vancomycin in empiric antimicrobial regimens for treatment of febrile neutropenic episodes.
- Describe situations in which antibiotic monotherapy versus combination therapy would be warranted for empiric treatment of febrile neutropenia.

PATIENT PRESENTATION

Chief Complaint

"I have a fever and chills."

■ HPI

Scarlet Hives is a 60-year-old woman with a history of IgG kappa multiple myeloma who is undergoing an autologous hematopoietic cell transplant. Her stem cells were collected by peripheral blood collection, which were mobilized with cyclophosphamide and filgrastim. During collection she developed a vesicular rash involving her left lower abdominal quadrant, which was documented by PCR analysis to be herpes zoster. This was treated with valacyclovir. Her preparative regimen for transplant was high-dose melphalan, followed by stem cell rescue with her peripheral blood stem cells. Eight days after stem cell infusion, she spiked a fever of 38.6°C (101.5°F). She now also complains of chills and nausea.

■ PMH

IgG kappa multiple myeloma
GERD
HTN
Hyperlipidemia
CAD
Peripheral neuropathy
Type 2 DM
Chronic back pain

■ Surgical History

Hysterectomy—17 years ago

■ FH

Mother died of CAD at early age; father died at age 67 from lung cancer; has one sister and one brother, both living and well.

■ SH

High school cafeteria manager of 22 years; now retired. She is married and lives with her husband. She has three children. Denies smoking or alcohol use.

■ Meds

Esomeprazole 40 mg PO once daily
Atorvastatin 80 mg PO once daily
Fentanyl patch 75 mcg Q 48 H
Neurontin 800 mg PO TID
Lisinopril 5 mg PO once daily
Metoprolol 75 mg PO BID
Multivitamin PO once daily
Oxycodone IR 15 mg Q 6 H PRN pain
Pioglitazone 15 mg PO once daily
Promethazine 25 mg PO Q 6 H PRN nausea
Valacyclovir 500 mg PO once daily, after previously completing 1000 mg TID × 7 days for treatment course
Fluconazole 400 mg PO once daily
Levofloxacin 500 mg PO once daily
Senna-docusate capsule one PO daily
Filgrastim 480 mcg subcutaneously daily

■ All

Ceftazidime—"bad rash"

■ ROS

(+) Fever/chills, (+) nausea; denies vomiting, cough, diarrhea

■ Physical Examination

Gen

Patient is a 60-year-old Caucasian woman who appears alert and oriented.

VS

BP 115/83 mm Hg, P 115 bpm, RR 16, T 38.6°C; O₂ sat 98%; Wt 191 lb, Ht 5'1"

Skin

Warm and dry. No erythema or induration around port on left chest. Resolving herpes zoster rash on abdomen; lesions are crusted and healing.

HEENT

PERRLA, EOMI, (–) tonsillar erythema, (–) rhinorrhea, (–) mucositis

Neck/Lymph Nodes

Neck supple; no lymphadenopathy

Lungs/Thorax

Normal; no wheezes, crackles, or rhonchi

Heart

Tachycardic but regular rhythm; no murmurs, rubs, or gallops

Abd

Soft, NT, (+) bowel sounds

Genit/Rect

Deferred

MS/Ext

No deformity, mild weakness, no peripheral edema

Neuro

A&O × 3; CN II–XII grossly intact

■ Labs

Na 135 mEq/L	WBC $0.2 \times 10^3/\text{mm}^3$	AST 16 IU/L
K 3.6 mEq/L	Hgb 8.9 g/dL	ALT 15 IU/L
Cl 95 mEq/L	Hct 25.3%	Alk phos 38 IU/L
CO ₂ 21 mEq/L	Plt $21 \times 10^3/\text{mm}^3$	LDH 187 IU/L
BUN 16 mg/dL	ANC $0.05 \times 10^3/\text{mm}^3$	T. bili 0.6 mg/dL
SCr 1.0 mg/dL	A1C 6.7%	Albumin 2.8 g/dL
Glu 149 mg/dL		
Ca 8.0 mg/dL		

■ UA

Pending

■ Blood Cultures

PICC line: Pending
Peripheral: Pending

■ Chest X-Ray

Presence of a 2.2-cm oval-shaped density projecting at the level of the retrocardiac aspect of the medial left lung base

■ CT Scan With IV Contrast

Normal, no evidence of pulmonary nodule that was a concern on chest x-ray

■ Assessment

1. Multiple myeloma s/p autologous stem cell transplant
2. Neutropenic fever
3. Concern for possible pneumonia, despite CT scan findings

■ Initial Plan

1. Begin empiric piperacillin–tazobactam 4.5 g IV Q 6 H (infused over 30 minutes).
2. Discontinue prophylactic levofloxacin.
3. Monitor for rash due to history of ceftazidime allergy.
4. Monitor renal function and hydrate with IV fluids due to IV contrast with CT scan.
5. Continue home medications.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of neutropenic fever and possible infection?
- 1.b. What additional information is needed to fully assess this patient's possible infection?

Assess the Information

- 2.a. Assess the severity of the possible infection based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient's possible infection?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the febrile neutropenic episode?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

On day 2 of admission, the patient is still febrile and the following results are reported:

SCr 2.1 mg/dL	Hgb 8.4 g/dL
	Hct 22.8%
	Platelets $9 \times 10^3/\text{mm}^3$
	WBC $0.2 \times 10^3/\text{mm}^3$
BP 120/75, P 100, RR 18, T 38.3°C, O ₂ sat 98% RA	
Urine and blood cultures (PICC line and peripheral): No growth at 24 hours	

The team continued to monitor the patient as planned. The patient started developing a systemic erythematous rash. On day 3, piperacillin–tazobactam was changed to imipenem–cilastatin due to the presumed drug rash. Her rash continued to worsen while taking imipenem. On day 5, the WBC was $0.3 \times 10^3/\text{mm}^3$, and caspofungin was added for empiric coverage for persistent fevers. On day 6, her WBC was $0.6 \times 10^3/\text{mm}^3$ with an ANC of $0.520 \times 10^3/\text{mm}^3$. At this time, blood cultures from the PICC line became positive for gram-positive cocci in pairs and chains. The team added vancomycin 1500 mg Q 24 H and stopped the imipenem–cilastatin because the rash was still worsening and the patient was no longer neutropenic. The PICC line was removed, and caspofungin was discontinued the next day. Final identification of the organism in the blood was reported on day 8 as *Enterococcus faecalis*, sensitive to ampicillin and vancomycin. The patient became afebrile after initiation of vancomycin. Her creatinine had normalized by this time, she was no longer neutropenic, and her rash was starting to resolve. She was discharged to complete a 2-week course of vancomycin. All subsequent blood and urine cultures were negative for microbial growth.

■ FOLLOW-UP QUESTIONS

1. What other antibiotic therapies could have been used for the treatment of this patient's bacteremia?
2. What is the possibility of cross-reactivity between ceftazidime and aztreonam?
3. When should vancomycin be considered as an initial empiric agent in febrile neutropenic patients?

■ SELF-STUDY ASSIGNMENTS

1. Review the criteria for classification of febrile neutropenic patients as either "low" or "high" risk. What types of neutropenic patients would be considered "low risk" and might benefit from oral antibiotic regimens?
2. Construct a treatment algorithm for neutropenic patients with bloodstream infections caused by vancomycin-resistant *Enterococcus faecium* (VRE). The algorithm should include decisions based on renal function and drug contraindications.

CLINICAL PEARL

Bacterial infections in neutropenic patients have evolved from the historical isolation of gram-negative pathogens to the most common bacteria isolated currently being gram-positive organisms. This is especially true when fluoroquinolone prophylaxis is used.

REFERENCES

1. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2011;52:e56–e93.
2. Taplitz RA, Kennedy EB, Bow EJ, et al. Outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology and Infectious Diseases Society of America Clinical Practice Guideline Update. *J Clin Oncol* 2018;36(14):1443–1453.
3. Shenoy ES, Macy E4, Rowe T, Blumenthal KG. Evaluation and management of penicillin allergy: a review. *JAMA* 2019;321(2):188–199.
4. Mermel LA, Farr BM, Sherertz RJ, et al. Guidelines for the management of intravascular catheter-related infections. *Clin Infect Dis* 2009;49:1–45.
5. National Comprehensive Cancer Network (NCCN) clinical practice guidelines in oncology (v1.2019). Prevention and treatment of cancer-related infections. Available at: https://www.nccn.org/professionals/physician_gls/pdf/infections.pdf. Accessed March 1, 2019.
6. Paul M, Dickstein Y, Schlesinger A, Grozinsky-Glasberg S, Soares-Weiser K, Leibovici L. Beta-lactam versus beta-lactam-aminoglycoside combination therapy in cancer patients with neutropenia. *Cochrane Database Syst Rev* 2013; 29(6):CD003038.
7. Rutter WC, Cox JN, Martin CA, Burgess DR, Burgess DS. Nephrotoxicity during vancomycin therapy in combination with piperacillin-tazobactam or ceftazidime. *Antimicrob Agents Chemother* 2017;61(2):e02089–16.
8. Gilbert DN, Chambers HF, Eliopoulos GM, Saag MS, Pavia AT eds. The Sanford Guide to Antimicrobial Therapy 2018. 48th ed. Sperryville, VA: Antimicrobial Therapy; 2018.
9. Frumin J, Gallagher JC. Allergic cross-sensitivity between penicillin, carbapenem, and monobactam antibiotics: what are the chances? *Ann Pharmacother* 2009;43:304–315.
10. Luther MK, Rice LB, LaPlante KL. Ampicillin in combination with ceftaroline, ceftazidime, or ceftriaxone demonstrates equivalent activities in a high-inoculum *Enterococcus faecalis* infection model. *Antimicrob Agents Chemother* 2016 Apr 22;60(5):3178–3182.

- Identify the pros and cons to using oral antimicrobial decontamination prior to colorectal surgery.
- Evaluate the need for perioperative antiplatelet therapy in a specific surgical patient.

PATIENT PRESENTATION

■ Chief Complaint

“I have colon cancer and I’m here for surgery.”

■ HPI

Edward Adler is a 72-year-old man who was recently diagnosed with anemia and generalized weakness. The workup for anemia included a colonoscopy, which showed a malignant neoplasm of the proximal ascending colon. The neoplasm was identified, and the biopsy revealed moderately differentiated adenocarcinoma. The patient denies any current abdominal pain or change in bowel habits but reports a 20-lb weight loss over the past several months. He is eating but has less of an appetite than normal.

■ PMH

Positive for HTN, CAD, TIA, and chronic rhinitis. History of gastritis and anemia.

■ PSH

Tonsillectomy, left inguinal hernia repair, colonoscopy with biopsy.

■ SH

Positive for smoking history of one-half of a pack daily; quit 20 years ago

■ Meds

Metoprolol succinate 50 mg PO daily
Hydrochlorothiazide 12.5 mg PO daily
Atorvastatin 40 mg PO daily
Sertraline 100 mg PO daily
Omeprazole 20 mg PO daily
Aspirin 81 mg PO daily
Triamcinolone nasal spray, two sprays in the morning
Ferrous sulfate 325 mg PO TID
Multivitamin one PO once daily

■ All

None

■ ROS

Cardiopulmonary: Denies chest pain, shortness of breath, or wheezing
Gastrointestinal: Denies history of hepatitis, ulcers, or jaundice
Genitourinary: He has no history of hematuria or renal calculi
Psychiatric: Positive for depression

■ Physical Examination

Gen

He has the appearance of a normally developed white man who appears his stated age. He is alert, awake, and in no obvious distress.

VS

BP 132/86 mm Hg, P 68 bpm, RR 11, T 37.1°C; Wt 69 kg, Ht 172.7 cm

144

ANTIMICROBIAL PROPHYLAXIS FOR SURGERY

In Life, Preparation Is Everything Level II

Curtis L. Smith, PharmD, FCCP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recommend appropriate antimicrobial prophylaxis for a given surgical procedure.
- Discuss the timing of antimicrobial prophylaxis for surgery, including doses prior to and after surgery.
- Describe the controversy regarding mechanical bowel preparation prior to colorectal surgery.

Skin

Warm and dry. Multiple seborrheic dermatomes over the abdomen and chest.

HEENT

Face reveals no asymmetry. Pupils are equal. Eyes have no icterus or exophthalmus, extraocular movements intact. He is wearing corrective lenses.

Neck/Lymph Nodes

No adenopathy or thyromegaly. There is no jugular venous distention.

Lungs/Thorax

Clear to auscultation

CV

Regular rate and rhythm without murmurs

Abd

The patient has a faint, left inguinal scar from prior left inguinal hernia repair. The abdomen is without palpable masses, splenomegaly, or hepatomegaly. No tenderness noted.

Genit/Rect

Not examined

MS/Ext

No scoliosis. He has mild lordotic and kyphotic components to the vertebral curvature. No paravertebral tenderness or spasm. Leg lengths and shoulder heights are grossly equal. Extremities: no gross deformities, rashes, or ecchymoses. 2+ pulses in all four extremities.

Neuro

No gross motor or sensory deficits or hyperreflexia. Good grip strength bilaterally.

Labs

Na 132 mEq/L	Hgb 11.9 g/dL	WBC $6.0 \times 10^3/\text{mm}^3$
K 4.1 mEq/L	Hct 39.2%	PMNs 70%
Cl 97 mEq/L	RBC $4.06 \times 10^6/\text{mm}^3$	Bands 0%
CO ₂ 26 mEq/L	Plt $324 \times 10^3/\text{mm}^3$	Eos 5%
BUN 14 mg/dL	MCV $84 \mu\text{m}^3$	Lymphs 13%
SCr 0.9 mg/dL	MCHC 34.8 g/dL	Monos 12%
Glu 93 mg/dL		
Alb 3.9 g/dL		

Assessment

1. Adenocarcinoma of the proximal ascending colon
2. Right hemicolectomy planned

QUESTIONS**Collect Information**

- 1.a. Do guidelines recommend antimicrobial prophylaxis for the surgical procedure planned for this patient?
- 1.b. What additional information is needed to fully assess this patient's need for surgical antimicrobial prophylaxis?

Assess the Information

- 2.a. Based on the planned surgical procedure, what is the risk for a surgical wound infection in this patient postoperatively?
- 2.b. Create a list of the patient's drug therapy problems and prioritize them, including potential postoperative problems.
- 2.c. Will a mechanical bowel preparation prior to surgery benefit this patient?
- 2.d. What are the potential advantages and disadvantages associated with giving oral antibiotics prior to a colorectal surgical procedure?

Develop a Care Plan

- 3.a. What are the goals of antimicrobial pharmacotherapy for preventing a surgical wound infection?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for surgical prophylaxis for this patient's type of surgery?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to this patient regarding the risk of surgical wound infections and the use of antibiotics to prevent this risk?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be monitored to assess the prevention or development of a surgical wound infection?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

SELF-STUDY ASSIGNMENTS

1. Construct a chart listing surgical procedures requiring preoperative antimicrobial prophylaxis and the recommended agent(s) to use.
2. Perform a literature search and assess the current information regarding use of oral antibiotics and mechanical bowel preparations prior to colorectal surgery.
3. Perform a literature search and assess the current information regarding using antiplatelets perioperatively (based on both patient characteristics and surgical procedure).

CLINICAL PEARL

Patients who receive antibiotics for surgical prophylaxis within 3 hours after the surgical incision have a three times higher risk of surgical wound infection compared to patients who receive antibiotics within 2 hours before the incision.

REFERENCES

1. Nelson RL, Gladman E, Barbateskovic M. Antimicrobial prophylaxis for colorectal surgery. *Cochrane Database Syst Rev* 2014 May 9;5:CD001181.
2. Hawn MT, Richman JS, Vick CC, et al. Timing of surgical antibiotic prophylaxis and the risk of surgical site infection. *JAMA Surg* 2013 Jul;148(7):649–657.
3. Fleisher LA, Fleischmann KE, Auerbach AD, et al. 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines. *Circulation* 2014 Dec 9;130(24):e278–e333.
4. Levine GN, Bates ER, Bittl JA, et al. 2016 ACC/AHA guideline focused update on duration of dual antiplatelet therapy in patients with coronary artery disease: a report of the American College of Cardiology/American Heart Association Task Force on Clinical Practice Guidelines: an update of the 2014 ACC/AHA guideline on perioperative cardiovascular evaluation and management of patients undergoing noncardiac surgery. *Circulation* 2016 Sep 6;134(10):e123–e155.
5. Devereaux PJ, Mirkobrada M, Sessler DI, et al. Aspirin in patients undergoing noncardiac surgery. *N Engl J Med* 2014;370:1484–1503.
6. Gould MK, Garcia DA, Wren SM, et al. American College of Chest Physicians. Prevention of VTE in nonorthopedic surgical patients: antithrombotic therapy and prevention of thrombosis, 9th ed. American College of Chest Physicians Evidence-Based Clinical Practice Guidelines. *Chest* 2012;141(2 Suppl):e227S–e277S.
7. Rollins KE, Javanmard-Emamghissi H, Lobo DN. Impact of mechanical bowel preparation in elective colorectal surgery: a meta-analysis. *World J Gastroenterol* 2018 Jan 28;24(4):519–536.
8. Bratzler DW, Dellinger EP, Olsen KM, et al. Clinical practice guidelines for antimicrobial prophylaxis in surgery. *Am J Health Syst Pharm* 2013;70:195–283.
9. Classen DC, Evans RS, Pestotnik SL, Horn SD, Menlove RL, Burke JP. The timing of prophylactic administration of antibiotics and the risk of surgical-wound infection. *N Engl J Med* 1992;326:281–286.
10. Berríos-Torres SI, Umscheid CA, Bratzler DW, et al. Centers for Disease Control and Prevention guideline for the prevention of surgical site infection, 2017. *JAMA Surg*. 2017 Aug 1;152(8):784–791.

145

PEDIATRIC IMMUNIZATION

Back to School Level II

Jean-Venable “Kelly” R. Goode, PharmD, BCPS, FAPhA, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Develop a plan for administering any needed vaccines when given a patient’s age, immunization history, and medical history.
- Describe appropriate use of pediatric vaccines.
- Educate a child’s parents on the risks associated with pediatric vaccines and ways to minimize adverse effects.
- Recognize inappropriate reasons for deferring immunization.

PATIENT PRESENTATION

■ Chief Complaint

“My daughter is here for the ‘Back to School’ program.”

■ HPI

Allison Showalter is a 4-year-old girl who is generally healthy. She presents today (August 30, 2019) to the pharmacy with her mother for evaluation and to receive any needed immunizations. Allison will be entering junior kindergarten in the fall, and she needs to have an updated immunization record.

■ PMH

Received prenatal care, delivered at 42 weeks’ gestation via uncomplicated vaginal delivery; birth weight 7 lb, 4 oz. Mother states that her child has had a couple of ear infections (currently on day 4 of treatment) and three or four “colds,” no other illnesses.

■ FH

Mother is 4 months pregnant.

■ SH

Lives with mother, age 30, and father, age 32. No siblings. Mother works part-time. Father works as an electrician. Both parents are Baptist.

■ Meds

Amoxicillin suspension 540 mg PO Q 8 H
No recent OTC medication use

■ All

NKDA

■ ROS

Negative

■ Physical Examination

Gen

Alert, happy, appropriately developed 4-year-old child in NAD.
Wt 18 kg (75th percentile), height 40 in (50th percentile).

VS

BP 105/65 mm Hg, P 110 bpm, RR 28, T 36.7°C (axillary)

HEENT

AF open, flat; PERRL; funduscopic exam not performed; ears slightly red; normal looking TMs, landmarks visualized, no effusion present; nose clear; throat normal

Lungs

Clear bilaterally

CV

RRR, no murmurs

Abd

Soft, nontender, no masses or organomegaly; normal bowel sounds

TABLE 145-1 Immunization Record Card

Immunization Record Card Name: Allison Showalter

Vaccine	Dose/Route/Site	Date	Health Professional	VIS
Hepatitis B	0.5 mL IM thigh	3/15/2015	Colter, RN	Hep B
Pediarix (DTaP, Hep B, IPV)	0.5 mL IM thigh	5/20/2015	Edwards, RN	DTaP, Hep B, IPV
PCV-13	0.5 mL IM thigh	5/20/2015	Edwards, RN	PCV
Hib (HibTITER)	0.5 mL IM thigh	5/20/2015	Edwards, RN	Hib
Pediarix	0.5 mL IM thigh	7/29/2015	Edwards, RN	DTaP, Hep B, IPV
PCV-13	0.5 mL IM thigh	7/29/2015	Edwards, RN	PCV
Hib (HibTITER)	0.5 mL IM thigh	7/29/2015	Edwards, RN	Hib
Pediarix	0.5 mL IM thigh	9/30/2015	Jones, RN	DTaP, Hep B, IPV
PCV-13	0.5 mL IM thigh	9/30/2015	Jones, RN	PCV
Hib (HibTITER)	0.5 mL IM thigh	9/30/2015	Jones, RN	Hib
Hib (HibTITER)	0.5 mL IM thigh	4/1/2016	Edwards, RN	Hib
PCV-13	0.5 mL IM thigh	4/1/2016	Edwards, RN	PCV

Genit/Rect

Normal external genitalia; rectal exam deferred, no fissures noted

Ext

Normal

Neuro

Alert; normal DTRs bilaterally

Labs

See Table 145-1 for immunization record card.

No other labs obtained

Assessment

Normal-appearing child, in need of immunizations

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates needs, precautions, or contraindications to immunization?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. How do healthcare providers determine which vaccines an infant or child needs?
- 2.b. Assess the urgency of the immunization needs based on the subjective and objective information available.
- 2.c. Create a list of the patient's drug therapy and immunization-related problems. Include assessment of medication appropriateness, effectiveness, safety, patient adherence, and any contraindications or precautions for vaccination.
- 2.d. What economic, psychosocial, cultural, racial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What feasible pharmacotherapeutic alternatives are available for pediatric immunizations?
- 3.c. Create an individualized, patient-centered, team-based care plan to optimize immunizations for this patient. Include the vaccines that should be administered to this child today, including dose, route, and schedule.

Implement the Care Plan

- 4.a. What information should be provided to the patient and parents/caregivers to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the response to immunization and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate follow-up for additional immunizations and achievement of a fully immunized patient.

ADDITIONAL CASE QUESTIONS

1. The next year, the mother brings the child to a pediatric influenza immunization clinic stating that the child was diagnosed with diabetes about 3 months ago. The child's immunization record reveals influenza vaccine 0.5 mL $\times$ 1 dose last fall. What is your recommendation for influenza vaccination for this child?
2. What other immunizations are indicated for this child who now has a chronic condition, diabetes mellitus?
3. What is the proper immunization administration technique for children, including location and needle size?

SELF-STUDY ASSIGNMENTS

1. Search the Internet for the immunization laws and allowed exemptions in your state. What vaccines are required for child-care and school entry?
2. Review the most current immunization recommendations for persons aged 0–18 years, and provide a summary of how your recommendations for this case would be different if a 6-month-old patient in need of immunizations came to your clinic today.
3. Search the Internet for immunization-related websites about vaccine-associated adverse effects; compare these sites and evaluate them against reliable websites for vaccine information.

CLINICAL PEARL

All states have immunization laws, but they differ in the requirements and types of exemptions allowed. Vaccine requirements for school entry help ensure that most people are protected through immunization. Pharmacists should advocate for parents and caregivers to have their children immunized on time to protect them against vaccine-preventable diseases.

REFERENCES

- Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices (ACIP). Recommended immunization schedules for persons aged 0–18 years—United States, 2018 (updated annually at <http://www.cdc.gov/vaccines/schedules/hcp/child-adolescent.html>). Accessed December 27, 2018.
- American Academy of Pediatrics. Active and passive immunization. In: Pickering LK, ed. Red Book—Report of the Committee on Infectious Diseases. 30th ed. Elk Grove Village, IL, American Academy of Pediatrics; 2018:1–111.
- Ventola CL. Immunization in the United States: recommendations, barriers, and measures to improve compliance. Part 1: childhood vaccinations. *P T* 2016;41(7):426–436.
- Liang JL, Tiwari T, Moro P, et al. Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2018;67(2):1–44.
- Marin M, Broder KR, Temte JL, et al. Use of combination measles, mumps, rubella, and varicella vaccine. Recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR Recomm Rep* 2010;59(RR-3):1–12.
- Das RR, Panigrahi I, Naik SS. The effect of prophylactic antipyretic administration on post-vaccination adverse reactions and antibody response in children: a systematic review. *PLoS One* 2014 Sep 2;9(9):e106629.
- Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States, 2018–19 Influenza Season. *MMWR Recomm Rep* 2018;67(RR-3):1–20.
- Centers for Disease Control and Prevention. Prevention of pneumococcal disease among infants and children—use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine. *MMWR* 2010;59(RR-11):1–18.
- Kroger AT, Duchin J, Vázquez M. General best practice guidelines for immunization. Best practices guidance of the Advisory Committee on Immunization Practices (ACIP). www.cdc.gov/vaccines/hcp/acip-recs/general-recs/downloads/general-recs.pdf. Accessed December 27, 2018.

146

ADULT IMMUNIZATION

Immunizations: Not Just Kid Stuff Level II

Jean-Venable “Kelly” R. Goode, PharmD, BCPS, FAPhA, FCCP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Develop a plan for administering any needed vaccines when given a patient’s age, immunization history, and medical history.
- Recognize appropriate precautions and contraindications for vaccination, including inappropriate reasons for deferring vaccination.
- Explain appropriate administration of vaccines, including timing and spacing of both inactive and live attenuated vaccines.
- Recognize the differences in vaccines for young adults currently in use in the United States.

PATIENT PRESENTATION

■ Chief Complaint

“I’m here to get my new prescription filled.”

■ HPI

Sandra Williams is a 23-year-old woman who presents to your pharmacy in January with a new prescription for prednisone 40 mg PO BID for 10 days. She has had a moderate asthma exacerbation. She just started her new job as an elementary school teacher. She is a new patient to your pharmacy. She inquires about your “One Less” signs which refers to a national HPV vaccination campaign.

■ PMH

Moderate persistent asthma
Chickenpox at age 5 per patient
Splenectomy secondary to car accident 3 months ago

■ FH

One sister who is healthy; mother is healthy; father has type 2 diabetes.

■ SH

Does not smoke; drinks alcohol socially; has healthcare coverage through her employer; religious affiliation is Baptist.

■ Meds

Albuterol MDI two inhalations PRN
Pulmicort DPI two inhalations once daily

■ All

NKDA

■ Immunization Record

No vaccines since kindergarten except:

- Meningococcal vaccine before she started her freshman year in college
- One dose of hepatitis B vaccine before she started her freshman year in college
- MMR vaccine before she started her freshman year in college, Td 10 years ago at her adolescent well checkup.

■ ROS

WDWN African-American woman in NAD

■ VS

BP 120/72 mm Hg (left arm, large cuff, seated), P 76 bpm; Wt 54 kg, Ht 5’5”

■ Physical Examination

Deferred

■ Assessment

A 23-year-old woman recently treated for a moderate asthma exacerbation. She is in need of immunizations today.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates needs, precautions, or contraindications to immunization?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. How do healthcare providers determine which vaccines an adult needs?
- 2.b. Assess the urgency of the immunization needs based on the subjective and objective information available.
- 2.c. Create a list of the patient's drug therapy and immunization-related problems. Include assessment of medication appropriateness, effectiveness, safety, patient adherence, and including any contraindications or precautions for vaccination.
- 2.d. What economic and psychosocial considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What feasible alternatives are available for adult immunizations?
- 3.c. Create an individualized, patient-centered, team-based care plan to optimize medication therapy and immunizations for this patient. Include the vaccines that should be administered today, including dose, route, and schedule.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the response to immunization and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate follow-up for additional immunizations and achievement of fully immunized patient.

■ ADDITIONAL CASE QUESTIONS

1. What screening questions should a patient be asked prior to administering any vaccinations?
2. What must be documented after a healthcare practitioner administers a vaccination?
3. What is the proper immunization administration technique for adults, including location and needle size?

■ SELF-STUDY ASSIGNMENTS

1. Review the most current immunization recommendations for adults and provide a summary of how your recommendations for this case would be different if this person were 65 years of age.

2. Develop a list of diseases and medications indicating that a patient may be a candidate for immunization.
3. Research the laws in your state to verify which vaccines pharmacists may administer. Also, explore how to implement an immunization service in your practice.
4. Review the guidelines for vaccination of pregnant women.
5. Search the Internet for immunization-related websites about vaccine-associated adverse effects; compare these sites and evaluate them against reliable websites for vaccine information.

CLINICAL PEARL

Delays in vaccination put patients at risk of vaccine-preventable diseases. However, there is no need to restart an immunization series if the interval between doses is longer than that recommended in the routine schedule. Instead of starting over, merely count the doses administered (provided that they were given at an acceptable minimum interval) and complete the series.

REFERENCES

1. Centers for Disease Control and Prevention. Advisory Committee on Immunization Practices. Recommended adult immunization schedule for immunization schedules for adults aged 19 years and older—United States, 2018. (Updated annually at <https://www.cdc.gov/vaccines/schedules/hcp/adult.html>). Accessed January 23, 2019.
2. Centers for Disease Control and Prevention. Use of 13-valent pneumococcal conjugate vaccine and 23-valent pneumococcal polysaccharide vaccine for adults with immunocompromising conditions: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2012;61(40):816–819.
3. Centers for Disease Control and Prevention. Prevention and control of meningococcal disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2013;62(RR02):1–22.
4. Recommendations from the National Vaccine Advisory Committee: Standards for Adult Immunization Practices. *Public Health Reports* 2014 March–April;129:115–123.
5. Kobayashi M, Bennett NM, Gierke R, et al. Intervals between PCV13 and PPSV23 vaccines: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2015;64(34):944–947.
6. Petrosky E, Bocchini JA, Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2015;64(11):300–304.
7. Liang JL, Twari T, Moro P, et al. Prevention of pertussis, tetanus, and diphtheria with vaccines in the United States: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2018;67(RR-2):1–44.
8. Centers for Disease Control and Prevention. Prevention and control of *Haemophilus influenza* type B disease: recommendations of the Advisory Committee on Immunization Practices (ACIP). *MMWR* 2014;63(RR01):1–14.
9. Grohskopf LA, Sokolow LZ, Broder KR, et al. Prevention and control of seasonal influenza with vaccines: recommendations of the Advisory Committee on Immunization Practices—United States 2018–19 Influenza Season. *MMWR* 2018;67(RR-3):1–20.
10. Petrosky E, Bocchini JA, Hariri S, et al. Use of 9-valent human papillomavirus (HPV) vaccine: updated HPV vaccination recommendations of the Advisory Committee on Immunization Practices. *MMWR* 2015;64(11):300–304.

147

HIV INFECTION

The Antiretroviral-Naïve Patient Level II

Rodrigo M. Burgos, PharmD

Sarah M. Michienzi, PharmD, BCPS, AAHIVP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe when antiretroviral therapy should be initiated in patients living with HIV.
- List the treatment goals of antiretroviral therapy.
- Design an appropriate antiretroviral regimen for an antiretroviral-naïve person living with HIV based on patient-specific data.
- Provide patient education on recommended antiretroviral agents to ensure adherence and minimize adverse effects.

PATIENT PRESENTATION

■ Chief Complaint

“I am here for regular care. It hurts to swallow.”

■ HPI

Jenny Baird is a 34-year-old woman diagnosed with HIV infection 2 years ago during a routine exam. She was asymptomatic at the time of diagnosis. She is currently antiretroviral therapy (ART) naïve, and since her diagnosis she has been following up regularly every 6 months. However, up to this point, she has not been ready to commit to ART. Today she returns to the HIV Specialty Clinic for a follow-up visit and reports painful and difficult swallowing over the past 2–3 weeks.

■ PMH

HIV positive, diagnosed 2 years ago; risk factor heterosexual contact
Asthma
GERD

■ FH

Noncontributory

■ SH

History of crack cocaine use, last use 1 month ago; smokes marijuana once per month, mainly as an appetite enhancer; cigarette smoking, 0.5 ppd; EtOH, one to two drinks on weekends; unemployed, lives with partner; sexually active with stable partner, 100% condom use; partner is HIV (–) and is aware of her HIV status

■ Medications

Multivitamin with minerals one tablet PO once daily
Albuterol HFA two puffs Q 6 H PRN SOB
Calcium carbonate antacid one to two tablets PRN heartburn
Oral contraceptive one tablet PO daily

■ All

TMP/SMX (rash)

■ ROS

Difficulty and pain on swallowing

■ Physical Examination

Gen

Thin, well-developed black woman in NAD, alert and oriented × 3

VS

BP 110/64 mm Hg, P 80 bpm, RR 18, T 35.9°C; Wt 58 kg, Ht 5'5"

Skin

Anicteric, has large tattoo on back, no other skin lesions noted

HEENT

(+) Oral lesions and white plaques, sinuses nontender, PERRLA, ears and nose clear

Neck/Lymph Nodes

Supple, no thyromegaly, (+) bilateral cervical lymph nodes 0.7 cm in diameter

Chest

Lungs clear to auscultation

Breasts

Soft and nontender without masses, discharge, or other lesions noted

CV

S₁, S₂ without S₃, S₄, or murmur

Abd

(+) BS, soft, nontender, without HSM; (+) bilateral inguinal lymph nodes 0.5 cm in diameter

Genit/Rect

WNL, no grossly visible lesions

MS/Ext

No wasting, no CCE

Neuro

No focal deficits

■ Labs

See Table 147-1.

■ Assessment

A 34-year-old ART-naïve woman living with HIV shows steady decline in CD4 cell count and rising levels of HIV viremia since her initial diagnosis 2 years ago, presenting with painful swallowing and white plaques on posterior pharynx, and mouth consistent with esophageal and oropharyngeal candidiasis.

TABLE 147-1 Laboratory Values for the Previous Visit and for Subsequent Visits

Parameter (Units)	2 Years Ago	This Visit	6 Weeks Later	12 Weeks Later
Weight (kg)	65	58	57	60
Hematology:				
Hgb (g/dL)	10.9	11.1	12.2	12.9
Hct (%)	32.9	33.6	36.5	37.3
Plt (×10 ³ /mm ³)	234	287	298	311
WBC (×10 ³ /mm ³)	7.1	5.7	6.9	7.1
Lymphs (%)	47.3	45.5	44.9	47.3
Monos (%)	6.4	6.6	6.1	6.4
Eos (%)	3.5	0.9	2.0	3.5
Basos (%)	0.3	0.2	0.4	0.3
Neutros (%)	42.5	46.8	46.6	42.5
ANC (×10 ³ /mm ³)	3.0	2.7	3.2	3.0
Chemistry:				
BUN (mg/dL)	5	10	9	7
SCr (mg/dL)	0.8	0.9	0.9	0.8
T. bili (mg/dL)	0.5	1.6	0.6	—
Alb (g/dL)	3.3	3.8	3.4	—
AST (IU/L)	17	19	18	—
ALT (IU/L)	12	13	14	—
Fasting glucose	115	93	92	—
Fasting lipid profile:				
T. chol	—	115	155	—
Triglycerides	—	41	93	—
LDL	—	67	108	—
HDL	—	40	28	—
Surrogate markers:				
CD4 (%)	20	12	—	13
CD4 (cells/mm ³)	377	180	—	200
HIV RNA (RT-PCR) ^a (copies/mL)	25,000	155,000	154	<20
Antiviral resistance test (genotypic resistance test)	L63P	—	—	—
Serologies:				
HBV surface Ab	Negative	—	—	—
HBV core Ab total	Negative	—	—	—
HBV surface Ag	Negative	—	—	—
HCV Ab	Negative	—	—	—
HAV Ab	Positive	—	—	—
Measles Ab	Positive	—	—	—
Mumps Ab	Positive	—	—	—
Rubella Ab	Positive	—	—	—
Other tests:				
Human chorionic gonadotropin (hCG)	Negative	Negative	—	—
G6PD	Not deficient	—	—	—
HLA-B*5701	Negative	—	—	—

^aReverse transcriptase polymerase chain reaction assay.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of HIV/AIDS?
- 1.b. What additional information is needed to fully assess this patient's HIV/AIDS?

Assess the Information

- 2.a. Assess the severity of HIV/AIDS based on the subjective and objective information available.

- 2.b. Create a list of the patient's HIV-related drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, and ethical considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for the patient's HIV-related drug therapy problems?
- 3.b. What nondrug therapies might be useful to this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating HIV?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's HIV-related drug therapy problems. Include specific drugs, dosage forms, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance adherence, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-Up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate ART for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient and care team accepted your treatment recommendations. The patient returns to the clinic for follow-up 6 and 12 weeks after treatment initiation. She reports nausea from her medications that resolved after several days of therapy. See Table 147-2 for her treatment flow sheet.

TABLE 147-2 Laboratory Values

Parameter	6 Weeks Later	12 Weeks Later
HIV RNA (RT-PCR) (copies/mL)	154	<20
CD4-lymphocyte count (cells/mm ³)	NA	200
CD4-lymphocyte percent (%)	NA	13
Symptoms of HIV infection	Asymptomatic	Asymptomatic
Adverse events reported	Mild nausea, no vomiting	None
Concomitant medications	Oral contraceptive 1 tablet PO daily MVI with minerals 1 tablet PO daily Dapsone 100 mg PO daily Albuterol HFA 2 puffs Q 6 H PRN Calcium carbonate antacid 1–2 tablets PRN	Oral contraceptive 1 tablet PO daily MVI with minerals 1 tablet PO daily Dapsone 100 mg PO daily Albuterol HFA 2 puffs Q 6 H PRN Calcium carbonate antacid 1–2 tablets PRN

■ FOLLOW-UP CASE QUESTIONS

1. Provide an assessment of the ART regimen efficacy at each follow-up visit.
2. Identify potential problems with her concomitant medications and discuss alternatives.

■ SELF-STUDY ASSIGNMENTS

1. Review the current literature regarding management of treatment-experienced patients living with HIV in the setting of virologic failure and optimizing ART in the setting of virologic suppression.
2. Review the current literature regarding development of resistance to ART and strategies for preventing and managing resistance.
3. Review the current literature regarding survival and life expectancy for persons living with HIV/AIDS.

CLINICAL PEARL

Updated guidelines recommend that ART be initiated in all patients living with HIV, regardless of CD4 count. Two randomized controlled trials, START and TEMPRANO, demonstrated greater clinical benefit when antiretroviral therapy is started early, as well an effort to prevent transmission. In addition to medication potency and efficacy, clinicians must consider a wide range of individual

factors for the particular regimen selected, including comorbid conditions, transmitted viral resistance, adherence, potential adverse events, drug–drug or drug–food interactions, and consequences of virologic failure. Clinicians should always individualize therapeutic choices based on available data and unique patient factors.

REFERENCES

1. Centers for Disease Control and Prevention. Revised surveillance case definitions for HIV infection—United States, 2014. *MMWR* 2014;63(RR-03):1–10.
2. Centers for Disease Control and Prevention. Appendix: Stage-3-defining opportunistic illness in HIV infection. *MMWR* 2014; 563(RR-03):11.
3. Panel on Opportunistic Infections in HIV-Infected Adults and Adolescents. Guidelines for the prevention and treatment of opportunistic infections in HIV-infected adults and adolescents: recommendations from the Centers for Disease Control and Prevention (CDC), the National Institutes of Health (NIH), and the HIV Medical Association of the Infectious Diseases Society of America. Available at: <http://aidsinfo.nih.gov/contentfiles/lvguidelines/AdultandAdolescentGL.pdf>. Accessed April 9, 2019.
4. Panel on Antiretroviral Guidelines for Adults and Adolescents. Guidelines for the use of antiretroviral agents in adults and adolescents living with HIV. Department of Health and Human Services (DHHS). Available at: http://aidsinfo.nih.gov/contentfiles/lvguidelines/adult_oi.pdf. Accessed April 9, 2019.
5. Anon. U=U taking off in 2017. *Lancet HIV* 2017;4(11):e475.

This page intentionally left blank

SECTION 17

ONCOLOGIC DISORDERS

148

BREAST CANCER

An Opportunity Lost Level II

Jonathan W. Malara, PharmD, BCOP

Bonnie Lin Boster, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Design a pharmacotherapeutic plan for treatment of locally advanced breast cancer.
- Develop an appropriate monitoring plan for patients receiving adjuvant hormonal therapy for treatment of breast cancer.
- Establish appropriate follow-up for patients after definitive treatment of breast cancer.
- Provide patient education on the proper dosing, administration, and adverse effects of letrozole and palbociclib.
- Compare and contrast the goals of treatment for locally advanced breast cancer versus metastatic breast cancer.

PATIENT PRESENTATION

■ Chief Complaint

"I have a lump in my breast."

■ HPI

Rosalita Garza is a 61-year-old woman presenting for evaluation of a new mass in her left breast. She first noticed a palpable breast mass on self-examination approximately 14 months ago but was unable to have this further investigated due to loss of health insurance. The patient describes the mass as intermittently painful. A mammogram was performed prior to her current visit, which was suspicious for malignancy.

■ PMH

Musculoskeletal injury 6 years ago. Fell from a chair while at work and suffered injuries to her cervical spine. The patient has required bone grafting from her right hip to her cervical spine. She has been prescribed multiple as-needed medications for pain control but uses them infrequently.

Depression (diagnosed 7 years ago)

■ FH

Sister diagnosed with breast cancer at age 60, now 5 years postsurgery. The patient was unable to recall any further details. No other significant cancer history is noted.

■ SH

Lives with and acts as primary caretaker for her mother, who has dementia. Denies alcohol use and is a nonsmoker. Has a 35-year-old daughter who also lives with her.

■ Endocrine History

Menarche age 13; menopause age 55; first child age 26; G₁P₁A₀. Last Pap smear at age 40. Took Premarin as HRT for 5 years after the onset of menopause.

■ Meds

Protonix 40 mg PO once daily
Zoloft 50 mg PO once daily
Ambien CR 12.5 mg PO at bedtime PRN sleep
Neurontin 300 mg PO TID
Hydrocodone/acetaminophen 5 mg/300 mg, one to two tablets PO Q 6 H PRN pain

■ All

NKDA

■ ROS

Negative except for complaints noted above

■ Physical Examination

Gen

WDWN 61-year-old Hispanic woman. Awake, alert, in NAD.

VS

BP 127/71 mm Hg, P 89 bpm, RR 16, T 36.7°C; Wt 137 lb, Ht 5'1"

HEENT

NC/AT; PERRLA; EOMI; ear, nose, and throat are clear.

Neck/Lymph Nodes

Supple. No lymphadenopathy, thyromegaly, or masses. No supraclavicular or infraclavicular adenopathy.

Lungs

CTA and percussion

Breasts

Left: Notable for a 2.5-cm mass at the 6 o'clock position, approximately 3 cm from the nipple margin, not fixated to skin; no nipple retraction or discharge is visualized; the mass is not tender to palpation; 1.5-cm, nontender, palpable mass in the axilla noted.

Right: Without mass or lymphadenopathy

CV

RRR; no murmurs, rubs, or gallops

Abd

Soft, NT/ND, normoactive bowel sounds. No appreciable hepatosplenomegaly.

Spine

Slight tenderness to percussion

Ext

No CCE

Neuro

No deficits noted

Labs

Na 142 mEq/L	Hgb 12.9 g/dL	WBC $8.7 \times 10^3/\text{mm}^3$	AST 36 IU/L
K 3.7 mEq/L	Hct 37.6%		ALT 17 IU/L
Cl 102 mEq/L	RBC $4.13 \times 10^6/\text{mm}^3$	Neutros 55%	LDH 488 IU/L
CO ₂ 26 mEq/L	Plt $410 \times 10^3/\text{mm}^3$	Lymphs 35%	T. bili 0.2 mg/dL
BUN 9 mg/dL	PT 11.9 seconds	Monos 8%	CA 27.29 36.2
SCr 0.7 mg/dL	INR 1.09	Eos 2%	U/mL
Glu 83 mg/dL	aPTT 30.1 seconds		

Chest X-Ray

Lungs are clear.

Other Diagnostic Tests

Diagnostic bilateral mammogram (Fig. 148-1):

1. American College of Radiology category V, highly suspicious for malignancy in the left breast. There is a high-density, irregular mass measuring 2.2 cm with indistinct margins seen in the left breast lower hemisphere at 6 o'clock located 3 cm from the nipple.
2. In the right breast, no dominant mass, distortion, or suspicious calcifications are identified.

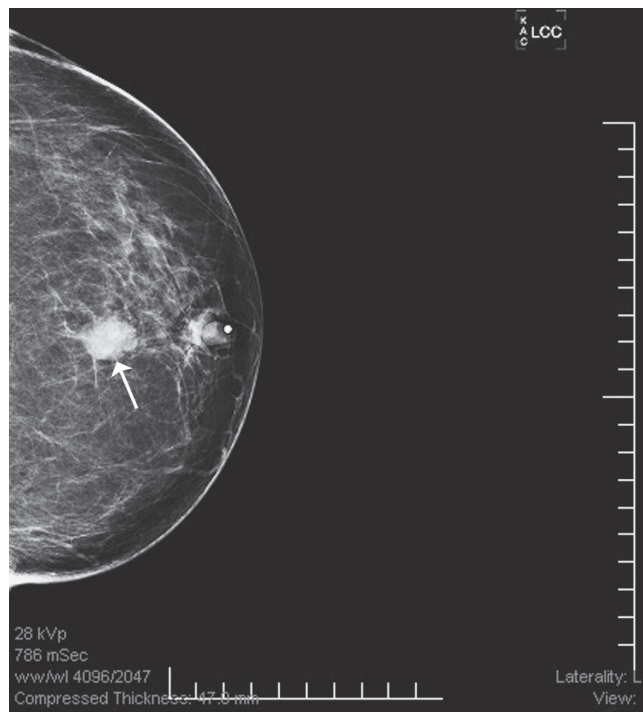


FIGURE 148-1. Mammogram of left breast. Arrow indicates area of abnormality highly suspicious for malignancy.

Unilateral ultrasound left breast and left axilla with biopsy:

1. An ill-defined, hypoechoic mass is noted in the 5:00–6:00 region. This measures approximately 2.5 cm $\times$ 2.3 cm $\times$ 1.5 cm and is located 3 cm from the nipple. A core biopsy of this mass was performed.
2. Suspicious lymph nodes are noted in the axilla. The largest node measures 1.8 cm $\times$ 1.8 cm $\times$ 1.4 cm. FNA of this lymph node was performed. In the infraclavicular region, a few hypoechoic lymph nodes were also seen and were located in the lateral aspect. The largest node measured 0.8 cm $\times$ 0.8 cm $\times$ 0.8 cm. FNA of this infraclavicular lymph node was performed. No suspicious internal mammary or supraclavicular lymph nodes were seen.

Core needle biopsy of left breast mass:

1. Left breast, 6 o'clock: infiltrating ductal carcinoma, modified Black's nuclear grade II (moderately differentiated), ER 95%, PR 95%, HER2 overexpression 2+, HER2 FISH negative (no amplification), and Ki-67 30% (moderate)

FNA of left axillary and infraclavicular lymph nodes:

1. Left axillary lymph node: metastatic adenocarcinoma consistent with breast primary
2. Left infraclavicular lymph node: metastatic adenocarcinoma consistent with breast primary

Bone scan:

1. No definite evidence of osseous metastases
2. Abnormality in cervical spine consistent with previous history of bone grafting

CT abdomen:

No lesions suggestive of metastases

CT chest:

No evidence of metastases

Assessment

Ms Garza is a 61-year-old woman who has newly diagnosed breast cancer.

QUESTIONS**Collect Information**

1. What subjective and objective information indicates the presence of breast cancer?

Assess the Information

- 2.a. Based on the information available, what is this patient's clinical stage of breast cancer?
- 2.b. In addition to the stage of disease, what other factors are important for determining the prognosis for breast cancer?
- 2.c. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What is the primary goal for cancer treatment in this patient?
- 3.b. What nondrug therapies might be useful for treating this patient's breast cancer?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's breast cancer?

- 3.d. Create an individualized, patient-centered, team-based care plan to treat this patient's breast cancer and optimize all medication therapy. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the efficacy and adverse effects of the therapy you recommended?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The patient tolerated your treatment plan well. Twelve months after its completion, she returns to clinic complaining of lower back pain for the past 3–4 weeks. She has been taking hydrocodone/acetaminophen more regularly, “about two or three pills per day.” This is a significant change since previously she reported not taking any. She is restaged with a bone scan, chest x-ray, abdominal CT, chest CT, and laboratory tests. Bone scan reveals metastases to the lumbar spine without spinal cord compression. Chest x-ray is negative. Abdominal CT shows a solitary liver metastasis. Chest CT is negative for metastases. LFTs are within normal limits. CA 27.29 is 100.7 U/mL. Biopsy of the liver lesion confirms recurrence of ER-positive, PR-positive, and HER2-negative breast cancer. The physician concludes that this patient's breast cancer is now metastatic to the bone and liver. The previous therapy is discontinued, and the patient is started on palbociclib and letrozole. The patient's updated information is as follows.

Labs

Na 140 mEq/L	Hgb 12.5 g/dL	WBC $6.7 \times 10^3/\text{mm}^3$	AST 40 IU/L
K 3.9 mEq/L	Hct 36.4%	Neutros 64%	ALT 24 IU/L
Cl 103 mEq/L	RBC $4.1 \times 10^6/\text{mm}^3$	Lymphs 30%	LDH 502 IU/L
CO ₂ 28 mEq/L	Plt $356 \times 10^3/\text{mm}^3$	Monos 3%	T. bili 0.5 mg/dL
BUN 11 mg/dL		Eos 3%	CA 27.29
SCr 0.65 mg/dL			100.7 U/mL
Glu 92 mg/dL			

Meds

Cardizem CD 180 mg PO once daily
 Protonix 40 mg PO once daily
 Zolof 50 mg PO once daily
 Ambien CR 12.5 mg PO at bedtime PRN sleep
 Hydrocodone/acetaminophen 5 mg/300 mg, one to two tablets PO Q 6 H PRN pain

FOLLOW-UP QUESTIONS

- What is this patient's current clinical stage of breast cancer, and what is the primary goal for cancer treatment for this patient now?
- Based on the patient's current medication list, create a list of potential drug therapy problems as she begins a new therapy for cancer.
- Since the patient has developed bone metastases, what other medication should be added to her treatment plan? At what dose and schedule?

- What information should be provided to the patient regarding her new chemotherapy for breast cancer?

SELF-STUDY ASSIGNMENTS

- Perform a literature search to obtain recent information regarding clinical trials utilizing trastuzumab and pertuzumab in patients with HER2 overexpressing breast cancer.
- Perform a literature search to obtain recent information regarding clinical trials using aromatase inhibitors (anastrozole, letrozole, or exemestane) in patients with early-stage hormone receptor-positive breast cancer.
- Develop a treatment plan for a patient presenting to the emergency center with febrile neutropenia after administration of chemotherapy.
- Provide educational information regarding genetic testing for a patient with a family history of breast cancer.

CLINICAL PEARL

Even though metastatic breast cancer is usually considered to be incurable, some patients can live for a relatively long time with hormonal therapy (if hormone receptor-positive) and palliative chemotherapy. These therapies are administered to increase the patient's quality of life and prolong disease progression, and are typically used in a sequential manner until they are no longer effective, or side effects preclude their use. Although the average life span after diagnosis of metastatic disease is a few years, some patients can live a decade or more with the disease.

REFERENCES

- Hortobagyi GN, Connolly JL, D'Orsi CJ, et al. Breast. In: Amin EB, Edge SB, Gress DM, et al, eds. AJCC Cancer Staging Manual. 8th ed. Chicago, IL: Springer; 2017:589–638.
- Peto R, Davies D, Godwin J, et al. Comparisons between different poly-chemotherapy regimens for early breast cancer: meta-analyses of long-term outcome among 100,000 women in 123 randomised trials. *Lancet* 2012;379(9814):432–444.
- De Laurentiis M, Cancellaro G, D'Agostino D, et al. Taxane-based combinations as adjuvant chemotherapy of early breast cancer: a meta-analysis of randomized trials. *J Clin Oncol* 2008;26:44–53.
- Early Breast Cancer Trialists' Collaborative Group (EBCTCG). Aromatase inhibitors versus tamoxifen in early breast cancer: patient-level meta-analysis of the randomized trials. *Lancet* 2015;386(10001):1341–1352.
- Davies C, Pan H, Godwin J, et al. Long-term effects of continuing adjuvant tamoxifen to 10 years versus stopping at 5 years after diagnosis of oestrogen receptor-positive breast cancer: ATLAS, a randomised trial. *Lancet* 2013;381:805–816.
- Francis PA, Regan MM, Fleming GF, et al. Adjuvant ovarian suppression in premenopausal breast cancer. *N Engl J Med* 2015;372:436–446.
- Khatcheressian JL, Hurley P, Bantug E, et al. Breast cancer follow-up and management after primary treatment: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2013;31(7):961–965.
- NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer V.3.2019 © National Comprehensive Cancer Network, Inc., 2019. https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf. Accessed December 13, 2019.
- Van Poznak C, Somerfield MR, Barlow WE, et al. Role of bone-modifying agents in metastatic breast cancer: an American Society of Clinical Oncology-Cancer Care Ontario Focused Guideline Update. *J Clin Oncol* 2017;35(35):3978–3986.
- Ibrance® Package Insert. New York, NY: Pfizer Laboratories, Inc.; 2018.

149

NON-SMALL CELL
LUNG CANCER

It Takes Your Breath Away Level II

Michelle L. Rocky, PharmD, BCOP, FHOPA

Julianna V. F. Roddy, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the most common symptoms of non-small cell lung cancer (NSCLC).
- Design a treatment plan for patients with NSCLC.
- Design a pharmacotherapeutic plan for the treatment of hypercalcemia.
- Describe appropriate treatment strategies for brain metastases in NSCLC.
- Educate patients on the anticipated side effects of carboplatin, paclitaxel, and nivolumab therapy.

PATIENT PRESENTATION

■ Chief Complaint

“I have been coughing up blood.”

■ HPI

This 66-year-old woman presents to her PCP with complaints of a dry, nonproductive cough for 2.5 months, dyspnea on exertion, and hemoptysis for 1 week.

■ PMH

Dyslipidemia

HTN

Anemia of unknown etiology × 1 year

Type 2 DM

PPD (–)

■ FH

Father died of colorectal cancer at age 68

Aunt died of breast cancer at age 70

■ SH

Married, lives with son and daughter; 30 pack-year cigarette smoking history (approximately 1 ppd × 30 years); occasional ETOH use; no known recent exposure to TB

■ Meds

Folic acid 1 mg PO daily

Ferrous sulfate 325 mg PO TID

Simvastatin 20 mg PO daily

Metformin 500 mg PO BID

Pantoprazole 40 mg PO daily

■ All

Penicillin (rash)

Sulfa (rash)

■ ROS

(+) For pulmonary symptoms as noted in HPI; no headaches, dizziness, or blurred vision

■ Physical Examination

Gen

Mildly overweight Caucasian woman in slight distress. ECOG performance status of 1.

VS

BP 169/100 mm Hg, P 90 bpm, RR 30, T 37.2°C; Wt 82 kg, Ht 5'6"

Skin

Patches of dry skin; no lesions

HEENT

PERRLA; EOMI; fundi benign; TMs intact

Neck/Lymph Nodes

No lymphadenopathy; neck supple

Lungs

Wheezing in RUL; remainder of lung fields clear

Heart

RRR; normal S₁, S₂; slight systolic murmur on left lateral side

Abd

Soft, nontender; no splenomegaly or hepatomegaly

Genit/Rect

Normal female genitalia; guaiac (–) stool

Neuro

A&O × 3; sensory and motor intact, 5/5 upper, 4/5 lower; CN II–XII intact; (–) Babinski

■ Labs

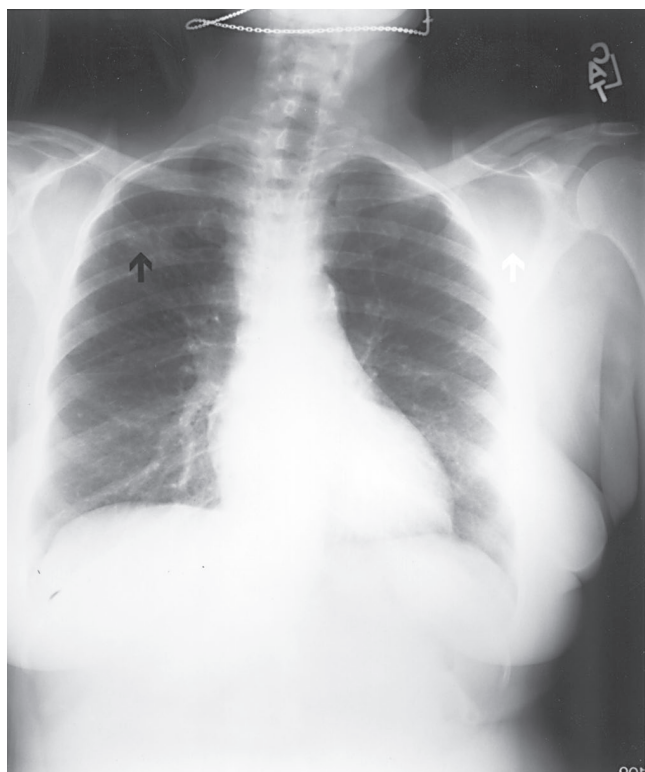
Na 138 mEq/L	Hgb 10.7 g/dL	Ca 9.7 mg/dL
K 3.6 mEq/L	Hct 34.6%	Mg 2.0 mg/dL
Cl 101 mEq/L	Plt 255 × 10 ³ /mm ³	
CO ₂ 23 mEq/L	WBC 9.9 × 10 ³ /mm ³	
BUN 11 mg/dL		
SCr 1.1 mg/dL		
Glu 182 mg/dL		

■ Chest X-Ray

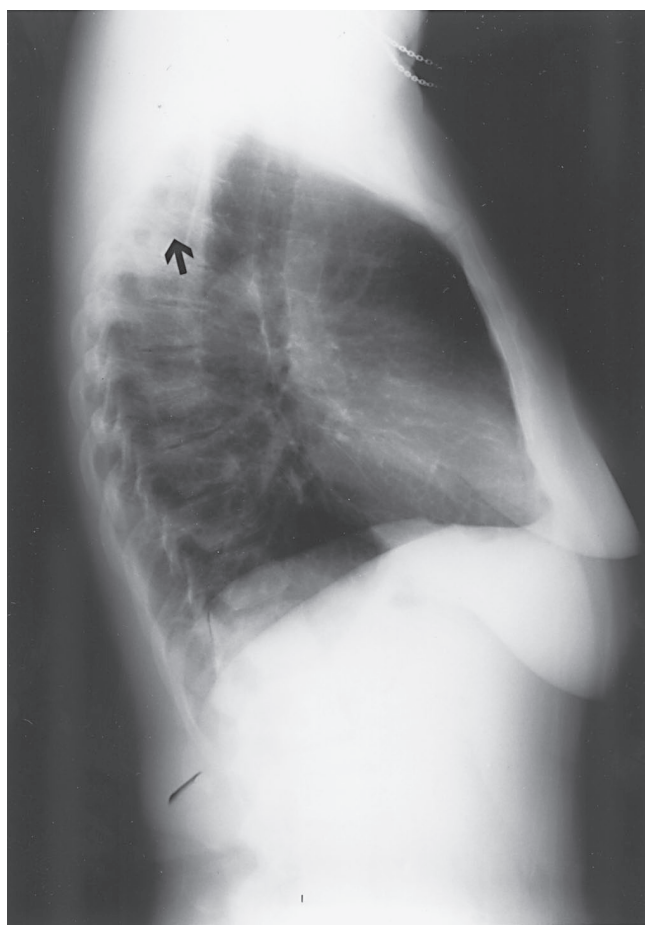
PA and lateral views reveal a possible mass in right upper lobe (Fig. 149-1).

■ Assessment

A 66-year-old woman with new-onset hemoptysis is admitted for workup of a possible lung mass. She has anemia and a history of dyslipidemia, DM type 2, and HTN.



A



B

FIGURE 149-1. Chest x-ray with PA (A) and lateral (B) views showing a possible mass in the right upper lobe (arrows).

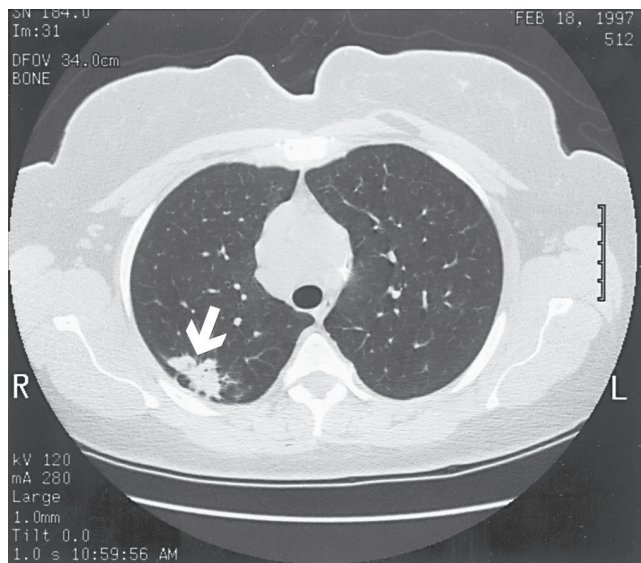


FIGURE 149-2. CT scan of the chest revealing a 2.5- × 2-cm right lung mass (arrow).

CLINICAL COURSE (PART 1)

The patient was further evaluated for lung cancer on an outpatient basis. A bronchoscopy (with biopsy) was performed that identified squamous cell carcinoma. The chest CT scan revealed a 3- × 2-cm right lung mass (Fig. 149-2). A mediastinoscopy was performed to determine the resectability of the tumor. The mediastinoscopy and biopsy revealed unresectable stage IIIB (T_2N_3) NSCLC with metastases to the contralateral mediastinal nodes. A brain MRI was negative for disease. Tumor EGFR status was positive by IHC (nonsensitizing), and *EML4-ALK* and *ROS1* gene rearrangement were negative. Additional testing showed the tumor to have 5% PD-L1 expression and V600E mutation negative. PFTs included FEV_1 1.49 L and FVC 1.9 L. An echocardiogram showed mild LVH with an LVEF of 55%. Patient has an EGOG performance status of 1.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of non-small cell lung cancer (NSCLC) in this patient?
- 1.b. What additional information is needed to fully assess this patient's lung cancer?

Assess the Information

- 2.a. Assess the severity of the NSCLC based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What is the goal for treating NSCLC in this patient? What is the likelihood of achieving this goal?
- 3.b. What nondrug therapies might be useful for treating NSCLC?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating stage IIIB NSCLC?

- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. For NSCLC chemotherapy, include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. In addition to chemotherapy, what measures should be taken to ensure the tolerability of the NSCLC regimen and to prevent adverse effects?

Implement the Care Plan

- 4.a. What additional laboratory and clinical information is needed before administration of the chemotherapy?
- 4.b. Calculate the patient's BSA, creatinine clearance, and the amount of each drug to be administered based on the regimen chosen.
- 4.c. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.d. Describe how care should be coordinated with other healthcare providers.
- 4.e. Would the treatment plan for this patient change if she had presented initially with stage IIIB NSCLC that was positive for a sensitizing EGFR mutation? If so, what would the treatment be?

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE (PART 2)

The patient's subsequent courses were complicated by the occurrence of DVT, weight loss, neutropenic fever, anemia, nausea/vomiting, and infections. At one point, she presented with a serum calcium level of 11.3 mg/dL and an albumin of 1.2 g/dL, with symptoms of weakness, confusion, nausea, and vomiting.

FOLLOW-UP QUESTIONS

1. Calculate the patient's corrected calcium level and provide an interpretation of that value.
2. What treatment modalities may be used to correct hypercalcemia?

CLINICAL COURSE (PART 3)

The patient completed concurrent chemotherapy with radiation followed by two cycles of carboplatin and paclitaxel. A repeat chest CT showed enlargement of the initial lesion, and a PET-CT demonstrated a 2- × 2-cm suspicious lesion in the liver. Her performance status remains an ECOG of 1.

FOLLOW-UP QUESTIONS

3. What treatment options are available for the patient at this time?
4. Design a specific chemotherapeutic regimen to treat this patient.

CLINICAL COURSE (PART 4)

Seven weeks after beginning the new chemotherapy regimen, the patient presents to the ED with complaints of headache and mental

status changes as per the patient's husband and caregiver. An MRI of the head reveals multiple lesions, most likely brain metastases.

FOLLOW-UP QUESTIONS

5. Briefly discuss options (drug and nondrug) to treat brain metastases.
6. What is the role of anticonvulsant agents in the setting of brain metastases?

SELF-STUDY ASSIGNMENTS

1. Review clinically important drug interactions for cancer patients started on phenytoin. Include appropriate monitoring parameters. Extend your review beyond the medications this patient is currently receiving.
2. The oncologist has decided to place this patient on nivolumab therapy. Design a patient education session for this drug therapy.

CLINICAL PEARL

Approximately 85–90% of lung cancers are attributable to cigarette smoking. Smoking cessation is the only proven method to decrease the risk of lung cancer. Low-dose computed tomography (CT) in select high-risk smokers and former smokers decreases the mortality rate in lung cancer.

REFERENCES

1. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Non-small cell lung cancer, version 1, 2019. Available at: https://www.nccn.org/professionals/physician_gls/pdf/nscl.pdf. Accessed November 3, 2018.
2. Antonia SJ, Villegas A, Daniel D, et al. Durvalumab after chemotherapy in stage III non-small-cell lung cancer. *N Engl J Med* 2017;377:1919–1929.
3. Belani CP, Choy H, Bonomi P, et al. Combined chemotherapy regimens of paclitaxel and carboplatin for locally advanced non-small-cell lung cancer: a randomized phase II locally advanced multi-modality protocol. *J Clin Oncol* 2005;23:5883–5891.
4. Fournier P, Robinet G, Thomas P, et al. Randomized phase III trial of sequential chemoradiotherapy compared with concurrent chemoradiotherapy in locally advanced non-small-cell lung cancer: Groupe Lyon-Saint-Etienne d'Oncologie Thoracique-Groupe Francis de Pneumo-Cancerologie NPC 95-01 study. *J Clin Oncol* 2005;23:5910–5917.
5. Hesketh PJ, Bohlke K, Lyman GH, et al. Antiemetics. American Society of Clinical Oncology Focused Guideline Update. *J Clin Oncol* 2015;33:1–8.
6. National Comprehensive Cancer Network Clinical Practice Guidelines in Oncology. Antiemesis, version 3, 2018. https://www.nccn.org/professionals/physician_gls/pdf/antiemesis.pdf. Accessed November 3, 2018.
7. Rizzo DJ, Brouwers M, Hurley P, et al. American Society of Clinical Oncology/American Society of Hematology clinical practice guideline update on the use of epoetin and darbepoetin in adult patients with cancer. *J Clin Oncol* 2010;28:4996–5010.
8. Garon EB, Ciuleanu T, Arrieta O, et al. Ramucirumab plus docetaxel versus placebo plus docetaxel for second-line treatment of stage IV non-small-cell lung cancer after disease progression on platinum-based therapy (REVEL): a multicentre, double-blind, randomised phase 3 trial. *Lancet* 2014;384:665–673.
9. Weiss GJ, Langer C, Rosell R, et al. Elderly patients benefit from second-line cytotoxic chemotherapy: a subset analysis of a randomized phase III trial of pemetrexed compared with docetaxel in patients with previously treated advanced non-small-cell lung cancer. *J Clin Oncol* 2006;24:4405–4411.

150

COLON CANCER

Drug Therapy by Design Level II

Lisa E. Davis, PharmD, FCCP, BCPS, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe the treatment goals associated with early and advanced stages of colon cancer.
- Design an appropriate chemotherapy regimen for colon cancer based on patient-specific data.
- Formulate a monitoring plan for a patient receiving a prescribed chemotherapy regimen for colon cancer based on patient-specific information.
- Recommend alterations in a drug therapy plan for a patient with colon cancer based on patient-specific information.
- Educate patients on the anticipated side effects of irinotecan, capecitabine, fluorouracil, oxaliplatin, bevacizumab, ziv-aflibercept, ramucirumab, regorafenib, cetuximab, panitumumab, trifluridine/tipiracil hydrochloride, nivolumab, pembrolizumab, ipilimumab, and vemurafenib.

PATIENT PRESENTATION

■ Chief Complaint

“The pain below my right ribs is getting worse. Also, I’m having more numbness, cramping, and burning sensations in my hands and feet, especially when I’m working a lot. I don’t think I can tolerate it much longer.”

■ HPI

Peter Robinson is a 56-year-old man who presents with worsening pain in his hands and feet and increasing RUQ pain. He was diagnosed with stage IV colon cancer 11 months ago after presenting with abdominal pain, bloating and distention, a history of intermittent changes in bowel movements, and no BM within the prior 4 days. He presented to the ED where an abdominal/pelvic CT scan revealed a complete bowel obstruction and extensive hypodense lesions in the liver, consistent with metastases (Fig. 150-1). His preoperative CEA was 13.6 ng/mL. He subsequently underwent a laparotomy with a left hemicolectomy and lymphadenectomy. The pathology revealed a moderately differentiated adenocarcinoma with extension through the bowel wall to the serosal surface. Ten of 13 lymph nodes were positive for tumor. Biopsy of a liver lesion confirmed hepatic metastases. A CT scan of the chest showed no evidence of lung metastases. The tumor was *KRAS*, *NRAS*, and *BRAF* gene wild-type, and classified as microsatellite instability-high (MSI-H; MMR-deficient; dMMR). *UGT1A1* testing showed that the patient was homozygous for the *UGT1A1**28 allele. Seven weeks later, chemotherapy was initiated with capecitabine, oxaliplatin (CapeOx), and bevacizumab. Except for minor fatigue and occasional nausea, the patient generally tolerated the chemotherapy well. However, over the past 2 months he has been experiencing

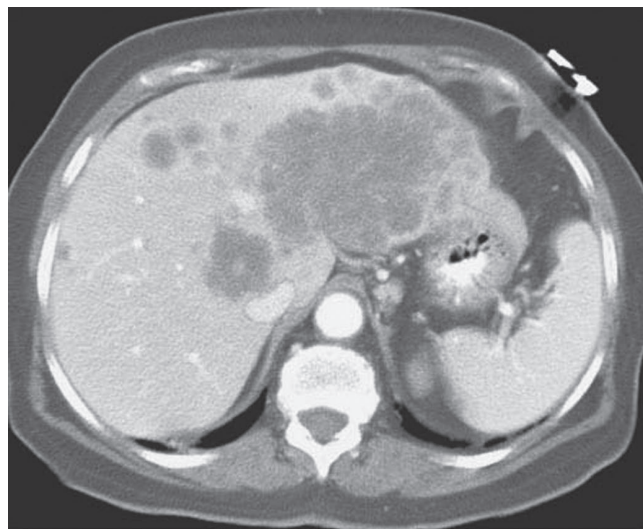


FIGURE 150-1. Abdominal/pelvic CT scan with extensive liver metastases. These multiple hypodense lesions are characteristic of metastases to the liver, the most common site for distant spread of gastrointestinal malignancies. (Reprinted with permission from Kaiser M. McGraw-Hill Manual: Colorectal Surgery: <http://www.accesssurgery.com>.)

worsening redness and pain on the palms of his hands with numbness and tingling in his fingers and toes. Six days ago he received his 19th cycle of chemotherapy.

■ PMH

Type 2 diabetes mellitus × 9 years
Hyperlipidemia × 5 years

■ FH

The patient is the oldest of three brothers; both siblings are alive and well. He has been married for 26 years and has one daughter who is 20 years old. Both his mother and father are in good health. His paternal grandfather died in his 60s from colon cancer, and his mother died in her 60s from ovarian cancer; he is aware of no other family history of malignancy.

■ SH

Self-employed as a graphic designer. He smoked cigarettes, one pack per day, since age 19 but quit 10 years ago. He does not drink alcohol and has never tried illicit drugs.

■ Meds

Morphine sustained-release 60 mg PO twice daily
Bisacodyl 5 mg PO daily as needed
Metformin 1000 mg PO twice daily
Simvastatin 20 mg PO once daily at bedtime

■ All

NKDA

■ ROS

The patient reports diffuse abdominal pain that is continuous with a “grabbing, gnawing” sensation and painful redness and swelling on the palms of his hands. He rates the abdominal pain severity as 5–6 out of 10. The numbness, tingling, and burning sensations in his hands and feet have worsened in frequency and severity over the past 2 months and have not responded well to morphine. He rates the severity of the tingling and burning pain as 6/10. He denies fever, headaches, shortness of breath, cough, nausea, vomiting, or

diarrhea. He reports no lesions in his mouth or difficulty swallowing. He has been having fewer bowel movements (about one every 3–4 days), but there is no pain or blood with passage of stool. He denies polyuria, polydipsia, and burning on urination. He has not noticed any bleeding or excessive bruising.

■ Physical Examination

Gen

Patient is a slightly overweight Caucasian man who appears fatigued.

VS

BP 164/93 mm Hg, P 79 bpm, RR 22, T 35.6°C; Wt 87 kg, Ht 5'9"

Skin

Redness and swelling of the palms of both hands and soles of feet

HEENT

PERRLA; EOMI; funduscopic exam without retinopathy; pale conjunctiva; no scleral icterus; moist mucous membranes; no lesions in oral cavity

Neck/Lymph Nodes

Supple neck; no lymphadenopathy

Lungs/Thorax

Symmetric chest expansion with respiratory effort; clear to A&P; regular breath sounds

CV

Normal heart sounds; regular rate and rhythm; no MGR

Abd

Well-healed scar on left upper abdomen; diffuse abdominal tenderness to palpation; no rebound tenderness; decreased bowel sounds

Genit/Rect

Prostate normal size; no masses palpated; stool heme negative

MS/Ext

Full ROM in all four extremities

Neuro

A&O × 3; cranial nerves II–XII grossly intact; reduced DTRs bilaterally; reduced feet sensitivity to light touch and pinprick bilaterally in stocking-glove distribution; vibration sensation reduced in distal legs

■ Labs

Na 137 mEq/L	Hgb 9.6 g/dL	WBC $8.1 \times 10^3/\text{mm}^3$	AST 52 IU/L
K 4.4 mEq/L	Hct 29%	Neutros 40%	ALT 45 IU/L
Cl 98 mEq/L	Plt $252 \times 10^3/\text{mm}^3$	Bands 3%	Alk phos 109 IU/L
CO ₂ 26 mEq/L	MCV 87 μm^3	Eos 4%	LDH 370 IU/L
BUN 17 mg/dL	MCHC 33 g/dL	Lymphs 45%	T. bili 2.2 mg/dL
SCr 1.0 mg/dL		Monos 8%	D. bili 0.2 mg/dL
Glu 117 mg/dL			T. chol 199 mg/dL
Ca 8.7 mg/dL			CEA 9.9 ng/mL
Phos 3.4 mg/dL			
Mg 2.3 mg/dL			

■ Urinalysis

1+ glucose, (–) ketones, 1+ protein, (–) leukocyte esterase and nitrites; (–) RBC; 2–3 WBC/hpf

■ Abdominal CT

Multiple liver metastases, increased approximately 30% in diameter compared to prior scan; multiple new lesions present in both lobes of the liver

■ Chest CT

No evidence of pulmonary metastases

■ Assessment

Unresectable stage IV colon cancer, with disease progression on CapeOx plus bevacizumab chemotherapy

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of colon cancer?
- What additional information is needed to fully assess this patient's colon cancer?

Assess the Information

- Assess the severity of colon cancer based on the subjective and objective information available.
- Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy for this patient?
- What nondrug therapies might be useful for this patient?
- What anticancer treatment options are appropriate for treating colon cancer in this patient?
- What treatment modifications are appropriate to address escalating oxaliplatin-induced neuropathy?
- Create an individualized, patient-centered, team-based care plan for anticancer and supportive treatment of this patient's colon cancer. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- Create team-based care plans to treat the other drug therapy problems you identified for this patient.

Implement the Care Plan

- What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- How is the response to the treatment regimen for the colon cancer assessed?
- Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.
- What acute adverse effects are anticipated with the anticancer regimen, and what parameters should be monitored?

- 5.d. What pharmacologic measures can be instituted to prevent or manage the acute toxicities associated with the anticancer regimen?
- 5.e. What are the potential late-onset toxicities of the anticancer regimen, and how can they be detected and prevented?

CLINICAL COURSE (PART 1)

The patient's hypertension resolved after two cycles of the chemotherapy regimen you recommended, and his neuropathic symptoms diminished over time and with drug therapy. He received PRBC transfusions when his hemoglobin dropped below 8 g/dL. His sustained-release morphine dose was increased to 120 mg PO Q 12 H, and immediate-release morphine sulfate 30 mg PO Q 4 H PRN pain was started. A scheduled regimen of docusate sodium 100 mg orally plus two senna tablets daily maintained a regular pattern of bowel movements. After seven more cycles of chemotherapy, he presented with worsening abdominal pain, fatigue, and new-onset dyspnea. An abdominal CT scan showed the liver lesions increased in size, and a chest CT showed multiple bilateral pulmonary nodules consistent with pulmonary metastases. His ALT and AST increased to five times the upper limit of normal.

FOLLOW-UP QUESTION

1. What treatment options would be appropriate to consider at this time?

ADDITIONAL CASE QUESTIONS

1. What is the role of *UGT1A1* genotyping in the treatment of colon cancer?
2. What is the role of *KRAS*, *NRAS*, and *BRAF* tumor gene testing in the treatment of colon cancer?
3. What is the relevance of MSI-H (MMR-deficient; dMMR) classification of colon cancer?

CLINICAL COURSE (PART 2)

The patient expressed interest in receiving further treatment for his colon cancer. After considering limited treatment options with his oncologist, he agreed to participate in a clinical trial. His analgesic therapy was modified, and his pain control was acceptable. His metastatic lesions remained stable (by clinical symptoms and CT scans) for 2 months.

SELF-STUDY ASSIGNMENTS

1. Develop an algorithm for treatment of colon cancer chemotherapy-induced diarrhea.
2. Develop patient-specific education materials regarding management of dermatologic toxicities of agents used in colon cancer treatment.

CLINICAL PEARL

There is no available test, including presence of tumor tissue epidermal growth factor receptor expression, that predicts response to cetuximab or panitumumab. However, tumors can be tested for the presence of *KRAS*, *NRAS*, and *BRAF* mutations that are predictive of lack of response to these agents. Also, tumors that are left-sided primary tumors have an improved overall survival with EGFR inhibitors, whereas patients who present with right-sided tumors (location from the cecum to hepatic flexure) do not. Patients with tumors that are *KRAS* or *NRAS* mutant are not appropriate candidates for treatment regimens that contain cetuximab or panitumumab. *BRAF* mutation testing can also be performed, because the *BRAF* V600E

mutation can be present in a small proportion of *KRAS* and *NRAS* wild-type tumors. Tumors with *BRAF* V600E mutation are unlikely to respond to an anti-EGFR antibody unless administered in combination with a *BRAF* inhibitor (eg, vemurafenib).

REFERENCES

1. Fakih MG. Metastatic colorectal cancer: current state and future directions. *J Clin Oncol* 2015;33:1809–1824.
2. Bennouna J, Sastre J, Arnold D, et al. Continuation of bevacizumab after first progression in metastatic colorectal cancer (ML18147): a randomised phase 3 trial. *Lancet Oncol* 2013;14:29–37.
3. Van Cutsem E, Tabernero J, Lakomy R, et al. Addition of aflibercept to fluorouracil, leucovorin, and irinotecan improves survival in a phase III randomized trial in patients with metastatic colorectal cancer previously treated with an oxaliplatin-based regimen. *J Clin Oncol* 2012;30:3499–3506.
4. Tabernero J, Yoshino T, Cohn AL, et al. Ramucirumab versus placebo in combination with second-line FOLFIRI in patients with metastatic colorectal carcinoma that progressed during or after first-line therapy with bevacizumab, oxaliplatin, and a fluoropyrimidine (RAISE): a randomised, double-blind, multicentre, phase 3 study. *Lancet Oncol* 2015;16:499–508.
5. Peeters M, Price TJ, Cervantes A, et al. Randomized phase III study of panitumumab with fluorouracil, leucovorin, and irinotecan (FOLFIRI) compared with FOLFIRI alone as second-line treatment in patients with metastatic colorectal cancer. *J Clin Oncol* 2010;28:4706–4713.
6. Gill S, Dowden S, Colwell B, Collins LL, Berry S. Navigating later lines of treatment for advanced colorectal cancer—optimizing targeted biological therapies to improve outcomes. *Cancer Treat Rev* 2014;40(10):1171–1181.
7. Overman MJ, Ernstoff MS, Morse MA. Where we stand with immunotherapy in colorectal cancer: deficient mismatch repair, proficient mismatch repair, and toxicity management. *Am Soc Clin Oncol Educ Book* 2018;38:239–247.
8. Berry SR, Cosby R, Asmis T, et al. Continuous versus intermittent chemotherapy strategies in metastatic colorectal cancer: a systematic review and meta-analysis. *Ann Oncol* 2015;26:477–485.
9. Ciombor KK, Bekaii-Saab T. A comprehensive review of sequencing and combination strategies of targeted agents in metastatic colorectal cancer. *Oncologist* 2018;23(1):25–34.
10. Atreya CE, Yaeger R, Chu E. Systemic therapy for metastatic colorectal cancer: from current standards to future molecular targeted approaches. *Am Soc Clin Oncol Educ Book* 2017; 37:246–256.

151

PROSTATE CANCER

Missed Opportunity Level II

Lisa M. Holle, PharmD, BCOP, FHOPA

Jessica M. Clement, MD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe typical symptoms associated with prostate cancer at initial diagnosis and at disease progression.
- Describe the standard initial treatment options for hormone-sensitive metastatic prostate cancer.

- Recommend a pharmacotherapeutic plan for patients with castrate-resistant metastatic prostate cancer.
- Counsel patients regarding the toxicities associated with the pharmacologic agents used in prostate cancer treatment.

PATIENT PRESENTATION

■ Chief Complaint

"I have blood in my urine, I'm using the bathroom all the time, and my shoulder is really hurting."

■ HPI

Paul Williams is a 73-year-old African-American man who usually has yearly physicals and PSA checks by his local physician. The levels have always been in the range of 4–6 ng/mL. He did not go in for his yearly physical last year, and he now presents with painless gross hematuria, shoulder pain, and a PSA level of 35.7 ng/mL. He has had increased urinary symptoms for the past 5 months.

■ PMH

Dyslipidemia
CHF
Diverticulitis
Severe GERD

■ FH

Father, lung cancer diagnosed age 71, died age 73; mother, breast cancer, died at age 93. The patient has a paternal aunt and paternal grandmother who both were diagnosed with unspecified malignancies.

■ SH

Retired highway maintenance employee. Christian by faith, Protestant by denomination. The patient has an associate degree. He drinks on average one beer per day. He smoked 10 cigarettes a day for 21 years; stopped smoking at age 42. He is married with two children. He is an only child.

■ Meds

Valsartan 160 mg PO BID
Carvedilol 12.5 mg PO twice daily
Aspirin 81 mg PO daily
Furosemide 40 mg PO daily
Allopurinol 300 mg PO daily
Tamsulosin 0.4 mg, two capsules PO daily
Atorvastatin 10 mg PO at bedtime
Acetaminophen 500 mg PO four times daily PRN pain
Esomeprazole 40 mg PO daily

■ All

None

■ ROS

The patient reports significant fatigue and severe pain in right shoulder. No fever, chills, or sweats. No epistaxis or dysphagia. Reports no chest pain, shortness of breath, dyspnea, or cough. No nausea, vomiting, diarrhea, or constipation. He reports dysuria × 5 months with dribbling, nocturia eight times per night, hesitancy, and incomplete voiding. He has recurring hematuria. He denies memory loss, diplopia, or neuropathy; he has had no falls recently.

■ Physical Examination

Gen

This is a pleasant, elderly man who appears to be in moderate discomfort. Pain is 7 over 10 multifocally. ECOG performance status 1+.

VS

BP 136/61 mm Hg, P 80 bpm, RR 20, T 36.9°C; Wt 91.5 kg, Ht 5'6"

Skin

Warm and dry; no lesions or rashes

HEENT

Sclerae are anicteric. PERRLA; EOMI. Tympanic membranes are within normal limits bilaterally.

Neck/Lymph Nodes

No cervical or supraclavicular adenopathy

Lungs/Thorax

Lungs are clear in all fields. Respirations are even and unlabored.

CV

Normal rate and rhythm; S₁, S₂ normal; no murmurs, gallops, or rubs

Abd

There is a large midline abdominal hernia that does not appear incarcerated. No hepatosplenomegaly.

Genit/Rect

Patient is circumcised with a normal phallus. There are bilaterally descended testicles. No inguinal hernia on examination. Prostate is markedly enlarged and is asymmetric on the right. Texture is firm, but no discrete nodule palpated. Normal rectal tone.

MS/Ext

The patient has significant pain to touch on the superior aspect of the right shoulder; there is also pain on range of motion. There is tenderness in lumbar area; 1+ ankle and pedal edema is present. Pedal pulses are 2+ bilaterally.

Neuro

CN II–XII grossly normal. Cerebellar function remains intact.

■ Labs

Na 139 mEq/L	Hgb 9.5 g/dL	WBC 7.2 × 10 ³ /mm ³	Total bilirubin 0.2 mg/dL
K 4.0 mEq/L	Hct 27.1%	Neutros 70.3%	ALT <12 IU/L
Cl 107 mEq/L	RBC 3.6 × 10 ⁶ /mm ³	Baso 0.2%	AST 20 IU/L
CO ₂ 24 mEq/L	Plt 215 × 10 ³ /mm ³	Eos 2.3%	LDH 742 IU/L
BUN 21 mg/dL	MCV 75 μm ³	Lymphs 16.6%	Alk phos 912 IU/L
SCr 0.9 mg/dL	MCHC 35.1 g/dL	Monos 10.6%	Albumin 4 g/dL
Glu 114 mg/dL		PSA 35.7 ng/mL	Calcium 8.7 mg/dL
		Testosterone 276 ng/dL	

■ Bone Scan

Skeletal metastases involving the skull × 2, left femur, right shoulder, and right humerus. Lesion noted in thoracic spine (T8).

■ Cystoscopy and Bladder Neck Biopsy

High-grade carcinoma consistent with prostatic adenocarcinoma, Gleason score 8 (4 + 4), extensively involving the bladder neck biopsy tissue

■ Transrectal Prostate Biopsy

Prostatic adenocarcinoma, Gleason score 9 (4 + 5), positive for perineural invasion

■ CT Abdomen/Pelvis

Prostate mass extending into bladder, with local extension to pelvic sidewall. Multiple small, external iliac lymph nodes are present, predominantly on the left; 2–3 cm, deep inguinal lymph nodes are also present.

■ Urinalysis

Clear; negative for glucose, ketones, leukocyte esterase, nitrites, and protein; trace hemoglobin; rare bacteria

■ Assessment

A 73-year-old man with newly diagnosed T4N1M1b prostate cancer presenting with painless gross hematuria, increased urinary symptoms, and elevated PSA of 35.7 ng/mL. Patient has high-volume, high-grade metastatic hormone-sensitive disease and is here for consideration of initial treatment options.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of metastatic prostate cancer?
- 1.b. What additional information is needed to fully assess this patient's prostate cancer?

Assess the Information

- 2.a. Assess the extent of this patient's metastatic prostate cancer (eg, low-volume vs high-volume, low-risk vs high-risk) based on the subjective and objective information available.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for prostate cancer, given this patient's disease stage and history?
- 3.b. What nondrug therapies might be useful for this patient's prostate cancer?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating the metastatic, hormone-dependent prostate cancer?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's prostate cancer and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What alternatives would be appropriate if the initial therapy for prostate cancer cannot be used?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

■ CLINICAL COURSE

Mr Williams has been compliant with his treatment plan. His testosterone has been castrate since therapy was begun 20 months ago. His pain has been better controlled with these interventions. The PSA 3 months ago was mildly elevated at 0.6 ng/mL, whereas it had been undetectable previously. His PSA has now increased to 38.5 ng/mL, and his testosterone level is 22 ng/mL. He is complaining of increased pain in his pelvis and more bone pain in his ribs and back over the past 2 months. He is still able to participate in church social activities and play golf on the weekends. A CT of the pelvis shows a new soft tissue mass on the posterolateral aspect of the urinary bladder on the right side and multiple new blastic lesions in the pelvis and spine. His bone scan shows numerous new intense foci in the skull, scapulae, spine, and femurs.

■ FOLLOW-UP QUESTIONS

- 4.b. What pharmacotherapeutic options are available to the patient for his progressive, metastatic castrate-resistant prostate cancer (CRPC)?
- 4.c. What therapeutic options are available for managing this patient's pain?
- 4.d. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Locate information resources that are available to prostate cancer patients and their families.
2. Provide the rationale for intermittent LHRH hormone ablation for locally advanced and metastatic hormone-sensitive prostate cancer patients.
3. Define the role of secondary hormonal agents (eg, abiraterone acetate, enzalutamide) for metastatic disease relapse.
4. Describe the clinical rationale for starting an antiandrogen 1–2 weeks before giving the first dose of an LHRH agonist.
5. Define the role of bone modulating agents (ie, bisphosphonates, receptor activator of nuclear factor κ -B [RANK] ligand inhibitors) in men with prostate cancer.

CLINICAL PEARL

Androgen deprivation therapy is continued when a metastatic prostate cancer patient progresses from a hormone-sensitive to a castrate-resistant state (ie, has a rising PSA and/or new metastatic lesions despite a castrate-level of testosterone).

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology, V4.2018 Prostate Cancer. Available at: http://www.nccn.org/professionals/physician_gls/pdf/prostate.pdf. Accessed November 9, 2018.
2. Klotz L, Boccon-Gibod L, Shore N, et al. The efficacy and safety of degarelix: a 12-month, comparative, randomized, open-label, parallel-group phase III study in patients with prostate cancer. *BJU Int* 2008; 102:1531–1538.
3. Wolters Kluwer Clinical Drug Information, Inc. Lexi-Drugs. Wolters Kluwer Clinical Drug Information, Inc.; November 9, 2018.
4. Morris MJ, Rumble B, Basch E, et al. Optimizing anticancer therapy in metastatic non-castrate resistant prostate cancer: American Society of Clinical Oncology Practice Guideline. *J Clin Oncol* 2018;36(15): 1521–1539.
5. Zytiga Package Insert. Horsham, PA: Janssen Biotech, Inc.; 2018.
6. Yonsa Package Insert. Cranbury, NJ: Sun Pharmaceuticals Industries, Inc.; 2018.
7. Nuhn P, De Bono JS, Fizai K, et al. Update on systemic prostate cancer therapies: management of metastatic castration-resistant prostate cancer in the era of precision oncology. *Eur Oncol* 2019;75(1):88–99.
8. Fizazi K, Carducci M, Smith M, et al. Denosumab versus zoledronic acid for treatment of bone metastases in men with castration-resistant prostate cancer: a randomised, double-blind study. *Lancet* 2011;377:813–822.
9. NCCN Clinical Practice Guidelines in Oncology, V1.2018. Adult cancer pain. Available at: http://www.nccn.org/professionals/physician_gls/pdf/pain.pdf. Accessed November 26, 2018.

152

NON-HODGKIN LYMPHOMA

Chemical Formula for Cancer Level II

Keith A. Hecht, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify and describe the components of the staging workup and the corresponding staging and classification systems for non-Hodgkin lymphoma (NHL).
- Recommend treatment for NHL with high-risk genetic features.
- Identify acute and chronic toxicities associated with the drugs used to treat NHL and the measures used to prevent or treat these toxicities.
- Identify monitoring parameters for response and toxicity in patients with NHL.
- Provide detailed patient education for the chemotherapeutic regimen selected to treat NHL.

PATIENT PRESENTATION

■ Chief Complaint

“What’s the next step for my lymphoma?”

■ HPI

Ben Burner is a 58-year-old man who presents to his oncologist’s office for recommendations about treatment of a newly diagnosed diffuse, large B-cell lymphoma. He had been in relatively good health other than his longstanding hypertension, hypercholesterolemia, and GERD. He initially presented to the ED 1 week ago with new-onset left lower extremity edema. He was then hospitalized for further evaluation and treatment. At that time, he stated that he had lost weight over the past few months. Vital signs on admission included elevated temperature of 100.8°F (38.2°C). Physical examination findings were significant for a round, protuberant abdomen that was soft on the right side but firm on left and 3+ pitting edema of the left lower extremity from foot to knee. Laboratory findings were significant for serum creatinine 1.9 mg/dL, serum calcium 11.6 mg/dL, and hemoglobin 10.6 g/dL. A renal ultrasound revealed severe hydronephrosis on the left side and displacement of the bladder with compression, possibly from a mass. A CT scan without contrast of the chest, abdomen, and pelvis was performed. Results showed multiple enlarged lymph nodes, including several mediastinal nodes, paraesophageal nodes, and retrocrural nodes. A large, confluent soft tissue mass was found, extending through the retroperitoneum and involving the left pelvis. The mass encased the distal left ureter. The mass in its widest dimension was 16.3 cm. A diagnosis of lymphoma was presumed based on the extent of lymph involvement. Urologists placed a left ureteral stent and performed ultrasound-guided biopsy of the mass. Pathology showed diffuse large non-Hodgkin B-cell lymphoma. Upon confirmation of diagnosis, a bone marrow biopsy was performed. Results were not available during hospitalization. The patient was insistent on discharge to attend his daughter’s wedding, so treatment was deferred after initial consultation with an oncologist in the hospital. His creatinine and calcium values were normalizing at the time of discharge.

■ PMH

HTN × 10 years

Hypercholesterolemia × 5 years

GERD × 15 years

■ FH

The patient is the oldest of seven children (four brothers and two sisters), all alive and well. He has two children, both in good health. Family history of terminal prostate cancer in his father (died at age 63). No other history of malignancy that he is aware of.

■ SH

The patient is employed by a large chemical company as a manager of the division that caters to aerospace applications. He has been with the company since graduating from college. He initially began work in the production areas and advanced to his current management position. He previously smoked 1–2 ppd for 25 years; he quit when he was diagnosed with GERD. He drinks one to two beers nightly. Diet is mostly unremarkable except that he states that he does not eat many vegetables, unless popcorn counts. He has been married for 34 years; his wife is with him today in the clinic.

■ ROS

The patient reports continuing fever, typically ranging from 100.2 to 101°F (37.9–38.3°C). He states his lower extremity swelling is much better since hospitalization and was pleased that he was able to wear his fancy dancing shoes for his daughter’s wedding. He reports an unexplained weight loss of approximately 25 lb over the past 3 months. He denies headaches, changes in vision, or fainting episodes.

He reports no lesions in his mouth, difficulty swallowing, or nosebleeds. He denies orthopnea and tachycardia. He has not had any back pain. He denies any changes in urination frequency, burning on urination, urinary frequency, dribbling, or blood in the urine. He has not noticed any abnormal bleeding or bruising. He has not received any prior transfusions.

■ Meds

Lisinopril 20 mg PO once daily
Furosemide 20 mg PO once daily
Simvastatin 20 mg PO at bedtime
Famotidine 20 mg PO twice daily
Temazepam 30 mg PO at bedtime as needed
Epoetin alfa 40,000 units subQ once weekly

■ All

Penicillin—rash

■ Physical Examination

Gen

Patient is a thin white man in no apparent distress.

VS

BP 145/100 mm Hg, P 95 bpm, RR 14, T 37.9°C; Wt 72 kg, Ht 5'9"

Skin

No rashes or moles noted

HEENT

PERRLA; TMs clear; no masses in the tonsils, palate, or floor of the mouth; no stomatitis. Several missing teeth, but no gingival inflammation is noted.

Neck

Supple; no masses; no JVD

Chest

CTA bilaterally

CV

RRR; no MRG

Abd

Soft, nontender, appears distended. No hepatomegaly or splenomegaly noted. Bowel sounds normoactive.

Genit/Rect

Normal male genitalia

Ext

1+ pitting edema of left lower extremity

Neuro

Symmetric cranial nerve function. Symmetric facial muscle movement, and the tongue is midline. The palate is symmetric. Balance and coordination of the upper extremities are intact, with no evidence of tremor. There is symmetric coordination of rapidly alternating movements. Motor strength in the upper and lower extremities is normal and symmetric.

Lymph Node Survey

The lymph node survey is negative for any palpable peripheral nodes in the preauricular, postauricular, submandibular, cervical, supraclavicular, infraclavicular, or axillary areas.

■ Labs

Na 132 mEq/L	Hgb 10.3 g/dL	AST 29 IU/L	Phos 4.0 mg/dL
K 4.6 mEq/L	Hct 30%	ALT 27 IU/L	Uric acid 5.6 mg/dL
Cl 97 mEq/L	Plt $338 \times 10^3/\text{mm}^3$	Alk phos 75 IU/L	PT 12.2 seconds
CO ₂ 26 mEq/L	WBC $9.9 \times 10^3/\text{mm}^3$	LDH 623 IU/L	aPTT 21.7 seconds
BUN 20 mg/dL	Neutros 70%	T. bili 0.6 mg/dL	
SCr 0.9 mg/dL	Bands 2%	T. prot 6.3 g/dL	
Glu 112 mg/dL	Lymphs 18%	Alb 3.7 g/dL	
Ca 9.7 mg/dL	Monos 9%		
	Eos 1%		

■ Bone Marrow Biopsy

Biopsy and aspiration were negative for blasts or atypical lymphocytes.

■ Tumor Pathology

Diffuse large B-cell lymphoma, germinal center type; CD 10+, CD19+, CD20+, CD23+, CD38+, CD5-. FISH indicates 75% of nuclei have MYC/IGH fusion and BCL2 rearrangement.

■ Initial Assessment

Diffuse large cell lymphoma. Further staging will include PET scan, HIV test, CT of the abdomen, and a baseline cardiac assessment in light of the patient's longstanding history of HTN.

■ Clinical Course

PET scanning revealed multiple foci of increased FDG uptake, consistent with findings of CT scan. No additional areas of involvement noted. MUGA scan reveals LVEF 65%.

■ Assessment

Double-hit diffuse large B-cell lymphoma, stage III; IPI score of 2.

QUESTIONS

Collect Information

1. What subjective and objective information is consistent with the diagnosis of non-Hodgkin lymphoma (NHL)?

Assess the Information

- 2.a. Explain what system of staging was used and how his stage of disease was determined.
- 2.b. What laboratory and clinical features does this patient have that may affect his prognosis and treatment? How is the IPI determined?
- 2.c. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for treating this patient's drug therapy problems?

- 3.c. What feasible pharmacotherapeutic alternatives are available for treating NHL in this patient?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's NHL. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.
- 3.e. What other interventions should be made to maintain control of the patient's other concurrent diseases?

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. How is the response to the treatment regimen for lymphoma assessed?
- 5.b. What acute adverse effects are associated with the chemotherapy regimen, and what parameters should be monitored?
- 5.c. What pharmacologic measures should be instituted to treat or prevent the acute toxicities associated with the chemotherapy regimen?
- 5.d. What are potential late complications of the chemotherapy regimen, and how can they be detected and prevented?
- 5.e. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE (PART 1)

The patient tolerated the first few cycles of chemotherapy well, with only some minimal nausea and vomiting. His antihypertensive medication was modified, increasing the lisinopril to 40 mg daily and achieving average systolic BPs in the 120s and average diastolic BPs in the 70s. His left lower extremity edema resolved, and furosemide was discontinued. His fasting lipid panel was checked and was found to be within his goals. One week after completing the fourth cycle of chemotherapy, he presented to the ED with fever (101.3°F [38.5°C]), cough, dyspnea, pain on inspiration, and fatigue. Laboratory evaluation showed an ANC of $0.352 \times 10^3/\text{mm}^3$. He was admitted to the hospital for evaluation and treatment of suspected neutropenic fever with pneumonia. Blood and sputum cultures were negative. The patient was treated with broad-spectrum antibiotics and became afebrile after 3 days. He was discharged from the hospital after the neutropenia resolved, completing a 14-day course of inpatient IV antibiotics. PET and CT scans performed while he was hospitalized to evaluate his lymphoma showed that he achieved a complete response.

FOLLOW-UP QUESTION

1. What measures should be taken to prevent neutropenic fever in subsequent courses of chemotherapy?

CLINICAL COURSE (PART 2)

The patient completed his planned course of chemotherapy without further event. Eighteen months later, he returns to the oncologist office after being diagnosed with relapsed lymphoma during a hospital admission for worsening dyspnea.

SELF-STUDY ASSIGNMENTS

1. What is the role of stem cell transplant in the treatment of aggressive NHL?
2. What therapeutic options are available for the treatment of relapsed diffuse large B-cell lymphomas?
3. What is the role of chimeric antigen receptor T-cell therapy (CAR-T) in the treatment of diffuse large B-cell lymphoma?
4. If the patient had a history of hepatitis B, what diagnostic tests would be indicated? What antiviral therapy, if any, should be considered for patients with a history of hepatitis B who are receiving chemo-immunotherapy for treatment of diffuse large B-cell lymphoma?

CLINICAL PEARL

Double-hit lymphoma is an aggressive type of B-cell NHL caused by changes in the DNA that affect the MYC gene and either the BCL2 or the BCL6 gene. It requires more aggressive chemotherapy than standard B-cell lymphomas. Some clinicians advocate for initial treatment with high-dose chemotherapy with stem cell transplantation, but evidence from clinical trials does not support this approach.

REFERENCES

1. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol* 2014;32:3059–3067.
2. Snuderl M, Kolman OK, Chen YB, et al. B-cell lymphomas with concurrent IGH-BCL2 and MYC rearrangements are aggressive neoplasms with clinical and pathologic features distinct from Burkitt lymphoma and diffuse large B-cell lymphoma. *Am J Surg Pathol* 2010; 34:327–340.
3. Zhou Z, Sehn LH, Rademaker AW, et al. An enhanced International Prognostic Index (NCCN-IPI) for patients with diffuse large B-cell lymphoma treated in the rituximab era. *Blood* 2014;123:837–842.
4. Coiffier B, Thieblemont C, Van Den Neste E, et al. Long-term outcome of patients in the LNH-98.5 trial, the first randomized study comparing rituximab-CHOP to standard CHOP chemotherapy in DLBCL patients: a study by the Groupe d'Etudes des Lymphomes de l'Adulte. *Blood* 2010;116:2040–2045.
5. Howlett C, Snedecor SJ, Landsburg DJ, et al. Front line, dose escalated immunochemotherapy is associated with significant progression-free survival advantage in patients with double-hit lymphomas: a systemic review and meta-analysis. *Br J Haematol* 2015; 170:405–514.
6. Purroy N, Bergua J, Gallur L, et al. Long-term follow-up of dose-adjusted EPOCH plus rituximab (DA-EPOCH-R) in untreated patients with poor prognosis large B-cell lymphoma. A phase II study conducted by the Spanish PETHEMA group. *Br J Haematol* 2015;169: 188–198.
7. Smith TJ, Bohlke K, Lyman GH, et al. Recommendations for the use of WBC growth factors: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2015;33:3199–3212.
8. Hesketh PJ, Kris MG, Basch E, et al. Antiemetics: American Society of Clinical Oncology clinical practice guideline update. *J Clin Oncol* 2017;35:3240–3261.
9. Ganz WI, Sridhar KS, Ganz SS, et al. Review of tests for monitoring doxorubicin-induced cardiomyopathy. *Oncology* 1996;53:461–470.
10. Flowers CR, Seidenfeld J, Bow EJ, et al. Antimicrobial prophylaxis and outpatient management of fever and neutropenia in adults treated for malignancy: American Society of Clinical Oncology clinical practice guideline. *J Clin Oncol* 2013;31(6):794–810.

153

HODGKIN LYMPHOMA

The Rock Climber Level I

Cindy L. O'Bryant, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms commonly associated with Hodgkin lymphoma (HL).
- Discuss the pharmacotherapeutic treatment of choice and the alternatives available for treating HL.
- Identify acute and chronic toxicities associated with the medications used to treat HL and the measures used to prevent, treat, and monitor these toxicities.
- Determine monitoring parameters for response and toxicity in patients with HL.
- Formulate appropriate educational information to provide to a patient receiving chemotherapy treatment for HL.

PATIENT PRESENTATION

■ Chief Complaint

"I have been having night sweats, fever, and weight loss despite health eating. I have also been a lot more tired lately. My neck has been swollen and I have a growth on my neck that has gotten bigger over the past month."

■ HPI

Mike McCaffrey is a 27-year-old man who presents to an outpatient medical oncology clinic with a 1-month history of night sweats, fever, fatigue, and a 9-kg weight loss. He noticed weight loss because he has been watching his weight while training for an upcoming 2-week climbing trip. His wife also noticed neck swelling and a neck mass that has gotten progressively larger over the past month. He initially associated the mass with a strep throat infection and went to see his primary care provider 5 weeks ago. He was started on a 10-day course of antibiotics, but the mass did not resolve. One week ago, his primary care provider scheduled an ultrasound of the neck due to persistent and worsening symptoms. At this visit, enlarged right and left supraclavicular lymph nodes were palpated on physical exam. The ultrasound of the neck showed a cervical lymph node that measured approximately 11 cm in diameter. As a result, an excisional lymph node biopsy was performed that day, which demonstrated classic HL, nodular sclerosing (NS) subtype.

■ PMH

Epidemiology of Epstein-Barr virus as a teenager

■ FH

The patient's mother, father, and two siblings (brother and sister) are all in good health. Paternal grandfather died of lung cancer.

■ SH

Works as structural engineer. Is a rock climber and is training for a 2-week climbing trip. Drinks socially, about three to four beers per week. He has never smoked. He does not use illicit drugs. The patient is married and wishes to start a family in the next 2 years.

■ Meds

Ibuprofen 400 mg PO Q 4–6 H PRN pain/fever

■ All

NKDA

■ ROS

(+) For fevers, night sweats, fatigue, and weight loss of approximately 9 kg over the past month.

(–) For vision changes, headaches, shortness of breath, chest pain, nausea, vomiting, diarrhea, constipation, or urinary symptoms. Denies feeling depressed or having loss of pleasure with activities. His performance status is 1 on the ECOG scale.

■ Physical Examination

Gen

The patient is a healthy-appearing man in no apparent distress.

VS

BP 118/70 mm Hg, P 64 bpm, RR 16, T 37.6°C; Wt 79.3 kg, Ht 6'1"

Skin

Soft, diffusely enlarged soft tissue swelling in the neck; no erythema or warmth; no rashes

HEENT

PERRL; EOMI; TMs intact

Lymph Nodes

Supraclavicular lymph nodes are enlarged on both the right and left. The left anterior cervical neck mass is palpable. No other lymph nodes are palpable bilaterally.

Chest

Respirations with normal rhythm; clear to auscultation

CV

RRR; no JVD, murmurs, or gallops

Abd

Soft and nontender with no masses; bowel sounds are normoactive

Genit/Rect

Normal male genitalia; stool is guaiac (–).

MS/Ext

Without edema

Neuro

A&O × 3; CN II–XII intact; remainder of exam is nonfocal.

■ Labs

Na 137 mEq/L	Hgb 10.1 g/dL	AST 19 IU/L	PT 12.9 seconds
K 4.1 mEq/L	Hct 32.3%	ALT 22 IU/L	aPTT 27.1 seconds
Cl 103 mEq/L	Plt 310 ×	Alk phos 74 IU/L	Phos 3.1 mg/dL
CO ₂ 24 mEq/L	10 ³ /mm ³	LDH 372 IU/L	Magnesium
BUN 14 mg/dL	WBC 10.9 ×	T. bili 0.4 mg/dL	1.2 mEq/L
SCr 0.7 mg/dL	10 ³ /mm ³	T. prot 7.7 g/dL	Uric acid 7.5 mg/dL
Glu 82 mg/dL	Neutros 80.5%	Alb 3.2 g/dL	ESR 63 mm/h
	Lymphs 13.2%		
	Monos 5.4%		
	Eos 0.9%		

■ Ultrasound

There are singular, enlarged abnormal lymph nodes in the right and left supraclavicular regions. The largest node on the right measures 2.8 cm × 1.5 cm × 2.1 cm and on the left 1.8 cm × 0.9 cm × 1.3 cm. The large left anterior cervical node is 11.1 cm × 6.8 cm × 8.9 cm. The nodes contain solid echogenic material and have increased vascular flow.

■ Tumor Pathology

Identification of Reed–Sternberg cells classifying this as HL, NS type (Fig. 153-1). Immunohistochemistry: CD15+, CD30+, CD20–, CD45–.

■ PET/Helical CT Scan

Enlarged nodes demonstrating hypermetabolic activity are noted in the bilateral supraclavicular chains and the superior mesenteric chain. There is involvement of the left anterior cervical node showing bulky disease. The bilateral lungs and myocardium are negative for disease. Normal physiologic liver, GI, and urinary activity are noted. Diffuse increased uptake within the bone marrow; it is unclear whether this is lymphoma or hyperplasia.

■ Bone Marrow Biopsy

Bilateral biopsies are negative for HL.

■ Assessment

Classic HL, nodular sclerosis subtype, stage IIIB.

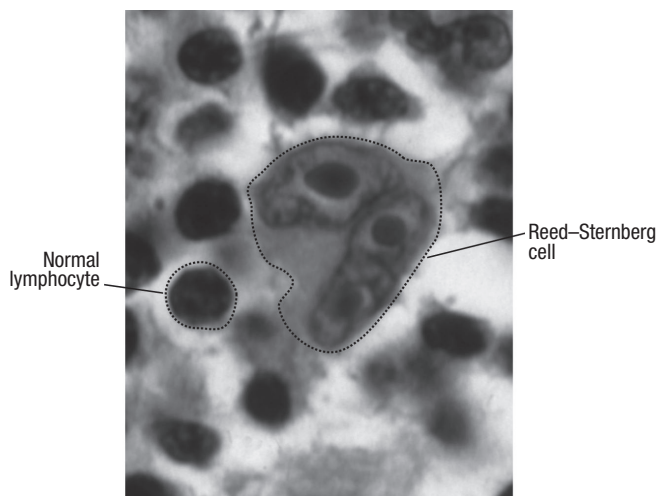


FIGURE 153-1. Reed–Sternberg cell (center) surrounded by normal lymphocytes. (Source: National Cancer Institute.)

QUESTIONS

Collect Information

1. What subjective and objective information is consistent with the diagnosis of Hodgkin lymphoma (HL)?

Assess the Information

- 2.a. What risk factors does the patient have for developing HL?
- 2.b. Explain what staging system was used and how his stage of disease was determined.
- 2.c. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. Are treatment measures other than chemotherapy indicated for treating this patient's HL?
- 3.c. What feasible pharmacotherapeutic alternatives are available for managing this patient's HL?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects for treatment of HL?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome for treatment of HL?
- 5.b. What acute adverse effects are associated with the chemotherapy regimen?
- 5.c. What clinical or laboratory parameters are necessary to detect and prevent acute and long-term adverse events commonly associated with treatment of HL?
- 5.d. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

The patient's treatment was administered in the outpatient setting. He received day 1 of his first cycle of chemotherapy and experienced acute nausea and vomiting. Five days after his first treatment, he experienced mild mucositis and mild constipation. He was instructed to maintain good oral hygiene, use a soft toothbrush, and avoid alcohol and spicy or acidic foods. He was started on a mouthwash (diphenhydramine, lidocaine, and aluminum/magnesium hydroxide) with instructions to swish and spit four times a day. He was educated to maintain good hydration, a high-fiber diet, and to start docusate sodium 50 mg orally once daily for constipation. He successfully received cycles 2 of chemotherapy in the outpatient clinic without incident. He was then restaged with a PET/CT scan to

assess his response to chemotherapy. Restaging showed the patient had a complete response with a Deauville score of 2, and he received four more cycles of chemotherapy followed by involved site radiation. On subsequent follow-up, the patient is in remission.

■ FOLLOW-UP QUESTION

1. What follow-up and long-term monitoring should this patient receive after completion of his cancer treatment?

■ SELF-STUDY ASSIGNMENTS

1. What are unfavorable prognostic factors for early and advanced HL, and how does this influence treatment?
2. What is the antiemetic regimen of choice to prevent acute nausea and vomiting for highly emetogenic chemotherapy?
3. What are the salvage therapy options for patients with relapsing HL?
4. What is the role for hematopoietic stem cell transplantation in HL?

CLINICAL PEARL

HL can be cured with chemotherapy, even in advanced stages. To achieve a cure, it is essential that a patient receives the appropriate treatment. This is based on several key factors, which include an accurate diagnosis of the type of HL with recommended immunostaining, determination of unfavorable prognostic factors, appropriate staging and use of combined chemotherapy and radiation treatment when appropriate.

REFERENCES

1. NCCN Hodgkin Lymphoma Clinical Practice Guidelines in Oncology (Version 3.2018). Available at: <http://www.nccn.org>. Accessed January 21, 2019.
2. Cheson BD, Fisher RI, Barrington SF, et al. Recommendations for initial evaluation, staging, and response assessment of Hodgkin and non-Hodgkin lymphoma: the Lugano classification. *J Clin Oncol* 2014;32:3059–3068.
3. Gordon LI, Hong F, Fisher RI, et al. Randomized phase III trial of ABVD versus Stanford V with or without radiation therapy in locally extensive and advanced-stage Hodgkin lymphoma: an intergroup study coordinated by the Eastern Cooperative Oncology Group (E2496). *J Clin Oncol* 2013;31:684–691.
4. Carde P, Karrasch M, Fortpied C, et al. Eight cycles of ABVD versus four cycles of BEACOPPescalated plus four cycles of BEACOPPbaseline in Stage III to IV, International Prognostic Score ≥ 3 , high-risk Hodgkin Lymphoma: first results of the phase III EORTC 20012 Intergroup Trial. *J Clin Oncol* 2016;34(17):2028–2036.
5. Longley J, Johnson PWM. Current treatment paradigms for advanced stage Hodgkin lymphoma. *Br J Haematol* 2019;184(1):60–71.
6. Johnson P, Frederico M, Kirkwood A, et al. Adapted treatment guided by interim PET-CT scan in advanced Hodgkin's lymphoma. *N Engl J Med* 2016;374:2419–2429.
7. NCCN Antiemesis Clinical Practice Guidelines in Oncology (Version 3.2018). Available at: <http://www.nccn.org>. Accessed January 21, 2019.
8. NCCN Myeloid Growth Factors Clinical Practice Guidelines in Oncology (Version 2.2018). Available at: <http://www.nccn.org>. Accessed January 21, 2019.
9. Schaapveld M, Aleman BM, van Eggermond A, et al. Second cancer risk up to 40 years after treatment for Hodgkin's lymphoma. *N Engl J Med* 2015;373:2499–2511.
10. Hodgson DC. Long-term toxicity of chemotherapy and radiotherapy in lymphoma survivors: optimizing treatment for individual patients. *Clin Adv Hematol Oncol* 2015;13:103–112.

154

OVARIAN CANCER

Family Ties Level II

Amber E. Proctor, PharmD, BCOP

Alexis Jones, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Recognize the signs and symptoms of ovarian cancer.
- Describe the genetic factors associated with ovarian cancer.
- Recommend a pharmacotherapeutic plan for the chemotherapy of newly diagnosed and relapsed ovarian cancer as well as maintenance treatment.
- Recognize the dose-limiting and most common toxicities associated with the chemotherapeutic agents used to treat ovarian cancer.

PATIENT PRESENTATION

■ Chief Complaint

"I'm very anxious about getting chemotherapy. My uncles have gone through chemotherapy for colorectal cancer and they became very sick. One of them was even admitted to the hospital due to the side effects. I don't want that to happen to me."

■ HPI

Edith Hillebrand is a 56-year-old woman who presents to the gynecology oncology clinic 1 week after surgery for stage IIIB (T3b N1 M0) serous epithelial ovarian adenocarcinoma. She originally presented to her PCP's office 1 month ago with complaints of a 15-lb weight gain, bloating, and abdominal pain. Her last physical exam was performed more than 15 months prior. The physician performed a complete history and physical exam and identified a left adnexal mass. CT scans of the abdomen and pelvis showed a large, soft tissue pelvic mass. Laboratory examination revealed a CA-125 level of 490 IU/mL.

Two weeks later, Mrs Hillebrand underwent an exploratory laparotomy, TAH-BSO, omentectomy, and bilateral pelvic and periaortic lymph node dissection with comprehensive staging by a gynecologic oncologist. On entering the abdomen, there was a relatively small amount of ascitic fluid. A large left adnexal mass measuring 15 cm $\times$ 5 cm $\times$ 10 cm was discovered and removed. Multiple small tumor nodules (≤ 2 cm) outside the pelvis were also removed. Numerous adhesions were seen throughout the omentum and surrounding organs. At completion of the surgery, the surgeon noted that the patient was optimally debulked with an R0 resection. Ascitic fluid, peritoneal washings, left adnexal mass, left and right ovaries, multiple pelvic and periaortic lymph nodes, and omentum were sent to pathology for further examination.

Gross examination of left and right ovaries revealed multiple adhesions extending from each ovary with interspersed broad regions of necrosis. Each ovary was serially sectioned for microscopic examination, which revealed numerous papillations of tumor

cells destructively permeating the stroma (grade 2). Based on this information, Mrs Hillebrand was diagnosed with stage IIIB (T3b N1 M0) serous epithelial ovarian adenocarcinoma.

■ PMH

Type 2 DM × 17 years
Dyslipidemia × 15 years

■ FH

Married × 37 years with a son age 35. Her father died of an MI at age 72, and her mother died at age 66 with ovarian cancer. Has two paternal uncles (age 80 and 76 years) alive with colorectal cancer.

■ SH

Consumes one glass of red wine with dinner every evening. Has a 20 pack-year history of cigarette smoking; quit 25 years ago. No recreational drug use. Poor adherence to medication as evidenced by inconsistent refill dates per pharmacy record.

■ Meds

Atorvastatin 40 mg PO daily
Metformin 1000 mg PO twice daily
Glyburide 10 mg PO twice daily
Lisinopril 40 mg PO daily

■ All

Penicillin (hives as a child)
Codeine (“sour stomach”)

■ ROS

Somewhat fatigued lately, progressively worsening over the past 2 months. Reports a 15-lb weight gain over the past month. She also reports requiring more sleep than usual, about 9–10 hours per night, but cannot recall when this change occurred. Her mood is depressed because of concern about her recent cancer diagnosis. Denies any changes in sight, smell, hearing, and taste.

■ Physical Examination

Gen

The patient appears to be her stated age. Appears anxious in the office on exam.

VS

BP 135/85 mm Hg, P 110 bpm, RR 18, T 37.0°C; Ht 5'7", Wt 70 kg

Skin

No erythema, rash, ecchymoses, or petechiae

LN

No cervical or axillary lymphadenopathy

HEENT

PERRLA, EOMI; TMs intact; fundus benign; OP dry

Breasts

Without masses, discharge, or adenopathy; no nipple or skin changes

Cor

RRR; no M/R/G

Pulm

CTA bilaterally

Abd

Soft, nontender; no HSM. Surgical wound healing well; no exudate or erythema; covered with 4 × 4 bandage with antibiotic ointment.

Genit/Rect

Normal female genitalia; heme (–) dark brown stool; no rectal wall tenderness or masses

Ext

No C/C/E. Residual erythema and swelling in LLE from prior DVT; no signs of ulceration.

Neuro

CN II–XII intact; sensation decreased to light touch and pinprick below the knees bilaterally; vibration sense diminished at the great toes bilaterally

■ Labs

Na 140 mEq/L	Hgb 12.8 g/dL	AST 25 IU/L
K 4.1 mEq/L	Hct 37%	ALT 40 IU/L
Cl 99 mEq/L	Plt $135 \times 10^3/\text{mm}^3$	T. bili 0.7 mg/dL
CO ₂ 24 mEq/L	WBC $5.2 \times 10^3/\text{mm}^3$	Alb 4.0 U/L
BUN 20 mg/dL	Neutros 60%	CA-125 490 IU/mL
SCr 1.1 mg/dL	Bands 3%	
Glu 135 mg/dL	Lymphs 30%	
Ca 9.8 mg/dL	Monos 5%	
Mg 2.0 mg/dL	Eos 1%	
Phos 3.5 mg/dL	Basos 1%	

■ UA

WBC 1–5/hpf, RBC 0/hpf, 1+ ketones, 1+ protein, pH 5.0

■ Genetic Results

Patient was offered a referral to a genetics counselor due to new diagnosis and history of ovarian cancer in her mother. She has declined genetics at this time.

■ Assessment/Plan

Mrs Hillebrand is a 56-year-old woman with advanced stage IIIB (T2c N1 M0) serous epithelial ovarian adenocarcinoma. She underwent optimal surgical debulking (2 weeks ago) with an R0 resection by a trained gynecologic oncologist and presents to the clinic for follow-up care. Based on the stage of diagnosis and risk for recurrence, first-line chemotherapy is recommended.

QUESTIONS

Collect Information

1. What subjective and objective information indicates the presence of ovarian cancer?

Assess the Information

- 2.a. What stage of ovarian cancer does this patient have, and how does the stage of disease affect the choice of therapy?
- 2.b. What is the significance of the size of residual tumor after primary cytoreductive surgery?

- 2.c. What genetic alteration in ovarian cancer is the reason for offering a genetic consult, and how would the genetic results influence the prognosis?
- 2.d. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What are the first-line chemotherapy options for treating ovarian cancer in this patient?
- 3.c. What are the specific toxicities and logistical issues related to intraperitoneal (IP) therapy?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's ovarian cancer and her other medical problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy for chemotherapy and for prevention/treatment of nausea and vomiting.

CLINICAL COURSE (PART 1)

The patient and oncologist agreed to begin treatment with the combination of IV docetaxel and carboplatin on day 1 every 21 days for six cycles as first-line treatment of her ovarian cancer.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE (PART 2)

Mrs Hillebrand completed six cycles of docetaxel 75 mg/m² IV over 1 hour followed by carboplatin AUC 5 IV over 1 hour on day 1 every 21 days. She tolerated therapy very well with no dose reductions or delays. Her serum CA-125 level slowly declined over the course of treatment and was 12 IU/mL 3 weeks after her sixth cycle. Based on her CA-125 level and the negative CT scans following the fourth and sixth cycles, Mrs Hillebrand was defined as a clinical complete response. Her CA-125 levels were followed monthly.

Starting 1 month after treatment was discontinued, monthly CA-125 levels were 8, 10, 14, 20, 30, 43, and 88 IU/mL. A CT scan performed at 8 months after treatment discontinuation revealed a pelvic mass (6 cm × 5 cm × 4 cm) arising from the retroperitoneum and a 2-cm mass in the head of the pancreas. Laboratory data were normal except for a CA-125 level of 150 IU/mL. She was diagnosed with recurrent ovarian cancer.

FOLLOW-UP QUESTIONS

1. Is it preferable to treat early relapsed disease based only on a rising CA-125 level rather than delaying treatment until there are clinical signs of relapse?
2. What therapeutic options are available for this patient's relapsed disease?
3. Which of the chemotherapeutic regimens would you recommend for the patient's locally relapsed ovarian cancer? Provide the rationale for your answer.

CLINICAL COURSE (PART 3)

The decision was made to start IV carboplatin AUC 5 and pegylated liposomal doxorubicin 30 mg/m² on day 1 every 28 days. Mrs Hillebrand received two cycles of carboplatin and pegylated liposomal doxorubicin. During this time her tumor tissue was sent for next generation sequencing (NGS). The genetic alterations identified are shown as follows:

BRCA2 S642FS*9
 PI3KCA C378R
 PRKCI amplification
 Microsatellite status: MS-stable

Radiologic imaging just prior to the third cycle showed no evidence of disease progression. During her third cycle, she complained of having trouble putting on her shoes and pain in her feet on walking. On physical exam, the patient's feet were red, swollen, and cracked. Her CA-125 levels were 155, 158, and 160 IU/mL after each of her first three cycles of carboplatin plus pegylated liposomal doxorubicin.

FOLLOW-UP QUESTION

4. What are the potential adverse effects of pegylated liposomal doxorubicin therapy that require monitoring and patient education?

CLINICAL COURSE (PART 4)

The fourth cycle of therapy was delayed for 2 weeks and restarted when her skin lesions resolved. She completed six cycles of chemotherapy; however, upon final imaging, she still had small lesions on CT scan (none of which were >4 cm in diameter). Because she experienced significant adverse effects from pegylated liposomal doxorubicin, she expresses a strong desire to take a break from cytotoxic chemotherapy but expresses concern about "doing nothing" to treat her cancer.

FOLLOW-UP QUESTIONS

5. Based on the information available, what would be the best treatment option for the patient at this time?
6. How would you explain "maintenance therapy" to a patient with ovarian cancer?
7. The oncologist decides that niraparib is the best treatment option for this patient. What are its possible adverse effects, and how would you monitor the therapy?

CLINICAL COURSE (PART 5)

After 4 months of niraparib therapy, the patient started to experience abdominal bloating and discomfort. A CT scan showed evidence of ascites and new disease within the peritoneal cavity.

■ FOLLOW-UP QUESTION

8. What options are available for salvage therapy, and which would you choose for this patient? Provide the rationale for your answer.

■ SELF-STUDY ASSIGNMENTS

1. What are the pharmacologic advantages of IV therapy versus IP therapy?
2. Why is the size of the residual tumor important with regard to IP therapy?
3. What are the probable causes of paclitaxel and docetaxel hypersensitivity?
4. What are the issues related to maintenance therapy in patients with advanced ovarian cancer after achieving complete response to consolidative chemotherapy?
5. How might cytochrome P450 3A4/5 polymorphism potentially affect docetaxel therapy of ovarian cancer?

CLINICAL PEARL

If patients with advanced age or poor performance status cannot undergo surgical cytoreduction followed by chemotherapy, another treatment option is neoadjuvant chemotherapy. This is given prior to the primary treatment (surgery) with the goal of reducing tumor volume and having a greater chance of a cure. Neoadjuvant chemotherapy simplifies surgery by decreasing tumor volume, blood loss, and transfusions during surgery, and can reduce surgical complications and length of stays.

REFERENCES

1. The NCCN Clinical Practice Guidelines in Oncology™ Ovarian Cancer (Version 2.2018). © 2018 National Comprehensive Cancer Network Inc. Available at: NCCN.org. Accessed November 1, 2016.
2. Boyd J, Sonoda Y, Federici MG, et al. Clinicopathologic features of BRCA-linked and sporadic ovarian cancer. *JAMA* 2000;283:2260–2265.
3. Ozols RF, Bundy BN, Greer BE, et al. Gynecologic Oncology Group. Phase III trial of carboplatin and paclitaxel compared with cisplatin and paclitaxel in patients with optimally resected stage III ovarian cancer: a gynecologic oncology group study. *J Clin Oncol* 2003;21:3194–3200.
4. du Bois A, Luck HJ, Meier W, et al; Arbeitsgemeinschaft Gynäkologische Onkologie Ovarian Cancer Study Group. A randomized clinical trial of cisplatin/paclitaxel versus carboplatin/paclitaxel as first-line treatment of ovarian cancer. *J Natl Cancer Inst* 2003;95:1320–1329.
5. Vasey PA, Jayson GC, Gordon A, et al; Scottish Gynaecological Cancer Trials Group. Phase III randomized trial of docetaxel–carboplatin versus paclitaxel–carboplatin as first-line chemotherapy for ovarian carcinoma. *J Natl Cancer Inst* 2004;96:1682–1691.
6. Armstrong DK, Bundy B, Wenzel L, et al; Gynecologic Oncology Group. Intraperitoneal cisplatin and paclitaxel in ovarian cancer. *N Engl J Med* 2006;354:34–43.
7. Rustin GJ, van der Burg ME, Griffin CL, et al. Early versus delayed treatment of relapsed ovarian cancer (MRC OV05/EORTC 55955): a randomised trial. *Lancet* 2010;376:1155–1163.
8. Wagner U, Marth C, Largillier R, et al. Final overall survival results of phase III GCIG CALYPSO trial of pegylated liposomal doxorubicin and carboplatin vs paclitaxel and carboplatin in platinum-sensitive ovarian cancer patients. *Br J Cancer* 2010;107:588–591.
9. Mirza MR, Monk BJ, Herrstedt J, et al. Niraparib maintenance therapy in platinum-sensitive, recurrent ovarian cancer. *N Engl J Med* 2016;375(22):2154–2164.
10. Pujade-Lauraine E, Hilpert F, Weber B, et al. Bevacizumab combined with chemotherapy for platinum resistant recurrent ovarian cancer: the AURELIA open-label randomized phase III trial. *J Clin Oncol* 2014;32:1302–1308.

155

ACUTE LYMPHOCYTIC LEUKEMIA

Ian's Unexpected Weight Loss Level II

Deborah A. Hass, PharmD, BCOP, BCPS

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Interpret the laboratory values that signify the response of acute lymphocytic leukemia (ALL) to chemotherapy.
- Describe the ancillary medications and supportive care measures that are necessary when administering chemotherapy to patients with ALL.
- Recommend the appropriate medications to treat neutropenic fever.
- Identify the backbone of therapy for treatment of adult ALL.
- State why CNS prophylaxis is routinely done in adult patients with ALL.

PATIENT PRESENTATION

■ Chief Complaint

Episodic sweating, dizziness, and progressively worsening weakness and shortness of breath on exertion × 1 month.

■ HPI

Ian Hamilton is a 58-year-old man with a past medical history of diabetes, hyperlipidemia, and hypertension who presents with episodic diaphoresis, dizziness, and progressively worsening weakness and dyspnea on exertion for 1 month. He has lost 40 lb in the past 9 months; he recently has been trying to eat more but is still losing 2 lb per week. Flow cytometry done 3 days ago at an outside hospital showed blastic B cells consistent with pre-B-cell lymphoblastic leukemia. The patient was found to have normocytic anemia (Hgb 9.9 g/dL). He also had a CT of the chest/abdomen/pelvis completed at the outside hospital due to weight loss and occasional abdominal pain and sensation that his stomach is “churning,” although no report was sent with his records. He denies diarrhea but admits to once having an episode of dry heaving. A CXR was unremarkable. The patient was previously taking Janumet for type 2 DM, but since this workup began, he stopped it and has had blood sugars in the 100–130s.

■ PMH

DM type 2
HTN
Dyslipidemia

■ FH

Father had MI at age 60 and leukemia at age 78 and expired shortly thereafter. Mother is alive with heart disease, skin cancer, an

unknown GI malignancy, and a recent diagnosis of lymphoma. He has five brothers and two sisters. One brother died at age 48 from Hodgkin lymphoma, diagnosed at age 18. Another brother has multiple sclerosis. The other three brothers and both sisters are healthy.

■ SH

Denies tobacco, EtOH, and illicit drugs. Drives a waste management truck, has three children, and lives with his wife.

■ Meds

None

■ All

NKDA

■ ROS

Constitutional: Positive for sweats, fatigue, anorexia, and weight loss
HEENT: Negative

Respiratory: Positive for dyspnea

CV: Negative

GI: Positive for nausea and abdominal pain

GU: Negative

Heme/lymph: Negative

MS: Negative

Neuro: Positive for dizziness and weakness

■ Physical Examination

Gen

A&O × 3; NAD

VS

BP 124/58 mm Hg, P 106 bpm, RR 18, T 37.2°C; Wt 100.8 kg, Ht 5'11", SpO₂: 98% (room air)

Skin

Normal, no rashes

HEENT

EOMI, no scleral icterus, no conjunctival pallor

Neck/Lymph Nodes

No cervical LAD

Lungs/Thorax

CTA bilaterally without crackles, wheezes, or rhonchi

CV

RRR; normal S₁, S₂; no murmurs, rubs, or gallops

Abd

Soft, obese, NT/ND, normoactive bowel sounds

Genit/Rect

Deferred

MS/Ext

No CCE

Neuro

UE/LE strength 5/5 bilaterally

■ Labs

Na 137 mEq/L
K 4.1 mEq/L
Cl 100 mEq/L
CO₂ 28 mEq/L
BUN 19 mg/dL
SCr 1.2 mg/dL
Glu 93 mg/dL

Hgb 9.9 g/dL
Hct 27.2%
MCV 93.5 μm³
RDW 17.1%
Plt 95 × 10³/mm³
WBC 7.1 × 10³/mm³
Segs 35%
Bands 0.2%
Lymphs 5.2%
Monos 8.6%
Myelos 1.6%
Blasts 49%

AST 16 IU/L
ALT 10 IU/L
T. bili 0.5 mg/dL
Alb 3 g/dL
Fe 23 mcg/dL
TIBC 252 mcg/dL
T. sat 35%
Ferritin 159 ng/L
TSH 3.3 μIU/mL
PSA 0.52 ng/mL
B₁₂ 311 ng/mL
Folate 9.5 ng/mL

■ Peripheral Blood Flow Cytometry

Large population of abnormal blasts, ~49% of leukocyte population expressing CD45. Blasts have precursor B-cell phenotype and express CD19, CD22, CD34, CD38, HLA-DR, and terminal deoxynucleotidyl transferase (TdT). About 59% of blasts express CD20. Blasts are negative for surface IG, T-cell-related antigens, and myeloid antigens. The mature lymphocyte population consists of a mix of unremarkable T and B cells.

■ Assessment and Plan

- Pre-B-cell lymphoblastic leukemia (Philadelphia chromosome negative):
 - Obtain LDH/uric acid
 - Bone marrow biopsy
 - MUGA scan
 - Central catheter placement
 - Will attempt to obtain CT report from outside hospital
 - Acute leukemia panel
- Type 2 DM with controlled BS despite stopping meds recently:
 - Accu-Chek QID
 - Diabetic diet
 - Obtain UA to check for proteinuria; patient recently on ACE inhibitor but taken off. SCr ranging from 0.9 to 1.2 mg/dL at outside hospital.
- Nausea:
 - Ondansetron PRN
- HTN:
 - Patient recently taken off meds due to weight loss; will monitor BP and restart meds as needed
- Thrombocytopenia:
 - Transfuse to keep platelets >10 × 10³/mm³
- Anemia:
 - Transfuse to keep hemoglobin >8 g/dL
- FEN:
 - Diabetic diet as above
 - Maintain K >4 mEq/L and Mg >2 mg/dL
- VTE prophylaxis:
 - SCD boots

QUESTIONS

Collect Information

- What subjective and objective information indicates the presence of acute lymphocytic leukemia (ALL)?

- 1.b. What additional information is needed to fully assess this patient's ALL?

Assess the Information

- 2.a. Assess the severity of ALL based on the subjective and objective information available.
- 2.b. Upon initial presentation, create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

CLINICAL COURSE

Within 2 days of admission, the patient receives a BM biopsy, MUGA (EF = 60%), and PICC line placement. The results of the biopsy were as follows:

The vast majority of cells in the aspirate and biopsy are large blasts with fine chromatin and many prominent cytoplasmic vacuoles. Nucleoli are not generally prominent, and flow cytometric studies indicated that this is a neoplasm of immature B cells. In addition, strong TdT expression is seen by immunohistochemistry. CD20 is expressed weakly to strongly in about half of the neoplastic cells.

WHO classification: Precursor B lymphoblastic leukemia.

The patient is started on the following medications:

- Pantoprazole delayed-release tablet 40 mg PO daily
- Ondansetron 8 mg PO Q 8 H PRN
- 0.9% normal saline by continuous IV infusion
- Allopurinol 300 mg PO daily

Following recovery from the PICC line placement, the patient was started on the R-Hyper-CVAD regimen based on Ht 180 cm, Wt 100.8 kg, and BSA = 2.2 m².

CHEMOTHERAPY

■ Regimen 1A

Cyclophosphamide 300 mg/m² (660 mg) IV over 3 hours every 12 hours for six doses on days 1–3
 Mesna 600 mg/m² (1320 mg) IV over 24 hours on days 1–3, ending 12 hours after the last dose of cyclophosphamide
 Vincristine 2 mg IV on days 4 and 11
 Doxorubicin 50 mg/m² (110 mg) IV on day 4
 Dexamethasone 40 mg PO on days 1–4 and 11–14
 Rituximab 375 mg/m² (825 mg) IV on day 1. (Patient did not receive it on day 1 to prevent tumor flare.)

■ Regimen 1B

(The patient will alternate cycles every 21 days with the following regimen, for a total of six to eight cycles depending on patient tolerability and disease progression; patient-specific doses will be based on the patient's weight at that time):

Methotrexate 200 mg/m² IV over 2 hours, followed by 800 mg/m² IV over 22 hours on day 1
 Leucovorin 25 mg PO Q 6 H starting 24 hours after completion of the methotrexate infusion until methotrexate level is <0.05 µmol/mL
 Cytarabine 3000 mg/m² IV over 2 hours every 12 hours for four doses on days 2–3
 Methylprednisolone 50 mg IV BID on days 1–3

■ CNS Prophylaxis

Methotrexate 12 mg intrathecally on day 2

Cytarabine 100 mg intrathecally on day 8

Repeat with each cycle of chemotherapy, depending on the risk of CNS disease. The CNS prophylaxis is given with both regimens 1 and 2.

■ Additional Medications With Chemotherapy

Ondansetron injection 8 mg IV push Q 12 H

Fluconazole 400 mg PO daily

Acyclovir 400 mg PO Q 12 H

Prochlorperazine 10 mg IV push Q 6 H PRN

Prochlorperazine 10 mg PO Q 6 H PRN

Lorazepam 0.5 mg PO Q 6 H PRN

CLINICAL COURSE

■ Day 2 of Induction Chemotherapy

Blood glucose remained in the 90s with one reading at 77 mg/dL early this morning. Patient denies any symptoms of hypoglycemia. He was started on a diabetic diet yesterday, which he has been tolerating. Given his recent weight loss, he may no longer have the same degree of insulin resistance as before. Continue to monitor BG levels. Hypoglycemic protocol is in place if patient's BG drops below 70 mg/dL.

■ Day 3 of Induction Chemotherapy

Patient c/o mild nausea but still has good appetite and is eating well; encouraged use of PRN antiemetics. Patient tolerated intrathecal chemotherapy. No acute events overnight.

■ Day 4 of Induction Chemotherapy

Patient spiked temp to 101°F (38.3°C). Denies any respiratory, urinary, or other symptoms. Started on cefepime 2 g IV Q 8 H.

■ Day 5 of Induction Chemotherapy

Patient continues to complain of nausea but has not vomited. He is able to tolerate a little solid food but reports that his appetite is not what it was. Reports two episodes of watery, nonbloody diarrhea early this morning with no further episodes since then.

■ Day 6 of Induction Chemotherapy

Patient reports that his appetite is improving. He still complains of nausea, which has improved only slightly, but he has had no episodes of vomiting. No further episodes of diarrhea. No acute events overnight. He will receive rituximab 375 mg/m² (825 mg) IV today.

■ Day 7 of Induction Chemotherapy

Patient reported chills and shaking during rituximab infusion yesterday. Acetaminophen 650 mg PO and diphenhydramine 50 mg IV were given. He felt better after that. No further symptoms during the day. Patient's only complaint is lack of bowel movement for 2 days. He is also still nauseated but is able to tolerate a regular meal without any emesis. No acute events overnight.

■ Day 8 of Induction Chemotherapy

Patient complains of severe hiccups throughout the day and night yesterday that prevented him from sleeping. He said that he also has epigastric discomfort associated with the hiccups. He has pain in

the epigastric region that he rates as 7/10 in intensity with no radiation. It is neither sharp nor dull and feels like a “knot.” He also feels very full and bloated. He says it feels better when he stands up and walks around and also subsides when the hiccups cease. No further episodes of diarrhea and no vomiting. Patient still nauseated but was able to tolerate meals. He had one small BM yesterday. No acute events overnight.

■ Day 15 of Induction Chemotherapy

The patient was discharged to home. He was instructed to call the hematology fellow on call at any sign of a fever or infection. He was also instructed to stay away from people who have active infections, such as an upper respiratory virus. He was told to avoid large crowds and not to do any gardening. This is all to decrease the risk of infection. He will return to the hospital in 6 days for cycle 2 of chemotherapy. He is sent home with the following prescriptions:

Fluconazole 400 mg PO daily
Acyclovir 400 mg PO Q 12 H
Prochlorperazine 10 mg PO Q 6 H PRN

- 2.c. Create and prioritize a new list of drug therapy problems resulting from treatment for ALL. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the short-term goals of pharmacotherapy in this case?
- 3.b. The patient will receive four cycles of R-Hyper-CVAD alternating with four cycles of high-dose methotrexate and cytarabine. What are the long-term goals of pharmacotherapy for this patient?
- 3.c. What nondrug therapies might be useful for this patient?
- 3.d. What effect will this chemotherapy regimen have on his diabetes?
- 3.e. What other chemotherapy regimens are available for treating this patient's ALL?
- 3.f. Why was the patient started on allopurinol prior to starting his chemotherapy?
- 3.g. Why was the patient started on fluconazole and acyclovir in the doses prescribed?
- 3.h. Why was the patient started on intrathecal chemotherapy with no current evidence of CNS disease?
- 3.i. What therapy would you recommend for a patient with relapsed or refractory ALL?

Implement the Care Plan

- 4.a. What information should be provided to the patient about the potential beneficial and adverse effects from the chemotherapy agents used during induction therapy?
- 4.b. Assume that the patient does not understand why he has to have so many courses of chemotherapy. Explain why he cannot be treated with just one cycle of chemotherapy.
- 4.c. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What laboratory parameters and other diagnostic tests indicate an adequate response to induction therapy?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. Discuss the value of colony-stimulating factors in the prophylaxis or treatment of therapy-related complications in patients with ALL.
2. Discuss the response criteria used to determine if a patient with ALL has obtained a complete remission or partial remission.
3. Define the terms *stable disease* and *progressive disease* as they relate to ALL.

CLINICAL PEARL

First-line therapy for ALL must contain the backbone of an anthracycline derivative, vincristine, and a corticosteroid. Asparaginase is also a useful agent due to the leukemic cells' unique lack of endogenous asparagine. Patients with Philadelphia chromosome-positive ALL are treated with BCR-ABL tyrosine kinase inhibitors such as imatinib or dasatinib, *in addition* to the induction chemotherapy regimen, such as R-Hyper-CVAD, which this patient received.

REFERENCES

1. Kantarjian H, Thomas D, O'Brien S, et al. Long-term follow-up results of hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone (Hyper-CVAD), a dose-intensive regimen, in adult acute lymphocytic leukemia. *Cancer* 2004;101:2788–2801.
2. Thomas DA, Cortes J, O'Brien S, et al. Hyper-CVAD program in Burkitt's-type adult acute lymphoblastic leukemia. *J Clin Oncol* 1999;17:2461–2470.
3. Weiser MA, Cabanillas ME, Konopleva M, et al. Relation between the duration of remission and hyperglycemia during induction chemotherapy for acute lymphocytic leukemia with a hyperfractionated cyclophosphamide, vincristine, doxorubicin, and dexamethasone/methotrexate-cytarabine regimen. *Cancer* 2004;100:1179–1185.
4. Nam J. Dexamethasone-induced hiccups in chemotherapy may be prevented by rotating to methylprednisolone. *Oncology Nurse Advisor*, July 11, 2017. Available at: <https://www.oncologynurseadvisor.com/home/hot-topics/side-effect-management/dexamethasone-induced-hiccups-in-chemotherapy-may-be-prevented-by-rotating-to-methylprednisolone/>. Accessed December 13, 2019.
5. Thomas DA, O'Brien S, Faderl S, et al. Chemoimmunotherapy with a modified hyper-CVAD and rituximab regimen improves outcome in de novo Philadelphia chromosome-negative precursor B-lineage acute lymphoblastic leukemia. *J Clin Oncol* 2010;28(24):3880–3889.
6. Wetzler M, Sanford BL, Kurtzberg J, et al. Effective asparagine depletion with pegylated asparaginase results in improved outcomes in adult acute lymphoblastic leukemia: Cancer and Leukemia Group B Study 9511. *Blood* 2007;109:4164–4167.
7. Stock W, Luger SM, Advani AS, et al. Favorable outcomes for older adolescents and young adults (AYA) with acute lymphoblastic leukemia (ALL): early results of U.S. Intergroup Trial C10403 [abstract]. *Blood* 2014;124: Abstract 796.
8. Linker C, Damon L, Ries C, Navarro W. Intensified and shortened cyclical chemotherapy for adult ALL. *J Clin Oncol* 2002;20:2464–2471.
9. Freifeld AG, Bow EJ, Sepkowitz KA, et al. Clinical practice guideline for the use of antimicrobial agents in neutropenic patients with cancer: 2010 update by the Infectious Diseases Society of America. *Clin Infect Dis* 2011;52(4):e56–e93.
10. Campana D. Minimal residual disease in acute lymphoblastic leukemia. *Hematology Am Soc Hematol Educ Program* 2010;2010:7–12.
11. O'Brien S, Schiller G, Lister J, et al. High-dose vincristine sulfate liposome injection for advanced, relapsed, and refractory adult Philadelphia chromosome-negative acute lymphoblastic leukemia. *J Clin Oncol* 2013; 31(6):676–683.
12. Kantarjian HM, DeAngelo DJ, Stelljes M, et al. Inotuzumab ozogamicin versus standard therapy for acute lymphoblastic leukemia. *N Engl J Med* 2016;375(8):740–753.

13. Topp MS, Gokbuget N, Stein AS, et al. Safety and activity of blinatumomab for adult patients with relapsed or refractory B-precursor acute lymphoblastic leukaemia: a multicentre, single-arm, phase 2 study. *Lancet Oncol* 2015;16(1):57–66.
14. Maude SL, Frey N, Shaw PA, et al. Chimeric antigen receptor T cells for sustained remissions in leukemia. *N Engl J Med* 2014;371(16):1507–1517.

156

CHRONIC MYELOID LEUKEMIA

It's Not Always Sunny in Philadelphia Level II

Allison L. Martin, PharmD, BCOP

Aaron Cumpston, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify the presenting signs and symptoms of chronic myeloid leukemia (CML).
- Determine important prognostic indicators for CML.
- Discuss available treatment options for newly diagnosed CML and refractory or relapsed CML and recommend an appropriate therapy.
- Choose appropriate parameters to monitor efficacy and potential adverse effects of treatment for CML.
- Educate patients on dosing and administration, the importance of adherence, and the most common side effects of the selected therapy for CML.
- Discuss potential mechanisms of resistance to first-line therapy for CML and formulate a treatment strategy for these patients.

PATIENT PRESENTATION

■ Chief Complaint

"I'm here for my routine visit for my back pain, but I have been feeling pretty tired lately and have this dull pain in my abdomen."

■ HPI

Carl Boyd is a 55-year-old man with a history of chronic back pain secondary to injury 5 years ago; he presents for his annual appointment and physical. Today he complains of left-sided abdominal discomfort and fullness that has resulted in some decreased appetite and increasing fatigue and inactivity over the past 3 months. When questioned, he reports experiencing intermittent drenching night sweats for the past 2 months that seem to be more frequent now.

■ PMH

Chronic back pain
Childhood asthma, last symptoms at age 21
Appendectomy 16 years ago

■ FH

Father died at age 66 due to MI. Mother is living, 71 years old with osteoporosis, depression, and GERD. He has one sister, age 52, living in Maine with no known medical issues. Paternal grandfather had prostate cancer but passed away from unrelated causes. Patient has no natural children.

■ SH

Married and has one stepson, age 19, who attends college overseas. The patient works as a nurse in a local long-term care facility, and his wife is a tax accountant. He has no smoking history but drinks alcohol on social occasions. He denies any illicit drug use.

■ Meds

One-A-Day multivitamin PO once daily
Cyclobenzaprine 10 mg PO BID as needed
Ibuprofen 800 mg PO TID as needed
Oxycodone 10 mg PO Q 6 H PRN

■ All

NKA

■ ROS

Positive for increased weakness and tiredness, frequent night sweats, mild shortness of breath on exertion, general musculoskeletal pain, and LUQ pain. Denies bleeding, headaches, vision changes, nausea, vomiting, chest pain, rashes, numbness or tingling in extremities, or urinary symptoms.

■ Physical Examination

Gen

Caucasian man who appears his stated age and is in no obvious distress

VS

BP 122/60 mm Hg, P 63 bpm, RR 20, T 36.3°C; Wt 77.5 kg, Ht 180 cm, pain score 0 on a 0–10 scale

Skin

Skin warm and dry, no rashes or lesions

HEENT

Head atraumatic and normocephalic; ENT without erythema or injection; mucous membranes moist; conjunctivae clear; PERRLA. No sinus discharge or tenderness. Lips, teeth, and gums without tenderness.

Neck

No JVD or thyromegaly appreciated

Lymph Nodes

No palpable cervical, supraclavicular, axillary, or inguinal adenopathy

Lungs

Diffuse expiratory wheezes bilaterally

CV

Regular rate and rhythm; S₁ and S₂ normal; 2/6 systolic murmur heard best along the upper left sternal border

Abd

Tender to palpation; tip of spleen palpable in LUQ. Normoactive bowel sounds. No hepatomegaly.

Rect

Deferred

MS/Ext

Normal gait, full range of motion in flexion and extension of the upper and lower extremities with 5/5 strength throughout. No cyanosis or edema; no synovitis or joint effusions.

Neuro

Grossly normal; CN II–XII intact; alert and oriented $\times 3$

Psychiatric

Normal affect, behavior, memory, thought content, judgment, and speech

■ Labs

Na 139 mEq/L	Hgb 10.3 g/dL	AST 24 IU/L	Ca 8.2 mg/dL
K 3.7 mEq/L	Hct 33.8%	ALT 38 IU/L	Mg 2.2 mEq/L
Cl 105 mEq/L	Plt 470 $\times 10^3/\text{mm}^3$	Alk phos 72 IU/L	Phos 3.8 mg/dL
CO ₂ 27 mEq/L	WBC 123 $\times 10^3/\text{mm}^3$	LDH 950 IU/L	Uric acid 6.5 mg/dL
BUN 28 mg/dL	T. bili 0.6 mg/dL	T. prot 6.9 g/dL	LAP absent
SCr 0.8 mg/dL	PMNs 53%	Alb 3.5 g/dL	
Glu 92 mg/dL	Bands 13%		
Retic 2.3%	Lymphs 7%		
	Myelos 9%		
	Metas 10%		
	Eos 4%		
	Basos 4%		

■ Bone Marrow Biopsy

The bone marrow is markedly hypercellular (essentially 100% cellular) due to extensive proliferation of granulocytes. The granulocytic series are left-shifted; however, blasts are not increased and no Auer rods or significant dysplasia is noted. Erythroid precursors are

slightly decreased and megakaryocytes are markedly increased with many small, hypolobated forms. Iron stores are decreased, and mild reticulin fibrosis is identified. Eosinophilia and basophilia are also present in the peripheral blood and bone marrow. FISH analysis is positive for BCR-ABL1 rearrangement.

Cytogenetic studies show translocation involving the long arms of chromosomes 9 and 22 [t(9q;22q)] (Philadelphia chromosome), with 95% of malignant cells analyzed found to be Ph-positive (Fig. 156-1). This information is consistent with the characteristics of CML, and the morphologic features are consistent with chronic phase (CML-CP).

QUESTIONS**Collect Information**

1. What subjective and objective information is consistent with a diagnosis of CML-CP?

Assess the Information

- 2.a. Describe the natural progression of CML.
- 2.b. List factors that signal a poor prognosis for CML patients in chronic phase.
- 2.c. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the long-term therapy goals for this case?
- 3.b. What nondrug therapies might be useful for this newly diagnosed patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating newly diagnosed CML-CP?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's CML and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

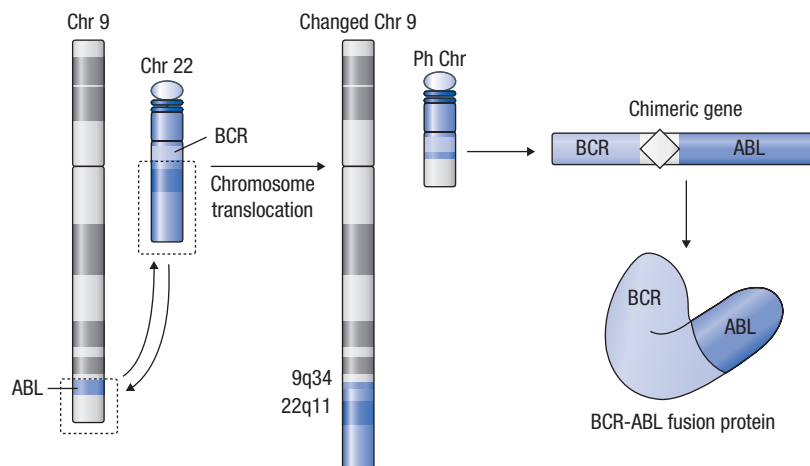


FIGURE 156-1. Specific chromosomal translocation seen in chronic myeloid leukemia (CML). The Philadelphia chromosome (Ph) is derived from a reciprocal translocation between chromosomes 9 and 22 with the breakpoint joining the sequences of the ABL oncogene with the BCR gene. The fusion of these DNA sequences allows for the generation of an entirely novel fusion protein with modified function. (Reprinted with permission from Morin PJ, Trent JM, Collins FS, Vogelstein B. Cancer genetics. In: Jameson JL, Fauci AS, Kasper DL, Hauser SL, Longo DL, Loscalzo J, eds. *Harrison's Principles of Internal Medicine*. 20th ed. New York, NY: McGraw-Hill; 2018.)

Implement the Care Plan

- 4.a. What information should be provided to the patient prior to treatment to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

The regimen you recommended was initiated. At the 2-week follow-up visit, the patient's WBC count was $34 \times 10^3/\text{mm}^3$. At the 4-week follow-up visit, his WBC count decreased to $9 \times 10^3/\text{mm}^3$. After 3 months of treatment, his WBC count was stable at $8.2 \times 10^3/\text{mm}^3$, platelet count stable at $425 \times 10^3/\text{mm}^3$, and he had a minimal cytogenetic response as evidenced by a bone marrow biopsy that revealed 70% Philadelphia chromosome-positive metaphases. After 6 months, he remained in complete hematologic response but minor cytogenetic response with 60% Ph-positive metaphases. Molecular analysis (qPCR testing for the Philadelphia chromosome) also showed less than a major response. Because he experienced a suboptimal response, mutation testing was performed and revealed the presence of a V299L mutation. Also, since beginning treatment with imatinib, the patient has noticed mild periorbital edema, moderate myalgias, and nausea. He presents to clinic today to discuss further treatment options with the healthcare team.

FOLLOW-UP QUESTIONS

1. What are the possible mechanisms of resistance to imatinib?
2. What therapeutic options are available for this patient with a suboptimal response to imatinib 400 mg PO once daily?
3. Compare dasatinib, nilotinib, bosutinib, and ponatinib in terms of efficacy and toxicity in patients with suboptimal responses to imatinib.
4. Is it possible to discontinue tyrosine kinase inhibitor (TKI) therapy and maintain remission, or will the patient need lifelong therapy?
5. How would your recommendations differ if the patient had a T315I mutation instead?

SELF-STUDY ASSIGNMENTS

1. Describe the criteria for hematologic complete response, cytogenetic response (complete, major, partial, minor, and no response), and molecular response (early, major) for therapy in patients with CML, including WBC count, splenomegaly, and percent of Ph+ marrow cells.
2. If a woman becomes pregnant while receiving TKI treatment for CML, how should the therapy be revised?
3. Discuss the progress being made to develop treatments for patients with the T315I mutation.

CLINICAL PEARL

Mutation testing in patients with chronic phase CML is generally not performed unless the patient has a suboptimal or lack of response to first-line TKI therapy because mutations can occasionally be found in patients without resistant disease.

REFERENCES

1. O'Brien SG, Guilhot F, Larson RA, et al. IRIS investigators. Imatinib compared with interferon and low-dose cytarabine for newly diagnosed chronic-phase chronic myeloid leukemia. *N Engl J Med* 2003;348:994–1004.
2. Hochhaus A, Larson RA, Guilhot F, et al. Long-term outcomes of imatinib treatment for chronic myeloid leukemia. *N Engl J Med* 2017;376:917–927.
3. Cortes JE, Saglio G, Kantarjian HM, et al. Final 5-year study results of DASISION: the dasatinib versus imatinib study in treatment-naïve chronic myeloid leukemia patients trial. *J Clin Oncol* 2016;34(20):2333–2340.
4. Hochhaus A, Saglio G, Hughes TP, et al. Long-term benefits and risks of frontline nilotinib vs imatinib for chronic myeloid leukemia in chronic phase: 5-year update of the randomized ENESTnd trial. *Leukemia* 2016;30(5):1044–1054.
5. Cortes JE, Khouury HJ, Kantarjian HM, et al. Long-term bosutinib for chronic phase chronic myeloid leukemia after failure of imatinib plus dasatinib and/or nilotinib. *Am J Hematol* 2016;91(9):1206–1214.
6. Rea D. Management of adverse events associated with tyrosine kinase inhibitors in chronic myeloid leukemia. *Ann Hematol* 2015;94(Suppl 2):S149–S158.
7. Baccarani M, Deininger MW, Rosti G, et al. European LeukemiaNet recommendations for the management of chronic myeloid leukemia: 2013. *Blood* 2013;122(6):872–884.
8. Shah NP, Rousselot P, Schiffer C, et al. Dasatinib in imatinib-resistant or -intolerant chronic-phase, chronic myeloid leukemia patients: 7-year follow-up of study CA180-034. *Am J Hematol* 2016;91(9):869–874.
9. Cortes JE, Kim DW, Pinilla-Ibarz J, et al. Ponatinib efficacy and safety in Philadelphia chromosome-positive leukemia: final 5-year results of the phase 2 PACE trial. *Blood* 2018;132(4):393–404.
10. Cortes J, Lipton JH, Rea D, et al. Phase 2 study of subcutaneous omacetaxine mepesuccinate after TKI failure in patients with chronic-phase CML with T315I mutation. *Blood* 2012;120:2573–2580.

157

KIDNEY CANCER

A Time for Decision Level II

Daniel J. Crona, PharmD, PhD, CPP
Jessica J. Auten, PharmD, BCPS, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Evaluate first-line pharmacotherapeutic options for patients with metastatic kidney cancer.
- Formulate a monitoring plan for a patient receiving treatment for metastatic kidney cancer based on patient-specific factors and the prescribed regimen.

- Recommend alternative pharmacotherapeutic treatment options for patients with relapsed or progressive metastatic kidney cancer.
- Provide appropriate and detailed educational information to patients about the targeted therapies for metastatic kidney cancer.

PATIENT PRESENTATION

■ Chief Complaint

“What treatment options do I have for my metastatic kidney cancer?”

■ HPI

Melanie Simmons is a 65-year-old woman who presented 3.5 years ago to her primary care physician with complaints of back pain, cough, and weight loss. She did not respond to an initial course of antibiotics for assumed pyelonephritis and developed gross hematuria a few days later. She was subsequently referred to a urologist, who detected a left kidney mass on renal ultrasound. CT scan of chest, abdomen, and pelvis revealed a 7-cm left upper-pole left kidney tumor and several bilateral small, subcentimeter lung nodules. Additional imaging found no evidence of metastatic disease in her brain, bones, or liver. She was referred to a nearby cancer center for further evaluation. A core needle biopsy of the kidney mass revealed neoplastic cells, but the sample was too small and heterogeneous to definitively determine a specific histology. In order to relieve worsening symptoms and further elucidate a specific histopathology of the mass, she underwent radical nephrectomy of her left kidney. Pathologic examination revealed kidney cancer with clear-cell histology. The patient recovered from surgery with resolution of back pain and hematuria. She received no treatment for the pulmonary nodules because interventional radiology determined that they were not cancerous; she agreed to undergo active surveillance of the nodules over time to identify changes or progression.

Now, more than 3 years later the patient presents to the outpatient oncology clinic for an appointment with the medical oncologist. Recently, a routine CT scan revealed lung metastases (which have increased in number and size since her initial scans and decision to pursue active surveillance). Imaging found no evidence of metastatic disease in her brain, bones, or liver. The patient has an estimated Karnofsky score of 90% and is interested in pursuing systemic treatment for her metastatic kidney cancer and would like to discuss appropriate and available treatment options.

■ PMH

Hypertension
Dyslipidemia

■ FH

Her mother died at age 75 due to complications related to MI, and her father died at age 73 due to PE. The patient has one brother, age 58, who is alive and living with asthma, but who is otherwise healthy. She has no family history of cancer.

■ SH

Mrs Simmons has been happily married for over 40 years. She has one grown son, age 33, who is alive and healthy. The patient reports an extensive smoking history (25 pack-years), but quit 5 years ago. She is overweight (BMI 29.3 kg/m²).

■ Meds

Hydrochlorothiazide 25 mg PO once daily
Enalapril 5 mg PO once daily
Atorvastatin 10 mg PO once daily

■ All

NKDA

■ ROS

No fever or chills; no headaches; no nausea or vomiting; feels very weak since the surgery

■ Physical Examination

Gen

WDWN Caucasian woman in NAD

VS

BP 130/84 mm Hg, P 64 bpm, RR 18, T 37.0°C; Wt 82.4 kg, Ht 5'6", BSA 1.96 m²

Skin

Olive complexion. Nephrectomy site is fully healed.

HEENT

PERRLA, EOMI; oropharynx without lesions

Neck/Lymph Nodes

Supple without adenopathy; thyroid without masses

Lung/Thorax

Slight wheezing in LUL

CV

RRR; normal S₁ and S₂; no MRG

Abd

Soft, NT/ND; (+) BS

Genit/Rect

Deferred

Ext

No clubbing, cyanosis, or edema

Neuro

A&O × 3; CN II–XII intact; DTRs 2+ throughout; motor and sensory levels intact; Babinski (–)

■ Labs

Na 137 mEq/L	Hgb 12 g/dL	WBC 6.1 × 10 ³ /mm ³	T. bili 0.8 mg/dL
K 4.0 mEq/L	Hct 36%	Neutros 66%	AST 25 IU/L
Cl 99 mEq/L	Plt 325 × 10 ³ /mm ³	Bands 4%	ALT 27 IU/L
CO ₂ 25 mEq/L		Lymphs 26%	Alk phos 125 IU/L
BUN 20 mg/dL		Monos 4%	Alb 3.8 g/dL
SCr 2.0 mg/dL			LDH 220 IU/L
Glu 75 mg/dL			Ca 8.5 mg/dL
			Mg 2.0 mg/dL

■ Assessment

A 65-year-old woman with metastatic clear-cell kidney cancer, who is S/P resection of her primary tumor via radical nephrectomy,

presents to the medical oncology clinic. Multiple subcentimeter metastatic lesions in lung persist; however, there is no evidence of additional metastatic disease. Briefly, she is not a candidate for high-dose IL-2 based on inadequate results of pulmonary function testing (both FVC and FEV₁ were <65% of predicted values) and an SCr value of 2.0 mg/dL. Nonpharmacologic options include surveillance and forgoing systemic treatment for now. However, she is interested in learning about possible pharmacotherapeutic options.

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence and severity of kidney cancer?
- 1.b. What additional information is needed to fully assess this patient's kidney cancer?

Assess the Information

2. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy for metastatic kidney cancer in this case?
- 3.b. What nondrug therapies might be useful for treating this patient's kidney cancer?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating kidney cancer?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient prior to treatment to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

Mrs Simmons was started on the treatment you recommended and achieved partial regression of some of her metastatic pulmonary lesions. She experienced adverse effects, including hypertension (maximum BP was 160/95), hand-foot skin reaction, a slight yellowing of her skin, hair depigmentation, and peripheral edema. Hypertension was controlled by increasing her enalapril dosage to 10 mg per day.

Unfortunately after 9 months of treatment, today's follow-up CT scan of the chest, abdomen, and pelvis indicates progression of the cancer in her lungs (eg, new and larger pulmonary lesions). The patient expressed a desire to continue treatment and is here to inquire about available second-line treatment options.

FOLLOW-UP QUESTIONS

1. Given this situation, what pharmacotherapeutic options are available at this time? Provide the rationale for your answer.
2. How would you monitor for the potential adverse effects of the treatment you recommended?
3. What education should the patient receive about the new regimen that you propose?
4. What alterations would you recommend to the patient's regimen if she were also receiving a strong inducer of hepatic CYP3A4 enzymes? What about a strong inhibitor of CYP3A4?

SELF-STUDY ASSIGNMENTS

1. Discuss the role of immunotherapies used in metastatic kidney cancer.
2. What role, if any, does adjuvant treatment play after surgery for localized kidney cancer?
3. What role does tumor histology play in treatment selection for metastatic kidney cancer?

CLINICAL PEARL

Until a decade ago, few effective treatment options were available to treat metastatic kidney cancer because most patients were unresponsive to traditional cytotoxic chemotherapy and radiation. Additionally, cytokine therapy (eg, interferon or high-dose IL-2) is toxic and rarely results in a durable remission. A deeper understanding of the molecular mechanisms involved in kidney cancer pathogenesis led to development and approval of nine targeted agents directed at signaling mechanisms in the VEGF or mTOR pathways and two immunotherapies (a CTLA-4 inhibitor and a PD-1 inhibitor). However, patients almost always progress after treatment with a first-line targeted agent, so treating patients with second-, third-, and even fourth-line targeted agents is not uncommon.

REFERENCES

1. Choueiri TK, Motzer RJ. Systemic therapy for metastatic renal-cell carcinoma. *N Engl J Med* 2017;376:354–366.
2. Heng DY, XIE W, Regan MM, et al. Prognostic factors for overall survival in patients with metastatic renal cell carcinoma treated with vascular endothelial growth factor–targeted agents: results from a large, multicenter study. *J Clin Oncol* 2009;27:5794–5799.
3. Choueiri TK, Halabi S, Sanford BL, et al. Cabozantinib versus sunitinib as initial targeted therapy for patients with metastatic renal cell carcinoma of poor or intermediate risk: the Alliance A031203 CABOSUN trial. *J Clin Oncol* 2017;35(6):591–597.
4. Motzer RJ, Tannir NM, McDermott DF, et al. Nivolumab plus ipilimumab versus sunitinib in advanced renal-cell carcinoma. *N Engl J Med* 2018;378:1277–1290.
5. Sternberg CN, Davis ID, Mardiak J, et al. Pazopanib in locally advanced or metastatic renal cell carcinoma: results of a randomized phase III trial. *J Clin Oncol* 2010;28:1061–1068.
6. Motzer R, Hutson TE, Cella D, et al. Pazopanib versus sunitinib in metastatic renal-cell carcinoma. *N Engl J Med* 2013;369:722–731.

7. Motzer RJ, Hutson TE, Tomczak P, et al. Overall survival and updated results for sunitinib compared with interferon alfa in patients with metastatic renal cell carcinoma. *J Clin Oncol* 2009;27:3584–3590.
8. Rini BI, Escudier B, Tomczak P, et al. Comparative effectiveness of axitinib versus sorafenib in advanced renal cell carcinoma (AXIS): a randomised phase 3 trial. *Lancet* 2011;378:1931–1939.
9. Choueiri TK, Escudier B, Powles T, et al. Cabozantinib versus everolimus in advanced renal-cell carcinoma. *N Engl J Med* 2015;373:1814–1823.
10. Motzer RJ, Hutson TE, Glen H, et al. Lenvatinib, everolimus, and the combination in patients with metastatic renal cell carcinoma: a randomised phase 2, open-label, multicentre trial. *Lancet Oncol* 2015;16(15):1473–1482.
11. Motzer RJ, Escudier B, McDermott DF, et al. Nivolumab versus everolimus in advanced renal-cell carcinoma. *N Engl J Med* 2015;373:1803–1813.

158

MELANOMA

Overexposure Level II

Jessica Michaud Davis, PharmD, BCOP, CPP

Marina Kanos, MSN, RN, FNP-C

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify risk factors for developing melanoma.
- Determine treatment options for metastatic melanoma.
- Prepare educational information to provide to a patient receiving treatment for metastatic melanoma.
- Discuss ways to prevent melanoma.

PATIENT PRESENTATION

■ Chief Complaint

“I have ongoing back pain for 8 weeks that has not resolved with over-the-counter treatments.”

■ HPI

James Conley is a 62-year-old Caucasian man who presents with an 8-week history of mid-back pain. He has no history of recent injury or trauma to the area. He reports that his back pain continues to increase despite rest and applications with cold and heat. He rates his pain at its worst as 5 on 0–10 scale. The pain is present with movement and at rest. The pain does not radiate. He denies associated numbness or tingling. He has tried various medications including ibuprofen, naproxen, and acetaminophen.

■ PMH

GERD

Type 2 DM

Stage IIIC melanoma of the right scapular area (T4b N1b M0; diagnosed 2 years ago in Australia; Breslow thickness 4.9 mm with

ulceration. S/P wide local excision with right axillary lymph node dissection; 1 out of 32 nodes showed evidence of involvement; there was no evidence of distant disease. Patient declined adjuvant treatment at the time because he was about to move to the United States to work for an advertising agency.

■ FH

Patient has two sisters; one with type 2 DM. Mother is 83 years old with a history of cutaneous basal cell carcinomas and stage IIA melanoma. Father died at age 71 secondary to heart disease.

■ SH

The patient is an advertising and commercial photographer. He is married with one daughter (age 27) who is healthy. He smoked one-half pack of cigarettes per day for 4 years while in college; has not smoked for the past 40 years. He has one to two alcoholic drinks on the weekends. He denies illicit drug use. As a child, he spent a significant amount of time outdoors in Australia. He was a summer lifeguard for 8 years. He did not routinely use sunscreen and has a history of sunburns, some blistering.

■ Medications

Omeprazole 20 mg orally once daily

Glipizide 10 mg orally once daily

Metformin 1000 mg orally twice daily

Ibuprofen 400 mg orally every 4–6 hours as needed for back pain

■ Allergies

NKDA

■ ROS

Low back pain as described above. Denies fatigue, fever, chills, night sweats, recent vision changes, tinnitus, nasal congestion, sore throat, cough, dyspnea, chest pain, palpitations, nausea, vomiting, diarrhea, constipation, abdominal pain, dysuria, hematuria, bowel/bladder retention or incontinence, easy bruising, polydipsia, polyuria, rash, pruritus, new or changing skin lesions, headache, or dizziness.

■ Physical Examination

General

Caucasian man with mild distress due to mid-back pain

Vital Signs

BP 129/72 mm Hg, P 86 bpm, RR 16, O₂ saturation 99% on room air, T 36.8°C; Wt 90 kg, Ht 5'10"

Skin

Fair complexion with multiple (>50) nevi on trunk and bilateral upper and lower extremities. Well-healed scars on right mid-upper back and right axilla.

HEENT

Normocephalic, TMs clear with normal light reflex, PERRLA, EOMI, normal sclerae, moist oral mucosa, no pharyngeal erythema or exudate, normal nasal mucosa without drainage, no frontal or maxillary sinus tenderness

Neck

Supple, nontender, no thyromegaly, no masses

Resp

Lungs clear to auscultation bilaterally, breath sounds equal, respirations nonlabored

CV

Regular rate and rhythm, no murmurs or gallops, good pulses equal bilaterally in upper and lower extremities, no peripheral edema

Abd

Soft, nontender, nondistended, normoactive bowel sounds in all four quadrants, no organomegaly

Genitourinary

No CVA tenderness

Lymphatics

No lymphadenopathy neck, axilla, or groin; trace right upper extremity lymphedema

Musculoskeletal

Discomfort to palpation along the thoracic spine at the T7–T9 area

Neuro

Alert and oriented $\times 4$, normal sensory and motor exam, CN II–XII intact, normal DTRs, negative Romberg, negative straight-leg raise

Psychiatric

Cooperative, appropriate mood and affect

■ Labs

Na 135 mEq/L	Hgb 15.8 g/dL	WBC $5.6 \times 10^6/\text{mm}^3$	T. bili 1.1 mg/dL
K 4.1 mEq/L	Hct 46%	Neutros 68%	AST 22 IU/L
Cl 100 mEq/L	RBC $5.2 \times 10^6/\text{mm}^3$	Bands 3%	ALT 28 IU/L
CO ₂ 25 mEq/L	Plt $322 \times 10^3/\text{mm}^3$	Eos 1%	Alk phos 165 IU/L
BUN 9 mg/dL		Lymphs 26%	Alb 4.2 g/dL
SCr 1.0 mg/dL		Monos 2%	LDH 340 IU/L
Glu 75 mg/dL			Ca 8.5 mg/dL
			Mg 2.1 mg/dL
			PO ₄ 3.6 mg/dL

■ CT Chest, Abdomen, and Pelvis

Two pulmonary nodules consistent with metastasis in the left upper and lower lobes. There is a lytic lesion in the vertebral body of T8.

■ CT-Guided Lung Biopsy

Pathology of the left lower lung nodule is consistent with metastatic melanoma. Molecular pathology confirmed BRAF V600E mutation not detected.

■ Assessment

A 62-year-old man with a 2-year history of melanoma with new metastases to the lungs and thoracic spine.

QUESTIONS**Collect Information**

- 1.a. What subjective and objective information indicates the presence and severity of melanoma?
- 1.b. What additional information is needed to fully assess this patient's melanoma?

Assess the Information

- 2.a. What risk factor(s) does this patient have for developing melanoma?
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals for treatment of melanoma in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating metastatic melanoma?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's metastatic melanoma and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ ADDITIONAL CASE QUESTIONS

1. Mr Conley's daughter is concerned that she is at risk for developing melanoma. How can melanoma be prevented?
2. What is the ABCDE rule in helping to distinguish features of a normal mole from an abnormal mole?
3. How should immune-related adverse events from CTLA-4 and PD-1 checkpoint inhibitors be managed?

■ SELF-STUDY ASSIGNMENTS

1. List options for treatment if this patient had a BRAF V600E mutation.
2. Describe how the dosing of ipilimumab plus nivolumab combination therapy would differ for patients with renal cell carcinoma.
3. Infusion reactions to checkpoint inhibitors are rare but may occur. Describe how an infusion reaction may present and how it should be treated. Describe how premedications may be given before future infusions to help prevent recurrent infusion reactions.

CLINICAL PEARL

Vitiligo (the presence of hypopigmented skin lesions) is a clinically visible immune-related adverse effect of nivolumab, which is thought to occur due to the involvement of the PD-1 pathway

in melanosomal proteins. The occurrence of vitiligo in melanoma patients treated with nivolumab has been associated with improved overall survival.¹⁰

REFERENCES

1. NCCN Clinical Practice Guidelines in Oncology. Cutaneous Melanoma. v.1.2019. Available at: www.nccn.org. Accessed November 3, 2018.
2. Larkin J, Chiarion-Sileni V, Gonzalez R, et al. Combined nivolumab and ipilimumab or monotherapy in untreated melanoma. *N Engl J Med* 2015;373(1):23–34.
3. Hodi FS, Chiarion-Sileni V, Gonzalez R, et al. Nivolumab plus ipilimumab or nivolumab alone versus ipilimumab alone in advanced melanoma (CheckMate 067): 4-year outcomes of a multicentre, randomised, phase 3 trial. *Lancet Oncol* 2018;19(11):1480–1492.
4. Robert C, Long GV, Brady B, et al. Nivolumab in previously untreated melanoma without BRAF mutation. *N Engl J Med* 2015;372:320–330.
5. Robert C, Schachter J, Long GV, et al. Pembrolizumab versus ipilimumab in advanced melanoma. *N Engl J Med* 2015;372:2521–2532.
6. Schachter J, Ribas A, Long GV, et al. Pembrolizumab versus ipilimumab for advanced melanoma: final overall survival results of a multicentre, randomised, open-label phase 3 study (KEYNOTE-006). *Lancet* 2017;390(10105):1853–1862.
7. National Comprehensive Cancer Network. Management of Immunotherapy-Related Toxicities (Version 1.2018). Available at: https://www.nccn.org/professionals/physician_gls/pdf/immunotherapy.pdf. Accessed December 11, 2018.
8. Brahmer JR, Lacchetti C, Schneider BJ, et al. Management of immune-related adverse events in patients treated with immune checkpoint inhibitor therapy: American Society of Clinical Oncology Clinical Practice Guideline. *J Clin Oncol* 2018;36(17):1714–1768.
9. Melanoma [Internet]. New York (NY): The Skin Cancer Foundation; 2018. Available at: <https://www.skincancer.org/skin-cancer-information/melanoma>. Accessed December 16, 2018.
10. Freeman-Keller M, Kim Y, Cronin H, Richards A, Gibney G, Weber JS. Nivolumab in resected and unresectable metastatic melanoma: characteristics of immune-related adverse events and association with outcomes. *Clin Cancer Res* 2016;22(4): 886–894.

159

HEMATOPOIETIC STEM CELL TRANSPLANTATION

Many Meds, Many Interactions Level III

Teresa C. Thakrar, PharmD, BCOP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Understand the regimen-related toxicities of immunosuppression medications used for allogeneic stem cell transplantation (SCT).
- Differentiate the presenting features of immunosuppressive medication adverse events from other medications.
- Recommend optimal therapeutic plans, taking into account drug interactions, efficacy, safety, and patient adherence in postalloge-neic SCT patients.

- Design appropriate pharmacotherapeutic plans for patients who develop toxicity from immunosuppression.

PATIENT PRESENTATION

■ Chief Complaint

The patient is being seen for follow-up in clinic and has developed bothersome headache and tremors with movement such as typing or holding a cup. She was seen recently by her PCP for dyslipidemia and hypertension and has had changes in her medication regimen.

■ HPI

Brenda Langer is a 68-year-old woman who presents to the BMT clinic 120 days post HLA-matched unrelated donor allogeneic SCT for high-risk AML. Her preparative regimen consisted of thiotepea (5 mg/kg IV Q 12 H × 3 doses) and cyclophosphamide (60 mg/kg IV Q 24 H × 2 doses). Her GVHD prophylaxis regimen consisted of tacrolimus and sirolimus, both starting on day −3. Her hospital course was complicated by febrile neutropenia, acute kidney injury, mucositis, and diarrhea. These complications had resolved at the time of discharge on day +20. Two weeks ago, she developed a skin rash and diarrhea and was diagnosed with grade 2 acute GVHD. She was started on prednisone 90 mg (1 mg/kg) orally BID, and fluconazole was switched to posaconazole 300 mg orally once daily. Her PCP also added gemfibrozil 600 mg orally twice daily to her lipid regimen.

■ PMH

High-risk AML treated with idarubicin and cytarabine induction, followed by high-dose cytarabine × 1 cycle. She was started on amlodipine at hospital discharge for newly diagnosed hypertension. Dyslipidemia was managed previously with atorvastatin and recently with addition of gemfibrozil.

■ FH

Married with two children. Father is deceased from atherosclerotic heart disease.

■ Meds (at Day +120)

Posaconazole 300 mg PO daily
Esomeprazole 40 mg PO daily
Tacrolimus 2 mg PO twice daily
Prednisone 90 mg PO twice daily
Valacyclovir 500 mg PO twice daily
Amlodipine 10 mg PO daily
Prochlorperazine 10 mg PO Q 8 H PRN nausea/vomiting
Sirolimus 2 mg PO once daily
Dapsone 100 mg PO daily
Atorvastatin 10 mg PO daily
Gemfibrozil 600 mg PO BID
Triamcinolone 1% cream—apply twice daily to chest and shoulders

■ All

Sulfa → urticaria

■ ROS

Worsening “annoying” motor tremors that interfere with activities of daily living such as typing and drinking. Patient also reports dull headache that started about a week ago. The rash has resolved, and she reports that the diarrhea has decreased to one to two loose stools per day.

■ Physical Examination

Gen

Patient is a WDN Caucasian woman.

VS

BP 158/76 mm Hg, P 92 bpm, T 37.4°C; O₂ sat 98% in room air; Wt 90 kg; Ht 5'4"

Skin

Red rash on chest and shoulders

HEENT

Moist mucous membranes

Neck/Lymph Nodes

Supple; no thyromegaly

Lungs

Clear without wheezes, rhonchi, or crackles

CV

RRR; normal heart sounds; no M/R/G

Abd

Slight distention, RUQ tenderness, mild hepatomegaly

MS/Ext

Grade I–II edema in LE bilaterally

Neuro

A&O × 3

■ Labs

Na 132 mEq/L	Hgb 8.8 g/dL	<i>Fasting lipid panel</i>
K 3.0 mEq/L	Hct 28%	Total cholesterol 369 mg/dL
CL 112 mEq/L	Plt $110 \times 10^3/\text{mm}^3$	LDL unknown
CO ₂ 19 mEq/L	WBC $4.1 \times 10^3/\text{mm}^3$	HDL 47 mg/dL
BUN 22 mg/dL	AST 55 IU/L	Trig 1,468 mg/dL
SCr 1.1 mg/dL	ALT 61 IU/L	Tacrolimus 19.6 ng/mL
Glu 298 mg/dL	Alk phos 222 IU/L	(target 5–10 ng/mL)
Mg 1.2 mg/dL	LDH 70 IU/L	Sirolimus 20.5 ng/mL
A1C 9.5%	T. bili 0.9 mg/dL	(target 5–10 ng/mL)
	Alb 2.9 g/dL	

■ Assessment

New-onset tremors, headaches, hypokalemia, hypomagnesemia, hyperglycemia, and hypertriglyceridemia

QUESTIONS

Collect Information

- 1.a. What subjective and objective information indicates the presence of toxicities from immunosuppressive medications?
- 1.b. What additional information is needed to fully assess this patient?

Assess the Information

- 2.a. What are the likely causes for the patient's tremors and headache?
- 2.b. What are potential causes for development of hypertriglyceridemia and hyperglycemia?
- 2.c. What are the potential causes of hypokalemia and hypomagnesemia?
- 2.d. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of pharmacotherapy in this case?
- 3.b. What nondrug therapies might be useful for this patient?
- 3.c. What feasible pharmacotherapeutic options are available for treating the patient's dyslipidemia?
- 3.d. What feasible pharmacotherapeutic options are available for treating the patient's hyperglycemia?
- 3.e. Create an individualized, patient-centered, team-based care plan to treat all of the patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient and her caregivers to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ SELF-STUDY ASSIGNMENTS

1. What options are available for prevention of graft-versus-host disease after allogeneic stem cell transplantation?
2. Which vaccinations and at what schedule should patients receive after allogeneic stem cell transplantation?

CLINICAL PEARL

Allogeneic SCT is often associated with multiple medical conditions, especially metabolic syndrome and cardiovascular disease exacerbated by secondary effects from immunosuppressive medications. Patients' medication regimens also often contain drug interactions requiring careful evaluation to prevent further toxicity.

REFERENCES

1. Glotzbecker B, Duncan C, Alyea E, Campbell B, Soiffer R. Important drug interactions in hematopoietic stem cell transplantation: what every physician should know. *Biol Blood Marrow Transplant* 2012;18:989–1006.

2. Cutler C, Logan BR, Nakamura R, et al. Tacrolimus/sirolimus vs tacrolimus/methotrexate as GVHD prophylaxis after matched, related donor allogeneic HCT. *Blood* 2014;124(8):1372–1377.
3. Griffith ML, Savani BN, Boord JB. Dyslipidemia after allogeneic stem cell transplantation: evaluation and management. *Blood* 2010;116:1197–1204.
4. Fuji S, Rovó A, Ohashi K, et al. How do I manage hyperglycemia/post-transplant diabetes mellitus after allogeneic HSCT. *Bone Marrow Transplant* 2016;51(8):1041–1049.
5. Ullmann AJ, Lipton JH, Vesole DH, et al. Posaconazole or fluconazole for prophylaxis in severe graft-versus-host disease. *N Engl J Med* 2007;356:335–347.
6. Tomblyn M, Chiller T, Einsele H, et al. Guidelines for preventing infectious complications among hematopoietic cell transplantation recipients: a global perspective. *Biol Blood Marrow Transplant* 2009;15:1143–1238.

This page intentionally left blank

SECTION 18

NUTRITION AND NUTRITIONAL DISORDERS

160

PARENTERAL NUTRITION

Getting Past the Obstruction Level III

Melissa R. Pleva, PharmD, BCPS, BCNSP, BCCCP

Michael D. Kraft, PharmD, BCNSP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Describe how a bowel obstruction can lead to nutritional, fluid, and electrolyte abnormalities.
- Characterize the severity of malnutrition based on subjective and objective patient data.
- Identify potential complications related to parenteral nutrition (PN) in patients with malnutrition (eg, refeeding syndrome) and steps to avoid or manage such complications.
- Design a patient-specific PN prescription that is based on the nutritional diagnosis and other subjective and objective patient data.
- Construct and evaluate appropriate monitoring parameters for a hospitalized patient receiving PN.

PATIENT PRESENTATION

■ Chief Complaint

“My stomach hurts and I can’t keep down any food or water.”

■ HPI

Steven Brown is a 49-year-old man familiar to the GI surgery service with a history of a ventral hernia, hypertension, dyslipidemia, and type 2 DM. He presented to the ED earlier today with abdominal pain, nausea, vomiting, and inability to tolerate PO intake. Approximately 2 months ago, he underwent an exploratory laparotomy with small bowel resection and primary anastomosis for repair of a ventral hernia with incarcerated small bowel. His postoperative course was complicated by an anastomotic leak, peritonitis, and sepsis, and he was ultimately discharged to home after a 3-week hospital stay. For the past 4 days, he has had worsening abdominal pain and has been unable to tolerate any PO intake. His last bowel movement was 6 days ago. He has lost ~25 lb (~11 kg) from his weight prior to his surgery 2 months ago. This weight loss includes ~14 lb (~6.5 kg) since his prior discharge due to poor appetite and limited PO intake at home.

The surgical team decides to admit Mr Brown to the hospital. On admission, they obtain an abdominal CT scan, which demonstrates dilated loops of small bowel consistent with a small bowel obstruction (SBO) and negative for anastomotic leak or abscess. The team believes this SBO is likely due to adhesions from his prior surgery.

■ PMH

Ventral hernia
Hypertension
Dyslipidemia
Type 2 DM

■ PSH

Exploratory laparotomy, small bowel resection with primary anastomosis for repair of ventral hernia with incarcerated small bowel 2 months ago

■ FH

Remarkable for DM in his mother, HTN and CAD in his father

■ SH

Married, lives with his wife; construction worker. Drinks two to three alcoholic beverages per week; quit smoking 2 years ago, 25 pack-year history prior to quitting.

■ ROS

Reports feeling thirsty, no appetite. Complains of moderate abdominal pain, nausea, and vomiting. Also complains his abdomen feels “crampy” and is very bloated. Complains of not passing flatus or having a bowel movement in 6 days; urinating infrequently over the past 2 days, and urine is dark and concentrated. Feels lightheaded and dizzy if he stands up quickly. Denies chills, fevers, or other pain.

■ Meds Prior to Admission

Simvastatin 40 mg PO at bedtime
Hydrochlorothiazide 25 mg PO daily
Metoprolol 25 mg PO twice daily
Glyburide/metformin 10 mg/1000 mg PO twice daily with meals

■ All

NKDA

■ Physical Examination

Gen

African-American man, uncomfortable because of abdominal pain, appears malnourished

VS

BP 96/60 mm Hg, P 108 bpm, RR 18, T 37.7°C; Wt 71 kg (Wt prior to surgery 2 months ago ~83 kg), Ht 71” (180 cm)

Skin

Dry, flaking in some spots, poor turgor

HEENT

PERRLA, EOMI, anicteric sclerae, normal conjunctivae. Mouth is dry, pharynx is clear, some evidence of wasting on temporal lobes, eyes appear sunken in. Orbital ridge protruding somewhat, evidence of moderate–severe wasting of muscle and subcutaneous fat.

Lungs/Thorax

CTA and percussion bilaterally; bilateral protruding scapulae

CV

RRR, no murmurs

Abd

Distended; hypoactive (nearly absent) bowel sounds; diffuse tenderness throughout all four quadrants

Genit/Rect

No lesions, no internal masses

MS/Ext

(–) Cyanosis, (–) edema, 2+ dorsalis pedis and posterior tibial pulses bilaterally, moderate–severe wasting of muscle and subcutaneous fat, especially around large muscle groups (biceps, triceps, and quadriceps)

Neuro

A&O × 3; CN II–XII intact; motor 5/5 upper and lower extremity bilaterally; sensation intact and reflexes symmetric with downgoing toes

■ Labs on Admission

Na 132 mEq/L	Hgb 12.1 g/dL	AST 24 IU/L	Ca 8.2 mg/dL
K 3.3 mEq/L	Hct 35.9%	ALT 21 IU/L	Mg 1.4 mEq/dL
Cl 94 mEq/L	Plt 334 × 10 ³ /mm ³	Alk phos 41 IU/L	Phos 2.6 mg/dL
CO ₂ 34 mEq/L	WBC 7.5 × 10 ³ /mm ³	GGT 45 IU/L	PT 12.3 seconds
BUN 17 mg/dL		T. bili 0.9 mg/dL	INR 0.8
SCr 0.5 mg/dL		T. prot 4.9 g/dL	
Glu 142 mg/dL		Alb 2.9 g/dL	

■ Radiology

A CT scan with contrast demonstrates dilated loops of small bowel consistent with SBO; negative for anastomotic leak; negative for abscess.

■ Assessment

This is a 49-year-old man with a history of a ventral hernia, hypertension, dyslipidemia and type 2 DM, S/P exploratory laparotomy, small bowel resection with primary anastomosis, and repair of incarcerated ventral hernia 2 months ago, who is admitted with abdominal pain, nausea, vomiting, and inability to tolerate PO intake. His symptoms and CT scan are consistent with SBO. His history and physical exam also demonstrate evidence of malnutrition.

■ Clinical Course

Given that the patient has had recent abdominal surgery, as well as significant weight loss and evidence of malnutrition, the surgical team elects to manage his SBO conservatively (nonoperatively). Because of recent abdominal surgery, the team would like to avoid reentering the abdomen for surgical intervention at this time (the patient is likely to still have inflammation and adhesions from his prior operation, and additional surgical intervention can further increase inflammation and risk of complications [eg, adhesions, fistula]).

The patient is made NPO, and home PO medications are held for now. An NG tube is placed for gastric decompression, and a PICC is inserted for administration of PN and IV fluids. The team gives the patient a 1000-mL IV fluid bolus with normal saline followed by normal saline at 100 mL/hr. Once PN is initiated and the patient has been resuscitated, IV fluids will be decreased to maintain a total fluid intake of 100 mL/hr. The surgical team obtains nutrition and pharmacy consults for PN recommendations.

QUESTIONS**Collect Information**

- What subjective and objective information indicates the presence of malnutrition in this patient?
- What additional nutrition assessment data should you obtain and why?

Assess the Information

- Characterize the type and severity of malnutrition, and describe why the patient is at risk for nutritional deficiencies.
- What are the advantages and limitations of using the serum albumin as a marker of nutritional status?
- How can small bowel obstruction lead to malnutrition? What other nutritional disorders (eg, fluid, electrolytes, and micronutrients) can develop in patients with small bowel obstruction?
- Create a list of the patient's nutrition, fluid and electrolyte, and drug therapy problems. Prioritize the problems and assess medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- What are the goals of pharmacotherapy and nutrition support therapy for this patient?
- What are the options for providing nutrition support, and which form is indicated for this patient? Provide the rationale for your answer.
- Create an individualized, patient-centered, team-based care plan for treating this patient's nutrition, fluid and electrolyte, and drug therapy problems.
- What are the ranges of estimated daily goals for calories (kcal/kg per day), protein (g/kg per day), and hydration (mL per day or mL/kg per day) for this patient?
- Design a goal PN formulation for this patient that includes the total volume (mL per day) and goal rate (mL/h), amino acids (g per day), dextrose (g per day), and IV lipid emulsion (ILE; g per day). Take into consideration the goals you developed in question 3.a, as well as the underlying nutrition problems identified previously in question 2.c.
- How would you initiate PN in this patient? How quickly would you advance to the goal infusion rate? Provide the rationale for your answers.

Implement the Care Plan

- What information should be provided to the patient and family during his hospitalization regarding the PN?
- Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What monitoring parameters should be assessed at the initiation of the PN?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy (eg, efficacy and safety of PN therapy, nutritional status).

CLINICAL COURSE

Mr Brown was managed conservatively with bowel rest, PN, NG tube decompression, and supportive care. His symptoms improved over 4–5 days, and he began having bowel sounds and passing flatus. On hospital day 7, he had a small bowel movement, and the team began to advance his diet and taper the PN.

FOLLOW-UP QUESTION

1. How should PN be tapered off in this patient? Develop a plan to taper PN based on PO intake in this patient.

SELF-STUDY ASSIGNMENTS

1. Mr Brown is at risk for a condition called *refeeding syndrome*. What is refeeding syndrome? What are its signs, symptoms, and potential complications? How can it be prevented? How should it be treated if signs and symptoms develop?
2. What other specific postoperative complications can develop in surgical patients with moderate to severe malnutrition? How can preoperative nutrition support impact a malnourished surgical patient's risk for postoperative complications?
3. Calculate how many milliliters per day of dextrose 70%, amino acids 10%, and ILE 20% stock solutions are needed to compound the daily PN prescription that you determined for this patient.
4. Using the calculated daily goals for amino acids, dextrose, and ILE, determine the minimum PN volume that could be compounded for this patient. Assume it will be compounded using a 10% amino acid solution, 70% dextrose solution, and 20% ILE, and use an estimate of 100 mL for all micronutrients and additives.

CLINICAL PEARLS

Refeeding syndrome is a nutritional emergency that can lead to serious complications, including death. A good rule of thumb in patients with moderate to severe malnutrition is to “start low and go slow” when initiating nutrition support and aggressively correct serum electrolyte abnormalities *before* initiating nutrition support as well as during therapy.

Achieving appropriate glycemic control while avoiding hyperglycemia and hypoglycemia can reduce morbidity and mortality. Current guidelines recommend a goal serum glucose of 140–180 mg/dL for adult hospitalized patients receiving nutrition support; hyperglycemia (>180 mg/dL), hypoglycemia (<70 mg/dL), and significant fluctuations in serum glucose should be avoided.⁹

REFERENCES

1. White JV, Guenter P, Jensen G, et al. Consensus statement: Academy of Nutrition and Dietetics and American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *JPEN J Parenter Enteral Nutr* 2012;36:275–283.

2. Kudsk KA, Tolley EA, DeWitt RC, et al. Preoperative albumin and surgical site identify surgical risk for major postoperative complications. *JPEN J Parenter Enteral Nutr* 2003;27:1–9.
3. Kraft MD, Btaiche IF, Sacks GS. Review of the refeeding syndrome. *Nutr Clin Pract* 2005;20:625–633.
4. Foster NM, McGory ML, Zingmond DS, Ko CY. Small bowel obstruction: a population-based appraisal. *J Am Coll Surg* 2006;203:170–176.
5. Brown KA, Dickerson RN, Morgan LM, et al. A new graduated dosing regimen for phosphorus replacement in patients receiving nutrition support. *JPEN J Parenter Enteral Nutr* 2006;30:209–214.
6. The American Society for Parenteral and Enteral Nutrition. Task Force for the Revision of Safe Practices for Parenteral Nutrition. Safe practices of parenteral nutrition. *JPEN J Parenter Enteral Nutr* 2004;28:S39–S70.
7. Boullata JJ, Gilbert K, Sacks G, et al. A.S.P.E.N. clinical guidelines: parenteral nutrition ordering, order review, compounding, labeling, and dispensing. *JPEN J Parenter Enteral Nutr* 2014;38:334–377.
8. Ayers P, Adams S, Boullata J, et al. A.S.P.E.N. parenteral nutrition safety consensus recommendations. *JPEN J Parenter Enteral Nutr* 2014;38:296–333.
9. Doig GS, Simpson F, Heighes PT, et al. Restricted versus continued standard caloric intake during the management of refeeding syndrome in critically ill adults: a randomised, parallel-group, multicentre, single-blind controlled trial. *Lancet Respir Med* 2015;3(12):943–952.
10. McMahon MM, Nystrom E, Braunschweig C, et al. A.S.P.E.N. Clinical Guidelines: nutrition support of adult patients with hyperglycemia. *JPEN J Parenter Enteral Nutr* 2013;37:23–36.

161

ADULT ENTERAL NUTRITION

Gut Check Level III

Carol J. Rollins, MS, RD, PharmD, BCNSP

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- List contraindications to enteral nutrition (EN) therapy.
- Calculate the protein, calorie, and fluid requirements for a patient who is to receive EN therapy.
- Recommend an appropriate enteral formula and feeding route.
- Implement an appropriate monitoring plan to achieve the desired nutritional endpoints and avoid complications.
- Design an appropriate regimen for administering medications via a feeding tube, including recommending alternate dosage forms for medications that cannot be crushed.

PATIENT PRESENTATION

Paula Ronin is a 60-year-old woman referred to the nutrition support team for evaluation and possible initiation of parenteral nutrition. The history on the referral states: admission to the hospital 2 days ago with c/o nausea, vomiting, and abdominal pain, primarily in the epigastric and LUQ region. Continued c/o nausea and abdominal pain; no vomiting in the last 24 hours. She is NPO except for sips of water for comfort.

QUESTIONS

Collect Information

1. What other information is necessary to evaluate the patient and provide recommendations for a nutrition support plan of care?

CLINICAL COURSE

After following appropriate procedures, you obtain the following additional information about the patient.

HPI

Ms Ronin began having symptoms of nausea and epigastric/LUQ pain about a week (per patient) prior to hospital admission. She thought this would “go away on its own by changing to a high carbohydrate diet; like in the past.” She began feeling weak and dizzy the day before she asked a friend to take her to the ED. She had several episodes of vomiting before going to the ED on the day of admission. Her history indicates five episodes with symptoms of nausea and abdominal pain in the past 6 months. With previous episodes, the pain was reported as less severe and lasted only a couple days; nausea occurred, but there was no vomiting; she tolerated a high-carbohydrate diet and was not weak or dizzy. She did not go to the hospital with the past episodes since the pain improved on its own.

In the ED, Ms Ronin received 6 L of 0.9% NaCl for hydration; D5%/0.45% NaCl + 20 mEq KCl/L has been infusing at 125 mL/hr since then. Imaging in the ED indicated multiple areas of cholelithiasis, potential choledocholithiasis, edema of the proximal pancreatic duct with possible stricture, and a small pancreatic pseudocyst.

Height: 70 in. Weight: no admission weight available; weight on hospital day 2 is 72 kg. Patient states, “I lost about 125 pounds over the past year; I’ve been about 150–155 pounds for the past 3 months and I’m happy with that weight. When my brother died, it really scared me. I started going for a walk after work and now walk a couple miles most days. My insurance pays for me to see a dietitian; she helped me with a weight-loss plan that has healthy meals and snacks. My last appointment was about 3 months ago.”

PMH

HTN
Pre-DM
GERD

DVT 4 months ago for which she receives warfarin 5 mg PO daily

FH

Mother died from a stroke 5 years ago; she had DM and HTN. Father is healthy; he is retired from working as a ranch hand. Per the patient, her father’s only health complaints are “aching bones” and need for glasses to read. Three siblings are healthy as far as the patient knows; however, her younger brother died from a stroke a year ago; he was obese and had complications from DM and HTN.

SH

Divorced; no contact with her ex-husband; no children. She works full time as a delivery driver. She smokes about one pack per week, down from about two packs per day for 15 years prior to her brother’s death; alcohol consumption is typically an occasional beer after work, although it was two to three beers at the end of the day before she decided to “do something to avoid ending up like my brother.” The patient has private health insurance through her

employer. Per the case manager, insurance coverage provides a drug benefit for oral medications but follows Medicare Parts A and B for hospitalization and home coverage.

ROS

From physician’s note today:

Constitutional: Moderate to severe pain and nausea

ENT: No vision changes or eye pain; no tinnitus or ear pain; no throat pain; no problem with swallowing

CV: No SOB, DOE, and chest pain

Resp: No cough or sputum production

GI: Continued persistent epigastric and LUQ abdominal pain; improved with fentanyl patch and more frequent breakthrough pain coverage; no emesis or diarrhea; complains of intermittent nausea and mild/moderate constipation

GU: No nocturia or hematuria

MS: (+) Abdominal pain; no other muscle aches or bone pain

Skin: No rashes, nodules, or itching. Patient pointed out a nonhealing wound on the right ankle, stating that she was bitten and badly scratched when trying to save her cat from a coyote a couple weeks ago. She was seen in Urgent Care at that time.

Neuro: No headaches, dizziness, unsteady gait, or seizures

Heme/lymph nodes: No recent blood transfusions or swollen glands

Meds

Metoprolol succinate tablet 200 mg PO daily

Morphine sulfate, immediate-release 15 mg PO Q 6 H PRN pain

Fentanyl transdermal patch 50 mcg, change every 72 hours

Lansoprazole 15 mg PO every morning

Bisacodyl tablet 5 mg PO at bedtime

Moxifloxacin 400 mg PO daily × 14 days (start today)

Amoxicillin/clavulanate (875/125 mg) twice daily for 5 days prescribed at urgent care. Patient stated “I took the last pill about 7 or 8 days ago and then the bottle was empty.”

Warfarin 5 mg PO daily

All

NKDA

Physical Examination

Gen

Well-developed mixed ethnic Caucasian–Hispanic woman; alert and conversant

VS

BP 144/88 mm Hg, P 88 bpm, RR 20, T 37.1°C; Wt 72 kg

Skin

No nodules, masses, or rash; no ecchymoses or petechiae. Venous access device in right hand.

HEENT

PERRLA; EOMs intact. Eyes anicteric. No mouth lesions; tongue normal size.

Neck

Neck supple; no thyromegaly or masses

Lymph Nodes

No cervical, supraclavicular, axillary, or inguinal adenopathy

Heart

RRR with no gallop, rubs, or murmur

Lungs

Clear

Abd

Tender to palpation; no masses palpable; no distension

Genit/Rect

Deferred

MS/Ext

Right ankle wound is red, warm, and swollen. No clubbing or cyanosis; 1+ bilateral ankle edema; 2+ sacral edema; no spine or CVA tenderness.

Neuro

Cranial nerves intact; DTRs active and equal

■ Endoscopy Report

From yesterday: ERCP, unable to enter pancreatic duct due to swelling and edema surrounding the area; suspected stricture although this could not be visualized. Biopsy was obtained from pancreatic duct opening and sent to pathology. Stent placement is not possible at this time. Recommendation for repeat ERCP and imaging in 2–3 weeks to determine the most appropriate plan of action; possible surgery for cholecystectomy versus more extensive pancreatic resection if evidence of malignancy based on pathology report. Continue patient on NPO except sips of clear liquids.

■ Labs

See Table 161-1.

■ Other

1. Peripheral blood smear: anisocytosis 3+, poikilocytosis 2+, macrocytosis 2+, microcytosis 1+, and hypersegmented neutrophils.
2. Tissue sample from right ankle wound sent for culture and sensitivities.

■ Assessment

Acute pancreatitis with pseudocyst, probably secondary to pancreatic duct stricture, possibly related to cholelithiasis or choledocholithiasis based on imaging completed in the ED, and/or alcohol. Serum markers for GI-related cancers are negative; pathology pending for pancreatic duct biopsy. Intolerance to diet; tolerates limited volume (150–200 mL per day) of clear liquids daily. Per GI service note, patient is to remain NPO except for sips of clear liquids.

Assess the Information

- 2.a. What is the appropriate timing for nutrition intervention?
- 2.b. Based on risk-versus-benefit considerations, is the consult for initiation of parenteral nutrition appropriate for this patient?
- 2.c. What information indicates the presence of malnutrition or increases the risk for malnutrition?
- 2.d. What type and degree of malnutrition does this patient exhibit? What evidence supports your assessment?
- 2.e. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

Develop a Care Plan

- 3.a. What are the goals of nutrition support in this case?
- 3.b. What are the potential alternatives for improving nutritional status in this patient other than initiating specialized nutrition support?
- 3.c. What are the potential routes for specialized nutrition support and the reason(s) why each is or is not appropriate for this patient?
- 3.d. By postponing invasive therapy (possible surgery for a cholecystectomy or stricture repair; awaiting pancreatic duct biopsy results to rule out pancreatic cancer) for several weeks, the potential of continuing nutrition support outside the hospital arises. Based on the information now available, does this patient meet criteria for home enteral therapy? Recall that her insurance follows Medicare guidelines for home coverage.
- 3.e. Estimate the protein, calorie, and fluid requirements for this patient.
- 3.f. What type of formula (eg, polymeric, monomeric) is most appropriate for this patient?
- 3.g. What administration regimen should be used for tube feedings?
- 3.h. Assuming that the patient is to continue her current medications during tube feedings, how should each of these be administered?
- 3.i. Create a care plan to manage the patient's drug therapy problems other than providing nutrition support. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Implement the Care Plan

- 4.a. What information should be provided to the patient or her caregiver to enhance compliance, ensure successful therapy, and minimize adverse effects of the nutritional support therapy?
- 4.b. Describe how care with nutrition support should be coordinated with other healthcare providers.

TABLE 161-1 Lab Values

Na 140 mEq/L	Hgb 8.5 g/dL	WBC $11.9 \times 10^3/\text{mm}^3$	AST 23 IU/L	Trig 105 mg/dL
K 3.9 mEq/L	Hct 26.7%	Segs 67%	ALT 34 IU/L	Ca 7.9 mg/dL
Cl 109 mEq/L	RBC $2.65 \times 10^6/\text{mm}^3$	Bands 14%	Alk phos 287 IU/L	Mg 1.9 mg/dL
CO ₂ 26 mEq/L	Plt $265 \times 10^3/\text{mm}^3$	Lymphs 17%	LDH 154 IU/L	Phos 3.5 mg/dL
BUN 7 mg/dL	MCV 104 μm^3	Monos 2%	T. bili 0.9 mg/dL	Amylase 462 mg/dL
SCr 0.9 mg/dL			T. prot 7.1 g/dL	Lipase 591 mg/dL
Glu 147 mg/dL			Alb 2.6 g/dL	CA 19-9 15 U/mL
			T. chol 239 mg/dL	CEA 1.2 ng/mL

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

CLINICAL COURSE

After discussing nutrition support during acute pancreatitis with the medical team, the nutrition support service discussed EN therapy with the patient. The patient consented to feeding tube placement. A 1.2-cal/mL, 55.5-g protein/L, 300-mOsm/kg polymeric formula was started using an enteral infusion pump via nasojunal tube at 35 mL/hr for 8 hours, and then advanced to the goal rate of 65 mL/hr. Basic metabolic panel results on day 2 of EN revealed electrolyte values WNL. The WBC decreased to $10.6 \times 10^3/\text{mm}^3$ with 75% segs, 9% bands, 14% lymphs, and 2% monos. The basic metabolic panel on day 3 of EN showed stable values and a prealbumin of 6 mg/dL. The plan for discharge to home was confirmed, and arrangements for home EN were finalized. The plan is for her diet to continue as limited clear liquids (<240 mL per day) and repeat imaging in 2–3 weeks to assess the small pancreatic pseudocyst and potentially schedule her for surgery the following week for the pancreatic duct stricture. If the biopsy results indicate cancer, more extensive surgery would likely be needed.

SELF-STUDY ASSIGNMENTS

1. Select another case from this Casebook where the patient is receiving several medications and design an appropriate regimen for administering medications via a feeding tube, including alternative dosage forms for medications that cannot be crushed and proper dosage adjustments for different forms where necessary.
2. Educate an actual patient or do a mock education with a classmate about medication administration through a feeding tube.
3. Select another case from this Casebook where the patient is receiving several medications and determine the potential cumulative sorbitol dose if all medications were changed to oral liquid dosage forms.
4. Identify the metabolic changes associated with refeeding syndrome and the characteristics that increase the risk of this complication.

CLINICAL PEARL

Medications administered through a feeding tube frequently clog the tube; avoid administration through the tube when possible. Administer medications orally if the patient can and will take them orally.

REFERENCES

1. White JV, Guenter P, Jensen G, Malone A, Schofield M; Academy of Nutrition and Dietetics Malnutrition Work Group; A.S.P.E.N. Malnutrition Task Force; A.S.P.E.N. Board of Directors. Consensus statement of the Academy of Nutrition and Dietetics/American Society for Parenteral and Enteral Nutrition: characteristics recommended for the identification and documentation of adult malnutrition (undernutrition). *J Acad Nutr Diet* 2012;112:730–738.

2. Mirtallo JM. Overview of parenteral nutrition. In: Mueller CM, ed. The A.S.P.E.N. Adult Nutrition Support Core Curriculum. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:e-book chapter 14:25.
3. McClave SA, Martindale RG, Vanek VW, et al. Guidelines for the provision and assessment of nutrition support therapy in the adult critically ill patient. Section K. Acute pancreatitis. *J Parenter Enteral Nutr* 2009;33:277–316.
4. Mirtallo JM, Forbes A, McClave SA, et al. International consensus guidelines for nutrition therapy in pancreatitis. *J Parenter Enteral Nutr* 2012;36:284–291.
5. Kruger K, McClave SA, Martindale RG. Pancreatitis. In: Mueller CM, ed. The A.S.P.E.N. Adult Nutrition Support Core Curriculum. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:e-book chapter 28:40.
6. Konrad D, Mitchell R, Hendrickson E. Home nutrition support. In: Mueller CM, ed. The A.S.P.E.N. Adult Nutrition Support Core Curriculum. 3rd ed. Silver Spring, MD: American Society for Parenteral and Enteral Nutrition; 2017:e-book chapter 38:51.
7. Boullata JJ, Carrera AL, Harvey L, et al. ASPEN Safe practices for enteral nutrition therapy. *J Parenter Enteral Nutr* 2017;41(1):15–103.
8. Rollins CJ. Drug–nutrient interactions in patients receiving enteral nutrition. In: Boullata JJ, Armenti VT, eds. *Handbook of Drug–Nutrient Interactions*. Totowa, NJ: Humana Press; 2009:515–552.

162

OBESITY

Oh, To Be 23 Again (BMI That Is) Level II

Dannielle C. O'Donnell, BS, PharmD

LEARNING OBJECTIVES

After completing this case study, the reader should be able to:

- Identify common obesity-related comorbidities.
- Calculate body mass index (BMI), and use waist circumference to determine a patient's risk of obesity-related morbidity.
- Develop a pharmacotherapeutic plan and treatment strategy for obese patients.
- Provide patient counseling on the expected benefits, possible adverse effects, and drug interactions with weight loss medications.

PATIENT PRESENTATION

Chief Complaint

"I've been through a painful divorce. I think I'm ready to try and get out and meet someone and start over, but I must've eaten my way through all of the stress of the separation and legal proceedings. Who's gonna even look at me when I'm this size? I may have to take up smoking again. It was easier to stay skinny when I smoked."

HPI

Francine Martinez is a 35-year-old Hispanic woman who emigrated to the United States from Guatemala as a child. She has "yo-yo'd"

with her weight since her teen years. She says she feels best at 55 kg, which was how much she weighed when she was 23 years old and got married. She states that she was a “chubby” kid who really worked in college to lose weight, mostly through trying to eat vegan like her roommate and going to exercise classes at the college gym. That was also when she started smoking. She and her ex-husband were smokers and stopped when she was 27 because they wanted a smoke-free home before starting a family. She remembers frustration that while she “did great going cold turkey with the cigs,” she put on 10 kg in the first 6 smoke-free months. She “worked out like crazy” and dropped 7 kg before they conceived their first child at the age of 29. She delivered a healthy baby, although her pregnancy was complicated by a diagnosis of gestational diabetes and excessive weight gain (27 kg). Her hyperglycemia resolved postdelivery, and she “was happy with how quickly most of the baby weight came off while nursing,” but then she plateaued 8 kg above her prepregnancy weight and “just couldn’t get the rest off; I don’t have time to commit to exercising while juggling a job and family.” She has now put on more weight over the course of the busy toddler years and then even more during the stress of the divorce and hectic new lifestyle as a single working mom. She now lives in an apartment with her 5-year-old and says she struggles a bit financially because her ex-husband often does not pay the alimony or child support on time, but she’s thankful she has good medical insurance and prescription benefits through her employer. She says she has tried weight loss shakes but finds herself just “starving” and “eating her way through the pantry” in the evening after she gets her son to bed. She says she does not have time for a gym membership or money for a “fancy program” where they provide meals for you. Also, she doesn’t think it would work with her having one thing and then just cooking for her son. She has bought some “herbal stuff” from a coworker that helped with end-of-day hunger but thinks cigarettes would be even “less of a dent in the wallet than those pills that I’m not sure even did very much.” To economize and accommodate her hectic single-mom schedule, they eat out quite a bit based on where the “kids eat free” meal nights are (ie, an all-you-can-eat buffet on Monday nights and a pancake house on Wednesday nights, drive-thru meals maybe one to two other nights each week). She drinks orange juice and coffee with sugar and creamer in the morning and more coffee or sweet tea throughout the day. On the weekends when she has her son, she likes to treat him to good home cooking of traditional meals that include flour tortillas (breakfast tacos, fajitas), refried beans, rice, tamales, chips, and guacamole. When her ex-husband has him, she doesn’t have any interest in cooking for herself so she often gets fast food or orders in from the local taqueria that delivers. That is also a time when she feels more alone and “down,” and she knows that she eats larger portions and snacks more often when feeling lonely or stressed.

■ PMH

GDM
Hemorrhoids
Insomnia
Tension headaches
Adjustment disorder post-divorce

■ FH

Her mother had an MI at the age of 62 years; father died in an MVA at the age of 67. Maternal grandmother died at age 63 with diabetes and “kidney problems.” She states that all women in her family “are what you would call ‘fluffy’ and have struggled with their weight.” No other family members have a significant medical history, although she states that her 5-year-old is “a big boy.” She blames his dad, stating that when he has their son all they do is eat

junk food and drink sodas, and he uses the TV and video games as a babysitter.

■ SH

The patient is a single working mom and a previous smoker (1 ppd $\times$ 4 years). Stopped 8 years ago. She denies IVDA. She has previously had success, albeit short term, with weight loss by focusing on exercising and doing a couple of “juice cleanses” but is not exercising now.

■ Diet

Has never had formal diet instruction. Her diet appears to be low in fiber, high in saturated fat, sugars, and calories. She denies regular or binge alcohol consumption.

■ Meds

Tylenol PM PRN sleep (one to two times per week)
Anusol HC PRN hemorrhoidal pain and/or itch
Citalopram 20 mg PO once daily
Unknown “herbal” weight loss product—discontinued 3 months ago

■ All

Macrolides—rash

■ ROS

She complains of general low energy and periods of apathy that she attributes to the divorce and a preoccupation with food and her weight and feeling “undesirable,” although her mood is improved since citalopram was increased from 10 to 20 mg 2 months ago. She denies symptoms of cold or heat intolerance; changes in skin, hair, or nails; nervousness; irritability; muscle pain or weakness; palpitations; diarrhea or constipation; polyuria; polydipsia; chest pain; or shortness of breath. Despite having low energy, she relates some difficulty sleeping and reports waking up feeling “unrested.” She denies binge eating or purging.

■ Physical Examination

Gen

The patient is in NAD but looks tired and older than her stated age. She is clean in appearance and dressed appropriately for the weather.

VS

BP 148/88 mm Hg (consistent with previous clinic reading), P 80 bpm, RR 16, T 36.4°C; Wt 80 kg, waist 100 cm, Ht 5’3”

Skin

Warm, with normal distribution of body hair. No significant lesions or discolorations.

HEENT

NC/AT; PERRLA; EOMI; TMs intact

Breasts

Deferred

CV

RRR, S₁ and S₂ normal; no murmurs, rubs, or gallops

Pulm

CTA & P bilaterally

Abd

Obese with multiple striae; NT; ND; (+) BS; no palpable masses

Genit/Rect

Pelvic and rectal exams deferred

Ext

LE varicosities present. Pedal pulses 2+ bilaterally. No joint swelling or tenderness.

Neuro

A&O $\times$ 3; CN II–XII intact; Romberg test (–); sensory and motor levels intact; 2+ triceps tendons and DTR; Babinski (–)

■ Labs (Fasting)

Na 138 mEq/L
K 3.9 mEq/L
Cl 96 mEq/L
CO₂ 26 mEq/L
BUN 13 mg/dL
SCr 1.0 mg/dL
Glu 115 mg/dL

AST 24 IU/L

Fasting lipid profile

T. chol 208 mg/dL
LDL-C 109 mg/dL
HDL-C 38 mg/dL
Trig 305 mg/dL

■ Assessment

This is an obese woman with obesity-related complications, including hypertension (diagnosed today based on her 2 clinic readings), dyslipidemia, and impaired fasting glucose (metabolic syndrome). With her history of GDM, she is at increased risk of developing type 2 DM. Weight loss would decrease her risk of developing type 2 DM and can improve BP and lipids.

QUESTIONS**Collect Information**

- 1.a. Calculate the patient's BMI.
- 1.b. What subjective and objective information indicates the presence of obesity?
- 1.c. What additional information is needed to fully assess this patient's obesity?

Assess the Information

- 2.a. By using her history, the BMI, and any other markers of adiposity, categorize her obesity and stratify her risk.
- 2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.
- 2.c. What economic, psychosocial, and cultural considerations are applicable to this patient?

Develop a Care Plan

- 3.a. What are the goals of therapy for this patient's obesity?
- 3.b. What nondrug therapies should be recommended for this patient's obesity?
- 3.c. What feasible pharmacotherapeutic alternatives are available for treating this patient's obesity?
- 3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's obesity

and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

- 3.e. What treatment alternatives would be appropriate if initial therapy for obesity fails?

Implement the Care Plan

- 4.a. What general and medication-specific information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?
- 4.b. Describe how care should be coordinated with other healthcare providers.

Follow-up: Monitor and Evaluate

- 5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?
- 5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

■ CLINICAL COURSE

At her first return visit 3 months later, Mrs Martinez had lost 4 kg (5% of her weight). By this second visit at the 6-month time point, she had lost some additional weight and weighs 73.5 kg; her waist circumference is 96 cm. She is now working out at home regularly 30 minutes each evening (typically four nights a week) with a video after her son goes to bed. She uses an app on her phone and does her best to get 10,000 steps each day. Although they still eat out a lot, she is making significantly different choices, increasing her lean meats, decreasing carbohydrates and saturated fats, monitoring portion sizes, abstaining from having seconds, and substituting a piece of fruit for dessert. She has eliminated sugary beverages (sweet tea, using Stevia in her coffee, eliminated orange juice in the morning) and is having good success sticking to her plan of not eating anything after her son goes to bed. If she is really struggling at night, she makes herself some horchata with sugar substitute. She has decreased fat and calories and increased fiber intake by switching from flour to corn tortillas and also by making her refried beans with vegetable oil instead of lard. She is logging her daily food intake and her steps onto the pedometer App, and has found it to be insightful to have to write down everything she eats and when she eats it.

Her FBG is now 102 mg/dL, and her FLP includes total cholesterol 202 mg/dL, LDL 110 mg/dL, HDL 45 mg/dL, and triglycerides 235 mg/dL. Her blood pressure has improved to 142/82 mm Hg, having also initiated lisinopril 10 mg/day at her visit 6 months ago.

She states that she is as compliant with her lifestyle modifications as in previous weeks and is in much better spirits overall. She has noticed a definite improvement in her clothing fit, but she is starting to become frustrated again that she has not seen any additional improvement on her home scale in the last 2 weeks and still does not like how she looks. She wants to know if there is something else she can take or if she could have the laparoscopic sleeve gastrectomy procedure since "I have good insurance and have met my deductible for the year." Although she is pleased with the improvement in her blood pressure and glucose, she is frustrated that her cholesterol did not improve more. She is wondering if it might further help her weight loss efforts if she picked up some of "that herbal dandelion tea from Paraguay" that her coworker sells for weight loss "to help move things along."

■ FOLLOW-UP QUESTIONS

1. What changes, if any, should be considered for her weight loss regimen today?
2. How would you educate her regarding use of the herbal weight loss tea?
3. What pharmacotherapeutic changes, if any, should be made for treating her dyslipidemia, hyperglycemia, and hypertension at this time? Is a medication indicated at this point to prevent or treat diabetes?

■ SELF-STUDY ASSIGNMENTS

1. List the limitations of height–weight charts or BMI determinations. What are the most accurate methods for quantifying body fat, and why are they not routinely employed?
2. Assume that you are a member of a pharmacy and therapeutics committee for a managed care corporation. Justify whether antiobesity drugs should be a covered benefit, and if so, which specific agent(s) should be added to the formulary. Should OTC weight loss products be covered? Justify your answer.
3. Compile a compendium of common herbal and dietary supplements that claim weight loss benefits, and make a list of the evidence for their safety and efficacy.
4. Make a list of the various prescription weight loss medications that have been introduced and subsequently withdrawn from the US and EU markets and the reasons for the withdrawal.

CLINICAL PEARL

Taking psyllium with orlistat has been reported to decrease the frequency and severity of orlistat GI side effects such as oily stool and leakage.

REFERENCES

1. Apovian CM, Aronne LJ, Bessesen DH, et al. Pharmacological management of obesity: an Endocrine Society clinical practice guideline. *J Clin Endocrinol Metab* 2015;100(2):342–362.
2. Jensen MD, Ryan DH, Apovian CM, et al. 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. *Circulation* 2013;63(25 Pt B):2985–3023.
3. Garvey WT, Mechanick JL, Brett EM, et al. American Association of Clinical Endocrinologists and American College of Endocrinology comprehensive clinical practice guidelines for medical care of patients with obesity. *Endocr Pract* 2016;22(Suppl 3):1–203.
4. Toplak H, Woodward E, Yumuk V, et al. 2014 EASO position statement on the use of anti-obesity drugs. *Obes Facts* 2015;8(3):166–174.
5. Khera R, Murad MH, Chandar AK, et al. Association of pharmacological treatments for obesity with weight loss and adverse events: a systematic review and meta-analysis. *JAMA* 2016;315(22):2424–2434.
6. American Diabetes Association. Position Statement: 5 Prevention or delay of type 2 diabetes: Standards of Medical Care in Diabetes—2018. *Diabetes Care* 2018;41(Suppl 1):S51–S54.

This page intentionally left blank

SECTION 19

COMPLEMENTARY AND ALTERNATIVE THERAPIES (LEVEL III)

Kelly M. Shields, PharmD

TO THE READER

Although use of many dietary supplements has leveled off or decreased in the past few years, many patients are still interested in trying supplements, either in place of (alternative) or along with (complementary) prescription and OTC therapies. Patients have a continued desire for knowledge on the potential benefits and risks of these therapies, and often expect pharmacists and other health-care providers to provide information they can use in determining what treatment option is preferred.

As part of providing appropriate care, clinicians have a duty to help individual patients avoid interactions with their drug therapies and prevent use of products unsafe for them because of other disease state contraindications. That is a fairly straightforward task when dealing with prescription and OTC therapies; there is so much information and research available that most problems and risks are well understood. If a patient is prescribed a contraindicated drug, we can ensure that he or she does not receive it. With dietary supplements, there is often not enough information available to make clear-cut judgments about risks. We also cannot prevent patients from taking supplements even if supplements are known to be unsafe or risky for them, because we do not control their access to those therapies. Instead, we are limited to providing as much guidance as possible to help maximize any possible benefit and minimize possible harm.

CASEBOOK QUESTIONS ABOUT DIETARY SUPPLEMENTS

The following questions regarding supplement therapy aid in the decision-making process and will be addressed in the “Clinical Course” section of the Casebook. It is assumed that necessary information about a patient’s medical history and current drug regimen has already been obtained.

1. What is the known or proposed mechanism of action?

- The pharmacology of FDA-approved prescription medications is generally understood, but many supplements are used with only limited knowledge about their pharmacologic activities. Botanical supplements, in particular, are extremely complex and may have multiple activities, some synergistic to the desired effect and some in opposition or unrelated. When there is little or no definitive human evidence for either efficacy or safety, we must often extrapolate based on in vitro or animal data in order to provide patients with information or instructions. For example, if a plant extract has been shown to improve glucose uptake in tissue studies, it is reasonable to expect that activity to some extent when taken by human beings. It would also be reasonable to offer cautions about use

with sulfonylurea drugs or other hypoglycemic agents, even when no case studies or clinical trials have reported interactions. Depending on the risks if an interaction should happen, appropriate real-life statements to patients can range from: “If you use this supplement, you will have to do additional blood sugar checks for the first 2 weeks to make sure it’s not interfering with your other medication” to “This particular supplement just isn’t safe for you at all.”

2. How extensive or conclusive are the clinical trial data on effectiveness?

- When clinical trial data conclude that a supplement has beneficial effects, it may be safer for a patient to try a supplement before a prescription drug with known adverse events. Whenever evidence of efficacy is lacking or contradictory, the severity of the patient’s condition becomes more important in the risk/benefit equation. For example, a patient wishing to try a supplement for the common cold or athlete’s foot is not at great risk of harm if the supplement is not effective—he or she will simply endure some unpleasant symptoms for a time, and then most likely use a standard medication. On the other hand, a patient with severe hypertension who tries an ineffective supplement may be at increased risk for a cardiovascular event.

3. What is known about safety?

- This question relates back to what is known about the mechanism of action: when there is a lack of information from long-term clinical trials, decisions about safety must be based on extrapolation from basic scientific studies and isolated case reports. It must be kept in mind that safety issues can be both overemphasized and underemphasized and that information (and therefore reasonable recommendations) can change. For example, ginger is often described as being associated with increased risk of bleeding. This is absolutely true at doses of 4 g per day or more but is unlikely at lower doses. However, even use at lower doses would become a major consideration in patients who have other medical conditions (eg, a clotting disorder) or if drug interactions are involved (eg, warfarin or chronic NSAID use). One safety rule of thumb for counseling patients is that *all* supplements should be stopped 10–14 days prior to scheduled surgery to minimize risks of interactions or increased risk of bleeding.

4. Does the product have any specific quality considerations?

- Two questions are associated with “quality.” First, is the product the “right” product—that is, the same strength or standardization as that used in the clinical trials that demonstrated any benefits? Second, is the product a “good quality product”—that is, contains what it is labeled to contain with no contaminants? The first question is answered by close attention to reliable information resources and clinical trials and to reading product labels to ensure the chosen product is the appropriate standardization or strength and doses are not subtherapeutic or toxic. The second question is best addressed by advising patients to only purchase products

from manufacturers that participate in quality seal programs or that have been tested by third-party laboratories. The first choice for a quality seal program is USP's Dietary Supplement Verification Program, but UL (Underwriters' Laboratories) and NSF International also have facility cGMP audit and certification programs. Third-party laboratories with consumer-accessible information include ConsumerLab.com and Labdoor.com.

- Certain products are more likely to have specific problems with quality or carry additional risk. For example, melatonin is usually produced synthetically, but a few available products are from "natural sources," generally meaning extracted from the pituitary glands of cattle. Because the pituitary gland is in the brain, these products do carry a small but real risk of contamination with prion proteins associated with bovine spongiform encephalopathy, also known as mad cow disease.
5. **Would this be an appropriate treatment choice in this particular patient?**
- Each patient may have different motivations to try a treatment. If clinical or basic science supports potential benefit of a supplement for a given condition, the next thing to consider is the patient's own expectations of therapy and ability to self-monitor for both efficacy and safety. For example, a postmenopausal woman who suffers 10 severe hot flashes a week and wants to end them entirely will probably be disappointed with a supplement, whereas another woman who also has 10 severe hot flashes a week and would like to reduce their frequency and/or severity may be very happy with the same product. Expectations must be appropriate; only rarely will a supplement work as strongly or as quickly as a prescription drug.
6. **If the patient is going to use the product, what counseling information will allow him or her to maximize any possible benefit and minimize any harm?**
- Counseling information should cover the same categories of information as prescription drugs: dose, schedule, duration of therapy, side effects, and interactions. Unfortunately, because there is usually less information available about side effects and interactions, it is impossible to warn patients about every possibility. It is best to counsel patients to contact their health-care providers if anything "unexpected or unusual" occurs. This provides protection for the patient and allows evaluation of any possible link to the supplement, which aids in expanding the supplement knowledge base.
 - Specificity is important in counseling. For example, if a patient is going to use *Ginkgo biloba*, he or she needs to be told to watch for easy bruising, not just that the ginkgo may increase bleeding risk. Specificity is even more important when a patient chooses to take a supplement despite being counseled against it because of safety issues.
 - In addition, there are extra categories of information to include in counseling that do not generally have to be addressed with prescription and OTC drugs: using the appropriate product and a high-quality product. For botanical supplements, it is generally necessary to specify information such as the standardization of an extract (eg, saw palmetto should be 160 mg of extract standardized to 85–95% fatty acids and sterols twice daily). For nonbotanical supplements, the salt form may need to be specified (eg, glucosamine sulfate for monotherapy has more evidence of efficacy than glucosamine hydrochloride for monotherapy and so is the preferred form).

OBTAINING CURRENT AND RELIABLE DIETARY SUPPLEMENT INFORMATION

Decisions made about using supplements are only as good as the information used in making the decisions. Unfortunately, incomplete or wrong information about dietary supplements is abundantly available, so using only reliable resources is vital. A brief list of recommended resources is provided at the end of this section, but practitioners need to know what to look for or to avoid as they come across new resources. The following questions and rules of thumb should be kept in mind:

- Avoid resources published or provided by manufacturers; their primary interest is selling the product.
- Investigate the authors or source of the information; is the resource actually created by trained professionals, or by a ghost-writing group?
- Are recommendations based on careful analysis of the quality of clinical trials? Recommendations based solely on the end results of trials are often wrong; it is not possible to get good decision-making data from a badly designed or poorly conducted trial.
- Are cautions (about interactions, contraindications, or adverse effects) based on all theoretical, animal, or human data available, or only on well-documented human trials or case reports? Although it may seem counterintuitive at first, there is such a lack of high-quality reports and information in humans that theoretical data (based on in vitro experiments or theorized mechanisms of action) or animal data becomes more important in generating cautions that help keep patients safe. Often these cautions should not be as strong, of course. If a supplement has been found to affect glucose utilization in tissue cultures, a diabetic patient starting to take the supplement may be warned appropriately to monitor blood glucose more frequently, whereas a case report of loss of glycemic control in two patients using the supplement would generate a strong warning not to use the supplement.
- Does the resource include up-to-date information? Supplement information changes rapidly, so publication dates can matter tremendously.

RECOMMENDED INFORMATION RESOURCES

■ Literature Search Strategies

One of the most essential resources is a comprehensive literature search, because this can retrieve the most current information. While it is recommended that more than one indexing system be used (such as both Medline and EMBASE), healthcare students and professionals often do not have access to anything other than Medline. Consequently, it is essential to use very thorough search strategies, as discussed here:

- Because pertinent articles can be incompletely or wrongly indexed, search using more than just MESH (or EMTREE) terms to ensure proper retrieval. For example, to search for saw palmetto, search the MESH term (*Serenoa*), and then perform keyword searches for the common name (saw palmetto), the botanical name (*Serenoa repens*), and any alternative botanical names (*Sabul serrulata*). Consider searching misspellings; the spelling "saw palmeto" may not be common, but "gingko" instead of "ginkgo" is very common. Combining

the results of these searches with “OR” will optimize retrieval of articles that may be relevant.

- Search the relevant disease state and any closely related terms. Continuing the example, search “BPH,” “benign prostatic hyperplasia,” “prostatic hyperplasia,” “prostate hypertrophy,” and “prostatic hypertrophy” as both MESH (or Emtree) terms and keywords. It may also be useful to search symptom or outcome measure terms, such as “urinary retention” or “micturition rate.”
- After combining product and disease state searches, if the retrieval set is so large as to be impossible to review, limitations can be used. For clinical decision making, the most useful types of limitations are clinical trials, evidence-based reviews, meta-analyses, and systematic reviews. Because it is not uncommon for articles about dietary supplement trials to report results of both animal and human studies, it is not recommended that a limitation of “human only” be used, because that could eliminate appropriate articles based on indexing.

■ Electronic Database Resources

Electronic databases available for purchase include:

- Natural Medicines (<https://naturalmedicines.therapeuticresearch.com/>). It is the most comprehensive resource available and includes a wide range of individual and combination products. It contains evidence-based recommendations and summaries of clinical and basic science information that are regularly reviewed and updated. The site allows for easy checking of supplement–drug interactions. It is available for purchase by individuals as well as institutions.
- ConsumerLab.com (www.consumerlab.com). This is a third-party laboratory that tests dietary supplements for compliance with labeled content and for appropriate dissolution and contaminants. No clinical recommendations are given; the site’s utility is primarily limited to aiding in the choice of a high-quality product. It is inexpensive (about \$40 per year) and is also appropriate for use by consumers.

Free electronic databases include:

- The Health Information site of the National Institutes of Health Office of Dietary Supplements (<http://ods.od.nih.gov/HealthInformation/>). This is a government site with links to several useful informational resources including tips for using supplements and fact sheets on a number of dietary supplements.
- Memorial Sloan-Kettering Cancer Center Integrative Medicine Service Web site (<http://www.mskcc.org/mskcc/html/1979.cfm>). It includes a database of individual supplements. Information is specifically focused on use of supplements in cancer patients, a population that has a high rate of use of complementary and alternative medicine therapies. The site includes more discussion of interactions with chemotherapeutic agents than other resources.
- Computer Access to Research on Dietary Supplements (CARDS; https://ods.od.nih.gov/Research/CARDS_Database.aspx). This is a database of federally funded clinical trials of supplements.
- The PubMed Dietary Supplement Subset (https://ods.od.nih.gov/Research/PubMed_Dietary_Supplement_Subset.aspx). This will automatically search Medline for dietary supplement-focused literature. The subset database is focused on medical use of plants, so it can be easier to search than other literature databases that contain citations for agricultural-focused studies.

- The Dietary Supplement Label Database (DSLD) became active in 2013 (<http://dsld.nlm.nih.gov/dsld/>). A project of both the National Library of Medicine and the Office of Dietary Supplements, it is a searchable database of labeling information for products both available and discontinued from the US market. It may be especially useful when gathering medication histories or when patients ask questions about brand name products that contain multiple ingredients.

■ Print Resources

Because of limitations on the timeliness of information in print resources, it is difficult to make strong recommendations. New print resources should be evaluated according to the criteria listed above to determine their usefulness.

CASE 14: DYSLIPIDEMIA

■ Garlic and Fish Oil for Dyslipidemia

Clinical Course

Mrs Thorngress is already taking garlic capsules, but she is not sure about the type or dose. Because you are making changes to her current prescription regimen, you need to investigate the advisability of continuing the garlic. If Mrs Thorngress does begin a statin drug as indicated, she would not be able to take red yeast rice, a common supplement used for dyslipidemia, because it contains monacolin K, a lovastatin analogue, and would be duplicative therapy. Would fish oil be a possible option for her?

■ FOLLOW-UP QUESTIONS

Garlic

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow her to maximize any possible benefit and minimize any harm?

Fish Oil/Omega-3 Fatty Acids

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow her to maximize any possible benefit and minimize any harm?

REFERENCES

1. Zeng T, Zhang CL, Zhao XL, Xie KQ. The role of garlic on the lipid parameters: a systematic review of the literature. *Crit Rev Food Sci Nutr* 2013;53:215–230.

- Shouk R, Abdou A, Shetty K, et al. Mechanisms underlying the antihypertensive effects of garlic bioactives. *Nutr Res* 2015;34:106–115.
- Ried K, Toben C, Fakler P. Effect of garlic on serum lipids: an updated meta-analysis. *Nutr Rev* 2013;71(5):282–299.
- Ried K. Garlic lowers blood pressure in hypertensive individuals, regulates serum cholesterol, and stimulates immunity: an updated meta-analysis and review. *J Nutr* 2016;146(2):389S–396S.
- Ried K, Travica N, Sali A. The effect of aged garlic extract on blood pressure and other cardiovascular risk factors in uncontrolled hypertensives: the AGE at Heart trial. *Integr Blood Press Control* 2016;9:9–21.
- Cho HJ, Yoon IS. Pharmacokinetic interactions of herbs with cytochrome p450 and p-glycoprotein. *Evid Based Complement Alternat Med* 2015;2015:736431.
- Adkins Y, Kelley DS. Mechanisms underlying the cardioprotective effects of omega-3 polyunsaturated fatty acids. *J Nutr Biochem* 2010;21:781–792.
- Lewis A, Lookinland S, Beckstrand RL, et al. Treatment of hypertriglyceridemia with omega-3 fatty acids: a systematic review. *J Am Acad Nurse Pract* 2004;16(9):384–395.
- Hartweg J, Farmer AJ, Perera R, et al. Meta-analysis of the effects of n-3 polyunsaturated fatty acids on lipoproteins and other emerging lipid cardiovascular risk markers in patients with type 2 diabetes. *Diabetologia* 2007;50(8):1593–1602.
- Eslick GD, Howe PRC, Smith C, Priest R, Bensoussan A. Benefits of fish oil supplementation in hyperlipidemia: a systematic review and meta-analysis. *Int J Cardiol* 2009;136:4–16.
- Leslie MA, Cohen CJA, Liddle DM, et al. A review of the effect of omega-3 polyunsaturated fatty acids on blood triacylglycerol levels in normolipidemic and borderline hyperlipidemic individuals. *Lipids Health Dis* 2015;14:53.
- GISSI-Prevenzione Investigators. Dietary supplementation with n-3 polyunsaturated fatty acids and vitamin E after myocardial infarction: results of the GISSI-Prevenzione trial. *Lancet* 1999;354:447–455.
- Khawaja OA, Gaziano JM, Djoussé L. N-3 fatty acids for prevention of cardiovascular disease. *Curr Atheroscler Rep* 2014;16:450.

CASE 40: NAUSEA AND VOMITING

■ Ginger for Nausea and Vomiting

Clinical Course

While discussing Mr Jones' antiemetic regimen, he says, "I remember that my sister used to take ginger to prevent sea sickness when she went on a cruise, and my cousin used ginger when he was having chemotherapy a few years ago. Would that be good for me to try?"

■ FOLLOW-UP QUESTIONS

Ginger

- What is the known or proposed mechanism of action?
- How extensive or conclusive are the clinical trial data on effectiveness?
- What is known about safety?
- Does the product have any specific quality concerns?
- Would this be an appropriate treatment choice in this particular patient?
- If the patient is going to use the product, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

- Lete I, Allué J. The effectiveness of ginger in the prevention of nausea and vomiting during pregnancy and chemotherapy. *Integrative Med Insights* 2016;11:11–17.

- Walstab J, Krüger D, Stark T, et al. Ginger and its pungent constituents non-competitively inhibit activation of human recombinant and native 5-HT₃ receptors of enteric neurons. *Neurogastroenterol Motil* 2013;25:439–448, e302.
- Ryan JL, Heckler CE, Roscoe JA, et al. Ginger (*Zingiber officinale*) reduces acute chemotherapy-induced nausea: a URCC CCOP study of 576 patients. *Support Care Cancer* 2012;20:1479–1489.
- Lee J, Oh H. Ginger as an antiemetic modality for chemotherapy-induced nausea and a systematic review and meta-analysis. *Oncol Nurs Forum* 2013;40(2):163–170.
- Marx WM, Teleni L, McCarthy AL, et al. Ginger (*Zingiber officinale*) and chemotherapy-induced nausea and vomiting: a systematic literature review. *Nutr Rev* 2013;71(4):245–254.

CASE 72: MIGRAINE HEADACHE

■ Butterbur and Feverfew for Prevention of Migraine

Clinical Course

While discussing possible alternatives to her valproic acid therapy, Ms Miller says that a friend who also has migraines had read about some herbal remedies used for migraine prevention. She asks whether any products like that could be used instead of or along with her prescription medications. Ms Miller is very interested in a more "natural" therapy, but only if it would reduce the number of migraines she experiences.

■ FOLLOW-UP QUESTIONS

Butterbur and Feverfew

- What are the known or proposed mechanisms of action?
- How extensive or conclusive are the clinical trial data on effectiveness of each?
- What is known about safety of each?
- Does either of the products have any specific quality concerns?
- Would either product be an appropriate treatment choice in this particular patient?
- If the patient is going to use either of the products, what counseling information will allow her to maximize any possible benefit and minimize any harm?
- Between the two products, which might be a better choice for Ms Miller?

REFERENCES

- Sutherland A, Sweet BV. Butterbur: an alternative therapy for migraine prevention. *Am J Health Syst Pharm* 2010;67:705–711.
- Agosti R, Duke RK, Chrubasik JE, Chrubasik S. Effectiveness of *Petasites hybridus* preparations in the prophylaxis of migraine: a systematic review. *Phytomedicine* 2006;13:743–746.
- Horak S, Koschak A, Stuppner H, Streissnig J. Use-dependent block of voltage-gated Cav2.1 Ca²⁺ channels by petasins and eudesmol isomers. *J Pharmacol Exp Ther* 2009;330:220–226.
- Lipton RB, Göbel H, Einhäupl KM, et al. *Petasites hybridus* root (butterbur) is an effective preventative treatment for migraine. *Neurology* 2004;63:2240–2244.
- Diener HC, Rahlfs VW, Danesch U. The first placebo-controlled trial of a special butterbur root extract for the prevention of migraine: reanalysis of efficacy criteria. *Eur Neurol* 2004;51:89–97.
- Rajapakse T, Pringsheim T. Nutraceuticals in migraine: a summary of existing guidelines for use. *Headache* 2016;56(4):808–816.
- Loder E, Burch R, Rizzoli P. The 2012 AHS/AAN guidelines for prevention of episodic migraine: a summary and comparison with other recent clinical practice guidelines. *Headache* 2012;52:930–945.

8. Wang YP, Yan J, Fu PP, Chou MW. Human liver microsomal reduction of pyrrolizidine alkaloid N-oxides to form the corresponding carcinogenic parent alkaloid. *Toxicol Lett* 2005;155:411–420.
9. Avula B, Wang YH, Wang M, et al. Simultaneous determination of sesquiterpenes and pyrrolizidine alkaloids from the rhizomes of *Petasites hybridus* (L.) G.M. et Sch. and dietary supplements using UPLC-UV and HPLC-TOF-MS methods. *J Pharm Biomed Anal* 2012;70:53–63.
10. Materazzi S, Benemei S, Fusi C, et al. Parthenolide inhibits nociception and neurogenic vasodilatation in the trigeminovascular systems by targeting the TRPA1 channel. *Pain* 2013;154:2750–2758.
11. Magni P, Ruscica M, Dozio E, et al. Parthenolide inhibits the LPS-induced secretion of IL-6 and NF- κ B nuclear translocation in BV-2 microglia. *Phytother Res* 2012;26(9):1405–1409.
12. Pittler MH, Ernst E. Feverfew for preventing migraine. *Cochrane Database Syst Rev* 2000;(3):CD002286.
13. Pfaffenrath V, Diener HC, Fischer M, et al. The efficacy and safety of *Tanacetum parthenium* (feverfew) in migraine prophylaxis—a double-blind, multicentre, randomized placebo-controlled dose-response study. *Cephalalgia* 2002;22:523–532.
14. Diener HC, Pfaffenrath V, Schnitker J, Friede et al. Efficacy and safety of 6.25 mg t.i.d. feverfew CO₂-extract (MIG-99) in migraine prevention—a randomized, double-blind, multicentre, placebo-controlled study. *Cephalalgia* 2005;25:1031–1041.

CASE 78: MAJOR DEPRESSION

■ St. John's Wort for Depression

Clinical Course

Mrs Flowers understands that she must stop the SJW she has been taking because of an interaction with her prescribed mirtazapine, but she wonders if it would have been helpful if she had started it when she first began feeling depressed.

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow her to maximize any possible benefit and minimize any harm?

REFERENCES

1. Russo E, Scicchitano F, Whalley BJ, et al. *Hypericum perforatum*: pharmacokinetic, mechanism of action, tolerability, and clinical drug-drug interactions. *Phytother Res* 2014;28:643–655.
2. Butterweck V. Mechanism of action of St. John's wort in depression: what is known? *CNS Drugs* 2003;17:539–562.
3. Hypericum Depression Trial Study Group. Effect of *Hypericum perforatum* (St. John's wort) in major depressive disorder. *JAMA* 2002;287:1807–1814.
4. Sarris J, Fava M, Schweitzer I, Mischoulon D. St. John's wort (*Hypericum perforatum*) versus sertraline and placebo in major depressive disorder: continuation data from a 26-week RCT. *Pharmacopsychiatry* 2012;45:275–278.
5. Shelton RC. St. John's wort (*Hypericum perforatum*) in major depression. *J Clin Psychiatry* 2009;70(Suppl 5):23–27.
6. Sarris J. St. John's wort for the treatment of psychiatric disorders. *Psychiatr Clin North Am* 2013;36:65–72.

7. Mannel M, Kuhn U, Schmidt U, Ploch M, Murck H. St. John's wort extract LI160 for the treatment of depression with atypical features—a double-blind, randomized, and placebo-controlled trial. *J Psychiat Res* 2010;44:760–767.
8. Rahimi R, Abdollahi M. An update on the ability of St. John's wort to affect the metabolism of other drugs. *Expert Opin Drug Metab Toxicol* 2012;8(6):691–708.
9. Kasper S, Gastpar M, Möller HJ, et al. Better tolerability of St. John's wort extract WS 5570 compared to treatment with SSRIs: a reanalysis of data from controlled clinical trials in acute major depression. *Int J Clin Psychopharmacol* 2010;25:204–213.

CASE 80: GENERALIZED ANXIETY DISORDER

■ Kava for Anxiety

Clinical Course

Mr Johnson is still worried about both the side effects of prescription drugs to treat his anxiety and whether he will be able to afford them. He states that he has read a lot of information about kava that “it really works for anxiety.” Mr Johnson says, “Maybe I was just using a bad product last time I tried it and that's why it didn't help much and hurt my stomach. Should I get a better product and try it again?”

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Singh YN, Singh NN. Therapeutic potential of kava in the treatment of anxiety disorders. *CNS Drugs* 2002;16:731–743.
2. Sarris J, LaPorte E, Schweitzer I. Kava: a comprehensive review of efficacy, safety, and psychopharmacology. *Aust NZ J Psychiatry* 2011;45:27–35.
3. Pittler M, Ernst E. Efficacy of kava extract for treating anxiety: systematic review and meta-analysis. *J Clin Psychopharmacol* 2000;20:84–89.
4. Pittler M, Ernst E. Kava extract versus placebo for treating anxiety. *Cochrane Database Syst Rev* 2003;1:CD003383.
5. Witte S, Loew D, Gaus W. Meta-analysis of the efficacy of the acetonic kava-kava WS®1490 in patients with non-psychotic anxiety disorders. *Phytother Res* 2005;19:183–188.
6. Smith K, Leiras C. The effectiveness and safety of kava kava for treating anxiety symptoms: a systematic review and analysis of randomized clinical trials. *Complement Ther Clin Pract* 2018;33:107–117.
7. Sarris J, Kavanagh DJ, Byrne G, et al. The kava anxiety depression spectrum study (KADSS): a randomized, placebo-controlled crossover trial using an aqueous extract of *Piper methysticum*. *Psychopharmacol* 2009;205:399–407.
8. Sarris J, Stough C, Bouseman CA, et al. Kava in the treatment of generalized anxiety disorder. A double-blind, randomized, placebo-controlled study. *J Clin Psychopharmacol* 2013;33(5):643–648.
9. Teschke R, Sarris J, Glass X, Schulze J. Kava, the anxiolytic herb: back to basics to prevent liver injury? *Br J Clin Pharmacol* 2011;71(3):445–448.

10. Kuchta K, Schmidt M, Nahrstedt A. German kava ban lifted by court: the alleged hepatotoxicity of kava (*Piper methysticum*) as a case of ill-defined herbal drug identity, lacking quality control, and misguided regulatory politics. *Planta Med* 2015;81(18):1647–1653.
11. Stevenson C, Huntley A, Ernst E. A systematic review of the safety of kava extract in the treatment of anxiety. *Drug Safety* 2002;25:251–261.
12. Brown AC. Liver toxicity related to herbs and dietary supplements: online table of case reports. *Food Chem Toxicol* 2017;107:472–501.

CASE 82: INSOMNIA

■ Melatonin for Insomnia

Clinical Course

Ms Miller states she knows her neighbor had suggested that using a melatonin product would help her be able to stay asleep. She'd like to learn whether that is a good option to help keep her from waking up after she has fallen asleep.

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Zisapel N. New perspectives on the role of melatonin in human sleep, circadian rhythms and their regulation. *Br J Pharmacol* 2018;175(16):3190–3199.
2. Auld F, Maschauer EL, Morrison I, et al. Evidence for the efficacy of melatonin in the treatment of primary adult sleep disorders. *Sleep Med Rev* 2017;34:10–22.
3. Luthringer R, Muzet M, Zisapel N, et al. The effect of prolonged-release melatonin on sleep measures and psychomotor performance in elderly patients with insomnia. *Int Clin Psychopharmacol* 2009;24(5):239–249.
4. Sateia MJ, Buysse DJ, Krystal AD, et al. Clinical practice guideline for the pharmacologic treatment of chronic insomnia in adults: an American Academy of Sleep Medicine clinical practice guideline. *J Clin Sleep Med* 2017;13(2):307–349.
5. Hansen MV, Danielsen AK, Hageman I, et al. The therapeutic or prophylactic effect of exogenous melatonin against depression and depressive symptoms: a systematic review and meta-analysis. *Eur Neuropsychopharmacol* 2014;24(11):1719–1728.
6. Foley HM, Steel AE. Adverse events associated with oral administration of melatonin: a critical systematic review of clinical evidence. *Complement Ther Med* 2019;42:65–81.

CASE 84: TYPE 2 DIABETES MELLITUS: NEW ONSET

■ Fish Oil, Cinnamon, and α -Lipoic Acid for Type 2 Diabetes Mellitus

Clinical Course

While discussing Mr Giuliani's diagnosis with him, he states that his neighbor with diabetes told him that she just follows her diabetic

diet and takes cinnamon and something called "alip acid" and does not have to take any prescriptions for her blood sugar. He also says that he has read about fish oil being used for diabetes. Mr Giuliani asks if he should start any of those to help get his blood sugar under control.

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action for each?
2. How extensive or conclusive are the clinical trial data on effectiveness for each?
3. What is known about safety of each?
4. Do any of the products have any specific quality concerns?
5. Would anyone or these be an appropriate treatment choice in this particular patient?
6. If the patient is going to use any of these products, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Fetterman JW Jr., Zdanowicz MM. Therapeutic potential of n-3 polyunsaturated fatty acids in disease. *Am J Health Syst Pharm* 2009;66:1169–1179.
2. Balk EM, Lichtenstein AH, Chung M, et al. Effects of omega-3 fatty acids on serum markers of cardiovascular disease risk: a systematic review. *Atherosclerosis* 2006;189(1):19–30.
3. Kabir M, Skurnik G, Naour N, et al. Treatment for 2 mo with n-3 polyunsaturated fatty acids reduces adiposity and some atherogenic factors but does not improve insulin sensitivity in women with type 2 diabetes: a randomized controlled study. *Am J Clin Nutr* 2007;86:1670–1679.
4. Zheng JS, Huang T, Yang J, Fu YQ. Marine n-3 polyunsaturated fatty acids are inversely associated with risk of type 2 diabetes in Asians: a systematic review and meta-analysis. *PLoS One* 2012;7(9):e44525.
5. Hartweg J, Perera R, Montori VM, Dinneen SF, Neil AHAWM, Farmer AJ. Omega-3 polyunsaturated fatty acids (PUFA) for type 2 diabetes mellitus. *Cochrane Database Syst Rev* 2008;(1):CD003205.
6. Gao H, Geng T, Huang T, et al. Fish oil supplementation and insulin sensitivity: a systematic review and meta-analysis. *Lipids Health Dis* 2017;16(1):131.
7. Lichtenstein AH, Appel LJ, Brands M, et al. Diet and lifestyle recommendations revision 2006: a scientific statement from the American Heart Association Nutrition Committee. *Circulation* 2006;114:82–96.
8. Medagama AB. The glycaemic outcomes of cinnamon, a review of the experimental evidence and clinical trials. *Nutr J* 2015;14:108.
9. Leach MJ, Kumar S. Cinnamon for diabetes mellitus. *Cochrane Database Syst Rev* 2012;(9):CD007170.
10. Akilen R, Tsiami A, Devendra D, Robinson N. Cinnamon in glycaemic control: systemic review and meta analysis. *Clin Nutr* 2012;31:609–615.
11. Davis PA, Yokoyama W. Cinnamon intake lowers fasting blood glucose: meta-analysis. *J Med Food* 2011;14(9):884–889.
12. Akilen R, Tsiami A, Devendra D, Robinson N. Glycated haemoglobin and blood pressure-lowering effect of cinnamon in multi-ethnic type 2 diabetic patients in the UK: a randomized, placebo-controlled, double-blind clinical trial. *Diabetic Med* 2010;27:1159–1167.
13. Lu T, Sheng H, Wu J, et al. Cinnamon extract improves fasting blood glucose and glycosylated hemoglobin level in Chinese patients with type 2 diabetes. *Nutr Res* 2012;32:408–412.
14. Allen RW, Schwartzman E, Baker WL, et al. Cinnamon use in type 2 diabetes: an updated systematic review and meta-analysis. *Ann Fam Med* 2013;11(5):452–459.
15. Chase CK, McQueen CE. The use of cinnamon in diabetes. *Am J Health Syst Pharm* 2007;64:1033–1035.
16. Rochette L, Ghibu S, Muresan A, Vergely C. Alpha-lipoic acid: molecular mechanisms and therapeutic potential in diabetes. *Can J Physiol Pharmacol* 2015;93:1021–1027.

17. Ansar H, Mazloom Z, Kazemi F, Hajazi N. Effect of alpha-lipoic acid on blood glucose, insulin resistance, and glutathione peroxidase of type 2 diabetic patients. *Saudi Med J* 2011;32(6):584–588.
18. Porasuphatana S, Suddee S, Nartnampong A, et al. Glycemic and oxidative status of patients with type 2 diabetes mellitus following oral administration of alpha-lipoic acid: a randomized double-blinded placebo-controlled study. *Asia Pac J Clin Nutr* 2012;21(1):12–21.
19. de Oliveira AM, Rondó PHC, Luzia LA, D'Abronzio FH, Illison VK. The effects of lipoic acid and α -tocopherol supplementation on the lipid profile and insulin sensitivity of patients with type 2 diabetes mellitus: a randomized, double-blind, placebo-controlled trial. *Diab Res Clin Pract* 2011;92:253–260.
20. Segermann J, Hotze A, Ulrich H, Rao GS. Effect of alpha-lipoic acid on the peripheral conversion of thyroxine to triiodothyronine and on serum lipid-, protein- and glucose levels. *Arzneimittelforschung* 1991;41(12):1294–1298.

CASE 96: MANAGING MENOPAUSAL SYMPTOMS

■ Black Cohosh and Soy for Menopausal Symptoms

Clinical Course

Ms Wilson is considering stopping her HT because her cousin was recently diagnosed with breast cancer. She still desires relief from hot flashes and asks for additional information on other alternatives. She has heard that black cohosh should not be used in women with breast cancer, but she has a friend who also has a family history of breast cancer who has been on black cohosh for about 9 months on the recommendation of her physician. Her friend has a checkup with lab tests every 6 months. Ms Wilson asks if black cohosh or soy would be an appropriate option to help keep her hot flushes under control.

■ FOLLOW-UP QUESTIONS

1. What are the known or proposed mechanisms of action?
2. How extensive or conclusive are the clinical trial data on effectiveness for each?
3. What is known about safety of each?
4. Do the products have any specific quality concerns?
5. Would either product be an appropriate treatment choice in this particular patient?
6. If the patient is going to use either of these products, what counseling information will allow her to maximize any possible benefit and minimize any harm?

REFERENCES

1. Powell SL, Gödecke T, Nikolic D, et al. In vitro serotonergic activity of black cohosh and identification of N_{ω} -methylserotonin as a potential active constituent. *J Agric Food Chem* 2008;56:11718–11726.
2. Borrelli F, Izzo AA, Ernst E. Pharmacological effects of *Cimicifuga racemosa*. *Life Sci* 2003;73:1215–1229.
3. Ruhlen RL, Haubner J, Tracy JK, et al. Black cohosh does not exert an estrogenic effect on the breast. *Nutr Cancer* 2007;59:269–277.
4. Fritz H, Seely D, McGowan J, et al. Black cohosh and breast cancer: a systematic review. *Integr Cancer Ther* 2014;13(1):12–29.
5. Borrelli F, Ernst E. Black cohosh (*Cimicifuga racemosa*) for menopausal symptoms: a systematic review of its efficacy. *Pharmacol Res* 2008;58:8–14.
6. Palacio C, Masi G, Mooradian AD. Black cohosh for the management of menopausal symptoms. A systematic review of clinical trials. *Drugs Aging* 2009;26:23–36.

7. Leach MJ, Moore V. Black cohosh (*Cimicifuga* spp.) for menopausal symptoms. *Cochrane Database Syst Rev* 2012;9:CD007244.
8. Shams T, Setia MS, Hemmings R, McCusker J, Sewitch CA. Efficacy of black cohosh-containing preparations on menopausal symptoms: a meta-analysis. *Altern Ther* 2010;16:36–44.
9. Beer AM, Osmers R, Schnitker J, et al. Efficacy of black cohosh (*Cimicifuga racemosa*) medicines for treatment of menopausal symptoms—comments on major statements of the Cochrane Collaboration report 2012 “black cohosh (*Cimicifuga* spp.) for menopausal symptoms (review).” *Gynecol Endocrinol* 2013;29(12):1022–1025.
10. Rebbeck TR, Troxel AB, Norman S, et al. A retrospective case-control study of the use of hormone-related supplements and association with breast cancer. *Int J Cancer* 2007;120:1523–1528.
11. Obi N, Chang-Claude J, Berger J, et al. The use of herbal preparations to alleviate climacteric disorders and risk of postmenopausal breast cancer in a German case-control study. *Cancer Epidemiol Biomarkers Prev* 2009;18(8):2207–2213.
12. McKenzie SC, Rahman A. Bradycardia in a patient taking black cohosh. *Med J Austral* 2010;193:479–481.
13. Dinman S. Black cohosh [sic]: a contraindication in general anesthesia. *Plastic Surg Nurs* 2006;26:42–43.
14. Naser B, Schnitker J, Minkin MJ, Garcia de Arriba S, Nolte KU, Osmers R. Suspected black cohosh hepatotoxicity: no evidence by meta-analysis of randomized controlled clinical trials for isopropanolic black cohosh extract. *Menopause* 2011;18(4):366–375.
15. Setchell KD, Brown NM, Lydeking-Olsen E. The clinical importance of the metabolite equol—a clue to the effectiveness of soy and its isoflavones. *J Nutr* 2002;132:3577–3584.
16. North American Menopause Society. The role of soy isoflavones in menopausal health: report of The North American Menopause Society/Wulf H. Utian Translational Science Symposium in Chicago, IL (October 2010). *Menopause* 2011;18(7):732–753.
17. Villaseca P. Non-estrogen conventional and phytochemical treatments for vasomotor symptoms: what needs to be known for practice. *Climacteric* 2012;15:115–124.
18. Duncan AM, Underhill KE, Xu X, et al. Modest hormonal effects of soy isoflavones in postmenopausal women. *J Clin Endocrinol Metab* 1999;84:3479–3484.
19. Ginsburg J, Prelevic GM. Lack of significant hormonal effects and controlled trials of phyto-oestrogens. *Lancet* 2000;355:163–164.
20. Schmidt M, Arjomand-Wölkart K, Birkhäuser MH, et al. Consensus: soy isoflavones as a first-line approach to the treatment of menopausal vasomotor complaints. *Gyn Endocrinol* 2016;32(6):427–430.
21. Taku K, Melby MK, Kronenberg F, Kurzer MS, Messina M. Extracted or synthesized soybean isoflavones reduce menopausal hot flash frequency and severity: systemic review and meta-analysis of randomized controlled trials. *Menopause* 2012;19(7):776–790.
22. Divi RL, Chang HC, Doerge DR. Anti-thyroid isoflavones from soybean: isolation, characterization, and mechanisms of action. *Biochem Pharmacol* 1997;54:1087–1096.

CASE 98: BENIGN PROSTATIC HYPERPLASIA

■ *Pygeum africanum* for BPH

Clinical Course

As the pharmacist in the team, you perform a literature search on the use of saw palmetto for BPH. You discover that there are reports of the dietary supplement both improving and worsening symptoms of ED. In addition, your readings indicate that saw palmetto should really only be used by patients with mild to moderate BPH. Based on this information, you do not recommend use of saw palmetto for the patient's BPH symptoms. However, because the patient is requesting information on natural products, you search for alternative dietary supplements that may provide some benefit for this patient's BPH without contributing to ED. Would *Pygeum africanum* be a reasonable option to consider?

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive is the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Quiles MT, Arbós MA, Fraga A, et al. Antiproliferative and apoptotic effects of the herbal agent *Pygeum africanum* on culture prostate stromal cells from patients with benign prostatic hyperplasia (BPH). *Prostate* 2010;70:1044–1053.
2. Papaioannou M, Schleich S, Roell D, et al. NBBS isolated from *Pygeum africanum* bark exhibits androgen antagonistic activity, inhibits AR nuclear translocation and prostate cancer cell growth. *Invest New Drugs* 2010;28:729–743.
3. Edgar AD, Levin R, Constantinou CE, Denis L. A critical review of the pharmacology of the plant extract of *Pygeum africanum* in the treatment of LUTS. *Neurourol Urodynam* 2007;26:458–463.
4. Shenouda NS, Sakla MS, Newton LG, et al. Physterol *Pygeum africanum* regulates prostate cancer in vitro and in vivo. *Endocrine* 2007;31:72–81.
5. Breza J, Dzurny O, Borowka A, et al. Efficacy and acceptability of Tadenan® (*Pygeum africanum* extract) in the treatment of benign prostatic hyperplasia (BPH): a multicentre trial in central Europe. *Cur Med Res Opin* 1998;14:127–139.
6. Chatelain C, Autet W, Brackman F. Comparison of once and twice daily dosage forms of *Pygeum africanum* extract in patients with benign prostatic hyperplasia: a randomized, double-blind study, with long-term open label extension. *Urology* 1999;54:473–478.
7. Ishani A, MacDonald R, Nelson D, Rutks I, Wilt TJ. *Pygeum africanum* for the treatment of patients with benign prostatic hyperplasia: a systematic review and quantitative meta-analysis. *Am J Med* 2000;109:654–664.
8. Wilt T, Ishani A, Mac Donald R, Rutks I, Stark G. *Pygeum africanum* for benign prostatic hyperplasia. *Cochrane Data Syst Rev* 2002;(1):CD001044.

CASE 103: OSTEOARTHRITIS

■ Glucosamine Sulfate, Glucosamine Hydrochloride, and Chondroitin for Osteoarthritis

Clinical Course

While discussing multiple treatment options with Mr Kansella, he says, “This may seem silly, but I have a neighbor a couple years older than me who was getting some pretty bad arthritis in both knees a few years ago. He says he hardly has any pain anymore because he’s taking these glucosamine and chondroitin pills. He even started back to golfing! Is there any way those could help me with my pain?”

■ FOLLOW-UP QUESTIONS

1. What are the known or proposed mechanisms of action?
2. How extensive or conclusive is the clinical trial data on effectiveness of each of the products or their combinations?
3. What is known about safety?
4. Do the products have any specific quality concerns?

5. Would any of these be appropriate treatment choice in this particular patient?
6. If the patient is going to use the products, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Nagaoka I, Igarashi M, Sakamoto K. Biological activities of glucosamine and its related substances. *Adv Food Nutr Res* 2012;65:337–352.
2. Volpi N. Anti-inflammatory activity of chondroitin sulphate: new functions from an old natural molecule. *Inflammopharmacology* 2011;19:299–306.
3. Calamia V, Mateos J, Fernández-Puente P, et al. A pharmacoproteomic study confirms the synergistic effect of chondroitin sulfate and glucosamine. *Sci Rep* 2014;4:5069.
4. Lee YH, Woo JH, Choi SJ, et al. Effect of glucosamine or chondroitin sulfate on the osteoarthritis progression: a meta-analysis. *Rheumatol Int* 2010;30:357–363.
5. Bruyère O, Altman RD, Reginster JY. Efficacy and safety of glucosamine sulfate in the management of osteoarthritis: evidence from real-life setting trials and surveys. *Semin Arthritis Rheum* 2016;45:S12–S17.
6. Wandel S, Jüni P, Tendal B, et al. Effects of glucosamine, chondroitin, or placebo in patients with osteoarthritis of hip or knee: network meta-analysis. *BMJ* 2010;34:c4675.
7. Sawitzke AD, Shi H, Finco MF, et al. Clinical efficacy and safety of glucosamine, chondroitin sulfate, their combination, celecoxib or placebo taken to treat osteoarthritis of the knee: 2-year results from GAIT. *Ann Rheum Dis* 2010;69:1459–1464.
8. Hochberg MC. Structure-modifying effects of chondroitin sulfate in knee osteoarthritis: an updated meta-analysis of randomized placebo-controlled trials of 2-year duration. *Osteoarthritis Cart* 2010;18:S28–S31.
9. Gabay C, Medinger-Sadowski C, Gascon D, et al. Symptomatic effects of chondroitin 4 and chondroitin 6 sulfate on hand osteoarthritis. *Arthritis Rheum* 2011;63(11):3383–3391.
10. Hochberg MC, Martel-Pelletier J, Monfort J, et al. Combined chondroitin sulfate and glucosamine for painful knee osteoarthritis: a multicentre, randomised, double-blind, non-inferiority trial versus celecoxib. *Ann Rheum Dis* 2016;75:37–44.
11. Provenza JR, Shinjo SM, Silva JM, et al. Combined glucosamine and chondroitin sulfate, once or three times daily, provides clinically relevant analgesia in knee osteoarthritis. *Clin Rheumatol* 2015;34:1455–1462.
12. Mazieres B, Combe B, Phan Van A, et al. Chondroitin sulfate in osteoarthritis of the knee: a prospective, double-blind, placebo-controlled multicenter clinical study. *J Rheumatol* 2001;28:173–181.
13. Villacis J, Rice TR, Bucci LR, et al. Do shrimp-allergic individuals tolerate shrimp-derived glucosamine? *Clin Exper Allergy* 2006;36:1457–1461.

CASE 108: ALLERGIC RHINITIS

■ Butterbur Extract for Allergic Rhinitis

Clinical Course

James’ mother is quite concerned about drowsiness associated with prescription treatments for his symptoms because he has a tendency to nap when he is supposed to be doing homework. Mrs Patrick uses butterbur extract for migraine prophylaxis and has heard that it is effective for allergy symptoms; she asks about using the same product for James.

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?

3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient?
6. If the patient is going to use the product, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Thomet OA, Schapowal A, Heinisch IV, et al. Anti-inflammatory activity of an extract of *Petasites hybridus* in allergic rhinitis. *Int Immunopharmacol* 2002;2:997–1006.
2. Dumitru AF, Shamji M, Wagenmann M, et al. Petasol butanoate complex (Ze 339) relieves allergic rhinitis-induced nasal obstruction more effectively than desloratadine. *J Allergy Clin Immunol* 2011;127:1515–1521.
3. Lee DK, Haggart K, Robb FM, Lipworth BJ. Butterbur, a herbal remedy, confers complementary anti-inflammatory activity in asthmatic patients receiving inhaled corticosteroids. *Clin Exp Allergy* 2004;34:110–114.
4. Giles M, Ulbricht C, Khalsa KP, Kirkwood CD, Park C, Basch E. Butterbur: an evidence-based systematic review by the Natural Standard Research Collaboration. *J Herb Pharmacother* 2005;5:119–143.
5. Guo R, Pittler MH, Ernst E. Herbal medicines for the treatment of allergic rhinitis: a systematic review. *Ann Allergy Asthma Immunol* 2007;99:483–495.
6. Nebel S, Kobi C, Zahner C. Effective treatment of early allergic and late inflammatory symptoms of allergic rhinitis with Ze 339 (Tesalin®): results of a non-interventional observational study. *Planta Med* 2014;80:16.
7. Anderson N, Meier T, Borlak J. Toxicogenomics applied to cultures of human hepatocytes enabled an identification of novel *Petasites hybridus* extracts for the treatment of migraine with improved hepatobiliary safety. *Toxicol Sci* 2009;112:507–520.
8. Wang YP, Yan J, Fu PP, Chou MW. Human liver microsomal reduction of pyrrolizidine alkaloid N-oxides to form the corresponding carcinogenic parent alkaloid. *Toxicol Lett* 2005;155:411–420.

CASE 125: INFLUENZA

■ Elderberry for Influenza

Clinical Course

As Mr Kharitonov is leaving, he thanks you and promises to follow your recommendations. He does say that he is worried about making anyone else sick, because of his son's upcoming wedding; "My cousins back in Russia keep telling me they use elderberry syrup to keep from getting sick during flu season. Could that help keep my wife from getting this flu?"

■ FOLLOW-UP QUESTIONS

1. What is the known or proposed mechanism of action?
2. How extensive or conclusive are the clinical trial data on effectiveness?
3. What is known about safety?
4. Does the product have any specific quality concerns?
5. Would this be an appropriate treatment choice in this particular patient or for the patient's wife?
6. If the patient is going to use the product, what counseling information will allow him to maximize any possible benefit and minimize any harm?

REFERENCES

1. Ulbricht C, Basch E, Cheung L, et al. An evidence-based systematic review of elderberry and elderflower (*Sambucus nigra*) by the Natural Standard Research Collaboration. *J Diet Suppl* 2014;11(1):80–120.
2. Krawitz C, Abu MM, Stein M, et al. Inhibitory activity of a standardized elderberry liquid extract against clinically-relevant human respiratory bacterial pathogens and influenza A and B viruses. *BMC Complement Altern Med* 2011;11:16.
3. Kinoshita E, Hayashi K, Katayama H, et al. Anti-influenza virus effects of elderberry juice and its fractions. *Biosci Biotechnol Biochem* 2012;76(9):1633–1638.
4. Zakay-Rones Z, Varsano N, Zlotnik M, et al. Inhibition of several strains of influenza virus in vitro and reduction of symptoms by an elderberry extract (*Sambucus nigra* L.) during an outbreak of influenza B Panama. *J Altern Complement Med* 1995;1:361–369.
5. Zakay-Rones Z, Thom E, Wollan T, et al. Randomized study of the efficacy and safety of oral elderberry extract in the treatment of influenza A and B virus infections. *J Int Med Res* 2004;32:132–140.
6. Rauš K, Pleschka S, Klein P, et al. Effect of an Echinacea-based hot drink versus oseltamivir in influenza treatment: a randomized, double-blind, double-dummy, multicenter, noninferiority clinical trial. *Curr Therapeutic Res* 2015;77:66–72.
7. Hawkins J, Baker C, Cherry L, et al. Black elderberry (*Sambucus nigra*) supplementation effectively treats upper respiratory symptoms: a meta-analysis of randomized, controlled clinical trials. *Complement Ther Med* 2019;42:361–365.
8. Curtis PJ, Kroom PA, Hollands WJ, et al. Cardiovascular disease risk biomarkers and liver and kidney function are not altered in postmenopausal women after ingesting and elderberry extract rich in anthocyanins for 12 weeks. *J Nutr* 2009;139:2266–2271.

ACKNOWLEDGMENT

This updated Casebook Section is based on the previous work of Cydney E. McQueen, PharmD. The author and editors gratefully acknowledge her previous contributions to this section.

This page intentionally left blank

APPENDIX A

CONVERSION FACTORS AND ANTHROPOMETRICS*

CONVERSION FACTORS

SI Units

SI (*le Système International d'Unités*) units are used in many countries to express clinical laboratory and serum drug concentration data. Instead of employing units of mass (such as micrograms), the SI system uses moles (mol) to represent the amount of a substance. A molar solution contains 1 mol (the molecular weight of the substance in grams) of the solute in 1 L of solution. The following formula is used to convert units of mass (mcg/mL to $\mu\text{mol/L}$ or, by substitution of terms, mg/mL to mmol/L or ng/mL to nmol/L).

Micromoles per Liter ($\mu\text{mol/L}$)

$$\mu\text{mol/L} = \frac{\text{drug concentration (mcg/mL)} \times 1000}{\text{molecular weight of drug (g/mol)}}$$

Milliequivalents

An equivalent weight of a substance is that weight which will combine with or replace 1 g of hydrogen; a milliequivalent is 1/1000 of an equivalent weight.

Milliequivalents per Liter (mEq/L)

$$\text{mEq/L} = \frac{\text{weight of salt (g)} \times \text{valence of ion} \times 1000}{\text{molecular weight of salt}}$$

$$\text{weight of salt (g)} = \frac{\text{mEq/L} \times \text{molecular weight of salt}}{\text{valence of ion} \times 1000}$$

Approximate Milliequivalents

Weights of Selected Ions		
Salt	mEq/g Salt	mg Salt/mEq
Calcium carbonate (CaCO_3)	20.0	50.0
Calcium chloride ($\text{CaCl}_2 \cdot 2\text{H}_2\text{O}$)	13.6	73.5
Calcium gluceptate ($\text{Ca}[\text{C}_7\text{H}_{13}\text{O}_8]_2$)	4.1	245.2
Calcium gluconate ($\text{Ca}[\text{C}_6\text{H}_{11}\text{O}_7]_2 \cdot \text{H}_2\text{O}$)	4.5	224.1
Calcium lactate ($\text{Ca}[\text{C}_3\text{H}_5\text{O}_3]_2 \cdot 5\text{H}_2\text{O}$)	6.5	154.1
Magnesium gluconate ($\text{Mg}[\text{C}_6\text{H}_{11}\text{O}_7]_2 \cdot \text{H}_2\text{O}$)	4.6	216.3
Magnesium oxide (MgO)	49.6	20.2
Magnesium sulfate (MgSO_4)	16.6	60.2
Magnesium sulfate ($\text{MgSO}_4 \cdot 7\text{H}_2\text{O}$)	8.1	123.2
Potassium acetate ($\text{K}[\text{C}_2\text{H}_3\text{O}_2]$)	10.2	98.1
Potassium chloride (KCl)	13.4	74.6
Potassium citrate ($\text{K}_3[\text{C}_6\text{H}_5\text{O}_7] \cdot \text{H}_2\text{O}$)	9.2	108.1
Potassium iodide (KI)	6.0	166.0
Sodium acetate ($\text{Na}[\text{C}_2\text{H}_3\text{O}_2]$)	12.2	82.0
Sodium acetate ($\text{Na}[\text{C}_2\text{H}_3\text{O}_2] \cdot 3\text{H}_2\text{O}$)	7.3	136.1
Sodium bicarbonate (NaHCO_3)	11.9	84.0
Sodium chloride (NaCl)	17.1	58.4
Sodium citrate ($\text{Na}_3[\text{C}_6\text{H}_5\text{O}_7] \cdot 2\text{H}_2\text{O}$)	10.2	98.0
Sodium iodide (NaI)	6.7	149.9
Sodium lactate ($\text{Na}[\text{C}_3\text{H}_5\text{O}_3]$)	8.9	112.1
Zinc sulfate ($\text{ZnSO}_4 \cdot 7\text{H}_2\text{O}$)	7.0	143.8

Valences and Atomic Weights of Selected Ions

Substance	Electrolyte	Valence	Molecular Weight
Calcium	Ca^{2+}	2	40.1
Chloride	Cl^-	1	35.5
Magnesium	Mg^{2+}	2	24.3
Phosphate	HPO_4^- (80%)	1.8	96.0 ^a
(pH = 7.4)	H_2PO_4^- (20%)		
Potassium	K^+	1	39.1
Sodium	Na^+	1	23.0
Sulfate	SO_4^{2-}	2	96.0 ^a

^aThe molecular weight of phosphorus only is 31; that of sulfur only is 32.1.

*This appendix contains information from Appendices 1 and 2 of Anderson PO, Knoben JE, Troutman WG, et al, eds. *Handbook of Clinical Drug Data*. 10th ed. New York, NY: McGraw-Hill; 2002:1053–1058, with permission.

■ Anion Gap

The anion gap is the concentration of plasma anions not routinely measured by laboratory screening. It is useful in the evaluation of acid–base disorders. The anion gap is greater with increased plasma concentrations of endogenous species (eg, phosphate, sulfate, lactate, and ketoacids) or exogenous species (eg, salicylate, penicillin, ethylene glycol, ethanol, and methanol). The formulas for calculating the anion gap are as follows:

$$\text{Anion gap} = (\text{Na}^+ + \text{K}^+) - (\text{Cl}^- + \text{HCO}_3^-)$$

or

$$\text{Anion gap} = \text{Na}^+ - (\text{Cl}^- + \text{HCO}_3^-)$$

where the expected normal value for the first equation is 11–20 mmol/L, and the expected normal value for the second equation is 7–16 mmol/L. Note that there is a variation in the upper and lower limits of the normal range.

■ Temperature

Fahrenheit to Centigrade: $(^{\circ}\text{F} - 32) \times 5/9 = ^{\circ}\text{C}$

Centigrade to Fahrenheit: $(^{\circ}\text{C} \times 9/5) + 32 = ^{\circ}\text{F}$

Centigrade to Kelvin: $^{\circ}\text{C} + 273 = \text{K}$

■ Calories

1 calorie = 1 kilocalorie = 1000 calories = 4.184 kilojoules (kJ)

1 kilojoule = 0.239 calories = 0.239 kilocalories = 239 calories

■ Weights and Measures

Metric Weight Equivalents

1 kilogram (kg) = 1000 grams

1 gram (g) = 1000 milligrams

1 milligram (mg) = 0.001 gram

1 microgram (mcg) = 0.001 milligram

1 nanogram (ng) = 0.001 microgram

1 picogram (pg) = 0.001 nanogram

1 femtogram (fg) = 0.001 picogram

Metric Volume Equivalents

1 liter (L) = 1000 milliliters

1 deciliter (dL) = 100 milliliters

1 milliliter (mL) = 0.001 liter

1 microliter (μL) = 0.001 milliliter

1 nanoliter (nL) = 0.001 microliter

1 picoliter (pL) = 0.001 nanoliter

1 femtoliter (fL) = 0.001 picoliter

Apothecary Weight Equivalents

1 scruple (℥) = 20 grains (gr)

60 grains (gr) = 1 dram (ʒ)

8 drams (ʒ) = 1 ounce (fl ʒ)

1 ounce (ʒ) = 480 grains

12 ounces (ʒ) = 1 pound (lb)

Apothecary Volume Equivalents

60 minims (℥) = 1 fluidram (fl ʒ)

8 fluidrams (fl ʒ) = 1 fluid ounce (fl ʒ)

1 fluid ounce (fl ʒ) = 480 minims

16 fluid ounces (fl ʒ) = 1 pint (pt)

Avoirdupois Equivalents

1 ounce (oz) = 437.5 grains

16 ounces (oz) = 1 pound (lb)

Weight/Volume Equivalents

1 mg/dL = 10 mcg/mL

1 mg/dL = 1 mg%

1 ppm = 1 mg/L

Conversion Equivalents

1 gram (g) = 15.43 grains

1 grain (gr) = 64.8 milligrams

1 ounce (ʒ) = 31.1 grams

1 ounce (oz) = 28.35 grams

1 pound (lb) = 453.6 grams

1 kilogram (kg) = 2.2 pounds

1 milliliter (mL) = 16.23 minims

1 minim (℥) = 0.06 milliliter

1 fluid ounce (fl oz) = 29.57 milliliter

1 pint (pt) = 473.2 milliliter

0.1 milligram = 1/600 grain

0.12 milligram = 1/500 grain

0.15 milligram = 1/400 grain

0.2 milligram = 1/300 grain

0.3 milligram = 1/200 grain

0.4 milligram = 1/150 grain

0.5 milligram = 1/120 grain

0.6 milligram = 1/100 grain

0.8 milligram = 1/80 grain

1 milligram = 1/65 grain

Metric Length Equivalents

2.54 cm = 1 inch

30.48 cm = 1 foot

1.6 km = 1 mile

ANTHROPOMETRICS

■ Creatinine Clearance Formulas

Formulas for Estimating Creatinine Clearance in Patients With Stable Renal Function

Cockcroft–Gault Formula

Adults (age ≥18 years)¹:

$$\text{CLcr (males)} = \frac{(140 - \text{age}) \times \text{weight}}{\text{Cr}_s \times 72}$$

$$\text{CLcr (males)} = 0.85 \times \text{above value}^\dagger$$

where CLcr is creatinine clearance (in mL/min), Cr_s is serum creatinine (in mg/dL), age is in years, and weight is in kilograms.

Children (age 1–18 years)²:

$$\text{CLcr} = \frac{0.48 \times \text{height} \times \text{BSA}}{\text{Cr}_s \times 1.73}$$

where BSA is body surface area (in m²), CLcr is creatinine clearance (in mL/min), Cr_s is serum creatinine (in mg/dL), and height is in centimeters.

[†]Some studies suggest that the predictive accuracy of this formula for women is better without the correction factor of 0.85.

Formula for Estimating Creatinine Clearance From a Measured Urine Collection

$$\text{CLcr (mL/minute)} = \frac{U \times V^{\ddagger}}{P \times T}$$

where U is the concentration of creatinine in a urine specimen (in same units as P), V is the volume of urine (in mL), P is the concentration of creatinine in serum at the midpoint of the urine collection period (in same units as U), and T is the time of the urine collection period in minutes (eg, 6 hours = 360 minutes; 24 hours = 1440 minutes).

MDRD Formula for Estimating Glomerular Filtration Rate (From the Modification of Diet in Renal Disease Study)³

Conventional calibration MDRD equation (used only with those creatinine methods that have not been recalibrated to be traceable to isotope dilution mass spectrometry [IDMS]).

For creatinine in mg/dL:

$$X = 186 \times \text{creatinine}^{-1.154} \times \text{age}^{-0.203} \times \text{constant}$$

For creatinine in $\mu\text{mol/L}$:

$$X = 32,788 \times \text{creatinine}^{-1.154} \times \text{age}^{-0.203} \times \text{constant}$$

where X is the glomerular filtration rate (GFR), constant for white males is 1 and for females is 0.742, and constant for African Americans is 1.21. Creatinine levels in $\mu\text{mol/L}$ can be converted to mg/dL by dividing by 88.4.

IDMS-Traceable MDRD Equation (Used Only With Creatinine Methods That Have Been Recalibrated to Be Traceable to IDMS)

For creatinine in mg/dL:

$$X = 175 \times \text{creatinine}^{-1.154} \times \text{age}^{-0.203} \times \text{constant}$$

For creatinine in $\mu\text{mol/L}$:

$$X = 175 \times (\text{creatinine}/88.4)^{-1.154} \times \text{age}^{-0.203} \times \text{constant}$$

where X is the glomerular filtration rate (GFR), constant for white males is 1 and for females is 0.742, and constant for African Americans is 1.21.

■ Ideal Body Weight (IBW)

IBW is the weight expected for a nonobese person of a given height. The following IBW formulas and various life insurance tables can be used to estimate IBW. Dosing methods described in the literature may use IBW as a method in dosing obese patients.

Adults (age ≥ 18 years)⁴:

$$\text{IBW (males)} = 50 + (2.3 \times \text{height in inches over 5 ft})$$

$$\text{IBW (females)} = 45.5 + (2.3 \times \text{height in inches over 5 ft})$$

where IBW is in kilograms.

Children (age 1–18 years)²:

Under 5 feet tall:

$$\text{IBW} = \frac{\text{height}^2 \times 1.65}{1000}$$

where IBW is in kilograms and height is in centimeters.

Five feet or taller:

$$\text{IBW (males)} = 39 + (2.27 \times \text{height in inches over 5 ft})$$

$$\text{IBW (females)} = 42.2 + (2.27 \times \text{height in inches over 5 ft})$$

where IBW is in kilograms.

REFERENCES

1. Cockcroft DW, Gault MH. Prediction of creatinine clearance from serum creatinine. *Nephron* 1976;16:31–41.
2. Traub SI, Johnson CE. Comparison of methods of estimating creatinine clearance in children. *Am J Hosp Pharm* 1980;37:195–201.
3. Levey AS, Bosch JP, Lewis JB, et al. A more accurate method to estimate glomerular filtration rate from serum creatinine: a new prediction equation. Modification of Diet in Renal Disease Study Group. *Ann Intern Med* 1999;130:461–470.
4. Devine BJ. Gentamicin therapy. *Drug Intell Clin Pharm* 1974;8:650–655.

[‡]The product of $U \times V$ equals the production of creatinine during the collection period and, at steady state, should equal 20–25 mg/kg per day for ideal body weight (IBW) in males and 15–20 mg/kg per day for IBW in females. If it is less than this, inadequate urine collection may have occurred and CLcr will be underestimated.

This page intentionally left blank

APPENDIX B

COMMON LABORATORY TESTS

The following table is an alphabetical listing of some common laboratory tests and their reference ranges for adults as measured in plasma or serum (unless otherwise indicated). Reference values differ among laboratories, so readers should refer to the published reference ranges used in each institution. For some tests, both SI units and conventional units are reported.

Laboratory	Conventional Units	Conversion Factor	SI Units
Acid phosphatase			
Male	2–12 units/L	16.7	33–200 nkat/L
Female	0.3–9.2 units/L	16.7	5–154 nkat/L
Activated partial thromboplastin time (aPTT)	25–40 sec		
Adrenocorticotrophic hormone (ACTH)	15–80 pg/mL or ng/L	0.2202	3.3–17.6 pmol/L
Alanine aminotransferase (ALT, SGPT)	7–53 IU/L	0.01667	0.12–0.88 μ kat/L
Albumin	3.5–5.0 g/dL	10	35–50 g/L
Albumin:creatinine ratio (urine)			
Normal	<30 mg/g creatinine		
Microalbuminuria	30–300 mg/g creatinine		
Proteinuria	>300 mg/g creatinine		
or	or		
Normal			
Male	<2.0 mg/mmol creatinine		
Female	<2.8 mg/mmol creatinine		
Microalbuminuria			
Male	2.0–20 mg/mmol creatinine		
Female	2.8–28 mg/mmol creatinine		
Proteinuria			
Male	>20 mg/mmol creatinine		
Female	>28 mg/mmol creatinine		
Aldosterone			
Supine	<16 ng/dL	27.7	<444 pmol/L
Upright	<31 ng/dL	27.7	<860 pmol/L
Alkaline phosphatase			
10–15 years	130–550 IU/L	0.01667	2.17–9.17 μ kat/L
16–20 years	70–260 IU/L	0.01667	1.17–4.33 μ kat/L
>20 years	38–126 IU/L	0.01667	0.13–2.10 μ kat/L
Alpha-fetoprotein (AFP)	<15 ng/mL	1	<15 mcg/L
Alpha ₁ -antitrypsin	80–200 mg/dL	0.01	0.8–2.0 g/L
Amikacin, therapeutic	15–30 mg/L peak	1.71	25.6–51.3 μ mol/L peak
	$\leq$ 8 mg/L trough		$\leq$ 13.7 μ mol/L trough
Amitriptyline	80–200 ng/mL or mcg/L	3.4	272–680 nmol/L
Ammonia (plasma)	15.33–56.20 mcg NH ₃ /dL	0.5872	9–33 μ mol NH ₃ /L
Amylase	25–115 IU/L	0.01667	0.42–1.92 kat/L
Androstenedione	50–250 ng/dL	0.0349	1.7–8.7 nmol/L
Angiotensin-converting enzyme	15–70 units/L	16.67	250–1,167 nkat/L
Anion gap	7–16 mEq/L	1	7–16 mmol/L
Anti-double-stranded DNA (anti-ds DNA)	Negative		
Anti-HAV	Negative		
Anti-HBc	Negative		
Anti-HBs	Negative		
Anti-HCV	Negative		
Anti-Sm antibody	Negative		
Antinuclear antibody (ANA)	Negative		
Apolipoprotein A-1			
Male	95–175 mg/dL	0.01	0.95–1.75 g/L
Female	100–200 mg/dL	0.01	1.0–2.0 g/L
Apolipoprotein B			
Male	50–110 mg/dL	0.01	0.5–1.10 g/L
Female	50–105 mg/dL	0.01	0.5–1.05 g/L

(continued)

Laboratory	Conventional Units	Conversion Factor	SI Units
Aspartate aminotransferase (AST, SGOT)	11–47 IU/L	0.01667	0.18–0.78 μ kat/L
Beta ₂ -microglobulin	<0.2 mg/dL	10	2 mg/L
Bicarbonate	22–26 mEq/L	1	22–26 mmol/L
Bilirubin			
Total	0.3–1.1 mg/dL	17.1	5.13–18.80 μ mol/L
Direct	0–0.3 mg/dL	17.1	0–5.1 μ mol/L
Indirect	0.1–1.0 mg/dL	17.1	1.71–17.1 μ mol/L
Bleeding time	3–7 min		
Blood gases (arterial)			
pH	7.35–7.45	1	7.35–7.45
PaO ₂	80–105 mm Hg	0.133	10.6–14.0 kPa
PaCO ₂	35–45 mm Hg	0.133	4.7–6.0 kPa
HCO ₃	22–26 mEq/L	1	22–26 mmol/L
O ₂ saturation	≥95%	0.01	0.95
Blood urea nitrogen	8–25 mg/dL	0.357	2.9–8.9 mmol/L
B-type natriuretic peptide (BNP)	0–99 pg/mL	1	0–99 ng/L
BUN-to-creatinine ratio	10:1 to 20:1		
C-peptide	0.51–2.70 ng/mL	330	170–900 pmol/L or
		0.33	0.172–0.900 nmol/L
C-reactive protein	<0.8 mg/dL	10	<8 mg/L
CA-125	<35 units/mL	1	<35 kilounits/L
CA 15-3	<30 units/mL	1	<30 kilounits/L
CA 19-9	<37 units/mL	1	<37 kilounits/L
CA 27-29	<38 units/mL	1	<38 kilounits/L
Calcium			
Total	8.6–10.3 mg/dL	0.25	2.15–2.58 mmol/L
	4.3–5.16 mEq/L	0.50	2.15–2.58 mmol/L
Ionized	4.5–5.1 mg/dL	0.25	1.13–1.28 mmol/L
	2.26–2.56 mEq/L	0.50	1.13–1.28 mmol/L
Carbamazepine, therapeutic	4–12 mg/L	4.23	17–51 μ mol/L
Carboxyhemoglobin (nonsmoker)	<2%	0.01	<0.02
Carcinoembryonic antigen (CEA)			
Nonsmoker	<2.5 ng/mL	1	<2.5 mcg/L
Smoker	<5 ng/mL		<5 mcg/L
Cardiac troponin I (see troponin I)	Variable ng/mL	1	Variable mcg/L
CD4 lymphocyte count	31–61% of total lymphocytes		
CD8 lymphocyte count	18–39% of total lymphocytes		
Cerebrospinal fluid (CSF)			
Pressure	75–175 mm H ₂ O		
Glucose	40–70 mg/dL	0.0555	2.2–3.9 mmol/L
Protein	15–45 mg/dL	0.01	0.15–0.45 g/L
WBC	<10/mm ³		
Ceruloplasmin	18–45 mg/dL	10	180–450 mg/L
		0.063	1.1–2.8 μ mol/L
Chloride	97–110 mEq/L	1	97–110 mmol/L
Cholesterol			
Desirable	<200 mg/dL	0.0259	<5.18 mmol/L
Borderline high	200–239 mg/dL	0.0259	5.18–6.19 mmol/L
High	≥240 mg/dL	0.0259	≥6.2 mmol/L
β-Human chorionic gonadotropin (β-hCG)	<5 milliunits/mL	1	<5 units/L
Clozapine	Minimum trough 300–350 ng/mL or mcg/L	3.06	918–1,071 nmol/L
CO ₂ content	22–30 mEq/L	1	22–30 mmol/L
Complement component 3 (C3)	70–160 mg/dL	0.01	0.7–1.6 g/L
Complement component 4 (C4)	20–40 mg/dL	0.01	0.2–0.4 g/L
Copper	70–150 mcg/dL	0.157	11–24 μ mol/L
Cortisol (fasting, morning)	5–25 mcg/dL	27.6	138–690 nmol/L
Cortisol (free, urinary)	10–100 mcg/day	2.76	28–276 nmol/day
Creatine kinase			
Male	30–200 IU/L	0.01667	0.50–3.33 μ kat/L
Female	20–170 IU/L	0.01667	0.33–2.83 μ kat/L
MB fraction	0–7 IU/L	0.01667	0.0–0.12 μ kat/L
Creatinine clearance (CLcr) (urine)	85–135 mL/min/1.73 m ²	0.00963	0.82–1.3 mL/sec/m ²
Creatinine			
Male 4–20 years	0.2–1.0 mg/dL	88.4	18–88 μ mol/L
Female 4–20 years	0.2–1.0 mg/dL	88.4	18–88 μ mol/L
Male (adults)	0.7–1.3 mg/dL	88.4	62–115 μ mol/L
Female (adults)	0.6–1.1 mg/dL	88.4	53–97 μ mol/L

(continued)

Laboratory	Conventional Units	Conversion Factor	SI Units
Cyclosporine			
Renal transplant	100–300 ng/mL or mcg/L	0.832	83–250 nmol/L
Cardiac, liver, or pancreatic transplant	200–350 ng/mL or mcg/L	0.832	166–291 nmol/L
Cryptococcal antigen	Negative		
D-dimers	<250 ng/mL	1	<250 mcg/L
Desipramine	75–300 ng/mL or mcg/L	3.75	281–1125 nmol/L
Dexamethasone suppression test (DST) (overnight)	8:00 AM cortisol <5 mcg/dL	0.0276	<0.14 µmol/L
DHEAS			
Male	170–670 mcg/dL	0.0271	4.6–18.2 µmol/L
Female			
Premenopausal	50–540 mcg/dL	0.0271	1.4–14.7 µmol/L
Postmenopausal	30–260 mcg/dL	0.0271	0.8–7.1 µmol/L
Digoxin, therapeutic	0.5–1.0 ng/mL or mcg/L	1.28	0.6–1.3 nmol/L
Erythrocyte count (blood) See under red blood cell count			
Erythrocyte sedimentation rate (ESR)			
Westergren			
Male	0–20 mm/hr		
Female	0–30 mm/hr		
Wintrobe			
Male	0–9 mm/hr		
Female	0–15 mm/hr		
Erythropoietin	2–25 mIU/mL	1	2–25 IU/L
Estradiol			
Male	10–36 pg/mL	3.67	37–132 pmol/L
Female	34–170 pg/mL	3.67	125–624 pmol/L
Ethanol, legal intoxication	≥50–100 mg/dL	0.217	10.9–21.7 mmol/L
	≥0.05–0.1%	217	
Ethosuximide, therapeutic	40–100 mg/L or mcg/mL	7.08	283–708 µmol/L
Factor VIII or factor IX			
Severe hemophilia	<1 IU/dL	0.01	<0.01 units/mL
Moderate hemophilia	1–5 IU/dL	0.01	0.01–0.05 units/mL
Mild hemophilia	>5 IU/dL	0.01	>0.05 units/mL
Usual adult levels	60–140 IU/dL	0.01	0.60–1.40 units/mL
Ferritin			
Male	20–250 ng/mL	1	20–250 mcg/L
Female	10–150 ng/mL	1	10–150 mcg/L
Fibrin degradation products (FDP)	2–10 mg/L		
Fibrinogen	200–400 mg/dL	0.01	2.0–4.0 g/L
Folate (plasma)	3.1–12.4 ng/mL	2.266	7.0–28.1 nmol/L
Folic acid (RBC)	125–600 ng/mL	2.266	283–1360 nmol/L
Follicle-stimulating hormone (FSH)			
Male	1–7 mIU/mL	1	1–7 IU/L
Female			
Follicular phase	1–9 mIU/mL	1	1–9 IU/L
Midcycle	6–26 mIU/mL	1	6–26 IU/L
Luteal phase	1–9 mIU/mL	1	1–9 IU/L
Postmenopausal	30–118 mIU/mL	1	30–118 IU/L
Free thyroxine index (FT ₄ I)	6.5–12.5		
Gamma glutamyl transferase (GGT)	0–30 IU/L	0.01667	0–0.5 µkat/L
Gastrin (fasting)	0–130 pg/mL	1	0–130 ng/L
Gentamicin, therapeutic	4–10 mg/L peak	2.09	8.4–21.0 µmol/L peak
	≤2 mg/L trough		≤4.2 µmol/L trough
Globulin	2.3–3.5 g/dL	10	23–35 g/L
Glucose (fasting, plasma)	65–109 mg/dL	0.0555	3.6–6.0 mmol/L
Glucose, 2-hr postprandial blood (PPBG)	<140 mg/dL	0.0555	<7.8 mmol/L
Granulocyte count	1.8–6.6 × 10 ³ /µL	10 ⁶	1.8–6.6 × 10 ⁹ /L
Growth hormone (fasting)			
Male	<5 ng/mL	1	<5 mcg/L
Female	<10 ng/mL	1	<10 mcg/L
Haptoglobin	60–270 mg/dL	0.01	0.6–2.7 g/L
HBeAg	Negative		
HBsAg	Negative		
HBV DNA	Negative		
Hematocrit			
Male	40.7–50.3%	0.01	0.407–0.503
Female	36.1–44.3%	0.01	0.361–0.443

(continued)

Laboratory	Conventional Units	Conversion Factor	SI Units
Hemoglobin (blood)			
Male	13.8–17.2 g/dL	10	138–172 g/L
		Alternative SI: 0.62	8.56–10.67 mmol/L
Female	12.1–15.1 g/dL	10	121–151 g/L
		Alternative SI: 0.62	7.5–9.36 mmol/L
Hemoglobin A _{1c}	4.0–6.0%	0.01	0.04–0.06
Heparin			
Via protamine titration method	0.2–0.4 mcg/mL		
Via anti-factor Xa assay	0.3–0.7 mcg/mL		
High-density lipoprotein (HDL) cholesterol	>35 mg/dL	0.0259	>0.91 mmol/L
Homocysteine	3.3–10.4 µmol/L		
Ibuprofen			
Therapeutic	10–50 mcg/mL	4.85	49–243 µmol/L
Toxic	100–700 mcg/mL or greater	4.85	485–3395 µmol/L or greater
Imipramine, therapeutic	100–300 ng/mL or mcg/L	3.57	357–1071 nmol/L
Immunoglobulin A (IgA)	85–385 mg/dL	0.01	0.85–3.85 g/L
Immunoglobulin G (IgG)	565–1765 mg/dL	0.01	5.65–17.65 g/L
Immunoglobulin M (IgM)	53–375 mg/dL	0.01	0.53–3.75 g/L
Insulin (fasting)	2–20 microunits/mL or milliunits/L	7.175	14.35–143.5 pmol/L
International normalized ratio (INR), therapeutic	2.0–3.0 (2.5–3.5 for some indications)		
Iron			
Male	45–160 mcg/dL	0.179	8.1–31.3 µmol/L
Female	30–160 mcg/dL	0.179	5.4–31.3 µmol/L
Iron-binding capacity (total)	220–420 mcg/dL	0.179	39.4–75.2 µmol/L
Iron saturation	15–50%	0.01	0.15–0.50
Lactate (plasma)	0.7–2.1 mEq/L	1	0.7–2.1 mmol/L
	6.3–18.9 mg/dL	0.111	
Lactate dehydrogenase	100–250 IU/L	0.01667	1.67–4.17 µkat/L
Lead	<25 mcg/dL	0.0483	<1.21 µmol/L
Leukocyte count	3.8–9.8 × 10 ³ /µL	10 ⁶	3.8–9.8 × 10 ⁹ /L
Lidocaine, therapeutic	1.5–6.0 mcg/mL or mg/L	4.27	6.4–25.6 µmol/L
Lipase	<100 IU/L	0.01667	1.7 µkat/L
Lithium, therapeutic	0.5–1.25 mEq/L	1	0.5–1.25 mmol/L
Low-density lipoprotein (LDL) cholesterol			
Desirable	<130 mg/dL	0.0259	<3.36 mmol/L
Borderline high risk	130–159 mg/dL	0.0259	3.36–4.11 mmol/L
High risk	≥160 mg/dL	0.0259	≥4.13 mmol/L
Luteinizing hormone (LH)			
Male	1–8 milliunits/mL	1	1–8 units/L
Female			
Follicular phase	1–12 milliunits/mL	1	1–12 units/L
Midcycle	16–104 milliunits/mL	1	16–104 units/L
Luteal phase	1–12 milliunits/mL	1	1–12 units/L
Postmenopausal	16–66 milliunits/mL	1	16–66 units/L
Lymphocyte count	1.2–3.3 × 10 ³ /µL	10 ⁶	1.2–3.3 × 10 ⁹ /L
Magnesium	1.3–2.2 mEq/L	0.5	0.65–1.10 mmol/L
	1.58–2.68 mg/dL	0.411	0.65–1.10 mmol/L
Mean corpuscular volume	80.0–97.6 µm ³	1	80.0–97.6 fL
Mononuclear cell count	0.2–0.7 × 10 ³ /µL	10 ⁶	0.2–0.7 × 10 ⁹ /L
Nortriptyline, therapeutic	50–150 ng/mL or mcg/L	3.8	190–570 nmol/L
NT-ProBNP (see Pro-BNP)			
Osmolality (serum)	275–300 mOsm/kg	1	275–300 mmol/kg
Osmolality (urine)	250–900 mOsm/kg	1	250–900 mmol/kg
Parathyroid hormone (PTH), intact	10–60 pg/mL or ng/L	0.107	1.1–6.4 pmol/L
Parathyroid hormone (PTH), N-terminal	8–24 pg/mL or ng/L		
Parathyroid hormone (PTH), C-terminal	50–330 pg/mL or ng/L		
Phenobarbital, therapeutic	15–40 mcg/mL or mg/L	4.31	65–172 µmol/L
Phenytoin, therapeutic	10–20 mcg/mL or mg/L	3.96	40–79 µmol/L
Phosphate	2.5–4.5 mg/dL	0.323	0.81–1.45 mmol/L
Platelet count	140–440 × 10 ³ /µL	10 ⁶	140–440 × 10 ⁹ /L
Potassium (plasma)	3.3–4.9 mEq/L	1	3.3–4.9 µmol/L
Prealbumin (adult)	19.5–35.8 mg/dL	10	195–358 mg/L
Primidone, therapeutic	5–12 mcg/mL or mg/L	4.58	23–55 µmol/L
ProBNP	<125 pg/mL or ng/L	0.118	<14.75 pmol/L
Procainamide, therapeutic	4–10 mcg/mL or mg/L	4.23	17–42 µmol/L

(continued)

Laboratory	Conventional Units	Conversion Factor	SI Units
Progesterone			
Male	13–97 ng/dL	0.0318	0.4–3.1 nmol/L
Female			
Follicular phase	15–70 ng/dL		0.5–2.2 nmol/L
Luteal phase	200–2500 ng/dL		6.4–79.5 nmol/L
Prolactin	<20 ng/mL	1	<20 mcg/L
Prostate-specific antigen (PSA)	<4 ng/mL	1	<4 mcg/L
Protein, total	6.0–8.0 g/dL	10	60–80 g/L
Prothrombin time (PT)	10–12 sec		
Quinidine, therapeutic	2–5 mcg/mL or mg/L	3.08	6.2–15.4 µmol/L
Radioactive iodine uptake (RAIU)	<6% in 2 hr		
Red blood cell (RBC) count (blood)			
Male	4–6.2 × 10 ⁶ /µL	10 ⁶	4–6.2 × 10 ¹² /L
Female	4–6.2 × 10 ⁶ /µL	10 ⁶	4–6.2 × 10 ¹² /L
Pregnant			
Trimester 1	4–5 × 10 ⁶ /µL	10 ⁶	4–5 × 10 ¹² /L
Trimester 2	3.2–4.5 × 10 ⁶ /µL	10 ⁶	3.2–4.5 × 10 ¹² /L
Trimester 3	3.0–4.9 × 10 ⁶ /µL	10 ⁶	3.0–4.9 × 10 ¹² /L
Postpartum	3.2–5 × 10 ⁶ /µL	10 ⁶	3.2–5.0 × 10 ⁶ /L
Red blood cell distribution width (RDW)	11.5–14.5%	0.01	0.115–0.145
Reticulocyte count			
Male	0.5–1.5% of total RBC count	0.01	0.005–0.015
Female	0.5–2.5% of total RBC count	0.01	0.005–0.025
Retinol-binding protein (RBP)	2.7–7.6 mg/dL	10	27–76 mg/L
Rheumatoid factor (RF) titer	Negative		
Salicylate, therapeutic	150–300 mcg/mL or mg/L	0.00724	1.09–2.17 mmol/L
	15–30 mg/dL	0.0724	
Sodium	135–145 mEq/L	1	135–145 mmol/L
Tacrolimus			
Renal transplant	6–12 ng/mL or mcg/L		
Liver transplant	4–10 ng/mL or mcg/L		
Pancreatic transplant	10–18 ng/mL or mcg/L		
Bone marrow transplant	10–20 ng/mL or mcg/L		
Testosterone (total)			
Men	300–950 ng/dL	0.0347	10.4–33.0 nmol/L
Women	20–80 ng/dL		0.7–2.8 nmol/L
Testosterone (free)			
Men	9–30 ng/dL	0.0347	0.31–1.04 nmol/L
Women	0.3–1.9 ng/dL		0.01–0.07 nmol/L
Theophylline			
Therapeutic	5–15 mcg/mL or mg/L	5.55	28–83 µmol/L
Toxic	20 or greater mcg/mL or mg/L	5.55	111 or greater µmol/L
Thrombin time	20–24 sec		
Thyroglobulin	<42 ng/mL	1	<42 mcg/L
Thyroglobulin antibodies	Negative		
Thyroxine-binding globulin (TBG)	1.2–2.5 mg/dL	10	12–25 mcg/L
Thyroid-stimulating hormone (TSH)	0.35–6.20 microunits/mL	1	0.35–6.20 milliunits/L
TSH receptor antibodies (TSH Rab)	0–1 unit/mL		
Thyroxine (T ₄)			
Total	4.5–12.0 mcg/dL	12.87	58–155 nmol/L
Free	0.7–1.9 ng/dL	12.87	9.0–24.5 pmol/L
Thyroxine index, free (FT ₄ I)	6.5–12.5		
TIBC, see Iron-binding capacity (total)			
Tobramycin, therapeutic	4–10 mcg/mL or mg/L peak	2.14	8.6–21.4 µmol/L
	≤2 mcg/mL mg/L trough	2.14	≤4.28 µmol/L
Transferrin	200–430 mg/dL	0.01	2.0–4.3 g/L
Transferrin saturation	30–50%	0.01	0.30–0.50
Triglycerides (fasting)	<160 mg/dL	0.0113	<1.8 mmol/L
Triiodothyronine (T ₃)	45–132 ng/dL	0.0154	0.91–2.70 nmol/L
Triiodothyronine (T ₃) resin uptake	25–35%		
Troponin I	<0.6 ng/mL	1	<0.6 g/L
Uric acid	3–8 mg/dL	59.48	179–476 µmol/L
Urinalysis (urine)			
pH	4.8–8.0		
Specific gravity	1.005–1.030		

(continued)

Laboratory	Conventional Units	Conversion Factor	SI Units
Protein	Negative		
Glucose	Negative		
Ketones	Negative		
RBC	1–2 per low-power field		
WBC	3–4 per low-power field		
Valproic acid, therapeutic	50–100 mcg/mL or mg/L	6.93	346–693 µmol/L
Vancomycin, therapeutic trough for CNS infections	20–40 mcg/mL or mg/L peak	0.690	14–28 µmol/L peak
	5–20 mcg/mL or mg/L trough	0.690	3–14 µmol/L trough
	15–20 mcg/mL or mg/L trough	0.690	10–14 µmol/L trough
Vitamin A (retinol)	30–95 mcg/dL	0.0349	1.05–3.32 µmol/L
Vitamin B ₁₂	180–1000 pg/mL	0.738	133–738 pmol/L
Vitamin D ₃ , 1,25-dihydroxy	20–76 pg/mL	2.4	48–182 pmol/L
Vitamin D ₃ , 25-hydroxy	10–50 ng/mL	2.496	25–125 nmol/L
Vitamin E (alpha tocopherol)	0.5–2.0 mg/dL	23.22	12–46 µmol/L
WBC count	4–10 × 10 ³ /µL or 4–10 × 10 ³ /mm ³	10 ⁶	4–10 × 10 ⁹ /L
WBC differential (peripheral blood)			
Polymorphonuclear neutrophils (PMNs)	50–65%		
Bands	0–5%		
Eosinophils	0–3%		
Basophils	1–3%		
Lymphocytes	25–35%		
Monocytes	2–6%		
WBC differential (bone marrow)			
Polymorphonuclear neutrophils (PMNs)	3–11%		
Bands	9–15%		
Metamyelocytes	9–25%		
Myelocytes	8–16%		
Promyelocytes	1–8%		
Myeloblasts	0–5%		
Eosinophils	1–5%		
Basophils	0–1%		
Lymphocytes	11–23%		
Monocytes	0–1%		
Zinc	60–150 mcg/dL	0.153	9.2–23.0 µmol/L

This table was reprinted with permission from: Chisholm-Burns MA, Wells BG, Schwinghammer TL, et al, eds. *Pharmacotherapy Principles and Practice*. New York, NY: McGraw-Hill; 2008.

APPENDIX C

PART I: COMMON MEDICAL ABBREVIATIONS

Note: Many of the medical abbreviations contained in Part I of this appendix are used in the Casebook. A more extensive list of abbreviations is available on the Internet at www.medilexicon.com and other sites.

A&O	Alert and oriented	Afeb	Afebrile
A&P	Auscultation and percussion; anterior and posterior; assessment and plan	AFP	α -Fetoprotein
A&W	Alive and well	A/G	Albumin–globulin ratio
A _{1C}	Hemoglobin A _{1C}	AGA	American Gastroenterological Association
aa	Of each (<i>ana</i>)	AGE	Acute viral gastroenteritis
AA	Aplastic anemia; Alcoholics Anonymous	AHA	American Heart Association
AAA	Abdominal aortic aneurysm	AI	Aortic insufficiency
AAL	Anterior axillary line	AIDS	Acquired immunodeficiency syndrome
AAO	Awake, alert, and oriented	AKA	Above-knee amputation; alcoholic ketoacidosis; all known allergies; also known as
AAP	American Academy of Pediatrics	AKI	Acute kidney injury
ABC	Absolute band count; absolute basophil count; aspiration, biopsy, and cytology; artificial β -cells	ALD	Alcoholic liver disease
Abd	Abdomen	ALFT	Abnormal liver function test
ABG	Arterial blood gases	ALK	Anaplastic lymphoma kinase
ABI	Ankle brachial index	ALL	Acute lymphocytic leukemia; acute lymphoblastic leukemia
ABP	Arterial blood pressure	ALP	Alkaline phosphatase
ABW	Actual body weight	ALS	Amyotrophic lateral sclerosis
ABx	Antibiotics	ALT	Alanine aminotransferase
AC	Before meals (<i>ante cibos</i>)	AMA	Against medical advice; American Medical Association; antimitochondrial antibody
ACC	American College of Cardiology	AMI	Acute myocardial infarction
ACE	Angiotensin-converting enzyme	AML	Acute myelogenous leukemia
ACEI	Angiotensin-converting enzyme inhibitor	Amp	Ampule
ACG	American College of Gastroenterology	AMPA	α -amino-3-hydroxy-5-methyl-4-isoxazolepropionic acid
ACL	Anterior cruciate ligament	ANA	Antinuclear antibody
ACLS	Advanced cardiac life support	ANC	Absolute neutrophil count
ACR	Albumin:creatinine ratio; American College of Rheumatology	ANLL	Acute nonlymphocytic leukemia
ACS	Acute coronary syndrome	Anti-CCP	Anticyclic citrullinated peptide
ACT	Activated clotting time	AODM	Adult-onset diabetes mellitus
ACTH	Adrenocorticotrophic hormone	A&O $\times$ 3	Awake and oriented to person, place, and time
AD	Alzheimer disease, right ear (<i>auris dextra</i>)	A&O $\times$ 4	Awake and oriented to person, place, time, and situation
ADA	American Diabetes Association; adenosine deaminase	AOM	Acute otitis media
ADE	Adverse drug effect (or event)	AP	Anteroposterior
ADH	Antidiuretic hormone	APACHE	Acute Physiology and Chronic Health Evaluation
ADHD	Attention-deficit hyperactivity disorder	APAP	Acetaminophen (<i>N</i> -acetyl- <i>p</i> -aminophenol)
ADL	Activities of daily living	aPTT	Activated partial thromboplastin time
ADR	Adverse drug reaction	ARB	Angiotensin receptor blocker
AED	Antiepileptic drug(s)	ARC	AIDS-related complex
AF	Atrial fibrillation	ARDS	Adult respiratory distress syndrome
AFB	Acid-fast bacillus; aortofemoral bypass; aspirated foreign body	ARF	Acute renal failure; acute respiratory failure; acute rheumatic fever

AROM	Active range of motion	BTFS	Breast tumor frozen section
AS	Left ear (<i>auris sinistra</i>)	BUN	Blood urea nitrogen
ASA	Aspirin (acetylsalicylic acid)	BV	Bacterial vaginosis
ASCVD	Atherosclerotic cardiovascular disease	Bx	Biopsy
ASD	Atrial septal defect	C&S	Culture and sensitivity
ASH	Asymmetric septal hypertrophy	CA	Cancer; calcium
ASHD	Arteriosclerotic heart disease	CABG	Coronary artery bypass graft
AST	Aspartate aminotransferase	CAD	Coronary artery disease
ATG	Antithymocyte globulin	CAH	Chronic active hepatitis
ATN	Acute tubular necrosis	CAM	Complementary and alternative medicine
AU	Each ear (<i>auris uterque</i>)	CAM-ICU	Confusion Assessment Method for the ICU
AV	Arteriovenous; atrioventricular	CAP	Community-acquired pneumonia
AVM	Arteriovenous malformation	CAPD	Continuous ambulatory peritoneal dialysis
AVR	Aortic valve replacement	CAT	COPD Assessment Test
AWMI	Anterior wall myocardial infarction	CBC	Complete blood count
BAC	Blood alcohol concentration	CBD	Common bile duct
BAL	Bronchioalveolar lavage	CBF	Cerebral blood flow
BBB	Bundle branch block; blood–brain barrier	CBG	Capillary blood gas; corticosteroid binding globulin
BC	Blood culture	CBT	Cognitive-behavioral therapy
BCACP	Board Certified Ambulatory Care Pharmacist	CC	Chief complaint
BCG	Bacillus Calmette Guerin	CCA	Calcium channel antagonist
BCL	B-cell lymphoma	CCB	Calcium channel blocker
BCNP	Board Certified Nuclear Pharmacist	CCE	Clubbing, cyanosis, edema
BCNSP	Board Certified Nutrition Support Pharmacist	CCK	Cholecystokinin
BCNU	Carmustine	CCMS	Clean catch midstream
BCOP	Board Certified Oncology Pharmacist	CCNU	Lomustine
BCP	Birth control pill	CCPD	Continuous cycling peritoneal dialysis
BCPP	Board Certified Psychiatric Pharmacist	CCT	Central corneal thickness
BCPS	Board Certified Pharmacotherapy Specialist	CCU	Coronary care unit
BCR-ABL	Breakpoint cluster region-Abelson	CD	Crohn disease
BE	Barium enema	CDAD	<i>Clostridium difficile</i> –associated diarrhea
BID	Twice daily (<i>bis in die</i>)	CDC	Centers for Disease Control and Prevention
BIS	Bispectral index	CEA	Carcinoembryonic antigen
BKA	Below-knee amputation	CF	Cystic fibrosis
BM	Bone marrow; bowel movement	CFS	Chronic fatigue syndrome
BMC	Bone marrow cells	CFU	Colony-forming unit
BMD	Bone mineral density	CHB	Chronic hepatitis B
BMR	Basal metabolic rate	CHC	Combined hormonal contraceptives
BMT	Bone marrow transplantation	CHD	Coronary heart disease
BNP	Brain natriuretic peptide	CHF	Congestive heart failure
BOO	Bladder outlet obstruction	CHO	Carbohydrate
BP	Blood pressure	CHOP	Cyclophosphamide, hydroxydaunorubicin (doxorubicin), Oncovin (vincristine), prednisone
BPD	Bronchopulmonary dysplasia	CI	Cardiac index
BPH	Benign prostatic hyperplasia	CIVI	Continuous intravenous infusion
bpm	Beats per minute	CK	Creatine kinase
BPRS	Brief Psychiatric Rating Scale	CKD	Chronic kidney disease
BPS	Behavior-based pain scale	CKD-EPI	Chronic Kidney Disease—Epidemiology Collaboration
BR	Bedrest	CKD-MBD	Chronic kidney disease—mineral and bone disorder
BRBPR	Bright red blood per rectum	CLcr	Creatinine clearance
BRM	Biological response modifier	CLL	Chronic lymphocytic leukemia
BRP	Bathroom privileges	CM	Costal margin
BS	Bowel sounds; breath sounds; blood sugar		
BSA	Body surface area		
BSO	Bilateral salpingo-oophorectomy		

CMG	Cystometrogram	DBP	Diastolic blood pressure
CML	Chronic myelogenous leukemia	D/C	Discontinue; discharge
CMRO ₂	Cerebral metabolic rate of oxygen	DCC	Direct current cardioversion
CMV	Cytomegalovirus	ddC	Zalcitabine
CN	Cranial nerve	ddI	Didanosine
CNCP	Chronic non-cancer pain	DES	Diethylstilbestrol
CNS	Central nervous system	DEXA	Dual-energy x-ray absorptiometry
c/o	Complains of	DI	Diabetes insipidus
CO	Cardiac output; carbon monoxide	DIC	Disseminated intravascular coagulation
COC	Combined oral contraceptive	Diff	Differential
COLD	Chronic obstructive lung disease	DIOS	Distal intestinal obstruction syndrome
COMT	Catechol-O-methyl transferase	DIP	Distal interphalangeal
COPD	Chronic obstructive pulmonary disease	DJD	Degenerative joint disease
CP	Chest pain; cerebral palsy	DKA	Diabetic ketoacidosis
CPA	Costophrenic angle	DKD	Diabetic kidney disease
CPAP	Continuous positive airway pressure	dL	Deciliter
CPK	Creatine phosphokinase	DM	Diabetes mellitus
CPOT	Critical-Care Pain Observation Tool	DMARD	Disease-modifying antirheumatic drug
CPP	Cerebral perfusion pressure	DNA	Deoxyribonucleic acid
CPR	Cardiopulmonary resuscitation	DNR	Do not resuscitate
CR	Complete remission	DO	Doctor of Osteopathy
CRF	Chronic renal failure; corticotropin-releasing factor	DOA	Dead on arrival; date of admission; duration of action
CRH	Corticotropin-releasing hormone	DOAC	Direct oral anticoagulant (see also NOAC)
CRI	Chronic renal insufficiency; catheter-related infection	DOB	Date of birth
CRNA	Certified Registered Nurse Anesthetist	DOE	Dyspnea on exertion
CRNP	Certified Registered Nurse Practitioner	DOT	Directly observed therapy
CRP	C-reactive protein	DP	Dorsalis pedis
CRPS	Complex regional pain syndrome	DPGN	Diffuse proliferative glomerulonephritis
CRTT	Certified Respiratory Therapy Technician	DPI	Dry powder inhaler
CS	Central Supply	DRE	Digital rectal examination
CSA	Cyclosporine	DRG	Diagnosis-related group
CSC	Corrected serum calcium	DRSP	Daily record of severity of problem
CSF	Cerebrospinal fluid; colony-stimulating factor	DS	Double strength
CSW	Cerebral salt wasting	DSM	Diagnostic and Statistical Manual of Mental Disorders
CT	Computed tomography; chest tube	DSHEA	Dietary Supplement Health and Education Act (1994)
CTA	Clear to auscultation	DST	Dexamethasone suppression test
CTB	Cease to breathe	DTIC	Dacarbazine
cTnI	Cardiac troponin I	DTP	Diphtheria-tetanus-pertussis
CTZ	Chemoreceptor trigger zone	DTR	Deep tendon reflex
CV	Cardiovascular	DVT	Deep vein thrombosis
CVA	Cerebrovascular accident; costovertebral angle	Dx	Diagnosis
CVAT	Costovertebral angle tenderness	DXA	Dual-energy x-ray absorptiometry (see also DEXA)
CVC	Central venous catheter	eAG	Estimated average glucose
CVP	Central venous pressure	EBL	Endoscopic band ligation
CVVH-DF	Continuous venovenous hemodiafiltration	EBV	Epstein-Barr virus
Cx	Culture; cervix	EC	Enteric-coated, emergency contraception, emergency contraceptive
CXR	Chest x-ray	ECF	Extended care facility
CYP	Cytochrome P-450 enzymes	ECG	Electrocardiogram
D&C	Dilatation and curettage	ECMO	Extracorporeal membrane oxygenator
d4T	Stavudine	ECOG	Eastern Cooperative Oncology Group
D ₅ NS	5% Dextrose in normal saline	ECT	Electroconvulsive therapy
D ₅ W5	% Dextrose in water		
DAA	Direct acting antivirals		
DAS	Disease activity score		

ED	Emergency department	FPIA	Fluorescence polarization immunoassay
EEG	Electroencephalogram	FRAX	Fracture Risk Assessment Tool
EENT	Eyes, ears, nose, throat	FSH	Follicle-stimulating hormone
EF	Ejection fraction	FTA	Fluorescent treponemal antibody
EGD	Esophagogastroduodenoscopy	f/u	Follow-up
EGFR	Epidermal growth factor receptor	FUDR	Floxuridine
EIA	Enzyme immunoassay	FUO	Fever of unknown origin
EMG	Electromyogram	Fx	Fracture
EML4-ALK	Echinoderm microtubule-associated protein-like 4-anaplastic lymphoma kinase	G6PD	Glucose-6-phosphate dehydrogenase
EMS	Emergency medical services	GABA	γ -aminobutyric acid
EMT	Emergency medical technician	GABHS	Group A β -hemolytic streptococcus
Endo	Endotracheal; endoscopy	GAD	Generalized anxiety disorder
EOMI	Extraocular movements (or muscles) intact	GB	Gallbladder
EPO	Erythropoietin	GBS	Group B <i>Streptococcus</i> ; Guillain-Barré syndrome
EPS	Extrapyramidal symptoms	GC	Gonococcus
EPT	Early pregnancy test; expedited partner therapy	G-CSF	Granulocyte colony-stimulating factor
ER	Estrogen receptor; emergency room	GDM	Gestational diabetes mellitus
ERCP	Endoscopic retrograde cholangiopancreatography	GE	Gastroesophageal; gastroenterology
ERT	Estrogen replacement therapy	GERD	Gastroesophageal reflux disease
ESA	Erythropoiesis-stimulating agent	GFR	Glomerular filtration rate
ESKD	End-stage kidney disease	GGT	γ -Glutamyltransferase
ESLD	End-stage liver disease	GGTP	γ -Glutamyl transpeptidase
ESR	Erythrocyte sedimentation rate	GI	Gastrointestinal
ESRD	End-stage renal disease	GM-CSF	Granulocyte-macrophage colony-stimulating factor
ESWL	Extracorporeal shockwave lithotripsy	GN	Glomerulonephritis; graduate nurse
ET	Endotracheal	GnRH	Gonadotropin-releasing hormone
ETOH	Ethanol	gr	Grain
EVL	Endoscopic variceal ligation	GT	Gastrostomy tube
FB	Finger-breadth; foreign body	gtt	Drops (<i>guttae</i>)
FBDSI	Functional Bowel Disorder Severity Index	GTT	Glucose tolerance test
FBS	Fasting blood sugar	GU	Gastric ulcer, genitourinary
FDA	Food and Drug Administration	GVHD	Graft-versus-host disease
FDC	Fixed dose combinations	GVL	Graft-versus-leukemia
FDP	Fibrin degradation products	Gyn	Gynecology
FEF	Forced expiratory flow (rate)	H&H	Hemoglobin and hematocrit
FEM-POP	Femoral-popliteal	H&P	History and physical examination
FEN	Fluids, electrolytes, and nutrition	HA or H/A	Headache
FE _{Na}	Fractional excretion of sodium	HAART	Highly active antiretroviral therapy
FEV ₁	Forced expiratory volume in 1 second	HAM-D	Hamilton Rating Scale for Depression
FFP	Fresh frozen plasma	HAP	Hospital-acquired pneumonia
FH	Family history	HAV	Hepatitis A virus
FiO ₂	Fraction of inspired oxygen	Hb, Hgb	Hemoglobin
FISH	Fluorescence in situ hybridization	HbA _{1C}	Hemoglobin A _{1C}
fL	Femtoliter	HBeAg	Hepatitis B early antigen
FLS	Fracture Liaison Service	HBIG	Hepatitis B immune globulin
FM	Face mask	HBP	High blood pressure
FNA	Fine-needle aspiration	HBsAg	Hepatitis B surface antigen
FOBT	Fecal occult blood test	HBV	Hepatitis B virus
FOC	Fronto-occipital circumference	HC	Hydrocortisone; home care
FODMAPs	Fermentable oligo-, di- and monosaccharides and polyols	HCAP	Healthcare-associated pneumonia (see new term: hospital-acquired pneumonia [HAP])
FOI	Flight of ideas	HCC	Hepatocellular carcinoma
FPG	Fasting plasma glucose	HCG	Human chorionic gonadotropin
		HCM	Hypercalcemia of malignancy

HCO ₃	Bicarbonate	ICDSC	Intensive Care Delirium Screening Checklist
Hct	Hematocrit	ICP	Intracranial pressure
HCTZ	Hydrochlorothiazide	ICS	Intercostal space
HAV	Hepatitis A virus	ICU	Intensive care unit
HBV	Hepatitis B virus	ID	Identification; infectious disease
HCV	Hepatitis C virus	IDDM	Insulin-dependent diabetes mellitus
Hcy	Homocysteine	IFN	Interferon
HD	Hodgkin disease; hemodialysis	Ig	Immunoglobulin
HDL	High-density lipoprotein	IgA	Immunoglobulin A
HE	Hepatic encephalopathy	IgD	Immunoglobulin D
HEC	High-emetic-risk chemotherapy	IHC	Immunohistochemistry
HEENT	Head, eyes, ears, nose, and throat	IHD	Ischemic heart disease
HEPA	High-efficiency particulate air	IJ	Internal jugular
HF	Heart failure	ILE	Intravenous lipid emulsion
HFA	Hydrofluoroalkane	IM	Intramuscular; infectious mononucleosis
H. flu	<i>Haemophilus influenzae</i>	IMV	Intermittent mandatory ventilation
HGH	Human growth hormone	INH	Isoniazid
HH	Hiatal hernia	INR	International normalized ratio
HHS	Hyperosmolar hyperglycemic state	IOP	Intraocular pressure
Hib	<i>Haemophilus influenzae</i> type b	IOR	Ideas of reference
HIV	Human immunodeficiency virus	IP	Intraperitoneal
HJR	Hepatojugular reflux	IPG	Impedance plethysmography
HL	Hodgkin lymphoma	IPI	International prognostic index
HLA	Human leukocyte antigen; human lymphocyte antigen	IPN	Interstitial pneumonia
HMG-CoA	Hydroxy-methylglutaryl coenzyme A	IPPB	Intermittent positive pressure breathing
H/O	History of	IPS	Idiopathic pneumonia syndrome
HOB	Head of bed	IRB	Institutional Review Board
HPA	Hypothalamic–pituitary axis	ISA	Intrinsic sympathomimetic activity
HPF	High-power field	ISDN	Isosorbide dinitrate
HPI	History of present illness	ISH	Isolated systolic hypertension
HPV	Human papilloma virus	ISMN	Isosorbide mononitrate
HR	Heart rate	IT	Intrathecal
HRQOL	Health-related quality of life	ITP	Idiopathic thrombocytopenic purpura
HRT	Hormone replacement therapy (see new term: hormone therapy, HT)	IU	International unit
HS	At bedtime (<i>hora somni</i>)	IUD	Intrauterine device
HSCT	Hematopoietic stem cell transplantation	IV	Intravenous; Roman numeral IV; symbol for Class 4 controlled substances
HSM	Hepatosplenomegaly	IVC	Inferior vena cava; intravenous cholangiogram
HSV	Herpes simplex virus	IVDA	Intravenous drug abuse
HT	Hormone therapy	IVF	Intravenous fluids
HTN	Hypertension	IVIG	Intravenous immunoglobulin
HVPG	Hepatic venous pressure gradient	IVP	Intravenous pyelogram; intravenous push
Hx	History	IVPB	Intravenous piggyback
I&D	Incision and drainage	IVSS	Intravenous Soluset
I&O	Intake and output	IWMI	Inferior wall myocardial infarction
IABP	Intra-arterial balloon pump	JODM	Juvenile-onset diabetes mellitus
IADL	Instrumental activities of daily living	JRA	Juvenile rheumatoid arthritis
IBD	Inflammatory bowel disease	JVD	Jugular venous distention
IBS	Irritable bowel syndrome	JVP	Jugular venous pressure
IBS-C	Irritable bowel syndrome with constipation	K	Potassium
IBS-D	Irritable bowel syndrome with diarrhea	kcal	Kilocalorie
IBS-SSS	Irritable Bowel Syndrome Symptom Severity Score	KCL	Potassium chloride
IBW	Ideal body weight	KDIGO	Kidney Disease: Improving Global Outcomes
ICD	Implantable cardioverter defibrillator	KOH	Potassium hydroxide
		KRAS	Kirsten rat sarcoma viral oncogene homolog

KUB	Kidney, ureters, bladder	mg	Milligram
KVO	Keep vein open	MHC	Major histocompatibility complex
L	Liter	MI	Myocardial infarction; mitral insufficiency
LAD	Left anterior descending; left axis deviation	MIC	Minimum inhibitory concentration
LAO	Left anterior oblique	MICU	Medical intensive care unit
LAP	Leukocyte alkaline phosphatase	MIDAS	Migraine Disability Assessment
LBBB	Left bundle branch block	mL	Milliliter
LBP	Low back pain	MM	Multiple myeloma
LCM	Left costal margin	MMA	Methylmalonic acid
LDH	Lactate dehydrogenase	MMEFR	Maximal midexpiratory flow rate
LDL	Low-density lipoprotein	MMR	Measles-mumps-rubella
LE	Lower extremity	MMSE	Mini mental state examination
LES	Lower esophageal sphincter	MOM	Milk of magnesia
LFT	Liver function test	MoCA	Montreal Cognitive Assessment
LHRH	Luteinizing hormone-releasing hormone	MPV	Mean platelet volume
LIMA	Left internal mammary artery	MRD	Minimal residual disease
LLE	Left lower extremity	MRAB	Medication-related aberrant behavior
LLL	Left lower lobe	MRG	Murmur/rub/gallop
LLQ	Left lower quadrant (abdomen)	MRI	Magnetic resonance imaging
LLSB	Left lower sternal border	MRSA	Methicillin-resistant <i>Staphylococcus aureus</i>
LMD	Local medical doctor	MRSE	Methicillin-resistant <i>Staphylococcus epidermidis</i>
LMP	Last menstrual period	MS	Mental status; mitral stenosis; musculoskeletal; multiple sclerosis; morphine sulfate
LMWH	Low molecular weight heparin	MSE	Mental status exam
LOA	Looseness of association	MSM	Men who have sex with men
LOC	Loss of consciousness; laxative of choice	MSW	Master of social work
LOS	Length of stay	MTD	Maximum tolerated dose
LP	Lumbar puncture	MTP	Metatarsophalangeal
LPF	Low-power field	MTX	Methotrexate
LPN	Licensed practical nurse	MUD	Matched unrelated donor
LPO	Left posterior oblique	MUGA	Multiple gated acquisition
LPT	Licensed physical therapist	MVA	Motor vehicle accident
LR	Lactated Ringer	MVI	Multivitamin
LS	Lumbosacral	MVR	Mitral valve replacement; mitral valve regurgitation
LTCF	Long-term care facility	MVS	Mitral valve stenosis; motor, vascular, and sensory
LUE	Left upper extremity	NAAT	Nucleic acid amplification test
LUL	Left upper lobe	NAD	No acute (or apparent) distress
LUQ	Left upper quadrant	NAFLD	Nonalcoholic fatty liver disease
LUTS	Lower urinary tract symptoms	NASH	Nonalcoholic steatohepatitis
LVEF	Left ventricular ejection fraction	N/C	Noncontributory; nasal cannula
LVH	Left ventricular hypertrophy	NC/AT	Normocephalic/atramatic
MAOI	Monoamine oxidase inhibitor	NDDI-E	Neurological Disorders Depression Inventory for Epilepsy
MAP	Mean arterial pressure	NG	Nasogastric
MAR	Medication administration record	NGT	Nasogastric tube
mcg	Microgram	NGTD	No growth to date (on culture)
MCH	Mean corpuscular hemoglobin	NHL	Non-Hodgkin lymphoma
MCHC	Mean corpuscular hemoglobin concentration	NIDDM	Non-insulin-dependent diabetes mellitus
MCL	Midclavicular line	NIH	National Institutes of Health
MCP	Metacarpophalangeal	NKA	No known allergies
MCV	Mean corpuscular volume	NKDA	No known drug allergies
MD	Medical doctor	NL	Normal
MDI	Metered-dose inhaler	NMDA	N-methyl-D-aspartate
MDRD	Modified Diet in Renal Disease		
MED	Morphine-equivalent dose		
MEFR	Maximum expiratory flow rate		
mEq	Milliequivalent		

NNRTI	Nonnucleoside reverse transcriptase inhibitor	P	Pulse, plan, percussion, pressure
NOAC	Nonwarfarin (also new, novel, or non-vitamin K) oral anticoagulant	P&A	Percussion and auscultation
NOS	Not otherwise specified	P&T	Peak and trough
NP	Nurse practitioner	PA	Physician assistant; posterior-anterior; pulmonary artery
NPH	Neutral protamine Hagedorn; normal pressure hydrocephalus	PAC	Premature atrial contraction
NPI	Neuropsychiatric Inventory	PaCO ₂	Arterial carbon dioxide tension
NPN	Nonprotein nitrogen	PAH	Pulmonary arterial hypertension
NPO	Nothing by mouth (<i>nil per os</i>)	PaO ₂	Arterial oxygen tension
NRAS	Neuroblastoma RAS viral (v-ras) oncogene homolog	PAOP	Pulmonary artery occlusion pressure
NRS	Numeric rating scale	PARP	Poly ADP ribose polymerase
NRTI	Nucleoside reverse transcriptase inhibitor	PAT	Paroxysmal atrial tachycardia
NS	Neurosurgery; normal saline	PBI	Protein-bound iodine
NSAID	Nonsteroidal antiinflammatory drug	PBSCT	Peripheral blood stem cell transplantation
NSCLC	Nonsmall cell lung cancer	PC	After meals (<i>post cibum</i>)
NSR	Normal sinus rhythm	PCA	Patient-controlled analgesia
NSS	Normal saline solution	PCI	Percutaneous coronary intervention
NSVD	Normal spontaneous vaginal delivery	PCKD	Polycystic kidney disease
NTG	Nitroglycerin	PCN	Penicillin
NT/ND	Nontender/nondistended	PCOS	Polycystic ovarian syndrome
N/V	Nausea and vomiting	PCP	Primary care physician; phencyclidine; <i>Pneumocystis (carinii) jirovecii</i> pneumonia
NVD	Nausea/vomiting/diarrhea; neck vein distention; nonvalvular disease; neovascularization of the disk	PCR	Polymerase chain reaction
NYHA	New York Heart Association	PCWP	Pulmonary capillary wedge pressure
O&P	Ova and parasites	PDA	Patent ductus arteriosus
OA	Osteoarthritis	PDE	Phosphodiesterase
OB	Obstetrics	PE	Physical examination; pulmonary embolism
OBS	Organic brain syndrome	PEEP	Positive end-expiratory pressure
OCD	Obsessive-compulsive disorder	PEFR	Peak expiratory flow rate
OCG	Oral cholecystogram	PEG	Percutaneous endoscopic gastrostomy; polyethylene glycol
OCT	Ocular coherence tomography	PERLA	Pupils equal, react to light and accommodation
OD	Right eye (<i>oculus dexter</i>); overdose; Doctor of Optometry	PERRLA	Pupils equal, round, and reactive to light and accommodation
ODT	Orally disintegrating tablet	PET	Positron emission tomography
OFC	Occipitofrontal circumference	PFT	Pulmonary function test
OGT	Oral glucose tolerance test	pH	Hydrogen ion concentration
OHTx	Orthotopic heart transplantation	PharmD	Doctor of Pharmacy
OIH	Opioid-induced hyperalgesia	PHQ	Patient health questionnaire
OLTx	Orthotopic liver transplantation	PI	Principal investigator; protease inhibitor
OME	Otitis media with effusion	PICC	Peripherally inserted central catheter
ONJ	Osteonecrosis of the jaw	PID	Pelvic inflammatory disease
OOB	Out of bed	PIP	Proximal interphalangeal
OPD	Outpatient department	PKU	Phenylketonuria
OPG	Ocular plethysmography	PMD	Private medical doctor
OPV	Oral poliovirus vaccine	PMH	Past medical history
OR	Operating room	PMI	Point of maximal impulse
ORT	Oral rehydration therapy	PMN	Polymorphonuclear leukocyte
OS	Left eye (<i>oculus sinister</i>)	PMP	Prescription monitoring program
OSA	Obstructive sleep apnea	PMS	Premenstrual syndrome
OT	Occupational therapy	PNC-E	Postnecrotic cirrhosis-ethanol
OTC	Over-the-counter	PND	Paroxysmal nocturnal dyspnea
OU	Each eye (<i>oculus uterque</i>)	PNH	Paroxysmal nocturnal hemoglobinuria
		PO	By mouth (<i>per os</i>)
		POAG	Primary open-angle glaucoma

POD	Postoperative day	RDP	Random donor platelets
POS	Polycystic ovarian syndrome	RDS	Respiratory distress syndrome
PP	Patient profile	RDW	Red cell distribution width
PPBG	Postprandial blood glucose	REM	Rapid eye movement
ppd	Packs per day	RES	Reticuloendothelial system
PPD	Purified protein derivative	RF	Rheumatoid factor; renal failure; rheumatic fever
PPE	Personal protective equipment	Rh	Rhesus factor in blood
PPH	Past psychiatric history	RHD	Rheumatic heart disease
PPI	Proton pump inhibitor	RLE	Right lower extremity
PPN	Peripheral parenteral nutrition	RLL	Right lower lobe
pr	Per rectum	RLQ	Right lower quadrant (abdomen)
PR	Progesterone receptor; partial remission	RLS	Restless legs syndrome
PRA	Panel-reactive antibody; plasma renin activity	RML	Right middle lobe
PRBC	Packed red blood cells	RN	Registered nurse
PRN	When necessary; as needed (<i>pro re nata</i>)	RNA	Ribonucleic acid
PSA	Prostate-specific antigen	R/O	Rule out
PSCT	Peripheral stem cell transplant	ROM	Range of motion
PSE	Portal systemic encephalopathy	ROS	Review of systems
PSH	Past surgical history	RPGN	Rapidly progressive glomerulonephritis
PSVT	Paroxysmal supraventricular tachycardia	RPh	Registered pharmacist
PT	Prothrombin time; physical therapy; patient; posterior tibial	RPR	Rapid plasma reagin
PTA	Prior to admission	RR	Respiratory rate; recovery room
PTCA	Percutaneous transluminal coronary angioplasty	RRR	Regular rate and rhythm
PTE	Pulmonary thromboembolism	RRT	Registered respiratory therapist
PTH	Parathyroid hormone	RSE	Refractory status epilepticus
PTHrP	Parathyroid hormone-related peptide	RSV	Respiratory syncytial virus
PTSD	Posttraumatic stress disorder	RT	Radiation therapy
PTT	Partial thromboplastin time	RTA	Renal tubular acidosis
PTU	Propylthiouracil	RTC	Return to clinic
PUD	Peptic ulcer disease	RT-PCR	Reverse transcriptase-polymerase chain reaction
PVC	Premature ventricular contraction	RUE	Right upper extremity
PVD	Peripheral vascular disease	RUL	Right upper lobe
Q	Every (<i>quaque</i>)	RUQ	Right upper quadrant (abdomen)
QA	Quality assurance	RVH	Right ventricular hypertrophy
QD	Every day (<i>quaque die</i>)	S ₁	First heart sound
QI	Quality improvement	S ₂	Second heart sound
QID	Four times daily (<i>quater in die</i>)	S ₃	Third heart sound (ventricular gallop)
QNS	Quantity not sufficient	S ₄	Fourth heart sound (atrial gallop)
QOD	Every other day	SA	Sinoatrial
QOL	Quality of life	SAAG	Serum ascites–albumin gradient
QOLIE	Quality of Life in Epilepsy	SAD	Seasonal affective disorder
QS	Quantity sufficient	SAH	Subarachnoid hemorrhage
R&M	Routine and microscopic	SaO ₂	Arterial oxygen percent saturation
RA	Rheumatoid arthritis; right atrium	SAS	Sedation-Agitation Scale
RADT	Rapid antigen detection test	SBE	Subacute bacterial endocarditis
RAIU	Radioactive iodine uptake	SBFT	Small bowel follow-through
RANKL	Receptor activator of nuclear factor- κ B ligand	SBGM	Self blood glucose monitoring
RAO	Right anterior oblique	SBO	Small bowel obstruction
RASS	Richmond Agitation Sedation Scale	SBP	Systolic blood pressure; spontaneous bacterial peritonitis
RBBB	Right bundle branch block	SC	Subcutaneous; subclavian
RBC	Red blood cell	SCD	Sequential compression device
RCA	Right coronary artery	SCID	Severe combined immunodeficiency
RCM	Right costal margin	SCLC	Small cell lung cancer
RCT	Randomized controlled trial		
RDA	Recommended daily allowance		

SCr	Serum creatinine	TEE	Transesophageal echocardiogram
SDP	Single donor platelets	TEN	Toxic epidermal necrolysis
SEM	Systolic ejection murmur	TENS	Transcutaneous electrical nerve stimulation
SG	Specific gravity	TFT	Thyroid function test
SGOT	Serum glutamic oxaloacetic transaminase	TG	Triglyceride
SCT	Stem cell transplantation	THA	Total hip arthroplasty
SGPT	Serum glutamic pyruvic transaminase	THC	Tetrahydrocannabinol
SH	Social history	TIA	Transient ischemic attack
SIADH	Syndrome of inappropriate antidiuretic hormone secretion	TIBC	Total iron-binding capacity
SIDS	Sudden infant death syndrome	TID	Three times daily (<i>ter in die</i>)
SIMV	Synchronized intermittent mandatory ventilation	TIH	Tumor-induced hypercalcemia
SIRS	Systemic inflammatory response syndrome	TIPS	Transjugular intrahepatic portosystemic shunt
SJS	Stevens–Johnson syndrome	TKA	Total knee arthroplasty
SL	Sublingual	TKI	Tyrosine kinase inhibitor
SLE	Systemic lupus erythematosus	TLC	Therapeutic lifestyle changes
SMBG	Self-monitoring of blood glucose	TLI	Total lymphoid irradiation
SNF	Skilled nursing facility	TLS	Tumor lysis syndrome
SNRI	Serotonin–norepinephrine reuptake inhibitor	TM	Tympanic membrane
SNS	Sympathetic nervous system	TMJ	Temporomandibular joint
SOB	Shortness of breath; side of bed	TMP/SMX	Trimethoprim-sulfamethoxazole
SOS	Sinusoidal obstruction syndrome	TMs	Tympanic membranes
S/P	Status post	TNF	Tumor necrosis factor
SPEP	Serum protein electrophoresis	TnI	Troponin I (cardiac)
SPF	Sun protection factor	TnT	Troponin T
SPS	Sodium polystyrene sulfonate	TNTC	Too numerous to count
SRI	Serotonin reuptake inhibitor	TOD	Target organ damage
SRMD	Stress-related mucosal damage	TPI	Trigger-point injection
SSKI	Saturated solution of potassium iodide	TPN	Total parenteral nutrition
SSRI	Selective serotonin reuptake inhibitor	TPR	Temperature, pulse, respiration
STAT	Immediately; at once	T. prot	Total protein
STD	Sexually transmitted disease	TSH	Thyroid-stimulating hormone
STI	Sexually transmitted infection	TSS	Toxic shock syndrome
SUP	Stress ulcer prophylaxis	TTP	Thrombotic thrombocytopenic purpura
SV	Stroke volume	TUIP	Transurethral incision of the prostate
SVC	Superior vena cava	TURP	Transurethral resection of the prostate
SVR	Supraventricular rhythm; systemic vascular resistance	Tx	Treat; treatment
SVRI	Systemic vascular resistance index	UA	Urinalysis; uric acid
SVT	Supraventricular tachycardia	UC	Ulcerative colitis
SW	Social worker	UCD	Usual childhood diseases
SWI	Surgical wound infection	UDS	Urine drug screen
Sx	Symptoms	UE	Upper extremity
T	Temperature	UFC	Urinary-free cortisol
T&A	Tonsillectomy and adenoidectomy	UFH	Unfractionated heparin
T&C	Type and crossmatch	UGI	Upper gastrointestinal
TAH	Total abdominal hysterectomy	UOQ	Upper outer quadrant
TB	Tuberculosis	UPDRS	Unified Parkinson's Disease Rating Scale
TBG	Thyroid-binding globulin	UPT	Urine pregnancy test
TBI	Total body irradiation; traumatic brain injury	URI	Upper respiratory infection
T. bili	Total bilirubin	USP	United States Pharmacopeia
T/C	To consider	UTI	Urinary tract infection
TCA	Tricyclic antidepressant	UV	Ultraviolet
TCN	Tetracycline	VA	Veterans' Affairs
TED	Thromboembolic disease	VAMC	Veterans' Affairs Medical Center
		VAP	Ventilator-associated pneumonia
		VBL	Variceal band ligation
		VDRL	Venereal Disease Research Laboratory

VF	Ventricular fibrillation	WA	While awake
VL	Viral load	WBC	White blood cell
VLDL	Very low-density lipoprotein	W/C	Wheelchair
VNA	Visiting Nurses' Association	WDWN	Well-developed, well-nourished
VO	Verbal order	Wes ESR	Westergren erythrocyte sedimentation rate
VOD	Veno-occlusive disease	WHO	World Health Organization
VP-16	Etoposide	WNL	Within normal limits
V _A /Q	Ventilation/perfusion	W/U	Workup
VRE	Vancomycin-resistant <i>Enterococcus</i>	Y-BOCS	Yale-Brown Obsessive–Compulsive Scale
VS	Vital signs	yo	Year-old
VSS	Vital signs stable	yr	Year
VT	Ventricular tachycardia	ZDV	Zidovudine
VTE	Venous thromboembolism		

PART II: Prevent Medication Errors by Avoiding These Dangerous Abbreviations, Symbols, and Dose Designations

Institute for Safe Medication Practices

ISMP'S LIST OF ERROR-PRONE ABBREVIATIONS, SYMBOLS, AND DOSE DESIGNATIONS

The abbreviations, symbols, and dose designations found in this table have been reported to ISMP through the ISMP National Medication Errors Reporting Program (ISMP MERP) as being frequently misinterpreted and involved in harmful medication errors. They should **NEVER** be used when communicating medical information. This includes internal communications, telephone/verbal prescriptions, computer-generated labels, labels for drug storage bins, medication administration records, as well as pharmacy and prescriber computer order entry screens.

Abbreviations	Intended Meaning	Misinterpretation	Correction
µg	Microgram	Mistaken as "mg"	Use "mcg"
AD, AS, AU	Right ear, left ear, each ear	Mistaken as OD, OS, OU (right eye, left eye, each eye)	Use "right ear," "left ear," or "each ear"
OD, OS, OU	Right eye, left eye, each eye	Mistaken as AD, AS, AU (right ear, left ear, each ear)	Use "right eye," "left eye," or "each eye"
BT	Bedtime	Mistaken as "BID" (twice daily)	Use "bedtime"
cc	Cubic centimeters	Mistaken as "u" (units)	Use "mL"
D/C	Discharge or discontinue	Premature discontinuation of medications if D/C (intended to mean "discharge") has been misinterpreted as "discontinued" when followed by a list of discharge medications	Use "discharge" and "discontinue"
IJ	Injection	Mistaken as "IV" or "intrajugular"	Use "injection"
IN	Intranasal	Mistaken as "IM" or "IV"	Use "intranasal" or "NAS"
HS	Half-strength	Mistaken as bedtime	Use "half-strength" or "bedtime"
hs	At bedtime, hours of sleep	Mistaken as half-strength	
IU**	International unit	Mistaken as IV (intravenous) or 10 (ten)	Use "units"
o.d. or OD	Once daily	Mistaken as "right eye" (OD-oculus dexter), leading to oral liquid medications administered in the eye	Use "daily"
OJ	Orange juice	Mistaken as OD or OS (right or left eye); drugs meant to be diluted in orange juice may be given in the eye	Use "orange juice"
Per os	By mouth, orally	The "os" can be mistaken as "left eye" (OS-oculus sinister)	Use "PO," "by mouth," or "orally"
q.d. or QD**	Every day	Mistaken as q.i.d., especially if the period after the "q" or the tail of the "q" is misunderstood as an "i"	Use "daily"
qhs	Nightly at bedtime	Mistaken as "qhr" or every hour	Use "nightly"
qn	Nightly or at bedtime	Mistaken as "qh" (every hour)	Use "nightly" or "at bedtime"
q.o.d. or QOD**	Every other day	Mistaken as "q.d." (daily) or "q.i.d." (four times daily) if the "o" is poorly written	Use "every other day"
q1d	Daily	Mistaken as q.i.d. (four times daily)	Use "daily"
q6PM, etc.	Every evening at 6 PM	Mistaken as every 6 hours	Use "daily at 6 PM" or "6 PM daily"
SC, SQ, sub q	Subcutaneous	SC mistaken as SL (sublingual); SQ mistaken as "5 every," the "q" in "sub q" has been mistaken as "every" (eg, a heparin dose ordered "sub q 2 hours before surgery" misunderstood as every 2 hours before surgery)	Use "subcut" or "subcutaneously"
ss	Sliding scale (insulin) or ½ (apothecary)	Mistaken as "55"	Spell out "sliding scale;" use "one-half" or "½"
SSRI	Sliding scale regular insulin	Mistaken as selective-serotonin reuptake inhibitor	Spell out "sliding scale (insulin)"
SSI	Sliding scale insulin	Mistaken as Strong Solution of Iodine (Lugol's)	

(continued)

i/d	One daily	Mistaken as “tid”	Use “1 daily”
TIW or tiw	3 times a week	Mistaken as “3 times a day” or “twice in a week”	Use “3 times weekly”
U or u**	Unit	Mistaken as the number 0 or 4, causing a 10-fold overdose or greater (eg, 4U seen as “40” or 4u seen as “44”); mistaken as “cc” so dose given in volume instead of units (eg, 4u seen as 4 cc)	Use “unit”
UD	As directed (“ut dictum”)	Mistaken as unit dose (eg, diltiazem 125 mg IV infusion “UD” misinterpreted as meaning to give the entire infusion as a unit [bolus] dose)	Use “as directed”
Dose Designations and Other Information	Intended Meaning	Misinterpretation	Correction
Trailing zero after decimal point (eg, 1.0 mg)**	1 mg	Mistaken as 10 mg if the decimal point is not seen	Do not use trailing zeros for doses expressed in whole numbers
“Naked” decimal point (eg, .5 mg)**	0.5 mg	Mistaken as 5 mg if the decimal point is not seen	Use zero before a decimal point when the dose is less than a whole unit
Abbreviations such as mg. or mL. with a period following the abbreviation	mg mL	The period is unnecessary and could be mistaken as the number 1 if written poorly	Use mg, mL, etc. without a terminal period
Drug name and dose run together (especially problematic for drug names that end in “l” such as Inderal 40 mg; Tegretol 300 mg)	Inderal 40 mg Tegretol 300 mg	Mistaken as Inderal 140 mg Mistaken as Tegretol 1300 mg	Place adequate space between the drug name, dose, and unit of measure
Numerical dose and unit of measure run together (eg, 10 mg, 100 mL)	10 mg 100 mL	The “m” is sometimes mistaken as a zero or two zeros, risking a 10- to 100-fold overdose	Place adequate space between the dose and unit of measure
Large doses without properly placed commas (eg, 100000 units; 1000000 units)	100,000 units 1,000,000 units	100000 has been mistaken as 10,000 or 1,000,000; 1000000 has been mistaken as 100,000	Use commas for dosing units at or above 1000, or use words such as 100 “thousand” or 1 “million” to improve readability
Drug Name Abbreviations	Intended Meaning	Misinterpretation	Correction
To avoid confusion, do not abbreviate drug names when communicating medical information. Examples of drug name abbreviations involved in medication errors include:			
APAP	acetaminophen	Not recognized as acetaminophen	Use complete drug name
ARA A	vidarabine	Mistaken as cytarabine (ARA C)	Use complete drug name
AZT	zidovudine (Retrovir)	Mistaken as azathioprine or aztreonam	Use complete drug name
CPZ	Compazine (prochlorperazine)	Mistaken as chlorpromazine	Use complete drug name
DPT	Demerol-Phenergan- Thorazine	Mistaken as diphtheria-pertussis-tetanus (vaccine)	Use complete drug name
DTO	Diluted tincture of opium, or deodorized tincture of opium (Paregoric)	Mistaken as tincture of opium	Use complete drug name
HCl	hydrochloric acid or hydrochloride	Mistaken as potassium chloride (The “H” is misinterpreted as “K”)	Use complete drug name unless expressed as a salt of a drug
HCT	hydrocortisone	Mistaken as hydrochlorothiazide	Use complete drug name
HCTZ	hydrochlorothiazide	Mistaken as hydrocortisone (seen as HCT250 mg)	Use complete drug name
MgSO ₄ **	magnesium sulfate	Mistaken as morphine sulfate	Use complete drug name
MS, MSO ₄ **	morphine sulfate	Mistaken as magnesium sulfate	Use complete drug name
MTX	methotrexate	Mistaken as mitoxantrone	Use complete drug name
PCA	procainamide	Mistaken as patient controlled analgesia	Use complete drug name
PTU	propylthiouracil	Mistaken as mercaptopurine	Use complete drug name
T3	Tylenol with codeine No. 3	Mistaken as liothyronine	Use complete drug name
TAC	triamcinolone	Mistaken as tetracaine, Adrenalin, cocaine	Use complete drug name
TNK	TNKase	Mistaken as “TPA”	Use complete drug name
ZnSO ₄	zinc sulfate	Mistaken as morphine sulfate	Use complete drug name

(continued)

Stemmed Drug Names	Intended Meaning	Misinterpretation	Correction
"Nitro" drip	nitroglycerin infusion	Mistaken as sodium nitroprusside infusion	Use complete drug name
"Norflex"	norfloxacin	Mistaken as Norflex	Use complete drug name
"IV Vanc"	intravenous vancomycin	Mistaken as Invanz	Use complete drug name
Symbols	Intended Meaning	Misinterpretation	Correction
3a	Dram	Symbol for dram mistaken as "3"	Use the metric system
m	Minim	Symbol for minim mistaken as "mL"	
x3d	For three days	Mistaken as "3 doses"	Use "for three days"
> and <	Greater than and less than	Mistaken as opposite of intended; mistakenly use incorrect symbol; "< 10" mistaken as "40"	Use "greater than" or "less than"
/ (slash mark)	Separates two doses or indicates "per"	Mistaken as the number 1 (eg, "25 units/10 units" misread as "25 units and 110" units)	Use "per" rather than a slash mark to separate doses
@	At	Mistaken as "2"	Use "at"
&	And	Mistaken as "2"	Use "and"
+	Plus or and	Mistaken as "4"	Use "and"
°	Hour	Mistaken as a zero (eg, q2° seen as q 20)	Use "hr," "h," or "hour"
Ø or ø	zero, null sign	Mistaken as numerals 4, 6, 8, and 9	Use 0 or zero, or describe intent using whole words

**These abbreviations are included on The Joint Commission's "minimum list" of dangerous abbreviations, acronyms, and symbols that must be included on an organization's "Do Not Use" list, effective January 1, 2004. Visit www.jointcommission.org for more information about this Joint Commission requirement. Reprinted with permission from the Institute for Safe Medication Practices (www.ismp.org), 200 Lakeside Drive; Suite 200, Horsham, PA 19044-2321. Report medication errors or near misses to the ISMP Medication Errors Reporting Program (MERP) at 1-800-FAIL-SAF(E) or online at www.ismp.org.

This page intentionally left blank

APPENDIX D

SAMPLE RESPONSES TO CASE QUESTIONS

114

VITAMIN B₁₂ DEFICIENCY

Like Hot Pizza to the Tongue Level II

Jon P. Wietholter, PharmD, BCPS

CASE SUMMARY

A 45-year-old woman presents with complaints of tongue pain, fatigue, paresthesias, anorexia, and early satiety. These complaints have been bothering her over the course of months to years, but she has recently noticed increased tongue swelling and pain. The physical exam and laboratory tests reveal findings consistent with vitamin B₁₂ deficiency, including low hemoglobin, hematocrit, and vitamin B₁₂ levels; elevated MCV and MCH; a low-grade fever; mild tachycardia; mild splenomegaly; and decreased pinprick, vibratory, and temperature sensations in the lower extremities. The peripheral blood smear showed abnormalities commonly seen in vitamin B₁₂ deficiency. Additionally, she is taking both metformin and omeprazole, which are potential causes of vitamin B₁₂ deficiency. Several options for replacement of vitamin B₁₂ are available, and intramuscular (IM), deep subcutaneous (SC), and oral replacement are all potential options for this patient.

QUESTIONS

Collect Information

1.a. What subjective and objective information indicates the presence of vitamin B₁₂ deficiency?

- Complaints of fatigue and lethargy¹
- (+) red, smooth, swollen, sore tongue with loss of papillae (atrophic glossitis)²
- (+) tingling and numbness in feet (paresthesias) and decreased pinprick, vibratory, and temperature sensations in both lower extremities²
- Decreased hemoglobin, hematocrit, and RBC count
- Decreased serum vitamin B₁₂ level
- Elevated MCV and MCH levels¹
- Low-reticulocyte count in the presence of anemia
- Mild splenomegaly
- Persistent low-grade fever
- Mild tachycardia¹
- Anorexia and early satiety
- Mild thrombocytopenia¹⁻³

- Peripheral blood smear containing macro-ovalocytosis, hypersegmented granulocytes, large platelets, and macrocytic red blood cells with megaloblastic changes¹⁻³

1.b. What additional information is needed to fully assess this patient's vitamin B₁₂ deficiency?

- The main causes of cobalamin deficiency are pernicious anemia, insufficient nutritional vitamin B₁₂ intake, ileal disease and/or resection, and food-cobalamin malabsorption usually caused by atrophic gastritis. This form of gastritis is usually caused by *Helicobacter pylori* infection or long-term antacid use. Other causes include chronic alcoholism, gastric reconstruction surgery, or chronic pancreatic disease.¹⁻³
- Information about the patient's diet would be extremely valuable. Vitamin B₁₂ deficiency is much more common in vegetarians and vegans due to their lack of intake of meat, fish, and dairy products.¹
- Knowing the length of time she has been taking her chronic medications would be valuable to determine whether the metformin and/or omeprazole could be playing a role in her vitamin B₁₂ deficiency.
- Currently, any vitamin B₁₂ level <150 pmol/L or <200 pg/mL is considered deficient. However, sensitivity and specificity lack with vitamin B₁₂ serum levels because clinical signs of deficiency can be seen in people with normal levels.¹ Elevated homocysteine (>13 mmol/L) and methylmalonic acid (MMA) (>0.4 mmol/L) levels can also be used due to their increased sensitivity for cobalamin deficiency (95.9% and 98.4%, respectively).⁴ Elevated homocysteine levels are also seen in folate and vitamin B₆ deficiency, so this test lacks specificity; MMA levels have increased specificity for vitamin B₁₂ deficiency.^{1-3,5} Evaluation of a patient's MMA level is recommended in patients with borderline vitamin B₁₂ levels (<350 pg/mL).² Normal homocysteine and MMA levels exclude vitamin B₁₂ deficiency.² A low serum holotranscobalamin (holoTC) level (<35 pmol/L) is actually the earliest marker of vitamin B₁₂ deficiency and more closely correlates with the biologically active fraction of vitamin B₁₂.^{1,3,5}

Assess the Information

2.a. Assess the severity of vitamin B₁₂ deficiency based on the subjective and objective information available.

- The patient has clinically relevant deficiency of at least moderate severity due to atrophic glossitis and paresthesias that could potentially be caused by vitamin B₁₂ deficiency.

2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

- *Problem #1:* Vitamin B₁₂ deficiency that may require treatment with drug therapy.
- *Problem #2:* Potential adverse drug reaction: exacerbation of vitamin B₁₂ deficiency by metformin and/or omeprazole.^{2,6,7}

- *Problem #3:* Diabetes mellitus type 2 treated with metformin with apparent control ($A_{1C} < 7\%$).
- *Problem #4:* Asthma treated with a long-term combination controller inhaler with availability of a rescue inhaler but with uncertain control and chronic asthma classification.
- *Problem #5:* GERD treated with omeprazole with uncertain control based on available information.
- *Problem #6:* 21+ pack-year history of tobacco use, which may require pharmacotherapy if cessation is attempted.

Develop a Care Plan

3.a. What are the goals of pharmacotherapy in this case?

- Reverse symptoms related to vitamin B₁₂ deficiency anemia, if possible.
- Replenish vitamin B₁₂ stores.
- Prevent further complications of vitamin B₁₂ deficiency.
- Correct abnormal laboratory values associated with vitamin B₁₂ deficiency anemia.
- Prevent worsening anemia with pharmacotherapy or diet.
- Continue therapies to maintain control of her asthma, type 2 diabetes, and GERD.

3.b. What nondrug therapies for vitamin B₁₂ deficiency might be useful for this patient?

- Physical therapy and occupational therapy are valuable non-pharmacologic options in patients with problems related to balance, gait, and arm function (if present). Assistance might be needed in the later stages of vitamin B₁₂ deficiency via a cane or walker for ambulation. These options would be appropriate if Mrs Kindred's paresthesias make ambulation more difficult.
- Dietary management to increase nutritional intake of vitamin B₁₂ is indicated if diet is deemed to be the source of the deficiency. Metabolic vitamin B₁₂ requirements are 2–5 mcg/day, and the recommended daily allowance of cobalamin for adults in the United States is 2.4 mcg/day, with higher-risk groups including pregnant women and elderly patients potentially requiring higher intake.¹ The typical nonvegetarian diet contains 5–8 mcg/day, and the body can store in excess of 2000 mcg (2 mg) of cobalamin, so it may take several years to develop a deficiency due to poor dietary intake or malabsorption.¹ Foods that are rich in vitamin B₁₂ include meat, fish, eggs, cheese, milk, and yogurt.¹ If it is deemed that this patient's deficiency stems from insufficient dietary intake of vitamin B₁₂, it would be wise to recommend increased consumption of meat and dairy products if she is willing to eat these products.

3.c. What feasible pharmacotherapeutic alternatives are available to treat this patient's vitamin B₁₂ deficiency?

- *Cyanocobalamin* and *hydroxocobalamin* are the two pharmacologic agents used to replace vitamin B₁₂. Cyanocobalamin is the preferred option and is available in parenteral and oral formulations.
- Traditional treatment involves parenteral administration of vitamin B₁₂ via IM or deep SC injection in the form of cyanocobalamin. In the United States, various dosing regimens are used to treat vitamin B₁₂ deficiency. One common dosing schedule is to administer 1000 mcg IM daily for 1 week, then 1000 mcg IM weekly for 4–8 weeks, followed by 1000 mcg IM monthly for the rest of the patient's life. Some clinicians skip the daily portion of the regimen and begin with 1000 mcg weekly for 1 month. This facilitates adherence with therapy; also, symptoms associated with longstanding vitamin B₁₂ deficiency may

take several months to resolve, so daily injections are often seen as unnecessary.

- Oral cobalamin administration is as effective as parenteral administration for replacing vitamin B₁₂ stores if given in adequate doses.^{3,4} Cobalamin can be absorbed by both intrinsic factor dependent and independent routes. The independent route of absorption is less effective; only 1–4% of vitamin B₁₂ is absorbed by passive diffusion in the intestine without intrinsic factor. Therefore, larger doses of oral vitamin B₁₂ are needed to provide adequate absorption.^{1,4} Oral administration avoids the discomfort of chronic injections and is more economical. Literature suggests the need for at least 200 times the recommended dietary allowance to effectively replace vitamin B₁₂ stores.⁴ The current dosing recommendation is 1000–2000 mcg orally daily for 1–2 weeks, followed by 1000 mcg daily indefinitely thereafter.
- Sublingual, intranasal, and lozenge preparations are also available and can be used in vitamin B₁₂ deficiency. The recommended dose is up to 2500 mcg sublingually daily, 500 mcg inhaled in one nostril once weekly, or one 1000-mcg lozenge daily, respectively.
- Hydroxocobalamin may allow for use of smaller doses compared with cyanocobalamin. However, it is no more effective in stabilizing hematocrit levels, and it may be associated with antibody formation to the transcobalamin–hydroxocobalamin complex. Hydroxocobalamin's main utility is in vitamin B₁₂ deficiency caused by the presence of cyanide. It is only available parenterally, and the usual dose is 30 mcg IM daily for 5–10 days followed by 100–200 mcg IM monthly thereafter, with higher doses being recommended for those with neurologic manifestations of vitamin B₁₂ deficiency.

3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's vitamin B₁₂ deficiency and other drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Problem #1: Vitamin B₁₂ deficiency that may require treatment with drug therapy.

- Based on the patient's signs and symptoms, it is appropriate to initiate cyanocobalamin therapy. All forms of cobalamin replacement would be considered acceptable. Because she has numerous signs and symptoms of vitamin B₁₂ deficiency, an appropriate regimen would be cyanocobalamin 1000 mcg IM daily for 1 week, then 1000 mcg IM weekly for 4–8 weeks, followed by 1000 mcg IM monthly for the rest of the patient's life. If the patient or her husband can administer the injection appropriately, therapy can be given at home. The patient may need to return to the clinic or her primary care provider for medication administration if home administration is not feasible.
- If the patient responds well to injectable therapy, it would be reasonable to suggest that she be switched to oral cyanocobalamin for the remainder of her lifetime with a dose of 1000 mcg daily. If oral cyanocobalamin is chosen initially for this patient and she does not respond adequately, a switch to parenteral therapy is warranted.

Problem #2: Potential adverse drug reaction: exacerbation of vitamin B₁₂ deficiency by metformin and/or omeprazole.^{2,6,7}

- Metformin is thought to cause vitamin B₁₂ deficiency through malabsorption.⁶ In a prospective clinical trial evaluating long-term metformin use, patients taking metformin had a 13% higher prevalence of vitamin B₁₂ deficiency per year of metformin use than patients taking placebo.⁶ A systematic review

also concluded that metformin reduced vitamin B₁₂ levels in a dose-dependent manner.⁸

- Prolonged use of acid suppression therapy with proton-pump inhibitors and H₂-receptor antagonists appears to be associated with vitamin B₁₂ deficiency due to impaired cobalamin release from dietary sources.^{2,9} Humans are not able to synthesize vitamin B₁₂ so it must be provided in the diet.^{1,2} Absorption of cobalamin depends primarily on intrinsic factor (IF), which is secreted by the gastric mucosa.⁴ The cobalamin/IF complex is then absorbed in the terminal ileum.¹ After transfer through the ileal membrane, cobalamin is released by proteolytic digestion by pepsin and transferred to transcobalamin II, and this complex is known as holotranscobalamin (holoTC). However, this process is not possible if cobalamin cannot be released during digestion by gastric acid.^{2,7} It has been estimated that acid-suppressive therapy may cause an 80% increased risk in vitamin B₁₂ deficiency.⁷
- Because both metformin and omeprazole can contribute to vitamin B₁₂ deficiency, their continued use in this patient for her diabetes and GERD should be reassessed, as described below.

Problem #3: Diabetes mellitus type 2 treated with metformin with apparent control (A_{1C} <7%).

- This patient's A_{1C} is 6.8%, meeting the American Diabetes Association (ADA) target of <7%. However, use of metformin should be reassessed to determine if its benefit on glucose control outweighs the risk for potential vitamin B₁₂ deficiency. Because her diabetes is controlled on the current regimen, it may be appropriate to continue metformin while replacing vitamin B₁₂. Alternatively, one could discontinue the metformin and attempt to control her diabetes by adding a different oral agent that has not been linked to vitamin B₁₂ deficiency.

Problem #4: Asthma treated with a long-term combination controller inhaler with availability of a rescue inhaler but with uncertain control and chronic asthma classification.

- Although the patient voiced no complaints related to asthma at this clinic visit, the physical exam did demonstrate minor wheezing on auscultation. At a future visit with her primary care provider, her degree of asthma control should be assessed, including review of adherence with her inhaled controller medication, frequency of need for the rescue inhaler, and reinforcement of correct inhaler technique.
- Identifying the patient's chronic asthma classification would be valuable to determine whether or not she is on optimal controller therapy.

Problem #5: GERD treated with omeprazole with uncertain control based on available information.

- Because omeprazole may contribute to vitamin B₁₂ deficiency, the primary care provider should assess how well controlled the GERD has been and, if possible, attempt discontinuation of omeprazole. H₂-receptor antagonists are also associated with this issue, making chronic acid suppressive therapy problematic in this patient. If feasible, low-dose on-demand therapy may have a less effect on vitamin B₁₂ levels than chronic daily acid suppressive therapy.

Problem #6: 21+ pack-year history of tobacco use, which may require pharmacotherapy if cessation is attempted.

- This patient has a long history of cigarette smoking, and the available information does not indicate whether attempts to quit have been made in the past. The medical records should be reviewed, and at a future visit with her primary care provider,

a conversation should be started about her degree of readiness to stop smoking. Although not all patients require pharmacotherapy for smoking cessation, various products are available, such as nicotine replacement patches, lozenges, and gum; varenicline; and bupropion.

Implement the Care Plan

4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

General instructions:

- This medication is called vitamin B₁₂ or *cyanocobalamin*. It is a water-soluble vitamin that can be stored by the body and is needed for normal growth and building of red blood cells, muscle, and nerve tissue. Vitamin B₁₂ deficiency may occur because of inadequate amounts in the diet, pernicious anemia (inability to absorb the vitamin after dietary intake), stomach disorders, medications, infections, or prior surgery.
- It is important to continue using vitamin B₁₂ for as long as your medical provider indicates (which may be lifelong) to correct the deficiency and prevent its recurrence.
- Inform your healthcare provider of any prescription and nonprescription medications you have tried to manage your symptoms. Also inform your provider if symptoms worsen significantly at any point during the treatment course.
- Store the medication away from heat, direct light, moisture, and children.
- During treatment with vitamin B₁₂, it may be necessary to have periodic laboratory testing performed to monitor how well you are responding to therapy.
- This medication is available in oral (by mouth), sublingual (under the tongue), intranasal, and injectable formulations.

Injectable cyanocobalamin:

- If you are taking an injectable form of cyanocobalamin, you may need to receive your shots in your provider's office, or they may be given to you by a home care nurse or someone who has been trained to give the injections.
- If you are self-administering the injections, you will need appropriate-size needles and syringes and a container for proper disposal of the needles after use. Injections should be given into a muscle (intramuscularly) with common locations being the gluteal (buttocks) or deltoid (upper arm) muscles.
- Vitamin B₁₂ injections should be protected from light.
- If a dose is missed, take the dose as soon as you remember and return to your normal schedule. If a provider is responsible for administering your shot, reschedule your appointment immediately. Never take two doses of the medication at the same time.

Oral cyanocobalamin:

- If you are using the lozenge or sublingual form of cyanocobalamin, place it under your tongue and allow it to melt. Some lozenges can be swallowed but should be held in your mouth for at least 30 seconds prior to swallowing.

Intranasal cyanocobalamin:

- If you are using the intranasal form of cyanocobalamin, separate your weekly dose by at least 1 hour from any hot liquids. Before the initial intranasal dose, prime the device by pumping the unit until a spray appears. At that point, prime the device two more times before instilling the weekly dose into your nostril.
- Intranasal cyanocobalamin should be protected from light.

Side effects of cyanocobalamin:

- Common side effects while using this medication include pain or irritation at the injection site (if the injectable form is being used), dizziness, headache, anxiety, and gastrointestinal upset. More serious side effects include hives, chest tightness, or trouble breathing, and if these occur, contact your healthcare provider immediately.

4.b. Describe how care should be coordinated with other health-care providers.

- The primary care provider can educate the patient about vitamin B₁₂ deficiency and its prognosis. Additionally, follow-up visits with the PCP should happen regularly, particularly early in the treatment course and should be consistently attended by the patient.
- A pharmacist can help with counseling on the cyanocobalamin product prescribed, including appropriate administration and common or serious adverse effects. Additionally, the pharmacist can provide an updated medication list, if requested.
- Referral to a dietician may be beneficial if it is determined that the vitamin B₁₂ deficiency is due to a dietary cause.
- Referral to a physical or occupational therapist may be beneficial if the patient begins to have issues with balance, gait or arm function.
- *If symptoms continue or worsen despite appropriate pharmacotherapeutic treatment, referral to a hematologist may be appropriate.¹*

Follow-up: Monitor and Evaluate**5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?****Efficacy parameters:**

- Reticulocytosis typically starts in 2–5 days and peaks at 1 week. Hemoglobin and hematocrit concentrations usually rise within 7–10 days, and hypersegmented neutrophils characteristically disappear in 1–2 weeks. Hematologic abnormalities should normalize within 2 months if vitamin B₁₂ deficiency is solely responsible for the patient's anemia (hemoglobin 12–16 g/dL for females and 13–18 g/dL for males).² Thrombocytopenia typically responds within 10–14 days of initiating therapy.
- Patients may subjectively improve within hours after initiation of cyanocobalamin therapy. Complaints of weakness and fatigue should improve dramatically over the course of treatment. It is likely that the paresthesias will also resolve over time, although this does not always occur.²
- Serum levels of MMA and homocysteine are elevated in patients with cobalamin deficiency. These tests are more sensitive than measuring serum vitamin B₁₂ levels because their elevations may precede a decline in vitamin B₁₂ concentration and a decrease in hematocrit. It would be reasonable to monitor these levels in addition to the patient's serum vitamin B₁₂ level.^{2,5}

Adverse effect parameters:

- Monitor the patient for the most common adverse effects of cyanocobalamin, which include dizziness, headache, arthralgia, GI upset, bronchitis, nasopharyngitis, urticaria, and fever.
- Instruct the patient to contact her provider immediately if wheezing, chest tightness, blue skin color, seizures, or swelling of the face, lips, tongue, or throat occur after vitamin B₁₂

administration. Obtain an allergy history from the patient before administering the first dose of vitamin B₁₂.

- Monitor the patient for adverse effects possibly associated with reticulocytosis, including hyperuricemia, hypokalemia, and sodium retention. Rebound thrombocytosis may precipitate thrombotic events. A sudden increase in production of red blood cells can lead to expansion of intravascular volume. Monitor serum potassium levels when initially replacing vitamin B₁₂ stores due to the possibility of hypokalemia from increased potassium utilization in hematopoiesis.
- The risk of gastric cancer is two- to threefold higher in patients with pernicious anemia.^{2,3} A Schilling test could be used to distinguish dietary vitamin B₁₂ deficiency from pernicious anemia (ie, lack of intrinsic factor), but since this would not change the clinical management of the individual patient, this particular test has become obsolete.^{1,2}

5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

- There is no consensus regarding monitoring parameters once vitamin B₁₂ replacement has been started. One simplified strategy is to monitor the vitamin B₁₂ level and reticulocyte count 1 month after beginning replacement therapy and every 3–6 months thereafter.
- It may also be appropriate to monitor a complete blood count and peripheral blood smear (optional) 1–2 weeks after initiation of therapy.
- Monitor complete blood counts and vitamin B₁₂ levels periodically for the patient's lifetime. Annual follow-up evaluations have been recommended.⁴

■ FOLLOW-UP QUESTIONS

1. Mrs Kindred returns to your clinic 3 months later reporting that she is feeling much less fatigued and is able to eat a more consistent diet but is still suffering from the tingling in her toes and a milder form of tongue soreness. What information can you give her regarding these remaining maladies?
 - Neurologic symptoms, including paresthesias, have been reported to worsen transiently after cobalamin therapy is initiated. However, most patients have a partial or complete response neurologically depending on pretreatment severity and duration of symptoms, with most improvements occurring during the first 6 months of therapy. Glossitis and tongue burning or soreness should resolve quickly with therapy. Based on Mrs Kindred's presentation today, it is reasonable to tell her that the paresthesias could last a while longer. However, the glossitis should have resolved by this point. Therefore, it is important to evaluate medication adherence. It is possible she began to feel better shortly after beginning cyanocobalamin treatment and has since become nonadherent with her regimen, thus explaining the continued tongue pain. Ask her if she is taking the medication as prescribed.
 - Additionally, it would be prudent to determine that Mrs Kindred is not solely taking a folic acid supplement without concomitantly taking cyanocobalamin. Patients with vitamin B₁₂ deficiency respond hematologically to treatment with either folic acid or vitamin B₁₂. However, bone marrow conversion to normoblastic morphology does not occur, and neurologic symptoms do not resolve with folic acid monotherapy, further risking permanent neurologic damage (including potential spinal cord degeneration) if vitamin B₁₂ deficiency is not properly diagnosed and treated.

REFERENCES

1. Green R. Vitamin B₁₂ deficiency from the perspective of a practicing hematologist. *Blood* 2017;129(19):2603–2611.
2. Briani C, Dalla Torre C, Citton V, et al. Cobalamin deficiency: clinical picture and radiological findings. *Nutrients* 2013;5:4521–4539.
3. Langan RC, Zawistoski KJ. Update on vitamin B₁₂ deficiency. *Am Fam Physician* 2011;83(12):1425–1430.
4. Chan CQ, Low LL, Lee KH. Oral vitamin B₁₂ replacement for the treatment of pernicious anemia. *Front Med (Lausanne)* 2016;3(38):1–6.
5. Oberley MJ, Yang DT. Laboratory testing for cobalamin deficiency in megaloblastic anemia. *Am J Hematol* 2013;88:522–526.
6. Aroda VR, Edelstein SL, Goldberg RB, et al. Long-term metformin use and vitamin B₁₂ deficiency in the Diabetes Prevention Program Outcomes Study. *J Clin Endocrinol Metab* 2016;101(4):1754–1761.
7. Maes ML, Fixen DR, Linnebur SA. Adverse effects of proton-pump inhibitor use in older adults: a review of the evidence. *Ther Adv Drug Saf* 2017;8(9):273–297.
8. Liu Q, Li S, Quan H, Li J. Vitamin B₁₂ status in metformin treated patients: systematic review. *PLoS One* 2014;9(6):e100379. doi: 10.1371/journal.pone.0100379.
9. Lewis JR, Barre D, Zhu K, et al. Long-term proton pump inhibitor therapy and falls and fractures in elderly women: a prospective cohort study. *J Bone Miner Res* 2014;29(11):2489–2497.

127

DIABETIC FOOT INFECTION

Let's Nail That Infection Level II

Renee-Claude Mercier, PharmD, BCPS-AQ ID, PhC, FCCP

Paulina Deming, PharmD, PhC

CASE SUMMARY

In this 67-year-old Hispanic man with poorly controlled type 2 diabetes mellitus and several comorbid conditions, an ingrown toenail has become infected, causing significant erythema and swelling of the right foot with purulent discharge from the wound. Physical and laboratory findings, including an elevated white blood cell (WBC), ESR, and fever, suggest a potential systemic infection secondary to cellulitis. The patient undergoes incision and drainage of the lesion, and tissue is submitted to the laboratory for culture. Empiric antimicrobial treatment must be initiated before results of wound culture and sensitivity testing are known. Because of the patient's comorbidities and the size and severity of the wound, parenteral antibiotic therapy should be initiated. Because this is an acutely infected wound, aerobic gram-positive bacteria (especially *Staphylococcus aureus*) are the most likely causative organisms. However, broad-spectrum coverage for gram-negative and anaerobic bacteria should also be instituted due to the location of the wound (bottom of foot), its size and severity, foul-smelling drainage, and the patient's diabetes. This patient has risk factors for hospital-acquired methicillin-resistant *S. aureus* (HA-MRSA) infection (ie, recent hospitalization and existing chronic illnesses), and empiric coverage of this organism should be considered. When tissue cultures are reported as positive for *S. aureus* (MRSA) and *Bacteroides fragilis*, the reader is asked to narrow to more specific therapy, which includes parenteral vancomycin or either oral or parenteral linezolid or tedizolid

with anaerobic coverage (metronidazole or clindamycin). Second-line agents include daptomycin, telavancin, ceftaroline, oritavancin, or dalbavancin all in combination with a drug with anaerobic coverage (metronidazole or clindamycin). This infection will require 2–3 weeks of therapy, so the patient will most likely be discharged on outpatient antibiotic therapy. Although parenteral therapy using any of a variety of agents, or oral linezolid or tedizolid, may be completed as an outpatient, attention must be paid to the patient's social and economic situation. Better glycemic control and education regarding techniques for proper foot care are important components of a comprehensive treatment plan for this patient.

QUESTIONS

Collect Information

1.a. What subjective and objective information indicates the presence of a diabetic foot infection?

- Swollen, sore, and red foot. Induration extend from first metatarsal to midfoot (4 × 5 cm)
- Purulent foul-smelling drainage with cellulitis
- 2+ edema of the foot increasing in amplitude
- Elevated WBC count (17.3 × 10³/mm³)
- X-ray showing tissue swelling from first metatarsal to midfoot consistent with cellulitis

1.b. What additional information is needed to fully assess this patient's diabetic foot infection?

- Risk factors for infection in this patient include:
 - ✓ Ingrown toenail; attempted self-treatment
 - ✓ Poorly controlled diabetes
 - ✓ Vascular calcifications in the foot per x-ray indicate a decreased blood supply
 - ✓ Decreased sensation of bilateral lower extremities
 - ✓ Poor foot care (presence of fungus and overgrown toenails)
 - ✓ Recent hospitalization and travel to Mexico (poor water purity)
- **Deep culture of the wound for both anaerobes and aerobes.**
 - ✓ Common aerobic isolates: *S. aureus*, *Streptococcus* spp., *Enterococcus* spp., *Proteus mirabilis*, *Escherichia coli*, *Klebsiella* spp., and *Pseudomonas aeruginosa*.
 - ✓ Common anaerobic isolates: *Peptostreptococcus* and *B. fragilis*.¹

Assess the Information

2.a. Assess the severity of the diabetic foot infection based on the subjective and objective information available.

- **Mild:** Local infection involving only the skin and subcutaneous tissues without systemic signs. Erythema >0.5 cm and ≤2 cm.
- **Moderate:** Local infection with erythema >2 cm, or involving structures deeper than skin and subcutaneous tissues, and *no* systemic inflammatory response signs (SIRS).
- **Severe (this patient):** Local infection with SIRS, which includes at least two of the following:
 - ✓ Temperature >38°C or <36°C
 - ✓ Heart rate >90 bpm
 - ✓ Respiratory rate >20 breaths/min or PaCO₂ <32 mm Hg
 - ✓ WBC count >12,000 or <4000 cells/μL or ≥10% immature forms

2.b. Create a list of the patient's drug therapy problems and prioritize them. Include assessment of medication appropriateness, effectiveness, safety, and patient adherence.

- *Problem #1:* Cellulitis and infection of the right foot in a patient with diabetes, requiring treatment.
 - ✓ Special consideration for drug selection: Recent travel abroad in Mexico where antibiotics are not controlled and antibiotic resistance is much higher. The patient could have been self-treating his infection or could have acquired more resistant pathogens.
 - ✓ Special consideration for drug selection: History of alcohol abuse; patient may have liver dysfunction, and the use of metronidazole should elicit discussion on the potential for a disulfiram drug reaction.
 - ✓ Fungal infection of toenails, requiring treatment—a possible portal of entry for bacteria causing foot infection.
- *Problem #2:* Poorly controlled type 2 diabetes mellitus despite therapy with three medications.
 - ✓ As evidenced by an A_{1C} of 11.8% (goal <7%) and recent episode of hyperglycemic hyperosmolar state (HHS). Metformin is contraindicated in this patient due to his SCr of 2.4 mg/dL and eGFR <30 mL/min/1.73 m². However, his renal function may improve with hydration, and this should be monitored.
 - ✓ Nonadherence with medication administration and home glucose monitoring.
- *Problem #3:* Renal insufficiency secondary to diabetic nephropathy, treated appropriately with lisinopril but without available information on progression of renal disease. Renal impairment may necessitate dose adjustment of antimicrobial agents.
- *Problem #4:* Dyslipidemia treated with atorvastatin but with no available information on the efficacy of therapy.
- *Problem #5:* Hypertension treated with lisinopril and currently controlled (BP 126/79 mm Hg), but without information about long-term blood pressure (BP) control.

2.c. What economic and psychosocial considerations are applicable to this patient?

- Poor adherence to current treatment for diabetes likely contributed to this situation. Cultural differences, lack of access to medical care, and challenges with health literacy may have contributed to nonadherence. Diabetic foot infections are complications of poorly controlled diabetes and hyperglycemia that can lead to neuropathy, decreased blood supply to extremities, and impaired immune status.
- A simplified drug regimen (monotherapy and less frequent dosing, whenever possible) should be selected because of his history of poor medication adherence. Addressing barriers to adherence will also be an important component of this patient's success with current treatment and prevention of future recurrence.
- The patient receives his healthcare primarily at First Choice Clinic. This may become an important consideration in selecting his future therapeutic plan.
- For this patient to receive appropriate wound care and home IV therapy if judged necessary, the healthcare team must establish that his family or a home healthcare nurse will be able to provide assistance.

Develop a Care Plan

3.a. What are the goals of pharmacotherapy in this case?

- Eradicate the bacteria.

- Prevent the development of osteomyelitis and the need for amputation.
- Preserve as much normal limb function as possible.
- Improve control of diabetes mellitus.
- Prevent infectious complications.
- Avoid adverse effects of medications.

3.b. What nondrug therapies might be useful for this patient's diabetic foot infection?

- Appropriate wound care by experienced podiatrists (incision and drainage, debridement of the wound, and toenail clipping), nurses (wound care, dressing changes of wound, and foot care teaching), and physical therapists (whirlpool treatments, wound debridement, and teaching about minimal weight-bearing with a walker or crutches).
- Bed rest, minimal weight-bearing, leg elevation, and control of edema.
- Proper education about wound care and the importance of good diabetes control, glucometer use, adherence to the medication regimens, and foot care in this patient with diabetes.

3.c. What feasible pharmacotherapeutic alternatives are available for the treatment of diabetic foot infection?

- Based on the most recent 2012 clinical practice guideline for the diagnosis and treatment of diabetic foot infections, treatment differs based on infection severity (mild vs moderate vs severe)¹:

Mild: Oral antimicrobial therapy may be used in mild, uncomplicated diabetic foot infections *only*.^{1,2} The following agents could be considered as preferred oral options because they target *S. aureus* and *Streptococcus* spp.:

- ✓ Amoxicillin/clavulanate
- ✓ Dicloxacillin
- ✓ Clindamycin
- ✓ Cephalexin
- ✓ Levofloxacin

- If MRSA coverage is needed, use either *doxycycline* or *trimethoprim/sulfamethoxazole* (activity against streptococci is uncertain).

- Although these regimens cover the most likely causative organisms, it is important to note that except for levofloxacin none of the antibiotics given above cover *P. aeruginosa*.

Moderate/Severe: Treatment of *moderate* infection may be with oral agents or initial parenteral therapy while *severe* infections should be treated with parenteral agents.¹ Consider coverage for MSSA, streptococci, Enterobacteriaceae, and obligate anaerobes. Options for IV monotherapy include:

- ✓ Piperacillin/tazobactam
- ✓ Imipenem/cilastatin
- ✓ Meropenem
- ✓ Doripenem
- ✓ Cefepime or levofloxacin could be used; however, additional coverage against obligate anaerobes should be considered with either metronidazole or clindamycin. Levofloxacin is also not optimal for *S. aureus* coverage.

- These agents cover all of the most likely causative organisms, including anaerobes and *P. aeruginosa*. However, imipenem/cilastatin is a potent β -lactamase inducer, so therapy with the other agents may be preferable initially.

- The following agents could also be used as IV therapy, but they do not cover *P. aeruginosa*:

- ✓ Ampicillin/sulbactam

- ✓ Ertapenem

- ✓ Cefoxitin or cefotetan

- ✓ Third-generation cephalosporin (ceftriaxone/cefotaxime) plus IV clindamycin combination

- A combination of clindamycin IV plus either aztreonam or an oral or IV fluoroquinolone (ciprofloxacin or levofloxacin) could be used in patients with moderate-to-severe infections who are allergic to penicillin and cephalosporins. Moxifloxacin is also now recommended for treatment of moderate infections and offers the advantage of once-daily dosing, no need of renal adjustments, and being relatively broad spectrum including most obligate anaerobic organisms.

- MRSA may be a suspected causative organism in some cases. There are two genetically distinct types of MRSA that can be of concern in diabetic foot infections: community-associated MRSA (CA-MRSA) and healthcare-associated MRSA (HA-MRSA). While acquisition of HA-MRSA is associated with well-defined risk factors (history of prolonged hospital or nursing home stay, past antimicrobial use, indwelling catheters, pressure sores, surgery, or dialysis), risk factors for acquisition of CA-MRSA are not as well established. CA-MRSA is susceptible to more antibiotics than is HA-MRSA.³

- Vancomycin IV, daptomycin IV, linezolid or tedizolid oral or IV, ceftaroline IV,⁴ dalbavancin IV, or oritavancin IV may be used if HA-MRSA is a suspected causative organism. Persons who are at high risk for HA-MRSA wound infection include those who: (a) have a previous history of HA-MRSA infection/colonization; (b) have positive nasal cultures for HA-MRSA; (c) have a recent history (within the last year) of prolonged hospitalization or intensive care unit stay; or (d) receive frequent and/or prolonged courses of broad-spectrum antibiotics.^{5,6} Should the above stated agents be used empirically, gram-negative and anaerobic coverage will need to be added to provide adequate empiric coverage.

- Should CA-MRSA be more of a concern (eg, in a patient with no HA-MRSA risk factors who is admitted from an area where the CA-MRSA rate is relatively high), the antibiotic regimen should include any of those agents active against HA-MRSA: clindamycin, sulfamethoxazole/trimethoprim, or doxycycline or minocycline.³

- Aminoglycosides should generally be avoided in diabetic patients because they are at increased risk for developing diabetic nephropathy and renal failure.

- Becaplermin 0.01% gel (Regranex) is FDA approved for treatment of diabetic ulcers on the lower limbs and feet. Becaplermin is a genetically engineered form of platelet-derived growth factor, a naturally occurring protein in the body that stimulates diabetic ulcer healing. It is to be used as adjunctive therapy, in addition to infection control and wound care. In one clinical trial, becaplermin applied once daily in combination with good wound care significantly increased the incidence of complete healing when compared with placebo gel (50% vs 35%, respectively). Becaplermin gel also significantly decreased the time to complete healing of diabetic ulcers by 32% (about 6 weeks faster). The incidence of adverse events, including infection and cellulitis, was similar in patients treated with becaplermin gel, placebo gel, or good diabetic wound care alone.⁷ Further studies are needed to assess which patients might best benefit from becaplermin use, particularly considering its cost

(average wholesale price \$1066.59 per 15-g tube at the time of this writing).

3.d. Create an individualized, patient-centered, team-based care plan to optimize medication therapy for this patient's drug therapy problems. Include specific drugs, dosage forms, doses, schedules, and durations of therapy.

Problem #1: Cellulitis and infection of the right foot in a patient with diabetes, requiring treatment.

- This diabetic foot infection has significant involvement of the skin and skin structures with deep tissue involvement. Moreover, the area of cellulitis and induration exceeds 2 cm (4 cm × 5 cm). Because this is an acutely infected wound, aerobic gram-positive bacteria (especially *S. aureus*) are the most likely causative organisms.¹ However, broad-spectrum coverage for gram-negative and anaerobic bacteria should also be instituted due to the location of the wound (bottom of foot), foul-smelling discharge, its size and severity, and the patient's diabetes. This patient does have risk factors for HA-MRSA infection (ie, recent hospitalizations and existing chronic illnesses), and empiric coverage of this organism should be considered as well. Initial empiric IV therapy is recommended in severe diabetic foot infections such as this one.
- A number of treatment options are appropriate for empiric therapy of this patient's diabetic foot infection. Drug selection may be based on institutional cost and drug availability through the formulary system. Dosage should be adjusted for the patient's renal function, as appropriate. This patient's calculated creatinine clearance, based on total body weight (patient's weight is below ideal body weight), is 25 mL/min. Antimicrobial resistance within the area and based on patient's prior culture and susceptibility should also be taken into consideration when selecting an empiric regimen.⁸
- All antibiotic regimens appropriate for this patient include two or more antibiotics (one to cover HA-MRSA and other gram-positive bacteria, and one or two to cover gram-negative and anaerobic bacteria). It would be best to limit it to no more than two antibiotics to optimize nursing ease and patient adherence and to minimize drug costs and toxicity. In most institutions, the patient would be started on vancomycin in addition to piperacillin/tazobactam as a first-line regimen. This is a dual therapy regimen that covers MRSA, gram-negative aerobic as well as anaerobic bacteria while reserving the carbapenems for use when absolutely necessary. There are concerns about increased renal toxicity associated with combined vancomycin and piperacillin/tazobactam use that warrant at least weekly to bi-weekly renal function monitoring.
- To cover HA-MRSA, one of the following agents is considered part of the preferred regimen:
 - ✓ Vancomycin 1 g IV Q 48 H (or other dosing regimen to achieve vancomycin trough of 10–15 mg/L);
 - ✓ Linezolid 600 mg PO Q 12 H; or
 - ✓ Tedizolid 200 mg PO Q 24 H; or
 - ✓ Daptomycin 240 mg IV Q 48 H is a second-line option.
 - ✓ Ceftaroline 300 mg IV every 12 hours is also a second-line option (covers some common gram-negative organisms).
 - ✓ Dalbavancin 1125 mg IV infused over 30 minutes as a single dose is a second-line option.
 - ✓ Oritavancin 1200 mg IV infused over 3 hours as a single dose is a second-line option. (Although dosing adjustment in severe renal impairment CrCl <30 mL/min has not been studied.)

- ✓ Telavancin (10 mg/kg [600 mg] Q 48 H) should be considered as a third-line option.
- To cover gram-negative bacteria and anaerobes, one of the following agents is preferred (dosed for renal dysfunction when indicated):
 - ✓ Piperacillin/tazobactam 2.25 g IV Q 6 H
 - ✓ Ampicillin/sulbactam 3 g IV Q 8 H
 - ✓ Ertapenem 500 mg IV Q 24 H
 - ✓ Imipenem/cilastatin 250 mg IV Q 6 H
 - ✓ Meropenem 1 g IV Q 12 H
 - ✓ Doripenem 250 mg IV Q 12 H
- Other acceptable IV alternatives for gram-negative and anaerobic coverage, with dose adjustments appropriate for Mr Chavez's renal function, include the combination of either clindamycin or metronidazole plus either a third- or fourth-generation cephalosporin (ceftazidime or cefepime), aztreonam, or a fluoroquinolone. However, this would cause the patient to be on a three-drug empiric regimen (including the antibiotic active against HA-MRSA), which may be costlier, inconvenient, and associated with more adverse drug reactions than monotherapy or dual therapy options (eg, clindamycin, fluoroquinolones, and cephalosporins are more highly associated with *Clostridioides difficile* colitis than other antibiotics).
- Start tolnaftate 1% topical cream BID as a treatment for his athlete's foot fungal infection that may have served as a portal of entry.

Problem #2: Poorly controlled type 2 diabetes mellitus despite therapy with three medications.

- The patient's eGFR is <30 mL/min/1.73 m², which is a contraindication to metformin use; it should be discontinued. The insulin regimen with both short- and long-acting insulins should be optimized to make sure patient has access to both forms and knows how to use them appropriately with regular blood sugar monitoring. Daily journaling would help the medical provider make appropriate adjustment at future appointments.

Problem #3: Renal insufficiency, treated appropriately with lisinopril but without available information on progression of renal disease. Renal impairment may necessitate dose adjustment of antimicrobial agents.

- In light of the chronic kidney disease associated with diabetes, the patient is appropriately prescribed an angiotensin-converting inhibitor, lisinopril. He may also have a component of acute kidney injury due to current illness and would benefit from hydration. As renal function improves, vancomycin dosing should be adjusted based on blood concentration and piperacillin/tazobactam dose will need to increase accordingly as well.
- The patient's history of renal insufficiency should be assessed to determine the rate at which his renal function is declining.

Problem #4: Dyslipidemia treated with atorvastatin but with no available information on the efficacy of therapy.

- At a future visit with his primary care provider, the most recent fasting lipid panel should be reviewed to assess the efficacy of the current regimen of atorvastatin 40 mg daily. If appropriate, another fasting lipid panel should be obtained. The patient should also be asked about his adherence with therapy and whether he is experiencing any potential adverse effects.

Problem #5: Hypertension treated with lisinopril but without information about long-term BP control.

- Although the current BP indicates control (BP 126/79 mmHg), the history of long-term control is unavailable. At a future visit with the healthcare provider, the medical record should be reviewed to assess long-term control. The patient should also be asked about adherence to the current regimen of lisinopril 20 mg daily and whether he is experiencing any potential adverse effects.

Implement the Care Plan

4.a. What information should be provided to the patient to enhance compliance, ensure successful therapy, and minimize adverse effects?

- A home health nurse (who speaks Spanish) will come to your home to show you and your family how the infusion set works.
- We will need to see you in the clinic each week to make sure the antibiotic is working. At these visits, we will draw some blood so that we can check for side effects of the medication.
- Vancomycin should be infused slowly, over 1–2 hours, to prevent flushing and BP decreases that are associated with rapid infusion.
- Contact your physician or me if any unusual side effects, such as rash, shortness of breath, diminished hearing or ringing in the ears, or decreased urine production, occur while taking this medicine.
- Contact your home healthcare provider if pain, redness, or swelling is observed at the IV site.
- Avoid alcohol intake as you may experience a significant drug interaction with metronidazole that could be characterized by intense flushing, breathlessness, headache, increased or irregular heart rate, low BP, nausea, and vomiting.
- *Note:* The patient needs to be made aware that osteomyelitis and limb amputation are possible consequences of these infections in diabetic patients. He also needs to be provided with personnel resources (telephone numbers and addresses) to contact if unusual reactions occur while on therapy, if infection worsens, or if he has questions or concerns. Adherence to outpatient clinic follow-up visits is of prime importance for success in this case.

4.b. Describe how care should be coordinated with other health-care providers.

- The patient's primary care provider will need to follow up for management of diabetes, hypertension, and dyslipidemia as well as medication adherence. An appointment with the provider should be made within the next 2–3 weeks after release from the hospital to adjust the patient's medication as necessary and address any barriers to adherence.
- Pharmacists are often available within several days from hospital discharge in primary care clinics to help with medication reconciliation and medication therapy management, which can decrease the burden on other primary care providers who have limited appointment availability. Pharmacists may also be able to assist with applicable patient assistance programs to facilitate drug acquisition and adherence. The primary care provider and pharmacist should emphasize education and the importance of adherence at every visit.
- Scheduling a meeting with a diabetes educator while in the hospital may facilitate adherence post-discharge.
- An infectious disease consult in the hospital will be beneficial to help coordinate with the outpatient parenteral antimicrobial

clinic to complete IV antibiotic in the outpatient setting. The patient should be seen in the outpatient parenteral antimicrobial therapy (OPAT) clinic within 1 week after discharge.

- Referral to a wound care specialist will be required upon discharge from the hospital for appropriate debridement of the wound and dressing changes.

Follow-up: Monitor and Evaluate

5.a. What clinical and laboratory parameters should be used to evaluate the therapy for achievement of the desired therapeutic outcome and to detect or prevent adverse effects?

- Regardless of the drug chosen, improvement in the signs and symptoms of infection and healing of the wound with prevention of limb amputation are the primary endpoints.
- Observe for decreased swelling, induration, and erythema. Improvement should be observed after 72–96 hours of appropriate antimicrobial therapy and surgical debridement.
- A decrease in cloudy drainage and formation of new scar tissue are signs of positive response to therapy that may take as long as 7–14 days to be seen.
- Obtain a WBC count and differential every 48–72 hours for the first week or until normalization if <1 week, and weekly thereafter until the end of therapy. Continue monitoring until therapy is completed because neutropenia is associated with many antibiotics (eg, ampicillin/sulbactam, vancomycin).
- Vancomycin used at high dose (trough goal of 15–20 mg/L) has been associated with higher incidence of renal dysfunction, and Mr Chavez already has an impaired renal function that increases the risk. Routine weekly SCr levels may be recommended to prevent vancomycin-associated nephrotoxicity and ototoxicity that can develop with accumulation of the drug should the patient's renal function worsen. It would be reasonable to order a weekly vancomycin trough level also to ensure that an adequate trough level (~10–15 mg/L) is being achieved.
- ESR and CRP are excellent makers of inflammation to follow while on therapy. Obtain levels at baseline before starting therapy and then weekly during therapy. Levels should decrease to normal by the end of therapy and are predictors of positive outcomes.
- Question the patient to detect any unusual side effects related to the drug or infusion (eg, rash, nausea, vomiting, and diarrhea) daily for the first 3–5 days and then weekly thereafter.

5.b. Develop a plan for follow-up that includes appropriate time frames to assess progress toward achievement of the goals of therapy.

- Assess the patient's infection daily for changes in swelling, induration, and erythema. Measure temperature at least twice daily and obtain a WBC count daily if it was initially increased. Improvements in these physical signs and laboratory parameters should be observed after 72–96 hours of appropriate antimicrobial therapy and surgical debridement. If the area of swelling and erythema increases, or if response to therapy appears inadequate, it may be necessary to broaden therapy so that gram-negative bacteria are covered as well. Response to therapy is often patient dependent, and in some cases, improvement may not be seen until after 7–10 days of treatment.
- The duration of therapy is controversial. The latest guidelines recommend continuing antibiotic therapy until, but not beyond, resolution of all signs and symptoms of infection, but not through complete healing of the wound. Wound healing in diabetic patients is often very slow. Therapy should be continued for at least 2–3 weeks total in severe infection.

- The patient should remain hospitalized until he is afebrile for 24–48 hours, has signs of improvement and positive response to therapy (decreased swelling, redness, purulent drainage; normalization of the WBC, ESR, or CRP), and outpatient wound care has been established, either by proper teaching to the patient (and his family) or through home healthcare services.

ADDITIONAL CASE QUESTIONS

1. What therapeutic alternatives are available for treating this patient after results of cultures are known to contain MRSA and *B. fragilis*?

- Once the culture results are available and the involved organism(s) is (are) considered pathogenic and responsible for the infectious process, therapy should be targeted at the specific organism(s).
 - ✓ Vancomycin given IV is often considered the drug of choice for skin and soft tissue infections caused by MRSA, as it has established efficacy, is generally well tolerated, and is inexpensive.
 - ✓ Linezolid is at least as effective as vancomycin in MRSA skin and soft tissue infections and has the advantage of oral administration, but it is expensive.⁹ A weekly CBC must be obtained from patients receiving linezolid because it carries a significant risk of thrombocytopenia that may require treatment discontinuation (0.3–10.0%).
 - ✓ Daptomycin is a lipopeptide antibiotic approved for treatment of complicated skin and soft tissue infections due to susceptible organisms including MRSA. It is expensive and is generally restricted to prevent the development of resistance.
 - ✓ Telavancin has been approved for treatment of complicated skin and soft tissue infections due to susceptible organisms including MRSA. It is fairly expensive, has been associated with renal dysfunction, and should be reserved for resistant bacteria or failure of first- and second-line therapy.
 - ✓ Ceftaroline has been approved for the treatment of complicated skin and soft tissue infections due to susceptible organisms including MRSA. It covers Enterobacteriaceae but lacks coverage against anaerobes, extended-spectrum β -lactamase (ESBL), AMP C or *Klebsiella pneumoniae* carbapenemase (KPC) producing strains, and *P. aeruginosa*. It is administered at least twice daily, but it lacks data in diabetic foot infection and should be reserved for patients failing first-line agents.
 - ✓ Dalbavancin and oritavancin are approved as single-dose IV agents for treatment of acute bacterial skin and soft tissue infection caused by gram-positive bacteria. Neither agent has activity against gram-negative organisms. Oritavancin must be infused over 3 hours compared to 30 minutes for dalbavancin. Both agents are well tolerated, although oritavancin has more drug and laboratory interactions than dalbavancin, and it has not yet been studied in patients like Mr Chavez who have a CrCl of approximately 25 mL/min. Both agents are also very expensive.
- None of the above agents has anaerobic coverage, and therefore metronidazole or clindamycin will need to be added. Either agent could be used orally or parenterally. Metronidazole may be associated with a disulfiram reaction if the patient consumes alcohol again. Clindamycin has an increased risk of *C. difficile* colitis.

- Tigecycline has activity against MRSA, and it would provide activity against *B. fragilis*. However, tigecycline should only be considered when other therapies cannot be used because it failed to meet noninferiority criteria in a diabetic foot infection trial.
- 2. Design an optimal drug treatment plan for treating the mixed infection while he remains hospitalized.**
- The patient's therapy should be streamlined to vancomycin 1 g IV Q 48 H. After the third dose, a vancomycin trough level should be recommended and therapy adjusted to maintain a trough ≥ 10 mg/L. Metronidazole 500 mg PO Q 8 H should be initiated to cover the *B. fragilis*.
- 3. Design an optimal pharmacotherapeutic plan for completion of his treatment after he is discharged from the hospital.**
- The decision about completion of therapy with IV versus oral therapy is often based on clinical experience because few clinical trials have been performed on long-term treatment of diabetic foot infections.¹⁰
 - In this patient, continued use of IV vancomycin would probably be the best choice. Either the drug could be infused at home, most likely with the wife's or daughter's assistance and frequent nursing care visits, or the patient may be required to visit a home infusion clinic to receive therapy, depending on what is economically feasible. Discharge planning should be involved in this case to ensure a smooth transition to outpatient therapy.
 - The patient should be seen in clinic at least once weekly while on therapy to assess therapeutic efficacy and safety. At each visit, a CBC should be obtained to evaluate for vancomycin-associated neutropenia or thrombocytopenia. An SCr should be obtained as well, and if any significant changes in renal function are observed, the vancomycin dose should be adjusted or the drug stopped and changed to a non-nephrotoxic agent. An ESR or CRP should be monitored weekly as a marker of inflammation and response to therapy.

REFERENCES

1. Lipsky BA, Berendt AR, Cornia PB, et al. 2012 Infectious Diseases Society of America clinical practice guideline for the diagnosis and treatment of diabetic foot infections. *Clin Infect Dis* 2012;54:132–173.
2. Levin ME. Management of the diabetic foot: preventing amputation. *South Med J* 2002;95:10–20.
3. Echániz-Aviles G, Velazquez-Meza ME, Vazquez-Larios Mdel R, Soto-Noguerón A, Hernández-Dueñas AM. Diabetic foot infection caused by community-associated methicillin-resistant *Staphylococcus aureus* (USA300). *J Diabetes* 2015;7(6):891–892.
4. Lipsky BA, Cannon CM, Ramani A, et al. Ceftaroline fosamil for treatment of diabetic foot infections: the CAPTURE study experience. *Diabetes Metab Res Rev* 2015;31(4):395–401.
5. Lipsky BA, Tabak YP, Johannes RS, Vo L, Hyde L, Weigelt JA. Skin and soft tissue infections in hospitalised patients with diabetes: culture isolates and risk factors associated with mortality, length of stay and cost. *Diabetologia* 2010;53:914–923.
6. Liu C, Bayer A, Cosgrove SE, et al. Clinical practice guidelines by the Infectious Diseases Society of America for the treatment of methicillin-resistant *Staphylococcus aureus* infections in adults and children. *Clin Infect Dis* 2011;52:1–38.
7. Martí-Carvajal AJ, Gluud C, Nicola S, et al. Growth factors for treating diabetic foot ulcers. *Cochrane Database Syst Rev* 2015;(10):CD008548. doi:10.1002/14651858.CD008548.pub2.
8. Guillet CV, Kollef MH. How to stratify patients at risk for resistant bugs in skin and soft tissue infections? *Curr Opin Infect Dis* 2016;29(2):116–123.
9. Weigelt J, Itani K, Stevens D, Lau W, Dryden M, Knirsch C. Linezolid versus vancomycin in the treatment of complicated skin and soft tissue infections. *Antimicrob Agents Chemother* 2005;46:2260–2266.
10. Nicolau DP, Stein GE. Therapeutic options for diabetic foot infections: a review with an emphasis on tissue penetration characteristics. *J Am Podiatr Med Assoc* 2010;100:52–63.