

19th Edition

HARRISON'S™

PRINCIPLES OF INTERNAL MEDICINE

KASPER

FAUCI

HAUSER

LONGO

JAMESON

LOSCALZO

Mc
Graw
Hill
Education

19th Edition



HARRISON'STM
P R I N C I P L E S O F
**INTERNAL
MEDICINE**

EDITORS OF PREVIOUS EDITIONS

T. R. Harrison

Editor-in-Chief, Editions 1, 2, 3, 4, 5

W. R. Resnick

Editor, Editions 1, 2, 3, 4, 5

M. M. Wintrobe

Editor, Editions 1, 2, 3, 4, 5
Editor-in-Chief, Editions 6, 7

G. W. Thorn

Editor, Editions 1, 2, 3, 4, 5, 6, 7
Editor-in-Chief, Edition 8

R. D. Adams

Editor, Editions 2, 3, 4, 5, 6, 7, 8, 9, 10

P. B. Beeson

Editor, Editions 1, 2

I. L. Bennett, Jr.

Editor, Editions 3, 4, 5, 6

E. Braunwald

Editor, Editions 6, 7, 8, 9, 10,
12, 13, 14, 16, 17
Editor-in-Chief, Editions 11, 15

K. J. Isselbacher

Editor, Editions 6, 7, 8, 10, 11, 12, 14
Editor-in-Chief, Editions 9, 13

R. G. Petersdorf

Editor, Editions 6, 7, 8, 9, 11, 12
Editor-in-Chief, Edition 10

J. D. Wilson

Editor, Editions 9, 10, 11, 13, 14
Editor-in-Chief, Edition 12

J. B. Martin

Editor, Editions 10, 11, 12, 13, 14

A. S. Fauci

Editor, Editions 11, 12, 13, 15, 16, 18
Editor-in-Chief, Editions 14, 17

R. Root

Editor, Edition 12

D. L. Kasper

Editor, Editions 13, 14, 15, 17, 18
Editor-in-Chief, Editions 16, 19

S. L. Hauser

Editor, Editions 14, 15, 16, 17, 18

D. L. Longo

Editor, Editions 14, 15, 16, 17
Editor-in-Chief, Edition 18

J. L. Jameson

Editor, Editions 15, 16, 17, 18

J. Loscalzo

Editor, Editions 17, 18

19th Edition



HARRISON'STM
P R I N C I P L E S O F
INTERNAL
MEDICINE

EDITORS

Dennis L. Kasper, MD

William Ellery Channing Professor of Medicine, Professor of Microbiology and Immunobiology, Department of Microbiology and Immunobiology, Harvard Medical School; Division of Infectious Diseases, Brigham and Women's Hospital
Boston, Massachusetts

Stephen L. Hauser, MD

Robert A. Fishman Distinguished Professor and Chairman, Department of Neurology, University of California, San Francisco
San Francisco, California

J. Larry Jameson, MD, PhD

Robert G. Dunlop Professor of Medicine; Dean, Perelman School of Medicine at the University of Pennsylvania; Executive Vice President, University of Pennsylvania for the Health System
Philadelphia, Pennsylvania

Anthony S. Fauci, MD

Chief, Laboratory of Immunoregulation;
Director, National Institute of Allergy and Infectious Diseases,
National Institutes of Health
Bethesda, Maryland

Dan L. Longo, MD

Professor of Medicine, Harvard Medical School; Senior Physician, Brigham and Women's Hospital; Deputy Editor, *New England Journal of Medicine*, Boston, Massachusetts

Joseph Loscalzo, MD, PhD

Hersey Professor of the Theory and Practice of Medicine, Harvard Medical School; Chairman, Department of Medicine, and Physician-in-Chief, Brigham and Women's Hospital
Boston, Massachusetts



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

Copyright © 2015 by McGraw-Hill Education. Previous editions copyright © 2012, 2008, 2005, 2001, 1998, 1994, 1991, 1987, 1983, 1980, 1977, 1974, 1970, 1966, 1962, 1958 by The McGraw-Hill Companies, Inc. 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, with the exception that the program listings may be entered, stored, and executed in a computer system, but they may not be reproduced for publication.

ISBN: 978-0-07-180216-1

MHID: 0-07-180216-9

The material in this eBook also appears in the print version of this title: ISBN: 978-0-07-180215-4,
MHID: 0-07-180215-0.

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.

Note: Dr. Fauci's work as editor and author was performed outside the scope of his employment as a U.S. government employee. This work represents his personal and professional views and not necessarily those of the U.S. government.

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.

Material from the disk that accompanies the printed version of this eBook may be obtained from McGraw-Hill Professional's MediaCenter at <http://www.mhprofessional.com/mediacenter/hpim19>

Some material may require a desktop or laptop computer for full access.

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.

COVER ILLUSTRATION

Budding HIV particle, computer artwork (*Credit: Animate4.com Ltd. / Science Source*)

This page intentionally left blank

CONTRIBUTORS xix
PREFACE xxxvii

PART 1 General Considerations in Clinical Medicine

1 The Practice of Medicine 1
The Editors

2 Global Issues in Medicine 7
Paul Farmer, Joseph Rhatigan

3 Decision-Making in Clinical Medicine 18
Daniel B. Mark, John B. Wong

4 Screening and Prevention of Disease 26
Katrina Armstrong, Gary J. Martin

5 Principles of Clinical Pharmacology 31
Dan M. Roden

 **6e Women's Health** 45
Andrea Dunaif

 **7e Men's Health** 45
Shalender Bhasin, Shehzad Basaria

8 Medical Disorders During Pregnancy 45
Robert L. Barbieri, John T. Repke

9 Medical Evaluation of the Surgical Patient 51
Wei C. Lau, Kim A. Eagle

10 Palliative and End-of-Life Care 55
Ezekiel J. Emanuel

11 Clinical Problems of Aging 70
Luigi Ferrucci, Stephanie Studenski

 **12e The Safety and Quality of Health Care** 85
David W. Bates

 **13e Primary Care in Low- and Middle-Income Countries** 85
Tim Evans, Kumanan Rasanathan

 **14e Complementary, Alternative, and Integrative Health Practices** 86
Josephine P. Briggs

 **15e The Economics of Medical Care** 86
Joseph P. Newhouse

 **16e Racial and Ethnic Disparities in Health Care** 86
Joseph R. Betancourt, Alexander R. Green

 **17e Ethical Issues in Clinical Medicine** 86
Bernard Lo, Christine Grady

PART 2 Cardinal Manifestations and Presentation of Diseases

PAIN

18 Pain: Pathophysiology and Management 87
James P. Rathmell, Howard L. Fields

19 Chest Discomfort 95
David A. Morrow

20 Abdominal Pain 103
Danny O. Jacobs, William Silen


21 Headache 107
Peter J. Goadsby, Neil H. Raskin

22 Back and Neck Pain 111
John W. Engstrom, Richard A. Deyo

ALTERATIONS IN BODY TEMPERATURE

23 Fever 123
Charles A. Dinarello, Reuven Porat

24 Fever and Rash 127
Elaine T. Kaye, Kenneth M. Kaye

 **25e Atlas of Rashes Associated with Fever** 135
Kenneth M. Kaye, Elaine T. Kaye

26 Fever of Unknown Origin 135
Chantal P. Bleeker-Rovers, Jos W. M. van der Meer

NERVOUS SYSTEM DYSFUNCTION

27 Syncope 142
Roy Freeman

28 Dizziness and Vertigo 148
Mark F. Walker, Robert B. Daroff

29 Fatigue 151
Jeffrey M. Gelfand, Vanja C. Douglas

30 Neurologic Causes of Weakness and Paralysis 154
Michael J. Aminoff

31 Numbness, Tingling, and Sensory Loss 158
Michael J. Aminoff

32 Gait and Balance Disorders 162
Lewis Sudarsky

 **33e Video Library of Gait Disorders** 165
Gail Kang, Nicholas B. Galifianakis, Michael D. Geschwind

34 Confusion and Delirium 166
S. Andrew Josephson, Bruce L. Miller

35 Dementia 170
William W. Seeley, Bruce L. Miller


36 Aphasia, Memory Loss, and Other Focal Cerebral Disorders 176
M.-Marsel Mesulam


 **37e Primary Progressive Aphasia, Memory Loss, and Other Focal Cerebral Disorders** 184
Maria Luisa Gorno-Tempini, Jennifer Ogar, Joel Kramer, Bruce L. Miller, Gil Rabinovici, Maria Carmela Tartaglia

38 Sleep Disorders 184
Charles A. Czeisler, Thomas E. Scammell, Clifford B. Saper

DISORDERS OF EYES, EARS, NOSE, AND THROAT

39 Disorders of the Eye 195
Jonathan C. Horton

 **40e Use of the Hand-Held Ophthalmoscope** 211
Homayoun Tabandeh, Morton F. Goldberg

 **41e Video Library of Neuro-Ophthalmology** 211
Shirley H. Wray

42 Disorders of Smell and Taste 211
Richard L. Doty, Steven M. Bromley


43 Disorders of Hearing 217
Anil K. Lalwani

44 Sore Throat, Earache, and Upper Respiratory Symptoms 225
Michael A. Rubin, Larry C. Ford, Ralph Gonzales

45 Oral Manifestations of Disease	235
<i>Samuel C. Durso</i>	

 46e Atlas of Oral Manifestations of Disease	242
<i>Samuel C. Durso, Janet A. Yellowitz</i>	


ALTERATIONS IN CIRCULATORY AND RESPIRATORY FUNCTIONS

 47e Dyspnea	243
<i>Richard M. Schwartzstein</i>	

48 Cough and Hemoptysis	243
<i>Patricia A. Kritek, Christopher H. Fanta</i>	

49 Hypoxia and Cyanosis	247
<i>Joseph Loscalzo</i>	

50 Edema	250
<i>Eugene Braunwald, Joseph Loscalzo</i>	

 51e Approach to the Patient with a Heart Murmur	253
<i>Patrick T. O'Gara, Joseph Loscalzo</i>	

52 Palpitations	254
<i>Joseph Loscalzo</i>	

ALTERATIONS IN GASTROINTESTINAL FUNCTION

53 Dysphagia	254
<i>Ikuo Hirano, Peter J. Kahrilas</i>	

54 Nausea, Vomiting, and Indigestion	258
<i>William L. Hasler</i>	

55 Diarrhea and Constipation	264
<i>Michael Camilleri, Joseph A. Murray</i>	


56 Involuntary Weight Loss	274
<i>Russell G. Robertson, J. Larry Jameson</i>	

57 Gastrointestinal Bleeding	276
<i>Loren Laine</i>	

58 Jaundice	279
<i>Savio John, Daniel S. Pratt</i>	

59 Abdominal Swelling and Ascites	285
<i>Kathleen E. Corey, Lawrence S. Friedman</i>	

ALTERATIONS IN RENAL AND URINARY TRACT FUNCTION

 60e Dysuria, Bladder Pain, and the Interstitial Cystitis/Bladder Pain Syndrome	288
<i>John W. Warren</i>	

61 Azotemia and Urinary Abnormalities	289
<i>Julie Lin, Bradley M. Denker</i>	

 62e Atlas of Urinary Sediments and Renal Biopsies	295
<i>Agnes B. Fogo, Eric G. Neilson</i>	

63 Fluid and Electrolyte Disturbances	295
<i>David B. Mount</i>	

 64e Fluid and Electrolyte Imbalances and Acid-Base Disturbances: Case Examples	312
<i>David B. Mount, Thomas D. DuBose, Jr.</i>	

65 Hypercalcemia and Hypocalcemia	313
<i>Sundeep Khosla</i>	

 64e Fluid and Electrolyte Imbalances and Acid-Base Disturbances: Case Examples	312
<i>David B. Mount, Thomas D. DuBose, Jr.</i>	

65 Hypercalcemia and Hypocalcemia	313
<i>Sundeep Khosla</i>	

66 Acidosis and Alkalosis	315
<i>Thomas D. DuBose, Jr.</i>	

ALTERATIONS IN SEXUAL FUNCTION AND REPRODUCTION

67 Sexual Dysfunction	324
<i>Kevin T. McVary</i>	

68 Hirsutism	331
<i>David A. Ehrmann</i>	

69 Menstrual Disorders and Pelvic Pain	335
<i>Janet E. Hall</i>	

ALTERATIONS IN THE SKIN

70 Approach to the Patient with a Skin Disorder	339
<i>Thomas J. Lawley, Kim B. Yancey</i>	

71 Eczema, Psoriasis, Cutaneous Infections, Acne, and Other Common Skin Disorders	344
<i>Leslie P. Lawley, Calvin O. McCall, Thomas J. Lawley</i>	

72 Skin Manifestations of Internal Disease	353
<i>Jean L. Bologna, Irwin M. Braverman</i>	

73 Immunologically Mediated Skin Diseases	370
<i>Kim B. Yancey, Thomas J. Lawley</i>	

74 Cutaneous Drug Reactions	377
<i>Kanade Shinkai, Robert S. Stern, Bruce U. Wintroub</i>	

75 Photosensitivity and Other Reactions to Light	385
<i>Alexander G. Marneros, David R. Bickers</i>	

 76e Atlas of Skin Manifestations of Internal Disease	391
<i>Thomas J. Lawley, Calvin O. McCall, Robert A. Swerlick</i>	


HEMATOLOGIC ALTERATIONS

77 Anemia and Polycythemia	392
<i>John W. Adamson, Dan L. Longo</i>	

78 Bleeding and Thrombosis	400
<i>Barbara A. Konkle</i>	

79 Enlargement of Lymph Nodes and Spleen	407
<i>Patrick H. Henry, Dan L. Longo</i>	

80 Disorders of Granulocytes and Monocytes	413
<i>Steven M. Holland, John I. Gallin</i>	

 81e Atlas of Hematology and Analysis of Peripheral Blood Smears	424
<i>Dan L. Longo</i>	

 81e Atlas of Hematology and Analysis of Peripheral Blood Smears	424
<i>Dan L. Longo</i>	

PART 3 Genes, the Environment, and Disease


82 Principles of Human Genetics	425
<i>J. Larry Jameson, Peter Kopp</i>	

 83e Chromosome Disorders	445
<i>Nancy B. Spinner, Laura K. Conlin</i>	

84 The Practice of Genetics in Clinical Medicine	446
<i>Susan M. Domchek, J. Larry Jameson, Susan Miesfeldt</i>	

 85e Mitochondrial DNA and Heritable Traits and Diseases	451
<i>Karl Skorecki, Doron Behar</i>	

 86e The Human Microbiome	451
<i>Jeffrey I. Gordon, Rob Knight</i>	

 87e Network Medicine: Systems Biology in Health and Disease	451
<i>Joseph Loscalzo</i>	

PART 4 Regenerative Medicine

- 88 Stem Cell Biology** 453
Minoru S. H. Ko
- 89e Hematopoietic Stem Cells** 455
David T. Scadden, Dan L. Longo
- 90e Applications of Stem Cell Biology in Clinical Medicine** 455
John A. Kessler
- 91e Gene Therapy in Clinical Medicine** 456
Katherine A. High
- 92e Tissue Engineering** 456
Anthony Atala

PART 5 Aging

- 93e World Demography of Aging** 457
Richard M. Suzman, John G. Haaga
- 94e The Biology of Aging** 457
Rafaël de Cabo, David G. Le Couteur

PART 6 Nutrition and Weight Loss

- 95e Nutrient Requirements and Dietary Assessment** 459
Johanna Dwyer
- 96e Vitamin and Trace Mineral Deficiency and Excess** 459
Robert M. Russell, Paolo M. Suter
- 97 Malnutrition and Nutritional Assessment** 459
Douglas C. Heimbarger
- 98e Enteral and Parenteral Nutrition Therapy** 465
Bruce R. Bistrian, L. John Hoffer, David F. Driscoll

PART 7 Oncology and Hematology

NEOPLASTIC DISORDERS

- 99 Approach to the Patient with Cancer** 467
Dan L. Longo
- 100 Prevention and Early Detection of Cancer** 475
Jennifer M. Croswell, Otis W. Brawley, Barnett S. Kramer
- 101e Cancer Genetics** 483
Pat J. Morin, Jeffrey M. Trent, Francis S. Collins, Bert Vogelstein
- 102e Cancer Cell Biology** 483
Jeffrey W. Clark, Dan L. Longo
- 103e Principles of Cancer Treatment** 483
Edward A. Sausville, Dan L. Longo
- 104 Infections in Patients with Cancer** 484
Robert W. Finberg
- 105 Cancer of the Skin** 493
Walter J. Urba, Brendan D. Curti
- 106 Head and Neck Cancer** 502
Everett E. Vokes
- 107 Neoplasms of the Lung** 506
Leora Horn, Christine M. Lovly, David H. Johnson

- 108 Breast Cancer** 523
Marc E. Lippman
- 109 Upper Gastrointestinal Tract Cancers** 532
Robert J. Mayer
- 110 Lower Gastrointestinal Cancers** 537
Robert J. Mayer
- 111 Tumors of the Liver and Biliary Tree** 544
Brian I. Carr
- 112 Pancreatic Cancer** 554
Elizabeth Smyth, David Cunningham
- 113 Endocrine Tumors of the Gastrointestinal Tract and Pancreas** 557
Robert T. Jensen
- 114 Bladder and Renal Cell Carcinomas** 575
Howard I. Scher, Jonathan E. Rosenberg, Robert J. Motzer
- 115 Benign and Malignant Diseases of the Prostate** 579
Howard I. Scher, James A. Eastham
- 116 Testicular Cancer** 588
Robert J. Motzer, Darren R. Feldman, George J. Bosl
- 117 Gynecologic Malignancies** 592
Michael V. Seiden
- 118 Primary and Metastatic Tumors of the Nervous System** 598
Lisa M. DeAngelis, Patrick Y. Wen
- 119e Soft Tissue and Bone Sarcomas and Bone Metastases** 608
Shreyaskumar R. Patel, Robert S. Benjamin
- 120e Carcinoma of Unknown Primary** 608
Gauri R. Varadhachary, James L. Abbruzzese
- 121 Paraneoplastic Syndromes: Endocrinologic/Hematologic** 608
J. Larry Jameson, Dan L. Longo
- 122 Paraneoplastic Neurologic Syndromes and Autoimmune Encephalitis** 614
Josep Dalmau, Myrna R. Rosenfeld
- 123e Thymoma** 619
Dan L. Longo
- 124e Neoplasia During Pregnancy** 620
Michael F. Greene, Dan L. Longo
- 125 Late Consequences of Cancer and Its Treatment** 620
Carl E. Freter, Dan L. Longo

HEMATOPOIETIC DISORDERS

- 126 Iron Deficiency and Other Hypoproliferative Anemias** 625
John W. Adamson
- 127 Disorders of Hemoglobin** 631
Edward J. Benz, Jr.
- 128 Megaloblastic Anemias** 640
A. Victor Hoffbrand
- 129 Hemolytic Anemias and Anemia Due to Acute Blood Loss** 649
Lucio Luzzatto
- 130 Bone Marrow Failure Syndromes Including Aplastic Anemia and Myelodysplasia** 662
Neal S. Young
- 131 Polycythemia Vera and Other Myeloproliferative Neoplasms** 672
Jerry L. Spivak
- 132 Acute Myeloid Leukemia** 678
Guido Marcucci, Clara D. Bloomfield



133	Chronic Myeloid Leukemia	687	155	Infective Endocarditis	816
	<i>Hagop Kantarjian, Jorge Cortes</i>			<i>Adolf W. Karchmer</i>	
134	Malignancies of Lymphoid Cells	695	156	Infections of the Skin, Muscles, and Soft Tissues	827
	<i>Dan L. Longo</i>			<i>Dennis L. Stevens</i>	
	135e Less Common Hematologic Malignancies	710	157	Infectious Arthritis	833
	<i>Ayalew Tefferi, Dan L. Longo</i>			<i>Lawrence C. Madoff</i>	
136	Plasma Cell Disorders	710	158	Osteomyelitis	838
	<i>Nikhil C. Munshi, Dan L. Longo, Kenneth C. Anderson</i>			<i>Werner Zimmerli</i>	
137	Amyloidosis	719	159	Intraabdominal Infections and Abscesses	846
	<i>David C. Seldin, John L. Berk</i>			<i>Miriam Baron Barshak, Dennis L. Kasper</i>	
	138e Transfusion Biology and Therapy	724	160	Acute Infectious Diarrheal Diseases and Bacterial Food Poisoning	852
	<i>Jeffery S. Dzieczkowski, Kenneth C. Anderson</i>			<i>Regina C. LaRocque, Edward T. Ryan, Stephen B. Calderwood</i>	
	139e Hematopoietic Cell Transplantation	725	161	<i>Clostridium difficile</i> Infection, Including Pseudomembranous Colitis	857
	<i>Frederick R. Appelbaum</i>			<i>Dale N. Gerding, Stuart Johnson</i>	

DISORDERS OF HEMOSTASIS

140	Disorders of Platelets and Vessel Wall	725	162	Urinary Tract Infections, Pyelonephritis, and Prostatitis	861
	<i>Barbara A. Konkle</i>			<i>Kalpana Gupta, Barbara W. Trautner</i>	
141	Coagulation Disorders	732	163	Sexually Transmitted Infections: Overview and Clinical Approach	869
	<i>Valder R. Arruda, Katherine A. High</i>			<i>Jeanne M. Marrazzo, King K. Holmes</i>	
142	Arterial and Venous Thrombosis	740	164	Meningitis, Encephalitis, Brain Abscess, and Empyema	883
	<i>Jane E. Freedman, Joseph Loscalzo</i>			<i>Karen L. Roos, Kenneth L. Tyler</i>	
143	Antiplatelet, Anticoagulant, and Fibrinolytic Drugs	745	165	Chronic and Recurrent Meningitis	906
	<i>Jeffrey I. Weitz</i>			<i>Walter J. Koroshetz, Avindra Nath</i>	

PART 8 Infectious Diseases

BASIC CONSIDERATIONS IN INFECTIOUS DISEASES

144	Approach to the Patient with an Infectious Disease	761		145e Molecular Mechanisms of Microbial Pathogenesis	768
	<i>Neeraj K. Surana, Dennis L. Kasper</i>			<i>Gerald B. Pier</i>	
146	Genomics and Infectious Disease	768			
	<i>Roby P. Bhattacharyya, Yonatan H. Grad, Deborah T. Hung</i>				
147	Approach to the Acutely Ill Infected Febrile Patient	779			
	<i>Tamar F. Barlam, Dennis L. Kasper</i>				
148	Immunization Principles and Vaccine Use	785			
	<i>Anne Schuchat, Lisa A. Jackson</i>				
149	Health Recommendations for International Travel	793			
	<i>Jay S. Keystone, Phyllis E. Kozarsky</i>				
	150e Laboratory Diagnosis of Infectious Diseases	802			
	<i>Alexander J. McAdam, Andrew B. Onderdonk</i>				
	151e Climate Change and Infectious Disease	803			
	<i>Aaron S. Bernstein</i>				
	152e Infections in Veterans Returning from Foreign Wars	803			
	<i>Andrew W. Artenstein</i>				

CLINICAL SYNDROMES: COMMUNITY-ACQUIRED INFECTIONS

153	Pneumonia	803		166e Infectious Complications of Burns	911
	<i>Lionel A. Mandell, Richard G. Wunderink</i>			<i>Lawrence C. Madoff, Florencia Pereyra</i>	
154	Lung Abscess	813		167e Infectious Complications of Bites	911
	<i>Rebecca M. Baron, Miriam Baron Barshak</i>			<i>Lawrence C. Madoff, Florencia Pereyra</i>	

CLINICAL SYNDROMES: HEALTH CARE–ASSOCIATED INFECTIONS

168	Infections Acquired in Health Care Facilities	911
	<i>Robert A. Weinstein</i>	
169	Infections in Transplant Recipients	919
	<i>Robert W. Finberg, Joyce Fingerh</i>	

APPROACH TO THERAPY FOR BACTERIAL DISEASES

170	Treatment and Prophylaxis of Bacterial Infections	930
	<i>David C. Hooper, Erica S. Shenoy, Christy A. Varughese</i>	

DISEASES CAUSED BY GRAM-POSITIVE BACTERIA

171	Pneumococcal Infections	946
	<i>David Goldblatt, Katherine L. O'Brien</i>	
172	Staphylococcal Infections	954
	<i>Franklin D. Lowy</i>	
173	Streptococcal Infections	963
	<i>Michael R. Wessels</i>	
174	Enterococcal Infections	971
	<i>Cesar A. Arias, Barbara E. Murray</i>	
175	Diphtheria and Other Corynebacterial Infections	977
	<i>William R. Bishai, John R. Murphy</i>	
176	<i>Listeria monocytogenes</i> Infections	982
	<i>Elizabeth L. Hohmann, Daniel A. Portnoy</i>	
177	Tetanus	984
	<i>C. Louise Thwaites, Lam Minh Yen</i>	
178	Botulism	987
	<i>Susan Maslanka, Agam K. Rao</i>	
179	Gas Gangrene and Other Clostridial Infections	990
	<i>Amy E. Bryant, Dennis L. Stevens</i>	

DISEASES CAUSED BY GRAM-NEGATIVE BACTERIA

- 180 Meningococcal Infections** 995
Andrew J. Pollard
- 181 Gonococcal Infections** 1003
Sanjay Ram, Peter A. Rice
- 182 Haemophilus and Moraxella Infections** 1010
Timothy F. Murphy
- 183e Infections Due to the HACEK Group and Miscellaneous Gram-Negative Bacteria** 1014
Tamar F. Barlam, Dennis L. Kasper
- 184 Legionella Infections** 1014
Victor L. Yu, M. Luisa Pedro-Botet, Yusef E. Lin
- 185 Pertussis and Other Bordetella Infections** 1021
Karina A. Top, Scott A. Halperin
- 186 Diseases Caused by Gram-Negative Enteric Bacilli** 1025
Thomas A. Russo, James R. Johnson
- 187 Acinetobacter Infections** 1036
David L. Paterson, Anton Y. Peleg
- 188 Helicobacter pylori Infections** 1038
John C. Atherton, Martin J. Blaser
- 189 Infections Due to Pseudomonas Species and Related Organisms** 1042
Reuben Ramphal
- 190 Salmonellosis** 1049
David A. Pegues, Samuel I. Miller
- 191 Shigellosis** 1055
Philippe J. Sansonetti, Jean Bergounioux
- 192 Infections Due to Campylobacter and Related Organisms** 1058
Martin J. Blaser
- 193 Cholera and Other Vibrios** 1061
Matthew K. Waldor, Edward T. Ryan
- 194e Brucellosis** 1066
Nicholas J. Beeching, Michael J. Corbel
- 195 Tularemia** 1066
Richard F. Jacobs, Gordon E. Schutze
- 196 Plague and Other Yersinia Infections** 1070
Michael B. Prentice
- 197 Bartonella Infections, Including Cat-Scratch Disease** 1078
Michael Giladi, Moshe Ephros
- 198e Donovanosis** 1083
Nigel O'Farrell

MISCELLANEOUS BACTERIAL INFECTIONS

- 199 Nocardiosis** 1084
Gregory A. Filice
- 200 Actinomycosis and Whipple's Disease** 1088
Thomas A. Russo
- 201 Infections Due to Mixed Anaerobic Organisms** 1094
Ronit Cohen-Poradosu, Dennis L. Kasper

MYCOBACTERIAL DISEASES

- 202 Tuberculosis** 1102
Mario C. Raviglione
- 203 Leprosy** 1122
Robert H. Gelber
- 204 Nontuberculous Mycobacterial Infections** 1128
Steven M. Holland
- 205e Antimycobacterial Agents** 1132
Max R. O'Donnell, Divya Reddy, Jussi J. Saukkonen

SPIROCHETAL DISEASES

- 206 Syphilis** 1132
Sheila A. Lukehart
- 207e Endemic Treponematoses** 1140
Sheila A. Lukehart
- 208 Leptospirosis** 1140
Rudy A. Hartskeerl, Jiří F. P. Wagenaar
- 209 Relapsing Fever** 1146
Alan G. Barbour
- 210 Lyme Borreliosis** 1149
Allen C. Steere

DISEASES CAUSED BY RICKETTSIAE, MYCOPLASMAS, AND CHLAMYDIAE

- 211 Rickettsial Diseases** 1154
David H. Walker, J. Stephen Dumler, Thomas Marrie
- 212 Infections Due to Mycoplasmas** 1163
R. Doug Hardy
- 213 Chlamydial Infections** 1165
Charlotte A. Gaydos, Thomas C. Quinn

VIRAL DISEASES: GENERAL CONSIDERATIONS

- 214e Medical Virology** 1174
Fred Wang, Elliott Kieff
- 215e Antiviral Chemotherapy, Excluding Antiretroviral Drugs** 1174
Lindsey R. Baden, Raphael Dolin

INFECTIONS DUE TO DNA VIRUSES

- 216 Herpes Simplex Virus Infections** 1175
Lawrence Corey
- 217 Varicella-Zoster Virus Infections** 1183
Richard J. Whitley
- 218 Epstein-Barr Virus Infections, Including Infectious Mononucleosis** 1186
Jeffrey I. Cohen
- 219 Cytomegalovirus and Human Herpesvirus Types 6, 7, and 8** 1190
Camille Nelson Kotton, Martin S. Hirsch
- 220e Molluscum Contagiosum, Monkeypox, and Other Poxvirus Infections** 1194
Fred Wang
- 221 Parvovirus Infections** 1195
Kevin E. Brown
- 222 Human Papillomavirus Infections** 1197
Aaron C. Ermel, Darron R. Brown

INFECTIONS DUE TO DNA AND RNA RESPIRATORY VIRUSES

- 223 Common Viral Respiratory Infections** 1202
Raphael Dolin
- 224 Influenza** 1209
Yehuda Z. Cohen, Raphael Dolin

INFECTIONS DUE TO HUMAN IMMUNODEFICIENCY VIRUS AND OTHER HUMAN RETROVIRUSES

- 225e The Human Retroviruses** 1215
Dan L. Longo, Anthony S. Fauci

- 226 Human Immunodeficiency Virus Disease: AIDS and Related Disorders** 1215
Anthony S. Fauci, H. Clifford Lane
- INFECTIONS DUE TO RNA VIRUSES**
- 227 Viral Gastroenteritis** 1285
Umesh D. Parashar, Roger I. Glass
- 228 Enterovirus, Parechovirus, and Reovirus Infections** 1289
Jeffrey I. Cohen
- 229 Measles (Rubeola)** 1295
Kaitlin Rainwater-Lovett, William J. Moss
-  **230e Rubella (German Measles)** 1299
Laura A. Zimmerman, Susan E. Reef
-  **231e Mumps** 1299
Steven A. Rubin, Kathryn M. Carbone
- 232 Rabies and Other Rhabdovirus Infections** 1299
Alan C. Jackson
- 233 Arthropod-Borne and Rodent-Borne Virus Infections** 1304
Jens H. Kuhn, Clarence J. Peters
- 234 Ebolavirus and Marburgvirus Infections** 1323
Jens H. Kuhn
- FUNGAL INFECTIONS**
- 235 Diagnosis and Treatment of Fungal Infections** 1329
John E. Edwards, Jr.
- 236 Histoplasmosis** 1332
Chadi A. Hage, L. Joseph Wheat
- 237 Coccidioidomycosis** 1334
Neil M. Ampel
- 238 Blastomycosis** 1337
Donna C. Sullivan, Rathel L. Nolan, III
- 239 Cryptococcosis** 1339
Arturo Casadevall
- 240 Candidiasis** 1342
John E. Edwards, Jr.
- 241 Aspergillosis** 1345
David W. Denning
- 242 Mucormycosis** 1350
Brad Spellberg, Ashraf S. Ibrahim
- 243 Superficial Mycoses and Less Common Systemic Mycoses** 1353
Carol A. Kauffman
- 244 Pneumocystis Infections** 1358
Henry Masur, Alison Morris
- PROTOZOAL AND HELMINTHIC INFECTIONS: GENERAL CONSIDERATIONS**
-  **245e Laboratory Diagnosis of Parasitic Infections** 1362
Sharon L. Reed, Charles E. Davis
-  **246e Agents Used to Treat Parasitic Infections** 1363
Thomas A. Moore
- PROTOZOAL INFECTIONS**
- 247 Amebiasis and Infection with Free-Living Amebas** 1363
Rosa M. Andrade, Sharon L. Reed
- 248 Malaria** 1368
Nicholas J. White, Joel G. Breman
- 249 Babesiosis** 1384
Edouard G. Vannier, Peter J. Krause
-  **250e Atlas of Blood Smears of Malaria and Babesiosis** 1387
Nicholas J. White, Joel G. Breman
- 251 Leishmaniasis** 1387
Shyam Sundar
- 252 Chagas Disease and African Trypanosomiasis** 1394
Louis V. Kirchhoff, Anis Rassi Jr.
- 253 Toxoplasma Infections** 1398
Kami Kim, Lloyd H. Kasper
- 254 Protozoal Intestinal Infections and Trichomoniasis** 1405
Peter F. Weller
- HELMINTHIC INFECTIONS**
-  **255e Introduction to Helminthic Infections** 1409
Peter F. Weller
- 256 Trichinellosis and Other Tissue Nematode Infections** 1410
Peter F. Weller
- 257 Intestinal Nematode Infections** 1413
Peter F. Weller, Thomas B. Nutman
- 258 Filarial and Related Infections** 1417
Thomas B. Nutman, Peter F. Weller
- 259 Schistosomiasis and Other Trematode Infections** 1423
Charles H. King, Adel A. F. Mahmoud
- 260 Cestode Infections** 1430
A. Clinton White, Jr., Peter F. Weller
-  **PART 9 Terrorism and Clinical Medicine**
-  **261e Microbial Bioterrorism** 1437
H. Clifford Lane, Anthony S. Fauci
-  **262e Chemical Terrorism** 1437
Charles G. Hurst, Jonathan Newmark, James A. Romano, Jr.
-  **263e Radiation Terrorism** 1437
Christine E. Hill-Kayser, Eli Glatstein, Zelig A. Tochner
-  **PART 10 Disorders of the Cardiovascular System**
- INTRODUCTION TO CARDIOVASCULAR DISORDERS**
- 264 Approach to the Patient with Possible Cardiovascular Disease** 1439
Joseph Loscalzo
-  **265e Basic Biology of the Cardiovascular System** 1441
Joseph Loscalzo, Peter Libby, Jonathan A. Epstein
-  **266e Epidemiology of Cardiovascular Disease** 1442
Thomas A. Gaziano, J. Michael Gaziano
- DIAGNOSIS OF CARDIOVASCULAR DISORDERS**
- 267 Physical Examination of the Cardiovascular System** 1442
Patrick T. O'Gara, Joseph Loscalzo

- 268 Electrocardiography** 1450
Ary L. Goldberger
- 269e Atlas of Electrocardiography** 1459
Ary L. Goldberger
- 270e Noninvasive Cardiac Imaging: Echocardiography, Nuclear Cardiology, and Magnetic Resonance/Computed Tomography Imaging** 1459
Marcelo F. Di Carli, Raymond Y. Kwong, Scott D. Solomon
- 271e Atlas of Noninvasive Imaging** 1460
Marcelo F. Di Carli, Raymond Y. Kwong, Scott D. Solomon
- 272 Diagnostic Cardiac Catheterization and Coronary Angiography** 1460
Jane A. Leopold, David P. Faxon
- DISORDERS OF RHYTHM**
- 273e Principles of Electrophysiology** 1466
David D. Spragg, Gordon F. Tomaselli
- 274 The Bradyarrhythmias: Disorders of the Sinoatrial Node** 1466
David D. Spragg, Gordon F. Tomaselli
- 275 The Bradyarrhythmias: Disorders of the Atrioventricular Node** 1470
David D. Spragg, Gordon F. Tomaselli
- 276 Supraventricular Tachyarrhythmias** 1476
Gregory F. Michaud, William G. Stevenson
- 277 Ventricular Arrhythmias** 1489
Roy M. John, William G. Stevenson
- 278e Atlas of Cardiac Arrhythmias** 1500
Ary L. Goldberger
- DISORDERS OF THE HEART**
- 279 Heart Failure: Pathophysiology and Diagnosis** 1500
Douglas L. Mann, Murali Chakinala
- 280 Heart Failure: Management** 1507
Mandeep R. Mehra
- 281 Cardiac Transplantation and Prolonged Assisted Circulation** 1516
Sharon A. Hunt, Hari R. Mallidi
- 282 Congenital Heart Disease in the Adult** 1519
Jamil A. Aboulhosn, John S. Child
- 283 Aortic Valve Disease** 1528
Patrick T. O’Gara, Joseph Loscalzo
- 284 Mitral Valve Disease** 1539
Patrick T. O’Gara, Joseph Loscalzo
- 285 Tricuspid and Pulmonic Valve Disease** 1547
Patrick T. O’Gara, Joseph Loscalzo
- 286 Multiple and Mixed Valvular Heart Disease** 1550
Patrick T. O’Gara, Joseph Loscalzo
- 287 Cardiomyopathy and Myocarditis** 1553
Neal K. Lakdawala, Lynne Warner Stevenson, Joseph Loscalzo
- 288 Pericardial Disease** 1571
Eugene Braunwald
- 289e Tumors and Trauma of the Heart** 1577
Eric H. Awtry, Wilson S. Colucci
- 290e Cardiac Manifestations of Systemic Disease** 1577
Eric H. Awtry, Wilson S. Colucci
- CORONARY AND PERIPHERAL VASCULAR DISEASE**
- 291e The Pathogenesis, Prevention, and Treatment of Atherosclerosis** 1578
Peter Libby
- 292e Atlas of Atherosclerosis** 1578
Peter Libby
- 293 Ischemic Heart Disease** 1578
Elliott M. Antman, Joseph Loscalzo
- 294 Non-ST-Segment Elevation Acute Coronary Syndrome (Non-ST-Segment Elevation Myocardial Infarction and Unstable Angina)** 1593
Christopher P. Cannon, Eugene Braunwald
- 295 ST-Segment Elevation Myocardial Infarction** 1599
Elliott M. Antman, Joseph Loscalzo
- 296e Percutaneous Coronary Interventions and Other Interventional Procedures** 1611
David P. Faxon, Deepak L. Bhatt
- 297e Atlas of Percutaneous Revascularization** 1611
Jane A. Leopold, Deepak L. Bhatt, David P. Faxon
- 298 Hypertensive Vascular Disease** 1611
Theodore A. Kotchen
- 299 Renovascular Disease** 1627
Stephen C. Textor
- 300 Deep Venous Thrombosis and Pulmonary Thromboembolism** 1631
Samuel Z. Goldhaber
- 301 Diseases of the Aorta** 1637
Mark A. Creager, Joseph Loscalzo
- 302 Arterial Diseases of the Extremities** 1643
Mark A. Creager, Joseph Loscalzo
- 303 Chronic Venous Disease and Lymphedema** 1650
Mark A. Creager, Joseph Loscalzo
- 304 Pulmonary Hypertension** 1655
Aaron B. Waxman, Joseph Loscalzo




PART 11 Disorders of the Respiratory System

DIAGNOSIS OF RESPIRATORY DISORDERS

- 305 Approach to the Patient with Disease of the Respiratory System** 1661
Patricia A. Kritek, Augustine M. K. Choi
- 306e Disturbances of Respiratory Function** 1663
Edward T. Naureckas, Julian Solway
- 307 Diagnostic Procedures in Respiratory Disease** 1663
Anne L. Fuhlbrigge, Augustine M. K. Choi
- 308e Atlas of Chest Imaging** 1669
Patricia A. Kritek, John J. Reilly, Jr.

DISEASES OF THE RESPIRATORY SYSTEM

- 309 Asthma** 1669
Peter J. Barnes
- 310 Hypersensitivity Pneumonitis and Pulmonary Infiltrates with Eosinophilia** 1681
Praveen Akuthota, Michael E. Wechsler
- 311 Occupational and Environmental Lung Disease** 1687
John R. Balmes, Frank E. Speizer
- 312 Bronchiectasis** 1694
Rebecca M. Baron, Miriam Baron Barshak
- 313 Cystic Fibrosis** 1697
Eric J. Sorscher
- 314 Chronic Obstructive Pulmonary Disease** 1700
John J. Reilly, Jr., Edwin K. Silverman, Steven D. Shapiro

315	Interstitial Lung Diseases	1708
	<i>Talmadge E. King, Jr.</i>	
316	Disorders of the Pleura	1716
	<i>Richard W. Light</i>	
317	Disorders of the Mediastinum	1719
	<i>Richard W. Light</i>	
318	Disorders of Ventilation	1720
	<i>John F. McConville, Babak Mokhlesi, Julian Solway</i>	
319	Sleep Apnea	1723
	<i>Andrew Wellman, Susan Redline</i>	
	320e Lung Transplantation	1727
	<i>Elbert P. Trulock</i>	

PART 12 Critical Care Medicine


RESPIRATORY CRITICAL CARE

321	Approach to the Patient with Critical Illness	1729
	<i>John P. Kress, Jesse B. Hall</i>	
322	Acute Respiratory Distress Syndrome	1736
	<i>Bruce D. Levy, Augustine M. K. Choi</i>	
323	Mechanical Ventilatory Support	1740
	<i>Bartolome R. Celli</i>	

SHOCK AND CARDIAC ARREST

324	Approach to the Patient with Shock	1744
	<i>Ronald V. Maier</i>	
325	Severe Sepsis and Septic Shock	1751
	<i>Robert S. Munford</i>	
326	Cardiogenic Shock and Pulmonary Edema	1759
	<i>Judith S. Hochman, David H. Ingbar</i>	
327	Cardiovascular Collapse, Cardiac Arrest, and Sudden Cardiac Death	1764
	<i>Robert J. Myerburg, Agustin Castellanos</i>	



NEUROLOGIC CRITICAL CARE

328	Coma	1771
	<i>Allan H. Ropper</i>	
	329e Examination of the Comatose Patient	1777
	<i>S. Andrew Josephson</i>	
330	Neurologic Critical Care, Including Hypoxic-Ischemic Encephalopathy, and Subarachnoid Hemorrhage	1777
	<i>J. Claude Hemphill, III, Wade S. Smith, Daryl R. Gress</i>	

ONCOLOGIC EMERGENCIES

331	Oncologic Emergencies	1787
	<i>Rasim Gucalp, Janice P. Dutcher</i>	

PART 13 Disorders of the Kidney and Urinary Tract

	332e Cellular and Molecular Biology of the Kidney	1799
	<i>Alfred L. George, Jr., Eric G. Neilson</i>	
	333e Adaptation of the Kidney to Injury	1799
	<i>Joseph V. Bonventre</i>	
334	Acute Kidney Injury	1799
	<i>Sushrut S. Waikar, Joseph V. Bonventre</i>	

335	Chronic Kidney Disease	1811
	<i>Joanne M. Bargman, Karl Skorecki</i>	
336	Dialysis in the Treatment of Renal Failure	1822
	<i>Kathleen D. Liu, Glenn M. Chertow</i>	
337	Transplantation in the Treatment of Renal Failure	1825
	<i>Jamil Azzi, Edgar L. Milford, Mohamed H. Sayegh, Anil Chandraker</i>	
338	Glomerular Diseases	1831
	<i>Julia B. Lewis, Eric G. Neilson</i>	
339	Polycystic Kidney Disease and Other Inherited Disorders of Tubule Growth and Development	1850
	<i>Jing Zhou, Martin R. Pollak</i>	
340	Tubulointerstitial Diseases of the Kidney	1856
	<i>Laurence H. Beck, David J. Salant</i>	
341	Vascular Injury to the Kidney	1863
	<i>Nelson Leung, Stephen C. Textor</i>	
342	Nephrolithiasis	1866
	<i>Gary C. Curhan</i>	
343	Urinary Tract Obstruction	1871
	<i>Julian L. Seifter</i>	

PART 14 Disorders of the Gastrointestinal System

DISORDERS OF THE ALIMENTARY TRACT

344	Approach to the Patient with Gastrointestinal Disease	1875
	<i>William L. Hasler, Chung Owyang</i>	
345	Gastrointestinal Endoscopy	1880
	<i>Louis Michel Wong Kee Song, Mark Topazian</i>	
	346e Video Atlas of Gastrointestinal Endoscopy	1900
	<i>Louis Michel Wong Kee Song, Mark Topazian</i>	
347	Diseases of the Esophagus	1900
	<i>Peter J. Kahrilas, Ikuo Hirano</i>	
348	Peptic Ulcer Disease and Related Disorders	1911
	<i>John Del Valle</i>	
349	Disorders of Absorption	1932
	<i>Henry J. Binder</i>	
	350e The Schilling Test	1946
	<i>Henry J. Binder</i>	
351	Inflammatory Bowel Disease	1947
	<i>Sonia Friedman, Richard S. Blumberg</i>	
352	Irritable Bowel Syndrome	1965
	<i>Chung Owyang</i>	
353	Diverticular Disease and Common Anorectal Disorders	1971
	<i>Rizwan Ahmed, Susan L. Gearhart</i>	
354	Mesenteric Vascular Insufficiency	1978
	<i>Rizwan Ahmed, Mahmoud Malas</i>	
355	Acute Intestinal Obstruction	1981
	<i>Danny O. Jacobs</i>	
356	Acute Appendicitis and Peritonitis	1985
	<i>Danny O. Jacobs</i>	

LIVER AND BILIARY TRACT DISEASE

357	Approach to the Patient with Liver Disease	1989
	<i>Marc G. Ghany, Jay H. Hoofnagle</i>	
358	Evaluation of Liver Function	1995
	<i>Daniel S. Pratt</i>	

359 The Hyperbilirubinemias 1999
Allan W. Wolkoff

360 Acute Viral Hepatitis 2004
Jules L. Dienstag


361 Toxic and Drug-Induced Hepatitis 2023
William M. Lee, Jules L. Dienstag


362 Chronic Hepatitis 2031
Jules L. Dienstag

363 Alcoholic Liver Disease 2052
Mark E. Mailliard, Michael F. Sorrell

364 Nonalcoholic Fatty Liver Diseases and Nonalcoholic Steatohepatitis 2054
Manal F. Abdelmalek, Anna Mae Diehl

365 Cirrhosis and Its Complications 2058
Bruce R. Bacon

 **366e Atlas of Liver Biopsies** 2067
Jules L. Dienstag, Atul K. Bhan

 **367e Genetic, Metabolic, and Infiltrative Diseases Affecting the Liver** 2067
Bruce R. Bacon

368 Liver Transplantation 2067
Raymond T. Chung, Jules L. Dienstag

369 Diseases of the Gallbladder and Bile Ducts 2075
Norton J. Greenberger, Gustav Paumgartner


DISORDERS OF THE PANCREAS


370 Approach to the Patient with Pancreatic Disease 2086
Darwin L. Conwell, Norton J. Greenberger, Peter A. Banks

371 Acute and Chronic Pancreatitis 2090
Darwin L. Conwell, Peter A. Banks, Norton J. Greenberger


 **PART 15 Immune-Mediated, Inflammatory, and Rheumatologic Disorders**

THE IMMUNE SYSTEM IN HEALTH AND DISEASE

 **372e Introduction to the Immune System** 2103
Barton F. Haynes, Kelly A. Soderberg, Anthony S. Fauci


 **373e The Major Histocompatibility Complex** 2103
Gerald T. Nepom

374 Primary Immune Deficiency Diseases 2103
Alain Fischer

 **375e Primary Immunodeficiencies Associated with (or Secondary to) Other Diseases** 2113
Alain Fischer

DISORDERS OF IMMUNE-MEDIATED INJURY

376 Allergies, Anaphylaxis, and Systemic Mastocytosis 2113
Joshua A. Boyce, K. Frank Austen

 **377e Autoimmunity and Autoimmune Diseases** 2124
Betty Diamond, Peter E. Lipsky

378 Systemic Lupus Erythematosus 2124
Bevra Hannahs Hahn

379 Antiphospholipid Syndrome 2134
Haralampos M. Moutsopoulos, Panayiotis G. Vlachoyiannopoulos

380 Rheumatoid Arthritis 2136
Ankooor Shah, E. William St. Clair

381 Acute Rheumatic Fever 2149
Jonathan R. Carapetis

382 Systemic Sclerosis (Scleroderma) and Related Disorders 2154
John Varga

383 Sjögren’s Syndrome 2166
Haralampos M. Moutsopoulos, Athanasios G. Tzioufas

384 The Spondyloarthritides 2169
Joel D. Taurog, John D. Carter

385 The Vasculitis Syndromes 2179
Carol A. Langford, Anthony S. Fauci

 **386e Atlas of the Vasculitic Syndromes** 2193
Carol A. Langford, Anthony S. Fauci

387 Behçet’s Syndrome 2194
Haralampos M. Moutsopoulos

388 Polymyositis, Dermatomyositis, and Inclusion Body Myositis 2194
Marinos C. Dalakas

389 Relapsing Polychondritis 2202
Carol A. Langford

390 Sarcoidosis 2205
Robert P. Baughman, Elyse E. Lower

 **391e IgG4-Related Disease** 2212
John H. Stone

392 Familial Mediterranean Fever and Other Hereditary Autoinflammatory Diseases 2212
Daniel L. Kastner

DISORDERS OF THE JOINTS AND ADJACENT TISSUES

393 Approach to Articular and Musculoskeletal Disorders 2216
John J. Cush

394 Osteoarthritis 2226
David T. Felson

395 Gout and Other Crystal-Associated Arthropathies 2233
H. Ralph Schumacher, Lan X. Chen

396 Fibromyalgia 2238
Leslie J. Crofford


397 Arthritis Associated with Systemic Disease, and Other Arthritides 2240
Carol A. Langford, Brian F. Mandell


398 Periarticular Disorders of the Extremities 2247
Carol A. Langford

 **PART 16 Endocrinology and Metabolism**



ENDOCRINOLOGY



399 Approach to the Patient with Endocrine Disorders 2251
J. Larry Jameson

 **400e Mechanisms of Hormone Action** 2255
J. Larry Jameson



 **401e Anterior Pituitary: Physiology of Pituitary Hormones** 2255
Shlomo Melmed, J. Larry Jameson

- 402 Hypopituitarism** 2255
Shlomo Melmed, J. Larry Jameson
- 403 Anterior Pituitary Tumor Syndromes** 2261
Shlomo Melmed, J. Larry Jameson
- 404 Disorders of the Neurohypophysis** 2274
Gary L. Robertson
- 405 Disorders of the Thyroid Gland** 2283
J. Larry Jameson, Susan J. Mandel, Anthony P. Weetman
- 406 Disorders of the Adrenal Cortex** 2309
Wiebke Arlt
- 407 Pheochromocytoma** 2329
Hartmut P. H. Neumann
- 408 Multiple Endocrine Neoplasia** 2335
Rajesh V. Thakker
- 409 Autoimmune Polyendocrine Syndromes** 2344
Peter A. Gottlieb
- REPRODUCTIVE ENDOCRINOLOGY**
- 410 Disorders of Sex Development** 2349
John C. Achermann, J. Larry Jameson
- 411 Disorders of the Testes and Male Reproductive System** 2357
Shalender Bhasin, J. Larry Jameson
- 412 Disorders of the Female Reproductive System** 2375
Janet E. Hall
- 413 Menopause and Postmenopausal Hormone Therapy** 2381
JoAnn E. Manson, Shari S. Bassuk
- 414 Infertility and Contraception** 2387
Janet E. Hall
- OBESITY, DIABETES MELLITUS, AND METABOLIC SYNDROME**
- 415e Biology of Obesity** 2392
Jeffrey S. Flier, Eleftheria Maratos-Flier
- 416 Evaluation and Management of Obesity** 2392
Robert F. Kushner
- 417 Diabetes Mellitus: Diagnosis, Classification, and Pathophysiology** 2399
Alvin C. Powers
- 418 Diabetes Mellitus: Management and Therapies** 2407
Alvin C. Powers
- 419 Diabetes Mellitus: Complications** 2422
Alvin C. Powers
- 420 Hypoglycemia** 2430
Philip E. Cryer, Stephen N. Davis
- 421 Disorders of Lipoprotein Metabolism** 2435
Daniel J. Rader, Helen H. Hobbs
- 422 The Metabolic Syndrome** 2449
Robert H. Eckel
- DISORDERS OF BONE AND MINERAL METABOLISM**
- 423 Bone and Mineral Metabolism in Health and Disease** 2454
F. Richard Bringhurst, Marie B. Demay, Stephen M. Krane, Henry M. Kronenberg
- 424 Disorders of the Parathyroid Gland and Calcium Homeostasis** 2466
John T. Potts, Jr., Harald Jüppner
- 425 Osteoporosis** 2488
Robert Lindsay, Felicia Cosman
- 426e Paget's Disease and Other Dysplasias of Bone** 2504
Murray J. Favus, Tamara J. Vokes
- DISORDERS OF INTERMEDIARY METABOLISM**
- 427 Heritable Disorders of Connective Tissue** 2504
Darwin J. Prockop, John F. Bateman
- 428 Hemochromatosis** 2514
Lawrie W. Powell
- 429 Wilson's Disease** 2519
George J. Brewer
- 430 The Porphyrrias** 2521
Robert J. Desnick, Manisha Balwani
- 431e Disorders of Purine and Pyrimidine Metabolism** 2533
Christopher M. Burns, Robert L. Wortmann
- 432e Lysosomal Storage Diseases** 2533
Robert J. Hopkin, Gregory A. Grabowski
- 433e Glycogen Storage Diseases and Other Inherited Disorders of Carbohydrate Metabolism** 2534
Priya S. Kishnani, Yuan-Tsong Chen
- 434e Inherited Disorders of Amino Acid Metabolism in Adults** 2534
Nicola Longo
- 435e Inherited Defects of Membrane Transport** 2534
Nicola Longo
- 436e Atlas of Clinical Manifestations of Metabolic Diseases** 2534
J. Larry Jameson
- PART 17 Neurologic Disorders**
- DIAGNOSIS OF NEUROLOGIC DISORDERS**
- 437 Approach to the Patient with Neurologic Disease** 2535
Daniel H. Lowenstein, Joseph B. Martin, Stephen L. Hauser
- 438e The Neurologic Screening Exam** 2540
Daniel H. Lowenstein
- 439e Video Atlas of the Detailed Neurologic Examination** 2540
Martin A. Samuels
- 440e Neuroimaging in Neurologic Disorders** 2540
William P. Dillon
- 441e Atlas of Neuroimaging** 2541
Andre D. Furtado, William P. Dillon
- 442e Electrodiagnostic Studies of Nervous System Disorders: EEG, Evoked Potentials, and EMG** 2541
Michael J. Aminoff
- 443e Technique of Lumbar Puncture** 2541
Elizabeth Robbins, Stephen L. Hauser
- 444e Biology of Neurologic Diseases** 2541
Stephen L. Hauser, Stanley B. Prusiner, M. Flint Beal
- DISEASES OF THE CENTRAL NERVOUS SYSTEM**
- 445 Seizures and Epilepsy** 2542
Daniel H. Lowenstein











446	Cerebrovascular Diseases	2559
	<i>Wade S. Smith, S. Claiborne Johnston, J. Claude Hemphill, III</i>	
447	Migraine and Other Primary Headache Disorders	2586
	<i>Peter J. Goadsby, Neil H. Raskin</i>	
448	Alzheimer's Disease and Other Dementias	2598
	<i>William W. Seeley, Bruce L. Miller</i>	
449	Parkinson's Disease and Other Movement Disorders	2609
	<i>C. Warren Olanow, Anthony H.V. Schapira, Jose A. Obeso</i>	
450	Ataxic Disorders	2626
	<i>Roger N. Rosenberg</i>	
	451e Classification of the Spinocerebellar Ataxias	2631
	<i>Roger N. Rosenberg</i>	
452	Amyotrophic Lateral Sclerosis and Other Motor Neuron Diseases	2631
	<i>Robert H. Brown, Jr.</i>	
	453e Prion Diseases	2637
	<i>Stanley B. Prusiner, Bruce L. Miller</i>	
454	Disorders of the Autonomic Nervous System	2637
	<i>Phillip A. Low, John W. Engstrom</i>	
455	Trigeminal Neuralgia, Bell's Palsy, and Other Cranial Nerve Disorders	2645
	<i>M. Flint Beal, Stephen L. Hauser</i>	
456	Diseases of the Spinal Cord	2650
	<i>Stephen L. Hauser, Allan H. Ropper</i>	
	457e Concussion and Other Traumatic Brain Injuries	2660
	<i>Allan H. Ropper</i>	
458	Multiple Sclerosis and Other Demyelinating Diseases	2661
	<i>Stephen L. Hauser, Douglas S. Goodin</i>	
NERVE AND MUSCLE DISORDERS		
459	Peripheral Neuropathy	2674
	<i>Anthony A. Amato, Richard J. Barohn</i>	
460	Guillain-Barré Syndrome and Other Immune-Mediated Neuropathies	2694
	<i>Stephen L. Hauser, Anthony A. Amato</i>	
461	Myasthenia Gravis and Other Diseases of the Neuromuscular Junction	2701
	<i>Daniel B. Drachman, Anthony A. Amato</i>	
	462e Muscular Dystrophies and Other Muscle Diseases	2707
	<i>Anthony A. Amato, Robert H. Brown, Jr.</i>	
	463e Special Issues in Inpatient Neurologic Consultation	2707
	<i>S. Andrew Josephson, Martin A. Samuels</i>	
CHRONIC FATIGUE SYNDROME		
	464e Chronic Fatigue Syndrome	2707
	<i>Gijs Bleijenberg, Jos W. M. van der Meer</i>	
PSYCHIATRIC AND ADDICTION DISORDERS		
	465e Biology of Psychiatric Disorders	2708
	<i>Robert O. Messing, Eric J. Nestler</i>	
466	Mental Disorders	2708
	<i>Victor I. Reus</i>	
467	Alcohol and Alcoholism	2723
	<i>Marc A. Schuckit</i>	
	468e Opioid-Related Disorders	2728
	<i>Thomas R. Kosten, Colin N. Haile</i>	

	469e Cocaine and Other Commonly Abused Drugs	2729
	<i>Nancy K. Mello, Jack H. Mendelson</i>	
470	Nicotine Addiction	2729
	<i>David M. Burns</i>	
	471e Neuropsychiatric Illnesses in War Veterans	2732
	<i>Charles W. Hoge</i>	

PART 18 Poisoning, Drug Overdose, and Envenomation

	472e Heavy Metal Poisoning	2733
	<i>Howard Hu</i>	
	473e Poisoning and Drug Overdose	2733
	<i>Mark B. Mycyk</i>	
474	Disorders Caused by Venomous Snakebites and Marine Animal Exposures	2733
	<i>Charles Lei, Natalie J. Badowski, Paul S. Auerbach, Robert L. Norris</i>	
475	Ectoparasite Infestations and Arthropod Injuries	2744
	<i>Richard J. Pollack, Scott A. Norton</i>	

PART 19 Disorders Associated with Environmental Exposures

	476e Altitude Illness	2753
	<i>Buddha Basnyat, Geoffrey Tabin</i>	
	477e Hyperbaric and Diving Medicine	2753
	<i>Michael H. Bennett, Simon J. Mitchell</i>	
	478e Hypothermia and Frostbite	2753
	<i>Daniel F. Danzl</i>	
	479e Heat-Related Illnesses	2753
	<i>Daniel F. Danzl</i>	
APPENDIX: Laboratory Values of Clinical Importance 2754		
	<i>Alexander Kratz, Michael A. Pesce, Robert C. Basner, Andrew J. Einstein</i>	
	480e The Clinical Laboratory in Modern Health Care	2770
	<i>Anthony A. Killeen</i>	
	481e Clinical Procedure Tutorial: Central Venous Catheter Placement	2770
	<i>Maria A. Yialamas, William E. Corcoran, Gyorgy Frenzl, Kurt Fink</i>	
	482e Clinical Procedure Tutorial: Thoracentesis	2770
	<i>Charles A. Morris, Andrea S. Wolf</i>	
	483e Clinical Procedure Tutorial: Abdominal Paracentesis	2770
	<i>Maria A. Yialamas, Anna E. Rutherford, Lindsay King</i>	
	484e Clinical Procedure Tutorial: Endotracheal Intubation	2770
	<i>Charles A. Morris, Emily Page Nelson</i>	
	485e Clinical Procedures Tutorial: Percutaneous Arterial Blood Gas Sampling	2770
	<i>Christian D. Becker</i> <i>Medical Editors: Sean Sadikot, Jeremy Matloff</i>	
	486e Clinical Procedures Tutorial: Lumbar Puncture	2770
	<i>Beth Rapaport, Stephen Krieger, Corey McGraw</i> <i>Medical Editors: Sean Sadikot, Jeremy Matloff</i>	

Index	I-1
------------------------	-----

PATIENT MANAGEMENT ALGORITHMS

AGING

- FIG. 11-16** Algorithm depicting assessment and management of delirium in hospitalized older patients 79
- FIG. 11-17** Algorithm depicting assessment and management of falls in older patients. 80

ALLERGY, IMMUNOLOGY, RHEUMATOLOGY

- FIG. 376-4** The diagnosis and management of rhinitis 2123
- FIG. 378-2** The diagnosis and initial therapy of systemic lupus erythematosus. 2128
- FIG. 383-1** Treatment for Sjögren's syndrome 2168
- FIG. 385-1** Approach to the patient with a suspected diagnosis of vasculitis 2181
- FIG. 390-8** Patient management for sarcoidosis 2210
- FIG. 390-9** Management of acute sarcoidosis 2211
- FIG. 390-10** Management of chronic sarcoidosis 2211
- FIG. 393-1** The diagnosis of musculoskeletal complaints 2217
- FIG. 393-2** The consideration of the most common musculoskeletal conditions 2218
- FIG. 393-6** Approach to synovial fluid aspiration and analysis. 2224

ALTERATIONS IN CIRCULATORY AND RESPIRATORY FUNCTIONS

- FIG. 50-1** Clinical conditions in which a decrease in cardiac output and a systemic vascular resistance cause arterial underfilling. 251
- FIG. 51e-5** Differential diagnosis of a holosystolic murmur 51e-5

CARDIOLOGY

- FIG. 9-1** Cardiac risk assessment and stratification in patients undergoing noncardiac surgery 52
- FIG. 51e-9** Strategy for evaluating heart murmurs 51e-8
- FIG. 264-1** Approach to the evaluation of a heart murmur 1441
- FIG. 276-9** Treatment algorithm for patients presenting with hemodynamically stable paroxysmal supraventricular tachycardia 1483
- FIG. 283-2** Management strategy for patients with aortic stenosis 1533
- FIG. 283-6** Management of patients with aortic regurgitation 1537
- FIG. 284-1** Management of rheumatic mitral stenosis. 1541
- FIG. 284-4** Management of mitral regurgitation. 1545
- FIG. 285-1** Management of tricuspid regurgitation. 1549
- FIG. 287-18** Treatment algorithm for hypertrophic cardiomyopathy 1570

- FIG. 293-2** Evaluation of the patient with known or suspected ischemic heart disease 1583
- FIG. 293-3** Management of the patient with ischemic heart disease 1591
- FIG. 294-3** Algorithm for evaluation and management of patients with suspected acute coronary syndrome 1595
- FIG. 295-5** The assessment of need for implantation of a cardioverter-defibrillator. 1609

CLINICAL GENETICS

- FIG. 84-2** Approach to genetic testing 448
- FIG. 85e-6** Clinical and laboratory investigation of a suspected mitochondrial DNA (mtDNA) disorder. 85e-7
- FIG. 101e-6** Genetic testing in a family with cancer predisposition 101e-8

CLINICAL NUTRITION

- FIG. 98e-1** Decision-making for the implementation of specialized nutritional support (SNS) 98e-2

CORONARY AND PERIPHERAL VASCULAR DISEASE

- FIG. 295-4** Reperfusion therapy for patients with T-segment elevation myocardial infarction (STEMI) 1604
- FIG. 296e-4** Algorithm for patients requiring revascularization: factors to consider when choosing between bare metal stents, drug-eluting stent, or CABG. 296e-3

DISORDERS OF THE URINARY TRACT

- FIG. 337-2** Typical algorithm for early posttransplant care of a kidney recipient 1830

EMERGENCY AND CRITICAL CARE

- FIG. 263e-1** General guidelines for treatment of radiation casualties. 263e-4
- FIG. 263e-2** Evacuation in a multicasualties radiologic event 263e-5
- FIG. 321-2** Approach to the patient in shock 1731
- FIG. 322-5** Algorithm for the initial management of acute respiratory distress syndrome 1739
- FIG. 326-2** Emergency management of patients with cardiogenic shock, acute pulmonary edema, or both 1761
- FIG. 327-3A** Cardiac arrest management: ventricular fibrillation 1769

FIG. 327-3B Cardiac arrest management: bradyarrhythmia/ asystole 1769

ENDOCRINOLOGY AND METABOLISM

FIG. 68-2 The evaluation and differential diagnosis of hirsutism 334

FIG. 402-1 Management of adult growth hormone (GH) deficiency 2260

FIG. 403-3 Management of prolactinoma 2268

FIG. 403-5 Management of acromegaly 2270

FIG. 403-6 Management of Cushing's syndrome 2273

FIG. 403-7 Management of a nonfunctioning pituitary mass 2274

FIG. 405-13 Approach to the patient with a thyroid nodule 2308

FIG. 406-10 Management of the patient with suspected Cushing's syndrome 2316

FIG. 406-12 Diagnostic flowchart for evaluating patients with possible mineralocorticoid excess 2320

FIG. 406-13 Management of the patient with an incidentally discovered adrenal mass 2322

FIG. 406-16 Diagnostic flowchart for evaluating patients with suspected adrenal insufficiency 2327

FIG. 411-5 Evaluation of gynecomastia 2367

FIG. 411-6 Evaluation of hypogonadism 2367

FIG. 416-1 Algorithm for the treatment of obesity 2395

FIG. 418-2 Essential elements in comprehensive care of type 2 diabetes 2413

FIG. 418-3 Glycemic management of type 2 diabetes 2416

FIG. 419-4 Screening for microalbuminuria 2425

FIG. 420-2 Hypoglycemia-associated autonomic failure in insulin-deficient diabetes 2432

FIG. 424-6 The evaluation of patients with hypercalcemia 2479

FIG. 428-3 Algorithm for screening for *HFE*-associated hemochromatosis 2518

GASTROENTEROLOGY AND HEPATOLOGY

FIG. 53-2 Approach to the patient with dysphagia 257

FIG. 55-2 Management of acute diarrhea 267

FIG. 55-3 Management of chronic diarrhea 271

FIG. 55-4 Management of constipation 273

FIG. 57-1 Management of acute upper gastrointestinal bleeding 278

FIG. 57-2 Algorithm for patients with acute lower gastrointestinal bleeding 279

FIG. 58-1 Evaluation of the patient with jaundice 281

FIG. 348-12 Overview of new-onset dyspepsia 1924

FIG. 357-1 Algorithm for evaluation of abnormal liver tests 1994

FIG. 358-1 Algorithm for the evaluation of chronically abnormal liver tests 1996

FIG. 363-2 Treatment algorithm for alcoholic hepatitis 2054

FIG. 365-3 Management of recurrent variceal hemorrhage 2064

FIG. 365-5 Treatment of refractory ascites 2065

FIG. 370-1 A stepwise diagnostic approach to the patient with suspected chronic pancreatitis 2088

HEMATOLOGY AND ONCOLOGY

FIG. 77-17 The physiologic classification of anemia 398

FIG. 77-18 An approach to diagnosing patients with polycythemia 400

FIG. 104-2 Diagnosis and treatment of fever and neutropenia 490

FIG. 106-1 Evaluation of a patient with cervical adenopathy 503

FIG. 107-3 Algorithm for management of non-small-cell lung cancer 512

FIG. 107-5 Algorithm for management of small-cell lung cancer 515

FIG. 107-6 Approach to a solitary pulmonary nodule 517

FIG. 107-7 Management of recurrent small-cell lung cancer 522

FIG. 107-8 Approach to first-line therapy in a patient with stage IV non-small-cell lung cancer 523

FIG. 108-1 Approach to a palpable breast mass 525

FIG. 108-2 The "triple diagnosis" technique in suspected breast cancer 525

FIG. 108-3 Management of a breast cyst 525

FIG. 108-4 Approaches to abnormalities detected by mammogram 526

FIG. 111-2 Treatment approach to patients with hepatocellular carcinoma 548

FIG. 120e-2 Treatment algorithm for adenocarcinoma and poorly differentiated adenocarcinoma of unknown primary 120e-3

FIG. 120e-3 Treatment algorithm for squamous cell carcinoma of unknown primary 120e-4

FIG. 127-3 Pathophysiology of sickle cell crisis 634

FIG. 132-2 The therapy of newly diagnosed acute myeloid leukemia 684

FIG. 137-1 Algorithm for the diagnosis of amyloidosis and determination of type 720

FIG. 140-2 Evaluating the thrombocytopenic patient 726

FIG. 143-1 Classification of antithrombotic drugs 745

FIG. 331-2 Management of cancer patients with back pain 1791

FIG. 331-4 Management of patients at high risk for the tumor lysis syndrome 1796

INFECTIOUS DISEASES

FIG. 44-2 Diagnosis and treatment of acute pharyngitis 232

FIG. 152e-1 Syndromic approach to differential diagnosis of suspected infection in a veteran who has returned from a foreign war 152e-7

FIG. 155-4 Diagnostic use of transesophageal and transtracheal echocardiography in infective endocarditis 821

FIG. 159-3	Management of patients with intraabdominal abscesses using percutaneous drainage	850
FIG. 160-1	Approach to patients with community-acquired infectious diarrhea or bacterial food poisoning	854
FIG. 162-4	Diagnostic approach to urinary tract infection	865
FIG. 177-1	Clinical and pathologic progression of tetanus	985
FIG. 188-1	Schematic of the relationships between colonization with <i>Helicobacter pylori</i> and diseases of the upper gastrointestinal tract among persons in developed countries	1039
FIG. 188-2	Management of <i>Helicobacter pylori</i> infection	1041
FIG. 206-4	Interpretation of results from syphilis enzyme immunoassays used for screening	1137
FIG. 209-3	Treatment of relapsing fever	1148
FIG. 210-2	Treatment of the various early or late manifestations of Lyme borreliosis	1153
FIG. 226-32	Acute HIV infection	1249
FIG. 226-36	Evaluation of diarrhea in patients with HIV infection	1257
FIG. 232-5	Rabies postexposure prophylaxis	1303

NEPHROLOGY

FIG. 61-1	Approach to the patient with azotemia	290
FIG. 61-2	Approach to the patient with hematuria	292
FIG. 61-3	Approach to the patient with proteinuria	293
FIG. 61-4	Approach to the patient with polyuria	294
FIG. 63-5	The diagnostic approach to hyponatremia	299
FIG. 63-6	The diagnostic approach to hypernatremia	303
FIG. 63-7	The diagnostic approach to hypokalemia	308
FIG. 63-8	The diagnostic approach to hyperkalemia	311
FIG. 67-3	The evaluation and management of patients with erectile dysfunction	327
FIG. 337-2	A typical algorithm for early posttransplant care of the kidney recipient	1830
FIG. 340-1	Algorithm for the treatment of allergic and other immune-mediated acute interstitial nephritis	1857
FIG. 343-1	Diagnostic approach for urinary tract obstruction in unexplained renal failure	1873

NEUROLOGY AND PSYCHIATRY

FIG. 164-1	The management of patients with suspected central nervous system infection	884
-------------------	--	-----

FIG. 164-2	The pathophysiology of the neurologic complications of bacterial meningitis	886
FIG. 445-2	Evaluation of the adult patient with a seizure	2549
FIG. 445-3	Pharmacologic treatment of generalized tonic-clonic status epilepticus in adults	2558
FIG. 446-1	Medical management of stroke and transient ischemic attack	2560
FIG. 449-7	Treatment algorithm for the management of Parkinson's disease	2619
FIG. 458-4	Therapeutic decision-making for multiple sclerosis	2671
FIG. 459-1	Approach to the evaluation of peripheral neuropathies	2675
FIG. 461-2	The management of myasthenia gravis	2704
FIG. 462e-1	Diagnostic evaluation of intermittent weakness	462e-1
FIG. 462e-2	Diagnostic evaluation of persistent weakness	462e-2
FIG. 466-1	Medical management of major depressive disorder	2716

PULMONOLOGY

FIG. 47e-2	The evaluation of the patient with dyspnea	47e-3
FIG. 48-2	Algorithm for the evaluation of hemoptysis	246
FIG. 300-3	How to decide whether diagnostic imaging is needed in suspected pulmonary thromboembolism and deep venous thrombosis	1632
FIG. 300-6	Imaging tests to diagnose deep venous thrombosis and pulmonary embolism	1634
FIG. 300-7	Acute management of pulmonary thromboembolism	1634
FIG. 316-1	Approach to the diagnosis of pleural effusions	1717

SYSTEMIC CONDITIONS

FIG. 10-2	Common and uncommon clinical courses in the last days of terminally ill patients	68
FIG. 26-1	Structured approach to patients with fever of unknown origin	139
FIG. 30-3	The initial workup of a patient with weakness	156
FIG. 43-2	An algorithm for the approach to hearing loss	218
FIG. 69-2	Algorithm for evaluation of amenorrhea	337
FIG. 75-1	An algorithm for the diagnosis of a patient with photosensitivity	390

This page intentionally left blank

James L. Abbruzzese, MD

Chief, Division of Medical Oncology, Department of Medicine; Associate Director, Clinical Research, Duke Cancer Institute, Durham, North Carolina [120e]

Manal F. Abdelmalek, MD, MPH

Associate Professor of Medicine, Division of Gastroenterology and Hepatology, Duke University, Durham, North Carolina [364]

Jamil Aboulhosn, MD

Assistant Professor of Medicine; Director Ahmanson/UCLA Adult Congenital Heart Disease Center, David Geffen School of Medicine, University of California, Los Angeles, Los Angeles, California [282]

John C. Achermann, MD, PhD, MB

Wellcome Trust Senior Research Fellow in Clinical Science, University College London; Professor of Paediatric Endocrinology, UCL Institute of Child Health, University College London, London, United Kingdom [410]

John W. Adamson, MD

Clinical Professor, Division of Hematology/Oncology, Department of Medicine, University of California at San Diego, San Diego, California [77, 126]

Rizwan Ahmed, MD

General Surgery Resident, Department of General Surgery, Johns Hopkins Hospital, Baltimore, Maryland [353, 354]

Praveen Akuthota, MD

Assistant Professor of Medicine, Harvard Medical School; Beth Israel Deaconess Medical Center, Boston, Massachusetts [310]

Anthony A. Amato, MD

Professor of Neurology, Harvard Medical School; Vice-Chairman, Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts [459-462e]

Michael J. Aminoff, MD, DSc, FRCP

Professor of Neurology, School of Medicine, University of California, San Francisco, San Francisco, California [30, 31, 442e]

Neil M. Ampel, MD

Professor of Medicine, University of Arizona; Staff Physician, Southern Arizona Veterans Affairs Health Care System, Tucson, Arizona [237]

Kenneth C. Anderson, MD

Kraft Family Professor of Medicine, Harvard Medical School; Chief, Jerome Lipper Multiple Myeloma Center, Dana-Farber Cancer Institute, Boston, Massachusetts [136, 138e]

Rosa M. Andrade, MD

Department of Medicine, Division of Infectious Diseases, University of California, San Diego, San Diego, California [247]

Elliott M. Antman, MD

Professor of Medicine, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital; Associate Dean for Clinical/Translational Research, Harvard Medical School, Boston, Massachusetts [293, 295]

Frederick R. Appelbaum, MD

Director, Division of Clinical Research, Fred Hutchinson Cancer Research Center, Seattle, Washington [139e]

Cesar A. Arias, MD, PhD, MSc

Associate Professor of Medicine, Microbiology and Molecular Genetics; Director, Laboratory for Antimicrobial Research, University of Texas Medical School at Houston, Houston, Texas; Director, Molecular Genetics and Antimicrobial Unit; Co-Director, International Center for Microbial Genomics, Universidad, El Bosque, Bogota, Colombia [174]

Wiebke Arlt, MD, DSc, FRCP, FMedSci

Professor of Medicine, Centre for Endocrinology, Diabetes and Metabolism, School of Clinical and Experimental Medicine, University of Birmingham; Consultant Endocrinologist, University Hospital Birmingham, Birmingham, United Kingdom [406]

Katrina Armstrong, MD, MS

Jackson Professor of Clinical Medicine, Physician in Chief, Massachusetts General Hospital, Boston Massachusetts [4]

Valder R. Arruda, MD, PhD

Associate Professor, Division of Hematology, Department of Pediatrics, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [141]

Andrew W. Artenstein, MD

Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts; Adjunct Professor of Medicine and Health Services, Policy and Practice, Alpert Medical School, Brown University, Providence, Rhode Island; Chair, Department of Medicine, Baystate Health, Springfield, Massachusetts [152e]

Anthony Atala, MD

Professor and Director, Wake Forest Institute for Regenerative Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina [92e]

John C. Atherton, MD, FRCP

Professor of Gastroenterology and Dean of the School of Medicine, University of Nottingham, Nottingham, United Kingdom [188]

Paul S. Auerbach, MD, MS, FACEP, FAWM

Redich Family Professor of Surgery, Division of Emergency Medicine, Stanford University School of Medicine, Stanford, California [474]

K. Frank Austen, MD

AstraZeneca Professor of Respiratory and Inflammatory Diseases, Director, Inflammation and Allergic Diseases Research Section, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [376]

Eric H. Awtry, MD

Cardiology Division, Boston Medical Center, Boston, Massachusetts [289e, 290e]

Jamil Azzi, MD

Instructor in Medicine, Harvard Medical School; Associate Physician, Brigham and Women's Hospital, Boston, Massachusetts [337]

Bruce R. Bacon, MD

James F. King, MD Endowed Chair in Gastroenterology; Professor of Internal Medicine, Saint Louis University Liver Center, Saint Louis University School of Medicine, St. Louis, Missouri [365, 367e]

Lindsey R. Baden, MD

Associate Professor of Medicine, Harvard Medical School; Dana-Farber Cancer Institute, Brigham and Women's Hospital, Boston, Massachusetts [215e]

Natalie J. Badowski, MD

Division of Emergency Medicine, Stanford University School of Medicine, Stanford, California [474]

John R. Balmes, MD

Professor of Medicine, University of California, San Francisco; Professor, School of Public Health, University of California, Berkeley; Chief, Division of Occupational and Environmental Medicine, San Francisco General Hospital, San Francisco, California [311]

Manisha Balwani, MD, MS

Assistant Professor, Department of Genetics and Genomic Sciences, Mount Sinai School of Medicine of New York University, New York, New York [430]

Peter A. Banks, MD

Professor of Medicine, Harvard Medical School; Senior Physician, Division of Gastroenterology, Brigham and Women's Hospital, Boston, Massachusetts [370, 371]

Robert L. Barbieri, MD

Kate Macy Ladd Professor of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School; Chair, Department of Obstetrics and Gynecology, Brigham and Women's Hospital, Boston, Massachusetts [8]

Alan G. Barbour, MD

Professor of Medicine and Microbiology and Molecular Genetics, University of California Irvine, Irvine, California [209]

Joanne M. Bargman, MD, FRCP

Professor of Medicine, University of Toronto; Staff Nephrologist, University Health Network, Toronto, Canada [335]

Tamar F. Barlam, MD, MSc

Associate Professor of Medicine, Infectious Disease Section, Boston University School of Medicine, Boston, Massachusetts [147, 183e]

Peter J. Barnes, DM, DSc, FMedSci, FRS

Head of Respiratory Medicine, Imperial College, London, United Kingdom [309]

Richard J. Barohn, MD

Chairman, Department of Neurology; Gertrude and Dewey Ziegler Professor of Neurology, University of Kansas Medical Center, Kansas City, Kansas [459]

Rebecca M. Baron, MD

Assistant Professor of Medicine, Harvard Medical School; Associate Physician, Brigham and Women's Hospital, Division of Pulmonary and Critical Care Medicine, Department of Medicine, Boston, Massachusetts [154, 312]

Miriam Baron Barshak, MD

Assistant Professor, Harvard Medical School; Associate Physician, Massachusetts General Hospital, Boston, Massachusetts [154, 159, 312]

Shehzad Basaria, MD

Men's Health: Aging and Metabolism, Brigham and Women's Hospital, Boston, Massachusetts [7e]

Robert C. Basner, MD

Professor of Clinical Medicine, Division of Pulmonary, Allergy, and Critical Care Medicine, Columbia University College of Physicians and Surgeons, New York, New York [Appendix]

Buddha Basnyat, MD, MSc, FACP, FRCP (Edinburgh)

Director, Oxford University Clinical Research Unit, Patan Academy of Health Sciences; Medical Director, Nepal International Clinic, Kathmandu, Nepal [476e]

Shari S. Bassuk, ScD

Epidemiologist, Division of Preventive Medicine, Brigham and Women's Hospital, Boston, Massachusetts [413]

John F. Bateman, PhD

Director, Cell Biology, Murdoch Children's Research Institute, Melbourne, Victoria, Australia; Murdoch Children's Research Institute, Parkville, Victoria, Australia [427]

David W. Bates, MD, MSc

Professor of Medicine, Harvard Medical School; Chief, General Internal Medicine and Primary Care Division, Brigham and Women's Hospital; Medical Director, Clinical and Quality Analysis, Partners HealthCare System, Inc., Boston, Massachusetts [12e]

Robert P. Baughman, MD

Department of Internal Medicine, University of Cincinnati Medical Center, Cincinnati, Ohio [390]

M. Flint Beal, MD

University Professor of Neurology and Neuroscience; Neurologist, New York Presbyterian Hospital; Weill Cornell Medical College, New York, New York [444e, 455]

Laurence H. Beck, MD, PhD

Assistant Professor of Medicine, Boston University School of Medicine, Boston, Massachusetts [340]

Christian D. Becker, MD, PhD, FCCP

Assistant Professor, Department of Internal Medicine, Division of Pulmonary, Critical Care and Sleep Medicine, Icahn School of Medicine at Mount Sinai New York, New York [485e]

Nicholas J. Beeching, MA, BM BCh, FRCP, FRACP, FFTM RCPS(Glasg), DCH, DTM&H

Senior Lecturer (Clinical) in Infectious Diseases, Liverpool School of Tropical Medicine; Clinical Director, Tropical and Infectious Disease Unit, Royal Liverpool University Hospital; NIHR Health Protection Research Unit in Emerging and Zoonotic Infections, Liverpool; Honorary Consultant, Public Health England and Honorary Civilian Consultant in Infectious Diseases, Army Medical Directorate, United Kingdom [194e]

Doron Behar, MD, PhD

Institute of Genetics, Rambam Health Care Campus, Haifa, Israel [85e]

Robert S. Benjamin, MD

P. H. and Faye E. Robinson Distinguished Professor of Medicine, Department of Sarcoma Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas [119e]

Michael H. Bennett, MD, MBBS, MM (Clin Epi)

Conjoint Associate Professor in Anesthesia and Hyperbaric Medicine; Faculty of Medicine, University of New South Wales; Academic Head of Department, Wales Anaesthesia, Prince of Wales Hospital, Sydney, Australia [477e]

Edward J. Benz, Jr., MD

Richard and Susan Smith Professor of Medicine; Professor of Genetics, Harvard Medical School; President and CEO, Dana-Farber Cancer Institute; Director and Principal Investigator, Dana-Farber/Harvard Cancer Center; Boston, Massachusetts [127]

Jean Bergounioux, MD, PhD, PhC

Pediatric Intensive Care Unit, Hôpital Raymond-Poincaré, Université de Versailles-Saint Quentin, Garches, France [191]

John L. Berk, MD

Associate Professor of Medicine, Boston University School of Medicine; Clinical Director, Amyloidosis Center, Boston Medical Center, Boston, Massachusetts [137]

Aaron S. Bernstein, MD, MPH

Instructor, Harvard Medical School; Associate Director, Center for Health and the Global Environment, Harvard School of Public Health; Pediatric Hospitalist, Boston Children's Hospital, Boston, Massachusetts [151e]

Joseph R. Betancourt, MD, MPH

Associate Professor of Medicine, Harvard Medical School; Director, The Disparities Solutions Center, Massachusetts General Hospital, Boston, Massachusetts [16e]

Atul K. Bhan, MD, MBBS

Professor of Pathology, Harvard Medical School, Department of Pathology, Massachusetts General Hospital, Boston, Massachusetts [366e]

Shalender Bhasin, MBBS

Professor of Medicine, Harvard Medical School; Director, Research Program in Men's Health: Aging and Metabolism; Director, Boston Claude D. Pepper Older Americans Independence Center; Site Director, Harvard Catalyst Clinical Research Center at BWH, Brigham and Women's Hospital, Boston, Massachusetts [7e, 411]

Deepak L. Bhatt, MD, MPH

Professor of Medicine, Harvard Medical School; Chief of Cardiology, VA Boston Healthcare System; Senior Physician, Brigham and Women's Hospital; Senior Investigator, TIMI Study Group, Boston, Massachusetts [296e, 297e]

Roby P. Bhattacharyya, MD, PhD

Instructor in Medicine, Harvard Medical School; Assistant in Medicine, Division of Infectious Disease, Massachusetts General Hospital, Boston, Massachusetts [146]

David R. Bickers, MD

Carl Truman Nelson Professor and Chair, Department of Dermatology, Columbia University Medical Center, New York, New York [75]

Henry J. Binder, MD

Professor Emeritus of Medicine, Senior Research Scientist, Yale University, New Haven, Connecticut [349, 350e]

William R. Bishai, MD, PhD

Professor and Co-Director, Center for Tuberculosis Research, Department of Medicine, Division of Infectious Diseases, Johns Hopkins University School of Medicine, Baltimore, Maryland [175]

Bruce R. Bistrian, MD, PhD, MPH

Professor of Medicine, Harvard Medical School; Chief, Clinical Nutrition, Beth Israel Deaconess Medical Center, Boston, Massachusetts [98e]

Martin J. Blaser, MD

Muriel and George Singer Professor of Medicine; Professor of Microbiology; Director, Human Microbiome Program, New York University Langone Medical Center, New York, New York [188, 192]

Chantal P. Bleeker-Rovers, MD, PhD

Department of Internal Medicine, Radboud University Nijmegen Medical Center, Nijmegen, The Netherlands [26]

Gijs Bleijenberg, PhD

Professor Emeritus, Expert Centre for Chronic Fatigue, Radboud University Medical Centre, Nijmegen, The Netherlands [464e]

Clara D. Bloomfield, MD

Distinguished University Professor; William G. Pace, III Professor of Cancer Research; Cancer Scholar and Senior Advisor, The Ohio State University Comprehensive Cancer Center; Arthur G. James Cancer Hospital and Richard J. Solove Research Institute, Columbus, Ohio [132]

Richard S. Blumberg, MD

Chief, Division of Gastroenterology, Hepatology and Endoscopy, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts [351]

Jean L. Bolognia, MD

Professor, Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut [72]

Joseph V. Bonventre, MD, PhD

Samuel A. Levine Professor of Medicine, Harvard Medical School; Chief, Renal Division; Chief, Division of Biomedical Engineering, Brigham and Women's Hospital, Boston, Massachusetts [333e, 334]

George J. Bosl, MD

Professor of Medicine, Weill Cornell Medical College; Chair, Department of Medicine; Patrick M. Byrne Chair in Clinical Oncology, Memorial Sloan-Kettering Cancer Center, New York, New York [116]

Joshua A. Boyce, MD

Professor of Medicine and Pediatrics; Albert L. Sheffer Professor of Medicine, Harvard Medical School; Director, Inflammation and Allergic Disease Research Section, Brigham and Women's Hospital, Boston, Massachusetts [376]

Eugene Braunwald, MD, MA (Hon), ScD (Hon), FRCP

Distinguished Hersey Professor of Medicine, Harvard Medical School; Founding Chairman, TIMI Study Group, Brigham and Women's Hospital, Boston, Massachusetts [50, 288, 294]

Irwin M. Braverman, MD

Professor Emeritus; Senior Research Scientist, Department of Dermatology, Yale University School of Medicine, New Haven, Connecticut [72]

Otis W. Brawley, MD, FACP

Professor of Hematology, Medical Oncology, Medicine and Epidemiology, Emory University; Chief Medical and Scientific Officer, American Cancer Society, Atlanta, Georgia [100]

Joel G. Breman, MD, DTPH

Senior Scientific Advisor, Fogarty International Center, National Institutes of Health, Bethesda, Maryland [248, 250e]

George J. Brewer, MD

Morton S. and Henrietta K. Sellner Emeritus, Professor of Human Genetics, Emeritus Professor of Internal Medicine, University of Michigan Medical School; Senior Vice President for Research and Development, Adeona Pharmaceuticals, Inc., Ann Arbor, Michigan [429]

Josephine P. Briggs, MD

Director, National Center for Complementary and Alternative Medicine (NCCAM) at the National Institutes of Health (NIH), Bethesda, Maryland [14e]

F. Richard Bringhurst, MD

Associate Professor of Medicine, Harvard Medical School; Physician, Massachusetts General Hospital, Boston, Massachusetts [423]

Steven M. Bromley, MD

Director, Outpatient Services, Virtua Neuroscience, Voorhees, New Jersey; Director, Bromley Neurology, PC, Audubon, New Jersey [42]

Darron R. Brown, MD

Professor of Medicine, Microbiology and Immunology, Division of Infectious Diseases, Simon Cancer Center, Indiana University School of Medicine, Indianapolis, Indiana [222]

Kevin E. Brown, MD, MRCP, FRCPATH

Virus Reference Department, Public Health England, London, United Kingdom [221]

Robert H. Brown, Jr., MD, PhD

Chairman, Department of Neurology, University of Massachusetts Medical School, Worcester, Massachusetts [452, 462e]

Amy E. Bryant, PhD

Affiliate Assistant Professor, University of Washington School of Medicine, Seattle, Washington; Research Scientist, Veterans Affairs Medical Center, Boise, Idaho [179]

Christopher M. Burns, MD

Associate Professor, Department of Medicine, Section of Rheumatology, Geisel School of Medicine at Dartmouth, Dartmouth Hitchcock Medical Center, Lebanon, New Hampshire [431e]

David M. Burns, MD

Professor Emeritus, Department of Family and Preventive Medicine, University of California, San Diego School of Medicine, San Diego, California [470]

Stephen B. Calderwood, MD

Morton N. Swartz, MD Academy Professor of Medicine (Microbiology and Immunobiology), Harvard Medical School; Chief, Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts [160]

Michael Camilleri, MD

Atherton and Winifred W. Bean Professor; Professor of Medicine, Pharmacology, and Physiology, Mayo Clinic College of Medicine, Rochester, Minnesota [55]

Christopher P. Cannon, MD

Professor of Medicine, Harvard Medical School; Senior Physician, Cardiovascular Division, Brigham and Women's Hospital, Boston, Massachusetts [294]

Jonathan R. Carapetis, MBBS, PhD, FRACP, FAFPHM

Director, Telethon Kids Institute, The University of Western Australia, Crawley, Western Australia [381]

Kathryn M. Carbone, MD

Deputy Scientific Director, Division of Intramural Research, National Institute of Dental and Craniofacial Research, Bethesda, Maryland [231e]

Brian I. Carr, MD, PhD, FRCP

IRCCS de Bellis National Center for GI Diseases, Castellana Grotte, BA, Italy [111]

John D. Carter, MD

Professor of Medicine, Division of Rheumatology; Director, University of South Florida Morsani College of Medicine, Tampa, Florida [384]

Arturo Casadevall, MD, PhD

Chair, Department of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, New York [239]

Agustin Castellanos, MD, FACC, FAHA

Professor of Medicine; Director, Clinical Electrophysiology, University of Miami Miller School of Medicine, Cardiovascular Division, Miami, Florida [327]

Bartolome R. Celli, MD

Professor of Medicine, Harvard Medical School; Staff Physician, Division of Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, Massachusetts [323]

Murali Chakinala, MD

Associate Professor of Medicine, Division of Pulmonary and Critical Care Medicine, Washington University School of Medicine, St. Louis, Missouri [279]

Anil Chandraker, MBChB, FRCP

Associate Professor of Medicine, Harvard Medical School; Medical Director of Kidney and Pancreas Transplantation; Interim Director, Schuster Family Transplantation Research Center, Brigham and Women's Hospital, Boston, Massachusetts [337]

Lan X. Chen, MD, PhD

Penn Presbyterian Medical Center, Philadelphia, Pennsylvania [395]

Yuan-Tsong Chen, MD, PhD

Duke University Medical Center, Division of Medical Genetics, Department of Pediatrics, Durham, North Carolina [433e]

Glenn M. Chertow, MD, MPH

Norman S. Coplson/Satellite Healthcare Professor of Medicine; Chief, Division of Nephrology, Stanford University School of Medicine, Palo Alto, California [336]

John S. Child, MD, FACC, FAHA, FASE

Streisand Professor of Medicine and Cardiology; Director, Ahmanson-UCLA Adult Congenital Heart Disease Center; Director, UCLA Adult Noninvasive Cardiodiagnostics Laboratory Ronald Reagan-UCLA Medical Center, Geffen School of Medicine, University of California, Los Angeles (UCLA), Los Angeles, California [282]

Augustine M. K. Choi, MD

Chairman, Department of Medicine, Weill Cornell Medical College, Physician-in-Chief, New York-Presbyterian Hospital-Weill Cornell Medical Center, New York, New York [305, 307, 322]

Raymond T. Chung, MD

Associate Professor of Medicine, Harvard Medical School; Director of Hepatology and Liver Center; Vice Chief, Gastroenterology, Massachusetts General Hospital, Boston, Massachusetts [368]

Jeffrey W. Clark, MD

Associate Professor of Medicine, Harvard Medical School; Medical Director, Clinical Trials Core, Dana-Farber Harvard Cancer Center; Massachusetts General Hospital, Boston, Massachusetts [102e]

Jeffrey I. Cohen, MD

Chief, Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [218, 228]

Yehuda Z. Cohen, MD

Clinical Fellow, Department of Medicine, Division of Infectious Diseases and Center for Virology and Vaccine Research, Beth Israel Deaconess Medical Center; Harvard Medical School, Boston, Massachusetts [224]

Ronit Cohen-Poradosu, MD

Senior Physician, Infectious Diseases Unit, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel [201]

Francis S. Collins, MD, PhD

Director, National Institutes of Health, Bethesda, Maryland [101e]

Wilson S. Colucci, MD, FAHA, FACC

Thomas J. Ryan Professor of Medicine, Boston University School of Medicine; Chief of Cardiovascular Medicine, Boston Medical Center, Boston, Massachusetts [289e, 290e]

Laura K. Conlin, PhD

Scientific Director, CytoGenomics Lab, The Children's Hospital of Philadelphia, Assistant Professor of Pathology and Laboratory Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [83e]

Darwin L. Conwell, MD, MS

Professor of Medicine, The Ohio State University College of Medicine; Director, Division of Gastroenterology, Hepatology and Nutrition; The Ohio State University Wexner Medical Center, Columbus, Ohio [370, 371]

Michael J. Corbel, PhD, DSc, FRCPath

Retired (previously Head, Division of Bacteriology, National Institute for Biological Standards and Control, Hertfordshire, United Kingdom) [194e]

William E. Corcoran, V, MD

Staff Anesthesiologist, Allcare Clinical Associates; Medical Director of Analgesia and Sedation, Mission Health; Patient Safety Officer, Mission Health, Asheville, North Carolina [481e]

Kathleen E. Corey, MD, MPH

Clinical and Research Fellow, Harvard Medical School; Fellow, Gastrointestinal Unit, Massachusetts General Hospital, Boston, Massachusetts [59]

Lawrence Corey, MD

Professor, Medicine and Laboratory Medicine, University of Washington; President Emeritus, Fred Hutchinson Cancer Research Center; Member, Vaccine and Infectious Disease Division; Principal Investigator, HIV Vaccine Trials Network, Fred Hutchinson Cancer Research Center, Seattle, Washington [216]

Jorge Cortes, MD

D. B. Lane Cancer Research Distinguished Professor for Leukemia Research; Deputy Chairman; Section Chief of AML and CML, The University of Texas M.D. Anderson Cancer Center, Houston, Texas [133]

Felicia Cosman, MD

Professor of Medicine, Columbia University College of Physicians and Surgeons, New York, New York [425]

Mark A. Creager, MD

Professor of Medicine, Harvard Medical School; Simon C. Fireman Scholar in Cardiovascular Medicine; Director, Vascular Center, Brigham and Women's Hospital, Boston, Massachusetts [301-303]

Leslie J. Crofford, MD

Professor, Division of Rheumatology and Immunology, Vanderbilt University, Nashville, Tennessee; Chief, Division of Rheumatology, University of Kentucky, Lexington, Kentucky [396]

Jennifer M. Crowell, MD, MPH

Medical Officer, Center for Oncology Prevention Trials Research Group, Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland [100]

Philip E. Cryer, MD

Professor of Medicine Emeritus, Washington University in St. Louis; Physician, Barnes-Jewish Hospital, St. Louis, Missouri [420]

David Cunningham, MD, MB, ChB, FRCP

Professor, Head of Gastrointestinal/Lymphoma Unit; Director of Clinical Research, Royal Marsden NHS Trust, London, United Kingdom [112]

Gary C. Curhan, MD

Professor of Medicine, Harvard Medical School, Professor of Epidemiology, Harvard School of Public Health, Channing Division of Network Medicine/Renal Division, Brigham and Women's Hospital, Boston, Massachusetts [342]

Brendan D. Curti, MD

Director, Biotherapy Program, Robert W. Franz Cancer Research Center, Providence Portland Medical Center, Portland, Oregon [105]

John J. Cush, MD

Professor of Medicine and Rheumatology, Baylor University Medical Center; Director of Clinical Rheumatology, Baylor Research Institute, Dallas, Texas [393]

Charles A. Czeisler, MD, PhD

Frank Baldino, Jr., PhD Professor of Sleep Medicine, Professor of Medicine and Director, Division of Sleep Medicine, Harvard Medical School; Chief, Division of Sleep and Circadian Disorders, Departments of Medicine and Neurology, Brigham and Women's Hospital, Boston, Massachusetts [38]

Marinos C. Dalakas, MD

Professor of Neurology, University of Athens Medical School, Athens, Greece; Thomas Jefferson University, Philadelphia, Pennsylvania [388]

Josep Dalmau, MD, PhD

ICREA Professor, Institut d'Investigació Biomèdica August Pi i Sunyer, University of Barcelona, Barcelona, Spain; Adjunct Professor, University of Pennsylvania, Philadelphia, Pennsylvania [122]

Daniel F. Danzl, MD

University of Louisville, Department of Emergency Medicine, Louisville, Kentucky [478e, 479e]

Robert B. Daroff, MD

Professor and Chair Emeritus, Department of Neurology, Case Western Reserve University School of Medicine; University Hospitals-Case Medical Center, Cleveland, Ohio [28]

Charles E. Davis, MD

Professor of Pathology and Medicine, Emeritus, University of California, San Diego School of Medicine; Director Emeritus, Microbiology, University of California, San Diego Medical Center, San Diego, California [245e]

Stephen N. Davis, MBBS, FRCP

Theodore E. Woodward Professor and Chairman of the Department of Medicine, University of Maryland School of Medicine; Physician-in-Chief, University of Maryland Medical Center, Baltimore, Maryland [420]

Rafael de Cabo, PhD

Senior Investigator, Experimental Gerontology Section, TGB, National Institute on Aging, National Institutes of Health, Baltimore, Maryland [94e]

Lisa M. DeAngelis, MD

Professor of Neurology, Weill Cornell Medical College; Chair, Department of Neurology, Memorial Sloan Kettering Cancer Center, New York, New York [118]

John Del Valle, MD

Professor and Senior Associate Chair of Medicine, Department of Internal Medicine, University of Michigan School of Medicine, Ann Arbor, Michigan [348]

Marie B. Demay, MD

Professor of Medicine, Harvard Medical School; Physician, Massachusetts General Hospital, Boston, Massachusetts [423]

Bradley M. Denker, MD

Associate Professor of Medicine, Harvard Medical School; Renal Division, Beth Israel Deaconess Medical Center; Chief of Nephrology and Associate Chief of Medical Specialties, Harvard Vanguard Medical Associates, Boston, Massachusetts [61]

David W. Denning, MBBS, FRCP, FRCPath, FMedSci

Professor of Medicine and Medical Mycology; Director, National Aspergillosis Centre, The University of Manchester and Wythenshawe Hospital, Manchester, United Kingdom [241]

Robert J. Desnick, MD, PhD

Dean for Genetics and Genomics, Professor and Chairman Emeritus, Department of Human Genetics and Genomic Sciences, Icahn School of Medicine at Mount Sinai, New York, New York [430]

Richard A. Deyo, MD, MPH

Kaiser Permanente Professor of Evidence-Based Family Medicine, Department of Family Medicine, Department of Medicine, Department of Public Health and Preventive Medicine, Oregon Institute of Occupational Health Sciences; Oregon Health and Science University; Clinical Investigator, Kaiser Permanente Center for Health Research, Portland, Oregon [22]

Betty Diamond, MD

The Feinstein Institute for Medical Research, North Shore LIJ Health System; Center for Autoimmunity and Musculoskeletal Diseases, Manhasset, New York [377e]

Marcelo F. Di Carli, MD

Professor, Department of Radiology, Harvard Medical School; Chief, Division of Nuclear Medicine and Molecular Imaging; Executive Director, Noninvasive Cardiovascular Imaging Program, Brigham and Women's Hospital, Boston, Massachusetts [270e, 271e]

Anna Mae Diehl, MD

Florence McAlister Professor of Medicine; Chief, Division of Gastroenterology, Duke University, Durham, North Carolina [364]

Jules L. Dienstag, MD

Carl W. Walter Professor of Medicine and Dean for Medical Education, Harvard Medical School; Physician, Gastrointestinal Unit, Department of Medicine, Massachusetts General Hospital, Boston, Massachusetts [360-362, 366e, 368]

William P. Dillon, MD

Professor and Executive Vice-Chair; Chief, Section of Neuroradiology, Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, California [440e, 441e]

Charles A. Dinarello, MD

Professor of Medicine and Immunology, University of Colorado Denver, Aurora, Colorado; Professor of Experimental Medicine, Radboud University Medical Center, Nijmegen, The Netherlands [23]

Raphael Dolin, MD

Maxwell Finland Professor of Medicine (Microbiology and Molecular Genetics), Harvard Medical School; Beth Israel Deaconess Medical Center; Brigham and Women's Hospital, Boston, Massachusetts [215e, 223, 224]

Susan M. Domchek, MD

Basser Professor of Oncology, Abramson Cancer Center, University of Pennsylvania, Philadelphia, Pennsylvania [84]

Richard L. Doty, PhD, MA

Director, Smell and Taste Center; Professor, Department of Otorhinolaryngology: Head and Neck Surgery, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [42]

Vanja C. Douglas, MD

Assistant Professor of Clinical Neurology and Sara and Evan Williams Foundation Endowed Neurohospitalist Chair, University of California, San Francisco, San Francisco, California [29]

Daniel B. Drachman, MD

Professor of Neurology and Neuroscience, W. W. Smith Charitable Trust Professor of Neuroimmunology, Department of Neurology, Johns Hopkins School of Medicine, Baltimore, Maryland [461]

David F. Driscoll, PhD

Associate Professor of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts [98e]

Thomas D. DuBose, Jr., MD, MACP

Emeritus Professor of Internal Medicine and Nephrology, Wake Forest University School of Medicine, Winston-Salem, North Carolina [64e, 66]

J. Stephen Dumler, MD

Professor, Division of Medical Microbiology, Department of Pathology, Johns Hopkins University School of Medicine, Baltimore, Maryland [211]

Andrea Dunaif, MD

Charles F. Kettering Professor of Endocrinology and Metabolism and Vice-Chair for Research, Department of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois [6e]

Samuel C. Durso, MD, MBA

Mason F. Lord Professor of Medicine; Director, Division of Geriatric Medicine and Gerontology, Johns Hopkins University School of Medicine, Baltimore, Maryland [45, 46e]

Janice P. Dutcher, MD

Associate Director, Cancer Research Foundation of New York, Chappaqua, New York; Former Professor, New York Medical College, Valhalla, New York [331]

Johanna Dwyer, DSc, RD

Jean Mayer USDA Human Nutrition Research Center on Aging; Professor, Tufts Medical Center and Director, Frances Stern Nutrition Center, Tufts Medical Center, Boston, Massachusetts [95e]

Jeffrey S. Dzieczkowski, MD

Physician, St. Alphonsus Regional Medical Center; Medical Director, Coagulation Clinic, Saint Alphonsus Medical Group, International Medicine and Travel Medicine, Boise, Idaho [138e]

Kim A. Eagle, MD

Albion Walter Hewlett Professor of Internal Medicine; Chief of Clinical Cardiology; Director, Frankel Cardiovascular Center, University of Michigan Health System, Ann Arbor, Michigan [9]

James A. Eastham, MD

Chief, Urology Service, Florence and Theodore Baumritter/Enid Ancell Chair of Urologic Oncology, Department of Surgery, Sidney Kimmel Center for Prostate and Urologic Cancers, Memorial Sloan Kettering Cancer Center, New York, New York [115]

Robert H. Eckel, MD

Professor of Medicine, Division of Endocrinology, Metabolism and Diabetes, Division of Cardiology; Professor of Physiology and Biophysics, Charles A. Boettcher, II Chair in Atherosclerosis, University of Colorado School of Medicine, Anschutz Medical Campus, Director Lipid Clinic, University of Colorado Hospital, Aurora, Colorado [422]

John E. Edwards, Jr., MD

Professor of Medicine, David Geffen School of Medicine, University of California, Los Angeles (UCLA), Los Angeles, California; Chief, Division of Infectious Diseases, Harbor/UCLA Medical Center, Torrance, California [235, 240]

David A. Ehrmann, MD

Professor, Department of Medicine, Section of Endocrinology, Diabetes, and Metabolism, The University of Chicago Pritzker School of Medicine, Chicago, Illinois [68]

Andrew J. Einstein, MD, PhD

Victoria and Esther Aboodi Assistant Professor of Medicine; Director, Cardiac CT Research; Co-Director, Cardiac CT and MRI, Department of Medicine, Cardiology Division, Department of Radiology, Columbia University College of Physicians and Surgeons, New York-Presbyterian Hospital, New York, New York [Appendix]

Ezekiel J. Emanuel, MD, PhD

Chair, Department of Medical Ethics and Health Policy, Levy University Professor, Perelman School of Medicine and Wharton School, University of Pennsylvania, Philadelphia, Pennsylvania [10]

John W. Engstrom, MD

Betty Anker Fife Distinguished Professor and Vice-Chairman; Neurology Residency Program Director, University of California, San Francisco, San Francisco, California [22, 454]

Moshe Ephros, MD

Clinical Associate Professor, Faculty of Medicine, Technion-Israel Institute of Technology; Pediatric Infectious Disease Unit, Carmel Medical Center; Haifa, Israel [197]

Jonathan A. Epstein, MD

William Wikoff Smith Professor; Chair, Department of Cell and Developmental Biology; Scientific Director, Penn Cardiovascular Institute, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [265e]

Aaron C. Ermel, MD

Assistant Research Professor; Assistant Professor of Clinical Medicine, Department of Internal Medicine, Division of Infectious Disease, Indiana University School of Medicine, Indianapolis, Indiana [222]

Tim Evans, MD, PhD

Senior Director, Health, Nutrition and Population, The World Bank Group, Washington, DC [13e]

Christopher H. Fanta, MD

Professor of Medicine, Harvard Medical School; Pulmonary and Critical Care Division, Brigham and Women's Hospital; Director, Partners Asthma Center, Boston, Massachusetts [48]

Paul Farmer, MD, PhD

Kolokotronis University Professor, Harvard University; Chair, Department of Global Health and Social Medicine, Harvard Medical School; Chief, Division of Global Health Equity, Brigham and Women's Hospital; Co-Founder, Partners In Health, Boston, Massachusetts [2]

Anthony S. Fauci, MD

Chief, Laboratory of Immunoregulation; Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [1, 225e, 226, 261e, 372e, 385, 386e]

Murray J. Favus, MD

Professor of Medicine, Department of Medicine, Section of Endocrinology, Diabetes and Metabolism, Director Bone Program, University of Chicago Pritzker School of Medicine, Chicago, Illinois [426e]

David P. Faxon, MD

Vice Chair of Medicine for Strategic Planning, Department of Medicine, Brigham and Women's Hospital; Senior Lecturer, Harvard Medical School, Boston, Massachusetts [272, 296e, 297]

Darren R. Feldman, MD

Associate Professor in Medicine, Weill Cornell Medical Center; Assistant Attending, Genitourinary Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, New York [116]

David T. Felson, MD, MPH

Professor of Medicine and Epidemiology; Chair, Clinical Epidemiology Unit, Boston University School of Medicine, Boston, Massachusetts [394]

Luigi Ferrucci, MD, PhD

Scientific Director, National Institute of Aging, National Institutes of Health, Baltimore, Maryland [11]

Howard L. Fields, MD, PhD

Professor, Department of Neurology, University of California, San Francisco, San Francisco, California [18]

Gregory A. Filice, MD

Professor of Medicine, Medical School, and Adjunct Professor of Epidemiology and Community Health, School of Public Health, University of Minnesota; Chief, Infectious Disease Section, Veterans Affairs Healthcare System, Minneapolis, Minnesota [199]

Robert W. Finberg, MD

Chair, Department of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts [104, 169]

Joyce Fingerhuth, MD

Professor of Medicine and MAPS, Division of Infectious Disease, University of Massachusetts Medical School, Worcester, Massachusetts [169]

Kurt Fink, MD

Palo Alto Medical Foundation, Palo Alto, California [481e]

Alain Fischer, MD, PhD

Director of INSERM U768; Director of Imagine Institute; Professor of Immunology and Pediatric Hematology; Université Paris Descartes, Paris, France [374, 375e]

Jeffrey S. Flier, MD

Caroline Shields Walker Professor of Medicine and Dean, Harvard Medical School, Boston, Massachusetts [415e]

Agnes B. Fogo, MD

John L. Shapiro Professor of Pathology; Professor of Medicine and Pediatrics, Vanderbilt University Medical Center, Nashville, Tennessee [62e]

Larry C. Ford, MD

Clinical Infectious Diseases, Intermountain Healthcare, Provo, Utah [44]

Jane E. Freedman, MD

Professor of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts [142]

Roy Freeman, MD

Professor of Neurology, Harvard Medical School; Director, Center for Autonomic and Peripheral Nerve Disorders, Beth Israel Deaconess Medical Center, Boston, Massachusetts [27]

Gyorgy Frendl, MD, PhD, FCCM

Assistant Professor; Director of Surgical Critical Care Research Center, Department of Anesthesiology, Perioperative Critical Care and Pain Medicine, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [481e]

Carl E. Freter, MD, PhD, FACP

Professor of Medicine; Director, Division of Hematology and Oncology; Associate Director, Cancer Center, Saint Louis University, St. Louis, Missouri [125]

Lawrence S. Friedman, MD

Professor of Medicine, Harvard Medical School; Professor of Medicine, Tufts University School of Medicine; Assistant Chief of Medicine, Massachusetts General Hospital, Boston, Massachusetts; Anton R. Fried, MD Chair, Department of Medicine, Newton-Wellesley Hospital, Newton, Massachusetts [59]

Sonia Friedman, MD

Associate Professor of Medicine, Harvard Medical School; Associate Physician, Brigham and Women's Hospital, Boston, Massachusetts [351]

Anne L. Fuhlbrigge, MD, MS

Assistant Professor of Medicine, Harvard Medical School, Pulmonary and Critical Care Division; Brigham and Women's Hospital, Boston, Massachusetts [307]

Andre D. Furtado, MD

Assistant Professor, Department of Radiology, School of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania [441e]

Nicholas B. Galifianakis, MD, MPH

Assistant Clinical Professor, Surgical Movement Disorders Center, Department of Neurology, University of California, San Francisco, San Francisco, California [33e]

John I. Gallin, MD

Director, Clinical Center, National Institutes of Health, Bethesda, Maryland [80]

Charlotte A. Gaydos, DrPh

Professor of Medicine, Johns Hopkins University, Division of Infectious Diseases, Baltimore, Maryland [213]

J. Michael Gaziano, MD, MPH

Professor of Medicine, Harvard Medical School; Chief, Division of Aging, Brigham and Women's Hospital; Director, Massachusetts Veterans Epidemiology Center, Boston VA Healthcare System, Boston, Massachusetts [266e]

Thomas A. Gaziano, MD, MSc

Assistant Professor of Medicine, Harvard Medical School; Assistant Professor, Health Policy and Management, Center for Health Decision Sciences, Harvard School of Public Health; Faculty Co-Leader, Chronic and Cardiovascular Diseases Working Group, Harvard Institute for Global Health, Harvard University; Associate Physician in Cardiovascular Medicine, Department of Cardiology, Brigham and Women's Hospital, Boston, Massachusetts [266e]

Susan L. Gearhart, MD

Associate Professor, Surgery, Johns Hopkins Medical Institutions, Baltimore, Maryland [353]

Robert H. Gelber, MD

Clinical Professor of Medicine and Dermatology, University of California, San Francisco, San Francisco, California [203]

Jeffrey M. Gelfand, MD, MAS

Assistant Professor of Clinical Neurology, Department of Neurology, University of California, San Francisco, San Francisco, California [29]

Alfred L. George, Jr., MD

Magerstadt Professor and Chair, Department of Pharmacology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois [332e]

Dale N. Gerding, MD

Professor of Medicine, Department of Medicine, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois; Research Physician, Edward Hines Jr. Veterans Affairs Hospital, Hines, Illinois [161]

Michael D. Geschwind, MD, PhD

Associate Professor of Neurology, Memory and Aging Center, University of California, San Francisco, San Francisco, California [33e]

Marc G. Ghany, MD, MHSC

Staff Physician, Liver Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland [357]

Michael Giladi, MD, MSc

Associate Professor of Medicine, Sackler Faculty of Medicine, Tel Aviv University; The Infectious Disease Unit and the Bernard Pridan Laboratory for Molecular Biology of Infectious Diseases, Tel Aviv Medical Center, Tel Aviv, Israel [197]

Roger I. Glass, MD, PhD

Director, Fogarty International Center, Bethesda, Maryland [227]

Eli Glatstein, MD

Professor and Vice Chairman, Department of Radiation Oncology, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania [263e]

Peter J. Goadsby, MD, PhD, DSc, FRACp, FRCP

Professor, NIHR-Wellcome Trust Clinical Research Facility, King's College, London, United Kingdom; Professor, Department of Neurology, University of California, San Francisco, San Francisco, California [21, 447]

Morton F. Goldberg, MD, FACS, FAOS

Director Emeritus and Joseph Green Professor of Ophthalmology, Wilmer Eye Institute, Johns Hopkins University School of Medicine and Johns Hopkins Hospital, Baltimore, Maryland [40e]

Ary L. Goldberger, MD

Professor of Medicine, Harvard Medical School; Wyss Institute for Biologically Inspired Engineering, Harvard University; Beth Israel Deaconess Medical Center, Boston, Massachusetts [268, 269e, 278e]

David Goldblatt, MB, ChB, PhD

Professor of Vaccinology and Immunology; Consultant in Paediatric Immunology; Director of Clinical Research and Development; Director, NIHR Biomedical Research Centre, Institute of Child Health; University College London; Great Ormond Street Hospital for Children NHS Trust, London, United Kingdom [171]

Samuel Z. Goldhaber, MD

Professor of Medicine, Harvard Medical School; Director, Thrombosis Research Group, Brigham and Women's Hospital, Boston, Massachusetts [300]

Ralph Gonzales, MD, MSPH

Professor of Medicine, University of California, San Francisco, San Francisco, California [44]

Douglas S. Goodin, MD

Professor, Department of Neurology, School of Medicine, University of California, San Francisco, San Francisco, California [458]

Jeffrey I. Gordon, MD

Dr. Robert J. Glaser Distinguished University Professor and Director, Center for Genome Sciences and Systems Biology, Washington University School of Medicine, St. Louis, Missouri [86e]

Maria Luisa Gorno-Tempini, MD, PhD

Professor, Department of Neurology; Language Neurobiology Lab, Memory and Aging Center; Dyslexia Center, University of California, San Francisco, San Francisco, California [37e]

Peter A. Gottlieb, MD

Professor of Pediatrics and Medicine, Barbara Davis Center, University of Colorado School of Medicine, Aurora, Colorado [409]

Gregory A. Grabowski, MD

Adjunct Professor of Pediatrics and Molecular Genetics, Biochemistry, and Microbiology, University of Cincinnati College of Medicine; Division of Human Genetics Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio; Chief Scientific Officer, Synageva BioPharma Corp., Lexington, Massachusetts [432e]

Yonatan H. Grad, MD, PhD

Assistant Professor of Immunology and Infectious Diseases, Harvard School of Public Health; Associate Physician, Division of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts [146]

Christine Grady, RN, PhD

Chief, Department of Bioethics, National Institutes of Health Clinical Center, Bethesda, Maryland [17e]

Alexander R. Green, MD, MPH

Assistant Professor of Medicine, Harvard Medical School; Associate Director, The Disparities Solutions Center, Massachusetts General Hospital, Boston, Massachusetts [16e]

Norton J. Greenberger, MD

Clinical Professor of Medicine, Harvard Medical School; Senior Physician, Division of Gastroenterology, Brigham and Women's Hospital, Boston, Massachusetts [369-371]

Michael F. Greene, MD

Professor of Obstetrics, Gynecology and Reproductive Biology, Harvard Medical School; Vincent Department of Obstetrics and Gynecology, Massachusetts General Hospital, Boston, Massachusetts [124e]

Daryl R. Gress, MD, FAAN, FCCM, FNCS

Associate Professor of Neurology, University of Virginia, Charlottesville, Virginia [330]

Rasim Gucalp, MD

Professor of Clinical Medicine, Albert Einstein College of Medicine; Associate Chairman for Educational Programs, Department of Oncology; Director, Hematology/Oncology Fellowship, Montefiore Medical Center, Bronx, New York [331]

Kalpna Gupta, MD, MPH

Associate Professor, Department of Medicine, Boston University School of Medicine; Chief, Section of Infectious Diseases, VA Boston Healthcare System, Boston, Massachusetts [162]

John G. Haaga, PhD

Deputy Associate Director, Behavioral and Social Research Program, National Institute on Aging, National Institutes of Health, Bethesda, Maryland [93e]

Chadi A. Hage, MD

Assistant Professor of Medicine, Thoracic Transplant Program, Indiana University Health, Indianapolis, Indiana [236]

Bevra Hannahs Hahn, MD

Professor Emerita Division of Rheumatology, University of California, Los Angeles, Los Angeles, California [378]

Colin N. Haile, MD, PhD

Assistant Professor, Menninger Department of Psychiatry and Behavioral Sciences, Baylor College of Medicine; Michael E. DeBakey VA Medical Center, Houston, Texas [468e]

Janet E. Hall, MD, MSc

Professor of Medicine, Harvard Medical School and Associate Chief, Reproductive Endocrine Unit, Massachusetts General Hospital, Boston, Massachusetts [69, 412, 414]

Jesse B. Hall, MD, FCCP

Professor of Medicine, Anesthesia and Critical Care; Chief, Section of Pulmonary and Critical Care Medicine, University of Chicago, Chicago, Illinois [321]

Scott A. Halperin, MD

Professor of Pediatrics and Microbiology and Immunology Head, Pediatric Infectious Diseases, Director, Canadian Center for Vaccinology, Dalhousie University, Halifax, Nova Scotia, Canada [185]

R. Doug Hardy, MD

Infectious Diseases Specialists, PA; Medical City Dallas Hospital and Medical City Children's Hospital, Dallas; Baylor Regional Medical Center, Plano, Texas [212]

Rudy A. Hartskeerl, PhD

Director WHO/FAO/OIE and National Leptospirosis Reference Centre, KIT Biomedical Research, KIT (Royal Tropical Institute), Amsterdam, The Netherlands [208]

William L. Hasler, MD

Professor, Division of Gastroenterology, University of Michigan Health System, Ann Arbor, Michigan [54, 344]

Stephen L. Hauser, MD

Robert A. Fishman Distinguished Professor and Chairman, Department of Neurology, University of California, San Francisco, San Francisco, California [1, 437, 443e, 444e, 455, 456, 458, 460]

Barton F. Haynes, MD

Frederic M. Hanes Professor of Medicine and Immunology, Departments of Medicine and Immunology; Director, Duke Human Vaccine Institute, Duke University School of Medicine, Durham, North Carolina [372e]

Douglas C. Heimbarger, MD, MS

Professor of Medicine, Associate Director for Education and Training, Vanderbilt Institute for Global Health, Vanderbilt University School of Medicine, Nashville, Tennessee [97]

J. Claude Hemphill, III, MD, MAS

Professor of Neurology and Neurological Surgery, University of California, San Francisco; Chief of Neurology, San Francisco General Hospital, San Francisco, California [330, 446]

Patrick H. Henry, MD

Clinical Adjunct Professor of Medicine, University of Iowa, Iowa City, Iowa [79]

Katherine A. High, MD

William H. Bennett Professor of Pediatrics, Perelman School of Medicine, University of Pennsylvania; Investigator, Howard Hughes Medical Institute, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania [91e, 141]

Christine E. Hill-Kayser, MD

Assistant Professor of Radiation Oncology, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [263e]

Ikuo Hirano, MD

Professor of Medicine, Division of Gastroenterology, Northwestern University Feinberg School of Medicine, Chicago, Illinois [53, 347]

Martin S. Hirsch, MD

Professor of Medicine, Harvard Medical School; Professor of Immunology and Infectious Diseases, Harvard School of Public Health; Physician, Massachusetts General Hospital, Boston, Massachusetts [219]

Helen H. Hobbs, MD

Professor, Internal Medicine and Molecular Genetics, University of Texas Southwestern Medical Center; Investigator, Howard Hughes Medical Institute, Dallas, Texas [421]

Judith S. Hochman, MD

Harold Snyder Family Professor of Cardiology, Clinical Chief, Leon Charney Division of Cardiology, Co-Director, NYU-HHC Clinical and Translational Science Institute; Director, Cardiovascular Clinical Research Center, New York University School of Medicine, New York, New York [326]

A. Victor Hoffbrand, DM

Emeritus Professor of Haematology, University College, London; Honorary Consultant Haematologist, Royal Free Hospital, London, United Kingdom [128]

L. John Hoffer, MD, PhD

Professor, Faculty of Medicine, McGill University; Senior Physician, Divisions of Internal Medicine and Endocrinology, Lady Davis Institute for Medical Research, Jewish General Hospital, Montreal, Quebec, Canada [98e]

Charles W. Hoge, MD

Senior Scientist, Center for Psychiatry and Neuroscience, Walter Reed Army Institute of Research, Silver Spring, Maryland [471e]

Elizabeth L. Hohmann, MD

Associate Professor of Medicine and Infectious Diseases, Harvard Medical School; Massachusetts General Hospital, Boston, Massachusetts [176]

Steven M. Holland, MD

Chief, Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [80, 204]

King K. Holmes, MD, PhD

Chair, Global Health; Professor of Medicine and Global Health; Adjunct Professor, Epidemiology; Director, Center for AIDS and STD; University of Washington School of Medicine; Head, Infectious Diseases Section, Harborview Medical Center, Seattle, Washington [163]

Jay H. Hoofnagle, MD

Director, Liver Diseases Research Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland [357]

David C. Hooper, MD

Professor, Harvard Medical School; Chief, Infection Control Unit; Associate Chief, Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts [170]

Robert J. Hopkin, MD

Associate Professor, Cincinnati Children's Hospital Medical Center, Cincinnati, Ohio [432e]

Leora Horn, MD, MSc

Assistant Professor, Division of Hematology and Medical Oncology, Vanderbilt University School of Medicine, Nashville, Tennessee [107]

Jonathan C. Horton, MD, PhD

William F. Hoyt Professor of Neuro-ophthalmology, Professor of Ophthalmology, Neurology and Physiology, University of California, San Francisco School of Medicine, San Francisco, California [39]

Howard Hu, MD, MPH, ScD

Dean; Professor of Environmental Health, Epidemiology and Global Health, Dalla Lana School of Public Health; Professor of Medicine, University of Toronto, Toronto, Ontario, Canada [472e]

Deborah T. Hung, MD, PhD

Associate Professor of Microbiology and Molecular Genetics, Assistant Professor of Medicine, Harvard Medical School; Brigham and Women's Hospital; Massachusetts General Hospital, Boston, Massachusetts; Co-director, Infectious Disease Initiative, Broad Institute of Harvard University and Massachusetts Institute of Technology, Cambridge, Massachusetts [146]

Sharon A. Hunt, MD, FACC

Professor of Medicine, Cardiovascular Medicine, Stanford University, Palo Alto, California [281]

Charles G. Hurst, MD

Chief, Chemical Casualty Care Division, United States Medical Research Institute of Chemical Defense, APG-Edgewood Area, Maryland [262e]

Ashraf S. Ibrahim, PhD

Professor, Department of Medicine, Geffen School of Medicine, University of California, Los Angeles (UCLA); Division of Infectious Diseases, Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center, Torrance, California [242]

David H. Ingbar, MD

Professor of Medicine, Pediatrics, and Physiology; Director, Pulmonary Allergy, Critical Care and Sleep Division, University of Minnesota School of Medicine, Minneapolis, Minnesota [326]

Alan C. Jackson, MD, FRCPC

Professor of Medicine (Neurology) and of Medical Microbiology, University of Manitoba; Section Head of Neurology, Winnipeg Regional Health Authority, Winnipeg, Manitoba, Canada [232]

Lisa A. Jackson, MD, MPH

Senior Investigator, Group Health Research Institute, Seattle, Washington [148]

Danny O. Jacobs, MD, MPH, FACS

Executive Vice President, Provost, and Dean of the School of Medicine; Thomas N. and Gleaves T. James Distinguished Chair, The University of Texas Medical Branch at Galveston, Galveston, Texas [20, 355, 356]

Richard F. Jacobs, MD

Robert H. Fiser, Jr., MD Endowed Chair in Pediatrics; Professor and Chairman, Department of Pediatrics, University of Arkansas for Medical Sciences; President, Arkansas Children's Hospital Research Institute, Little Rock, Arkansas [195]

J. Larry Jameson, MD, PhD

Robert G. Dunlop Professor of Medicine; Dean, Perelman School of Medicine at the University of Pennsylvania; Executive Vice President, University of Pennsylvania for the Health System, Philadelphia, Pennsylvania [1, 56, 82, 84, 121, 399-403, 405, 410, 411, 436e]

Robert T. Jensen, MD

Chief, Cell Biology Section, National Institutes of Diabetes, Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland [113]

Roy M. John, MBBS, PhD, FRCP

Assistant Professor of Medicine, Harvard Medical School; Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts [277]

Savio John, MD

Assistant Professor of Medicine, Division of Gastroenterology and Hepatology, State University of New York Upstate Medical University, Syracuse, New York [58]

David H. Johnson, MD

Donald W. Seldin Distinguished Chair in Internal Medicine; Professor and Chairman, Department of Internal Medicine, University of Texas Southwestern School of Medicine, Dallas, Texas [107]

James R. Johnson, MD

Professor of Medicine, University of Minnesota, Minneapolis, Minnesota [186]

Stuart Johnson, MD

Associate Professor of Medicine, Loyola University Chicago Stritch School of Medicine; Staff Physician, Edward Hines Jr. VA Hospital, Hines, Illinois [161]

S. Clairborne Johnston, MD, PhD

Dean, Dell Medical School; Frank Denius Distinguished Dean's Chair in Medical Leadership; Vice President for Medical Affairs, University of Texas, Austin, Austin, Texas [446]

S. Andrew Josephson, MD

Associate Professor; Vice Chairman, Department of Neurology, University of California, San Francisco, San Francisco, California [34, 329e, 463e]

Harald Jüppner, MD

Professor of Pediatrics, Endocrine Unit and Pediatric Nephrology Unit, Massachusetts General Hospital, Boston, Massachusetts [424]

Peter J. Kahrilas, MD

Gilbert H. Marquardt Professor of Medicine, Feinberg School of Medicine, Northwestern University, Chicago, Illinois [53, 347]

Gail Kang, MD

San Francisco, California [33e]

Hagop Kantarjian, MD

Chairman, Leukemia Department; Professor of Leukemia, The University of Texas M.D. Anderson Cancer Center, Houston, Texas [133]

Adolf W. Karchmer, MD

Professor of Medicine, Harvard Medical School, Division of Infectious Diseases, Beth Israel Deaconess Medical Center, Boston, Massachusetts [155]

Dennis L. Kasper, MD, MA

William Ellery Channing Professor of Medicine, Professor of Microbiology and Immunobiology, Department of Microbiology and Immunobiology, Harvard Medical School; Division of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts [1, 144, 147, 159, 183e, 201]

Lloyd H. Kasper, MD

Professor of Microbiology/Immunology and Medicine, Geisel School of Medicine, Dartmouth College, Hanover, New Hampshire [253]

Daniel L. Kastner, MD, PhD

Scientific Director, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland [392]

Carol A. Kauffman, MD

Professor of Internal Medicine, University of Michigan Medical School; Chief, Infectious Diseases Section, Veterans Affairs Ann Arbor Healthcare System, Ann Arbor, Michigan [243]

Elaine T. Kaye, MD

Assistant Clinical Professor of Dermatology, Harvard Medical School; Boston Children's Hospital, Boston, Massachusetts [24, 25e]

Kenneth M. Kaye, MD

Associate Professor of Medicine, Harvard Medical School; Division of Infectious Diseases, Brigham and Women's Hospital, Boston, Massachusetts [24, 25e]

John A. Kessler, MD

Davee Professor of Stem Cell Biology, Department of Neurology, Feinberg School of Medicine, Northwestern University, Chicago, Illinois [90e]

Jay S. Keystone, MD, FRCPC, MSc(CTM)

Professor of Medicine, University of Toronto, Toronto, Ontario, Canada [149]

Sundeep Khosla, MD

Professor of Medicine and Physiology, College of Medicine, Mayo Clinic, Rochester, Minnesota [65]

Elliott Kieff, MD, PhD

Harriet Ryan Albee Professor of Medicine, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [214e]

Anthony A. Killeen, MD, PhD

Professor, Department of Laboratory Medicine and Pathology, University of Minnesota, Minneapolis, Minnesota [480e]

Kami Kim, MD

Professor, Departments of Medicine, Pathology, and Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, New York [253]

Charles H. King, MD, MS

Professor, Center for Global Health and Diseases, School of Medicine, Case Western Reserve University, Cleveland, Ohio [259]

Lindsay King, MD, MPH

Advanced Transplant/Hepatology Fellow, Department of Medicine, Gastrointestinal Unit, Massachusetts General Hospital, Boston, Massachusetts [483e]

Talmadge E. King, Jr., MD

Professor and Chair, Department of Medicine, University of California, San Francisco, San Francisco, California [315]

Louis V. Kirchhoff, MD, MPH

Professor, Departments of Internal Medicine (Infectious Diseases) and Epidemiology, University of Iowa; Staff Physician, Department of Veterans Affairs Medical Center, Iowa City, Iowa [252]

Priya S. Kishnani, MD

Professor of Pediatrics, Division Chief, Medical Genetics, Duke University Medical Center, Durham, North Carolina [433e]

Rob Knight, PhD

Professor, Howard Hughes Medical Institute; Departments of Chemistry and Biochemistry and Computer Science, BioFrontiers Institute, University of Colorado, Boulder, Colorado [86e]

Minoru S. H. Ko, MD, PhD

Mitsunada Sakaguchi Professor and Chair, Department of Systems Medicine, Keio University School of Medicine, Tokyo, Japan [88]

Barbara A. Konkle, MD

Professor of Medicine, Hematology, University of Washington; Director, Translational Research, Puget Sound Blood Center, Seattle, Washington [78, 140]

Peter Kopp, MD

Associate Professor, Division of Endocrinology, Metabolism and Molecular Science and Center for Genetic Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois [82]

Walter J. Koroshetz, MD

National Institute of Neurological Disorders and Stroke, National Institutes of Health, Bethesda, Maryland [165]

Thomas R. Kosten, MD

J. H. Waggoner Professor of Psychiatry, Pharmacology, Immunology, Neuroscience, Baylor College of Medicine, Houston, Texas [468e]

Theodore A. Kotchen, MD

Professor Emeritus, Department of Medicine; Associate Dean for Clinical Research, Medical College of Wisconsin, Milwaukee, Wisconsin [298]

Camille Nelson Kotton, MD, FIDSA

Clinical Director, Transplant and Immunocompromised Host Infectious Diseases, Infectious Diseases Division, Massachusetts General Hospital; Harvard Medical School, Boston, Massachusetts [219]

Phyllis E. Kozarsky, MD

Professor of Medicine and Infectious Diseases, Emory University School of Medicine, Atlanta, Georgia [149]

Barnett S. Kramer, MD, MPH, FACP

Director, Division of Cancer Prevention, National Cancer Institute, Bethesda, Maryland [100]

Joel Kramer, PsyD

Professor of Neuropsychology in Neurology; Director of Neuropsychology, Memory and Aging Center, University of California, San Francisco, San Francisco, California [37e]

Stephen M. Krane, MD

Persis, Cyrus and Marlow B. Harrison Distinguished Professor of Medicine, Harvard Medical School; Massachusetts General Hospital, Boston, Massachusetts [423]

Alexander Kratz, MD, MPH, PhD

Associate Professor of Clinical Pathology and Cell Biology, Columbia University College of Physicians and Surgeons; Director, Core Laboratory, Columbia University Medical Center and the New York Presbyterian Hospital; Director, the Allen Hospital Laboratory, New York, New York [Appendix]

Peter J. Krause, MD

Senior Research Scientist, Yale School of Public Health; Yale School of Medicine, New Haven, Connecticut [249]

John P. Kress, MD

Professor of Medicine, Director, Medical Intensive Care Unit, University of Chicago, Chicago, Illinois [321]

Stephen Krieger, MD

Assistant Professor, Department of Neurology; Director, Neurology Residency Program, Icahn School of Medicine at Mount Sinai; Attending Physician, The Corinne Goldsmith Dickinson Center for MS, New York, New York [486e]

Patricia A. Kritek, MD, EdM

Associate Professor, Division of Pulmonary and Critical Care Medicine, University of Washington, Seattle, Washington [48, 305, 308e]

Henry M. Kronenberg, MD

Professor of Medicine, Harvard Medical School; Chief, Endocrine Unit, Massachusetts General Hospital, Boston, Massachusetts [423]

Jens H. Kuhn, MD, PhD, MS

Principal, Tunnell Government Services (TGS), Inc.; Lead Virologist, Integrated Research Facility at Fort Detrick (IRF-Frederick); TGS IRF-Frederick Team Leader, NIH/NIAID/DCR, Fort Detrick, Frederick, Maryland [233, 234]

Robert F. Kushner, MD, MS

Professor of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois [416]

Raymond Y. Kwong, MD, MPH

Associate Professor of Medicine, Harvard Medical School; Director of Cardiac Magnetic Resonance Imaging, Cardiovascular Division, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts [270e, 271e]

Loren Laine, MD

Professor of Medicine, Yale University School of Medicine, New Haven, Connecticut; VA Connecticut Healthcare System, West Haven, Connecticut [57]

Neil K. Lakdawala, MD

Instructor in Medicine, Harvard Medical School; Associate Physician, Cardiovascular Medicine, Brigham and Women's Hospital; Boston VA Healthcare; Boston, Massachusetts [287]

Anil K. Lalwani, MD

Professor and Vice Chair for Research; Director, Division of Otolaryngology and Skull Base Surgery; Director, Columbia Cochlear Implant Center, Columbia University College of Physicians and Surgeons, New York, New York [43]

H. Clifford Lane, MD

Clinical Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [226, 261e]

Carol A. Langford, MD, MHS

Harold C. Schott Endowed Chair; Director, Center for Vasculitis Care and Research, Department of Rheumatic and Immunologic Diseases, Cleveland Clinic, Cleveland, Ohio [385, 386e, 389, 397, 398]

Regina C. LaRocque, MD, MPH

Assistant Professor of Medicine, Harvard Medical School; Assistant Physician, Massachusetts General Hospital, Boston, Massachusetts [160]

Wei C. Lau, MD, FAHA

Emeritus Associate Professor, Department of Anesthesiology, Section Cardiovascular Anesthesiology, University of Michigan Health System Cardiovascular Center, Ann Arbor, Michigan [9]

Leslie P. Lawley, MD

Assistant Professor, Department of Dermatology, School of Medicine, Emory University, Atlanta, Georgia [71]

Thomas J. Lawley, MD

William P. Timmie Professor of Dermatology, Dean, Emory University School of Medicine, Atlanta, Georgia [70, 71, 73, 76e]

David G. Le Couteur, MD, PhD, FRACP

Professor of Geriatric Medicine, Director of the Centre for Education and Research on Ageing, University of Sydney and Sydney Research, Sydney, Australia [94e]

William M. Lee, MD

Professor of Internal Medicine; Meredith Mosle Chair in Liver Diseases, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas [361]

Charles Lei, MD

Assistant Professor, Department of Emergency Medicine, Vanderbilt University Medical Center, Nashville, Tennessee [474]

Jane A. Leopold, MD

Associate Professor of Medicine, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [272, 297e]

Nelson Leung, MD

Associate Professor of Medicine, Division of Nephrology and Hypertension, Division of Hematology, Mayo Clinic Rochester, Rochester, Minnesota [341]

Bruce D. Levy, MD

Associate Professor of Medicine, Harvard Medical School; Pulmonary and Critical Care Medicine, Brigham and Women's Hospital, Boston, Massachusetts [322]

Julia B. Lewis, MD

Professor, Department of Medicine, Division of Nephrology, Vanderbilt University Medical Center, Nashville, Tennessee [338]

Peter Libby, MD

Mallinckrodt Professor of Medicine, Harvard Medical School; Chief, Cardiovascular Medicine, Brigham and Women's Hospital, Boston, Massachusetts [265e, 291e, 292e]

Richard W. Light, MD

Professor of Medicine, Division of Allergy, Pulmonary, and Critical Care Medicine, Vanderbilt University, Nashville, Tennessee [316, 317]

Julie Lin, MD, MPH

Lecturer on Medicine, Harvard Medical School; Associate Physician, Renal Division, Brigham and Women's Hospital, Boston, Massachusetts, Boston, Massachusetts [61]

Yusen E. Lin, PhD, MBA

Professor and Director, Center for Environmental Laboratory Services; National Kaohsiung Normal University, Kaohsiung, Taiwan [184]

Robert Lindsay, MD, PhD

Chief, Internal Medicine; Professor of Clinical Medicine, Helen Hayes Hospital, West Haverstraw, New York [425]

Marc E. Lippman, MD, MACP, FRCP

Kathleen and Stanley Glaser Professor, Department of Medicine, Deputy Director, Sylvester Comprehensive Cancer Center, University of Miami Miller School of Medicine, Miami, Florida [108]

Peter E. Lipsky, MD

Charlottesville, Virginia [377e]

Kathleen D. Liu, MD, PhD, MAS

Associate Professor, Division of Nephrology, Department of Medicine, Division of Critical Care Medicine, Department of Anesthesiology, University of California, San Francisco, San Francisco, California [336]

Bernard Lo, MD

President, The Greenwall Foundation, New York; Professor of Medicine Emeritus and Director Emeritus of the Program in Medical Ethics, University of California, San Francisco, San Francisco, California [17e]

Dan L. Longo, MD

Professor of Medicine, Harvard Medical School; Senior Physician, Brigham and Women's Hospital; Deputy Editor, *New England Journal of Medicine*, Boston, Massachusetts [1, 77, 79, 81e, 89e, 99, 102e, 103e, 121, 123e, 124e, 125, 134, 135e, 136, 225e]

Nicola Longo, MD, PhD

Professor and Chief, Division of Medical Genetics, Departments of Pediatrics and Pathology; Medical Co-Director, Biochemical Genetics Laboratory, ARUP Laboratories, University of Utah, Salt Lake City, Utah [434e, 435e]

Joseph Loscalzo, MD, PhD

Hersey Professor of the Theory and Practice of Medicine, Harvard Medical School; Chairman, Department of Medicine; Physician-in-Chief, Brigham and Women's Hospital, Boston, Massachusetts [1, 49-52, 87e, 142, 264, 265e, 267, 283-287, 293, 295, 301-304]

Christine M. Lovly, MD, PhD

Academic, Vanderbilt Ingram Cancer Center, Vanderbilt University School of Medicine, Nashville, Tennessee [107]

Phillip A. Low, MD, FRACP, FRCP(Hon)

Robert D. and Patricia E. Kern Professor of Neurology, Mayo Clinic, College of Medicine, Rochester, Minnesota [454]

Daniel H. Lowenstein, MD

Dr. Robert B. and Mrs. Ellinor Aird Professor of Neurology; Director, Epilepsy Center, University of California, San Francisco, San Francisco, California [437, 438e, 445]

Elyse E. Lower, MD

Medical Oncology and Hematology, University of Cincinnati, Oncology Hematology Care, Inc., Cincinnati, Ohio [390]

Franklin D. Lowy, MD

Professor of Medicine and Pathology, Columbia University College of Physicians and Surgeons, New York, New York [172]

Sheila A. Lukehart, PhD

Professor, Departments of Medicine and Global Health, University of Washington, Seattle, Washington [206, 207e]

Lucio Luzzatto, MD, FRCP, FRCPATH

Professor of Hematology, University of Genova, Genova; Scientific Director, Istituto Toscano Tumori, Florence, Italy [129]

Lawrence C. Madoff, MD

Professor of Medicine, University of Massachusetts Medical School, Worcester, Massachusetts; Director, Division of Epidemiology and Immunization, Massachusetts Department of Public Health, Jamaica Plain, Massachusetts [157, 166e, 167e]

Adel A. F. Mahmoud, MD, PhD

Professor in Molecular Biology and Public Policy, Princeton University, Princeton, New Jersey [259]

Ronald V. Maier, MD

Jane and Donald D. Trunkey Professor and Vice-Chair, Surgery, University of Washington; Surgeon-in-Chief, Harborview Medical Center, Seattle, Washington [324]

Mark E. Mailliard, MD

Frederick F. Paustian Professor; Chief, Division of Gastroenterology and Hepatology, Department of Internal Medicine, University of Nebraska College of Medicine, Omaha, Nebraska [363]

Mahmoud Malas, MD, MHS, FACS

Associate Professor of Surgery, Johns Hopkins University; Director of Endovascular Surgery; Director of The Vascular and Endovascular Clinical Research Center, Johns Hopkins Bayview Medical Center, Baltimore, Maryland [354]

Hari R. Mallidi, MD

Associate Professor of Surgery and Chief, Division of Transplant and Assist Devices; Lester and Sue Smith Endowed Chair in Surgery, Baylor College of Medicine, Houston, Texas [281]

Susan J. Mandel, MD, MPH

Professor of Medicine; Associate Chief, Division of Endocrinology, Diabetes and Metabolism, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [405]

Brian F. Mandell, MD, PhD

Professor and Chairman of Medicine, Cleveland Clinic Lerner College of Medicine, Department of Rheumatic and Immunologic Disease, Cleveland Clinic, Cleveland, Ohio [397]

Lionel A. Mandell, MD, FRCPC

Professor of Medicine, McMaster University, Hamilton, Ontario, Canada [153]

Douglas L. Mann, MD

Lewin Chair and Chief, Cardiovascular Division; Professor of Medicine, Cell Biology and Physiology, Washington University School of Medicine, Cardiologist-in-Chief, Barnes Jewish Hospital, St. Louis, Missouri [279]

JoAnn E. Manson, MD, DrPH

Professor of Medicine and the Elizabeth Fay Brigham Professor of Women's Health, Harvard Medical School; Chief, Division of Preventive Medicine, Brigham and Women's Hospital, Boston, Massachusetts [413]

Eleftheria Maratos-Flier, MD

Professor of Medicine, Harvard Medical School; Division of Endocrinology, Beth Israel Deaconess Medical Center, Boston, Massachusetts [415e]

Guido Marcucci, MD

Professor of Medicine; John B. and Jane T. McCoy Chair in Cancer Research; Associate Director of Translational Research, Comprehensive Cancer Center, The Ohio State University College of Medicine, Columbus, Ohio [132]

Daniel B. Mark, MD, MPH

Professor of Medicine, Duke University Medical Center; Director, Outcomes Research, Duke Clinical Research Institute, Durham, North Carolina [3]

Alexander G. Marneros, MD, PhD

Assistant Professor, Department of Dermatology, Harvard Medical School; Cutaneous Biology Research Center, Massachusetts General Hospital, Boston, Massachusetts [75]

Jeanne M. Marrazzo, MD, MPH

Professor of Medicine, Division of Allergy and Infectious Diseases, University of Washington, Seattle, Washington [163]

Thomas Marrie, MD

Dean, Faculty of Medicine; Professor, Department of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada [211]

Gary J. Martin, MD

Raymond J. Langenbach, MD Professor of Medicine; Vice Chairman for Faculty Affairs, Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois [4]

Joseph B. Martin, MD, PhD

Edward R. and Anne G. Lefler Professor, Department of Neurobiology, Harvard Medical School, Boston, Massachusetts [437]

Susan Maslanka, PhD

Enteric Diseases Laboratory Branch, Centers for Disease Control and Prevention, Atlanta, Georgia [178]

Henry Masur, MD

Chief, Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, Maryland [244]

Jeremy Matloff, MD

Fellow, Department of Gastroenterology, Icahn School of Medicine at Mount Sinai, New York, New York [485e, 486e]

Robert J. Mayer, MD

Faculty Vice President for Academic Affairs, Dana-Farber Cancer Institute; Stephen B. Kay Family Professor of Medicine, Harvard Medical School, Boston, Massachusetts [109, 110]

Alexander J. McAdam, MD, PhD

Associate Professor of Pathology, Harvard Medical School; Medical Director, Infectious Diseases Diagnostic Laboratory, Children's Hospital of Boston, Boston, Massachusetts [150e]

Calvin O. McCall, MD

Associate Professor, Department of Dermatology, Virginia Commonwealth University Medical Center, Richmond, Virginia; Chief, Dermatology Section, Hunter Holmes McGuire Veterans Affairs Medical Center, Richmond, Virginia [71, 76e]

John F. McConville, MD

Associate Professor of Medicine and Director, Internal Medicine Residency Program, University of Chicago, Chicago, Illinois [318]

Corey A. McGraw, MD

Assistant Professor, The Saul R. Korey Department of Neurology, Albert Einstein College of Medicine, Yeshiva University, New York, New York [486e]

Kevin T. McVary, MD, FACS

Professor and Chairman, Division of Urology, Southern Illinois University School of Medicine, Springfield, Illinois [67]

Mandeep R. Mehra, MD, FACC, FACP

Professor of Medicine, Harvard Medical School; Executive Director, Center for Advanced Heart Disease, Brigham and Women's Hospital; Co-Director, Brigham and Women's Hospital Heart and Vascular Center, Boston, Massachusetts [280]

Nancy K. Mello,[†] PhD

Professor of Psychology (Neuroscience), Harvard Medical School, Boston, Massachusetts; Director, Alcohol and Drug Abuse Research Center, McLean Hospital, Belmont, Massachusetts [469e]

Shlomo Melmed, MD

Senior Vice President and Dean of the Medical Faculty, Cedars-Sinai Medical Center, Los Angeles, California [401e-403]

Jack H. Mendelson,[†] MD

Professor of Psychiatry (Neuroscience), Harvard Medical School, Belmont, Massachusetts [469e]

Robert O. Messing, MD

Professor, Division of Pharmacology and Toxicology, College of Pharmacy; Associate Director, Waggoner Center for Alcohol and Addiction Research, University of Texas at Austin, Austin, Texas [465e]

M.-Marsel Mesulam, MD

Professor of Neurology, Psychiatry and Psychology, Cognitive Neurology and Alzheimer's Disease Center, Northwestern University Feinberg School of Medicine, Chicago, Illinois [36]

Gregory F. Michaud, MD

Assistant Professor of Medicine, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [276]

Susan Miesfeldt, MD

Medical Oncology, Medical Director, Cancer Risk and Prevention Clinic, Maine Medical Center, Scarborough, Maine [84]

Edgar L. Milford, MD

Associate Professor of Medicine, Harvard Medical School; Director, Tissue Typing Laboratory, Brigham and Women's Hospital, Boston, Massachusetts [337]

Bruce L. Miller, MD

A. W. and Mary Margaret Clausen Distinguished Professor of Neurology, University of California, San Francisco School of Medicine, San Francisco, California [34, 35, 37e, 448, 453e]

Samuel I. Miller, MD

Professor, Departments of Microbiology, Medicine and Genome Sciences, University of Washington, Seattle, Washington [190]

Simon J. Mitchell, MB ChB, PhD, FUHM, FANZCA

Associate Professor, Department of Anaesthesiology, University of Auckland and Auckland City Hospital, Auckland, New Zealand [477e]

Babak Mokhlesi, MD, MSc

Professor of Medicine, Department of Medicine, Section of Pulmonary and Critical Care; Director, Sleep Disorders Center and Sleep Fellowship Program, University of Chicago, Chicago, Illinois [318]

Thomas A. Moore, MD, FACP, FIDSA

Chairman, Department of Infectious Diseases, Ochsner Health System, New Orleans, Louisiana [246e]

Pat J. Morin, PhD

Senior Director, Scientific Review and Grants Administration, American Association for Cancer Research, Philadelphia, Pennsylvania [101e]

Alison Morris, MD, MS

Associate Professor, Departments of Medicine and Immunology; Director, University of Pittsburgh HIV Lung Research Center, Division of Pulmonary, Allergy, and Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania [244]

Charles A. Morris, MD, MPH

Instructor in Medicine, Harvard Medical School; Staff Physician, Brigham and Women's Hospital, Boston, Massachusetts [482e, 484e]

David A. Morrow, MD, MPH

Associate Professor of Medicine, Harvard Medical School; Director, Levine Cardiac Intensive Care Unit; Senior Investigator, TIMI Study Group, Brigham and Women's Hospital, Boston, Massachusetts [19]

William J. Moss, MD, MPH

Professor, Departments of Epidemiology, International Health, and Molecular Microbiology and Immunology, Johns Hopkins Bloomberg School of Public Health, Baltimore, Maryland [229]

Robert J. Motzer, MD

Professor of Medicine, Joan and Sanford Weill College of Medicine of Cornell University D. Attending Physician, Genitourinary Oncology Service, Memorial Sloan-Kettering Cancer Center, New York, New York [114, 116]

David B. Mount, MD

Assistant Professor of Medicine, Harvard Medical School; Renal Division, Brigham and Women's Hospital, Renal Division, Boston VA Healthcare System, Boston, Massachusetts [63, 64e]

Haralampos M. Moutsopoulos, MD, FACP, FRCP(hc), Master ACR

Professor and Director, Department of Pathophysiology, Medical School, National University of Athens, Athens, Greece [379, 383, 387]

Robert S. Munford, MD

Senior Clinician, Laboratory of Clinical Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [325]

Nikhil C. Munshi, MD

Professor of Medicine, Harvard Medical School; Boston VA Healthcare System; Director of Basic and Correlative Sciences; Associate Director, Jerome Lipper Myeloma Center, Dana-Farber Cancer Institute, Boston, Massachusetts [136]

John R. Murphy, PhD

Professor of Medicine and Microbiology; Director ad interim, National Emerging Infectious Diseases Laboratories Institute, Boston University School of Medicine, Boston, Massachusetts [175]

Timothy F. Murphy, MD

SUNY Distinguished Professor; Director, Clinical and Translational Research Center, University at Buffalo, the State University of New York, Buffalo, New York [182]

Barbara E. Murray, MD

J. Ralph Meadows Professor and Director, Division of Infectious Diseases, University of Texas Medical School, Houston, Texas [174]

Joseph A. Murray, MD

Professor of Medicine, Departments of Internal Medicine and Immunology, Mayo Clinic, Rochester, Minnesota [55]

Mark B. Mycyk, MD

Associate Professor, Department of Emergency Medicine, Northwestern University Feinberg School of Medicine; Associate Professor, Department of Emergency Medicine, Rush University School of Medicine; Research Director, Toxikon Consortium; Attending Physician, Department of Emergency Medicine, Cook County Hospital, Chicago, Illinois [473e]

Robert J. Myerburg, MD

Professor, Departments of Medicine and Physiology, Division of Cardiology; AHA Chair in Cardiovascular Research, University of Miami Miller School of Medicine, Miami, Florida [327]

Avindra Nath, MD

Chief, Section of Infections of the Nervous System; Clinical Director, National Institute of Neurological Disorders and Stroke (NINDS), National Institutes of Health, Bethesda, Maryland [165]

Edward T. Naureckas, MD

Professor of Medicine, and Director, Pulmonary Function Laboratory, and Adult Cystic Fibrosis Laboratory, Section of Pulmonary and Critical Care Medicine, University of Chicago, Chicago, Illinois [306e]

Eric G. Neilson, MD

Lewis Landsberg Dean, and Vice President, Medical Affairs, Feinberg School of Medicine, Northwestern University, Chicago, Illinois [62e, 332e, 338]

Emily Page Nelson, MD

Clinical Instructor, Department of Anesthesiology, Perioperative, and Pain Medicine, Brigham and Women's Hospital, Boston, Massachusetts [484e]

Gerald T. Nepom, MD, PhD

Professor (Affiliate), University of Washington School of Medicine; Director, Benaroya Research Institute at Virginia Mason; Director, Immune Tolerance Network, Seattle, Washington [373e]

[†]Deceased

Eric J. Nestler, MD, PhD

Nash Family Professor and Chair, Department of Neuroscience; Director, Friedman Brain Institute, Ichan School of Medicine at Mount Sinai, New York, New York [465e]

Hartmut P. H. Neumann, MD

Universitaet Freiburg, Medizinische Universitaetsklinik, Freiburg im Breisgau, Germany [407]

Joseph P. Newhouse, PhD

John D. MacArthur Professor of Health Policy and Management, Department of Health Care Policy, Harvard Medical School; Faculty, John F. Kennedy School of Government, Harvard School of Public Health, Faculty of Arts and Sciences, Harvard University, Boston, Massachusetts [15e]

Jonathan Newmark, MD

Colonel, Medical Corps, U.S. Army; Deputy Joint Program Executive Officer, Medical Systems, Joint Program Executive Office for Chemical/Biological Defense, U.S. Department of Defense, Falls Church, Virginia; Adjunct Professor of Neurology, F. Edward Hebert School of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland [262e]

Rathel L. Nolan, III, MD

Professor, Department of Medicine, Division of Infectious Diseases, University of Mississippi Medical Center, Jackson, Mississippi [238]

Robert L. Norris, MD

Professor, Department of Surgery; Chief, Division of Emergency Medicine, Stanford University School of Medicine, Stanford, California [474]

Scott A. Norton, MD, MPH, MSc

Chief of Dermatology, Children's National Health Systems, Washington, DC [475]

Thomas B. Nutman, MD

Head, Helminth Immunology Section, Head, Clinical Parasitology Unit, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [257, 258]

Jose A. Obeso, MD

Professor of Neurology and Director, CIINAC, Hospital de Madrid; Medical School, CEU-San Pablo, Madrid, Spain [449]

Katherine L. O'Brien, MD, MPH

Professor, Department of International Health, Bloomberg School of Public Health, Johns Hopkins University, Baltimore, Maryland [171]

Max R. O'Donnell, MD, MPH

Assistant Professor of Medicine and Epidemiology, Division of Pulmonary, Allergy, and Critical Care Medicine, Columbia University Medical Center, New York, New York [205e]

Nigel O'Farrell, MD, MSc, FRCP

Ealing Hospital, London, United Kingdom [198e]

Jennifer Ogar, MS CCC-SLP

Speech-Language Pathologist, Memory and Aging Center, University of California, San Francisco, San Francisco, California [37e]

Patrick T. O'Gara, MD

Professor of Medicine, Harvard Medical School; Director, Clinical Cardiology, Brigham and Women's Hospital, Boston, Massachusetts [51e, 267, 283-286]

C. Warren Olanow, MD, FRCP, FRCP(hon)

Henry P. and Georgette Goldschmidt Professor and Chairman Emeritus, Department of Neurology; Professor, Department of Neuroscience, Mount Sinai School of Medicine, New York, New York [449]

Andrew B. Onderdonk, PhD

Professor of Pathology, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [150e]

Chung Owyang, MD

H. Marvin Pollard Professor of Internal Medicine; Chief, Division of Gastroenterology, University of Michigan Health System, Ann Arbor, Michigan [344, 352]

Umesh D. Parashar, MBBS, MPH

Lead, Viral Gastroenteritis Epidemiology Team, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia [227]

Shreyaskumar R. Patel, MD

Robert R. Herring Distinguished Professor of Medicine; Center Medical Director, Sarcoma Center, The University of Texas M.D. Anderson Cancer Center, Houston, Texas [119e]

David L. Paterson, MD, PhD

Professor of Medicine, University of Queensland Centre for Clinical Research; Royal Brisbane and Women's Hospital, Brisbane, Australia [187]

Gustav Paumgartner, MD

Professor Emeritus of Medicine, University of Munich, Munich, Germany [369]

M. Luisa Pedro-Botet, MD, PhD

Professor of Medicine, Autonomous University of Barcelona; Infectious Diseases Section (Senior Consultant), Germans Trias i Pujol University Hospital, Badalona, Barcelona, Spain [184]

David A. Pegues, MD

Professor of Medicine, Division of Infectious Diseases, Perelman School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania [190]

Anton Y. Peleg, MBBS, PhD, MPH, FRACP

Associate Professor, Department of Infectious Diseases and Microbiology, The Alfred Hospital and Monash University, Melbourne, Victoria, Australia [187]

Florencia Pereyra, MD

Instructor in Medicine, Harvard Medical School; Associate Physician, Infectious Disease Division, Brigham and Women's Hospital, Boston, Massachusetts [166e, 167e]

Michael A. Pesce, PhD

Professor Emeritus of Pathology and Cell Biology, Columbia University College of Physicians and Surgeons; Director, Biochemical Genetics Laboratory, Columbia University Medical Center, New York Presbyterian Hospital, New York, New York [Appendix]

Clarence J. Peters, MD

John Sealy Distinguished University Chair in Tropical and Emerging Virology; Professor, Department of Microbiology and Immunology; Department of Pathology; Director for Biodefense, Center for Biodefense and Emerging Infectious Diseases, University of Texas Medical Branch, Galveston, Texas [233]

Gerald B. Pier, PhD

Professor of Medicine (Microbiology and Immunobiology), Harvard Medical School; Brigham and Women's Hospital, Division of Infectious Diseases, Boston, Massachusetts [145e]

Richard J. Pollack, PhD

Instructor, Department of Immunology and Infectious Disease, Harvard School of Public Health, Boston, Massachusetts; Senior Environmental Public Health Officer, Department of Environmental Health and Safety, Harvard University, Cambridge, Massachusetts; President and Chief Scientific Officer, IdentifyUS LLC, Newton, Massachusetts [475]

Martin R. Pollak, MD

Professor of Medicine, Harvard Medical School; Beth Israel Deaconess Medical Center, Boston, Massachusetts [339]

Andrew J. Pollard, PhD, FRCPCH

Professor of Paediatric Infection and Immunity, Department of Paediatrics, University of Oxford, Oxford, United Kingdom [180]

Reuven Porat, MD

Professor of Medicine, Department of Internal Medicine, Tel Aviv Sourasky Medical Center; Sackler Faculty of Medicine, Tel Aviv University, Tel Aviv, Israel [23]

Daniel A. Portnoy, PhD

Professor, Department of Molecular and Cell Biology and the School of Public Health, University of California, Berkeley, Berkeley, California [176]

John T. Potts, Jr., MD

Jackson Distinguished Professor of Clinical Medicine, Harvard Medical School; Physician-in-Chief and Director of Research Emeritus, Massachusetts General Hospital, Boston, Massachusetts [424]

Lawrie W. Powell, MD, PhD

Professor of Medicine, The University of Queensland; Director, Centre for the Advancement of Clinical Research, Royal Brisbane and Women's Hospital, Brisbane, Australia [428]

Alvin C. Powers, MD

Joe C. Davis Chair in Biomedical Science; Professor of Medicine, Molecular Physiology and Biophysics; Director, Vanderbilt Diabetes Center; Chief, Division of Diabetes, Endocrinology, and Metabolism, Vanderbilt University School of Medicine, Nashville, Tennessee [417-419]

Daniel S. Pratt, MD

Assistant Professor of Medicine, Harvard Medical Center; Massachusetts General Hospital, Boston, Massachusetts [58, 358]

Michael B. Prentice, MB ChB, PhD, MRCP(UK), FRCPath, FFPRCP

Professor of Medical Microbiology, Departments of Microbiology and Pathology, University College Cork, Cork, Ireland [196]

Darwin J. Prockop, MD, PhD

Director and Professor, Institute for Regenerative Medicine, Texas A&M Health Science Center College of Medicine at Scott & White, Temple, Texas [427]

Stanley B. Prusiner, MD

Director, Institute for Neurodegenerative Diseases; Professor, Department of Neurology, University of California, San Francisco, San Francisco, California [444e, 453e]

Thomas C. Quinn, MD

Professor of Medicine, Johns Hopkins University, Baltimore, Maryland; Senior Investigator, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland [213]

Gil Rabinovici, MD

Associate Professor in Neurology, Memory and Aging Center, University of California, San Francisco, San Francisco, California [37e]

Daniel J. Rader, MD

Seymour Gray Professor of Molecular Medicine; Chair, Department of Genetics; Chief, Division of Translational Medicine and Human Genetics, Department of Medicine, Perelman School of Medicine at the University of Pennsylvania, Philadelphia, Pennsylvania [421]

Kaitlin Rainwater-Lovett, PhD, MPH

Research Fellow, Division of Infectious Diseases, Department of Pediatrics, Johns Hopkins University School of Medicine, Baltimore, Maryland [229]

Sanjay Ram, MBBS

Associate Professor of Medicine, Division of Infectious Diseases and Immunology, University of Massachusetts Medical School, Worcester, Massachusetts [181]

Reuben Ramphal, MD

Adjunct Professor of Medicine, Division of Infectious Diseases and Global Medicine, University of Florida College of Medicine, Gainesville, Florida [189]

Agam K. Rao, MD

Medical Officer, Division of Foodborne, Waterborne, and Environmental Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia [178]

Beth Rapaport, MD

Attending Physician, Elmhurst Hospital Center, Mount Sinai Medical Affiliate, Elmhurst, New York [486e]

Kumanan Rasanathan, MBChB, MPH, FAFPHM

Technical Officer, Department of Ethics, Equity, Trade, and Human Rights, World Health Organization, Geneva, Switzerland [13e]

Neil H. Raskin, MD

Department of Neurology, University of California, San Francisco, San Francisco, California [21, 447]

Anis Rassi, Jr., MD, PhD, FACC, FACP, FAHA

Scientific Director, Anis Rassi Hospital, Goiânia, Brazil [252]

James P. Rathmell, MD

Henry Knowles Beecher Professor of Anesthesiology, Harvard Medical School; Executive Vice Chair and Chief, Division of Pain Medicine, Department of Anesthesia, Critical Care and Pain Medicine, Massachusetts General Hospital, Boston, Massachusetts [18]

Mario C. Raviglione, MD

Director, Global TB Programme, World Health Organization, Geneva, Switzerland [202]

Divya Reddy, MBBS, MPH

Faculty, Department of Medicine, Pulmonary Division, Albert Einstein College of Medicine; Montefiore Medical Center, Bronx, New York [205e]

Susan Redline, MD, MPH

Peter C. Farrell Professor of Sleep Medicine, Harvard Medical School; Brigham and Women's Hospital; Beth Israel Deaconess Medical Center, Boston, Massachusetts [319]

Sharon L. Reed, MD, MSCTM, D(ABMM)

Professor of Pathology and Medicine; Director, Microbiology Laboratory, University of California, San Diego School of Medicine, La Jolla, California [245e, 247]

Susan E. Reef, MD

Medical Epidemiologist, Centers for Disease Control and Prevention, Atlanta, Georgia [230e]

John J. Reilly, Jr., MD

Jack D. Myers Professor of Medicine and Chair, Department of Medicine; Vice Chair for Clinical Affairs, University of Pittsburgh, Pittsburgh, Pennsylvania [308e, 314]

John T. Repke, MD, FACOG

University Professor and Chairman, Department of Obstetrics and Gynecology, Pennsylvania State University College of Medicine; Obstetrician-Gynecologist In-Chief, The Milton S. Hershey Medical Center, Hershey, Pennsylvania [8]

Victor I. Reus, MD

Department of Psychiatry, University of California, San Francisco School of Medicine; Langley Porter Neuropsychiatric Institute, San Francisco, California [466]

Joseph J. Rhatigan, MD

Assistant Professor, Harvard Medical School, Harvard School of Public Health; Associate Chief, Division of Global Health Equity, Brigham and Women's Hospital, Boston, Massachusetts [2]

Peter A. Rice, MD

Professor of Medicine, Division of Infectious Diseases and Immunology, University of Massachusetts Medical School, Worcester, Massachusetts [181]

Elizabeth Robbins, MD

Clinical Professor of Pediatrics, University of California, San Francisco, San Francisco, California [443e]

Gary L. Robertson, MD

Emeritus Professor of Medicine, Northwestern University School of Medicine, Chicago, Illinois [404]

Russell G. Robertson, MD

Professor of Family Medicine, Chicago Medical School, Rosalind Franklin University of Medicine and Science, Chicago, Illinois [56]

Dan M. Roden, MD

William Stokes Professor of Experimental Therapeutics; Professor of Medicine and Pharmacology, Assistant Vice-Chancellor for Personalized Medicine, Director, Oates Institute for Experimental Therapeutics, Vanderbilt University School of Medicine, Nashville, Tennessee [5]

James A. Romano, Jr., PhD, DABT

Principal Senior Life Scientist Advisor, Tunnell Government Services, Inc., Rockville, Maryland [262e]

Karen L. Roos, MD

John and Nancy Nelson Professor of Neurology; Professor of Neurological Surgery, Indiana University School of Medicine, Indianapolis, Indiana [164]

Allan H. Ropper, MD, FRCP, FACP

Professor of Neurology, Harvard Medical School; Raymond D. Adams Master Clinician; Executive Vice Chair, Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts [328, 456, 457e]

Jonathan E. Rosenberg, MD

Associate Attending; Section Chief, Non-Prostate Program, Division of Solid Tumor Oncology, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York [114]

Roger N. Rosenberg, MD

Zale Distinguished Chair and Professor of Neurology, Department of Neurology, University of Texas Southwestern Medical Center, Dallas, Texas [450, 451e]

Myrna R. Rosenfeld, MD, PhD

Department of Neurology, Hospital Clínic/IDIBAPS, Barcelona, Spain [122]

Michael A. Rubin, MD, PhD

Assistant Professor of Medicine, University of Utah School of Medicine, Salt Lake City, Utah [44]

Steven A. Rubin, PhD

Acting Principal Investigator, Center for Biologics Evaluation and Research, Food and Drug Administration, Bethesda, Maryland [231e]

Robert M. Russell, MD

Professor Emeritus of Medicine and Nutrition, Tufts University, Boston, Massachusetts; Office of Dietary Supplements, National Institutes of Health, Bethesda, Maryland [96e]

Thomas A. Russo, MD, CM

Staff Physician, Western New York VA Healthcare System; Professor of Medicine and Microbiology and Immunology; Vice Chair of Medicine; Head, Division of Infectious Disease, University at Buffalo, State University of New York, Buffalo, New York [186, 200]

Anna E. Rutherford, MD, MPH

Assistant Professor, Harvard Medical School; Associate Physician, Brigham and Women's Hospital, Boston, Massachusetts [483e]

Edward T. Ryan, MD, FACP, FIDSA, FASTMH

Professor of Medicine, Harvard Medical School; Professor of Immunology and Infectious Diseases, Harvard School of Public Health; Director, Global Infectious Diseases, Division of Infectious Diseases, Massachusetts General Hospital, Boston, Massachusetts [160, 193]

Sean Sadikot, MD

Department of Internal Medicine, Critical Care and Pulmonary Disease, Hackensack University Medical Center, Hackensack, New Jersey [485e, 486e]

David J. Salant, MD

Professor of Medicine, Boston University School of Medicine; Chief, Section of Nephrology, Boston Medical Center, Boston, Massachusetts [340]

Martin A. Samuels, MD

Professor of Neurology, Harvard Medical School; Chair, Department of Neurology, Brigham and Women's Hospital, Boston, Massachusetts [439e, 463e]

Philippe J. Sansonetti, MD

Professor, Collège de France; Institut Pasteur, Paris, France [191]

Clifford B. Saper, MD, PhD

James Jackson Putnam Professor of Neurology and Neuroscience, Harvard Medical School; Chairman, Department of Neurology, Beth Israel Deaconess Medical Center, Boston, Massachusetts [38]

Jussi J. Saukkonen, MD

Associate Professor of Medicine, Section of Pulmonary, Allergy, and Critical Care Medicine, Boston University School of Medicine, Boston, Massachusetts [205e]

Edward A. Sausville, MD, PhD

Professor of Medicine, University of Maryland School of Medicine; Associate Director for Clinical Research, Marlene and Stewart Greenbaum Cancer Center, Baltimore, Maryland [103e]

Mohamed H. Sayegh, MD

Raja N. Khuri Dean, Faculty of Medicine; Professor of Medicine and Immunology; Vice President of Medical Affairs, American University of Beirut, Beirut, Lebanon; Senior Lecturer, Harvard Medical School; Schuster Family Transplantation Center, Brigham and Women's Hospital, Boston, Massachusetts [337]

David T. Scadden, MD

Gerald and Darlene Professor of Medicine; Co-Chair, Harvard Stem Cell Institute; Co-chair, Department of Stem Cell and Regenerative Biology, Harvard Medical School; Director, Center for Regenerative Medicine; Chief, Hematologic Malignancies, Cancer Center, Massachusetts General Hospital, Boston, Massachusetts [89e]

Thomas E. Scammell, MD

Professor, Harvard Medical School; Beth Israel Deaconess Medical Center; Boston Children's Hospital, Boston, Massachusetts [38]

Anthony H. V. Schapira, MD, DSc, FRCP, FMedSci

Chair and Professor of Clinical Neurosciences, UCL Institute of Neurology, London, United Kingdom [449]

Howard I. Scher, MD

Professor of Medicine, Joan and Sanford Weill College of Medicine of Cornell University; D. Wayne Calloway Chair in Urologic Oncology; Attending Physician and Chief, Genitourinary Oncology Service, Department of Medicine, Memorial Sloan-Kettering Cancer Center, New York, New York [114, 115]

Anne Schuchat, MD

RADM, U.S. Public Health Service; Assistant Surgeon General, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia [148]

Marc A. Schuckit, MD

Distinguished Professor of Psychiatry, University of California, San Diego School of Medicine, La Jolla, California [467]

H. Ralph Schumacher, Jr., MD

Professor of Medicine, Division of Rheumatology, University of Pennsylvania, School of Medicine, Philadelphia, Pennsylvania [395]

Gordon E. Schutze, MD, FAAP

Professor of Pediatrics; Vice-Chairman for Educational Affairs; Martin I. Lorin, MD Chair in Medical Education, Department of Pediatrics, Section of Retrovirology, Vice President, Baylor International Pediatric AIDS Initiative at Texas Children's Hospital, Baylor College of Medicine, Texas Children's Hospital, Houston, Texas [195]

Richard M. Schwartzstein, MD

Ellen and Melvin Gordon Professor of Medicine and Medical Education, Harvard Medical School; Associate Division Chief, Division of Pulmonary, Critical Care, and Sleep Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts [47e]

William W. Seeley, MD

Associate Professor of Neurology and Pathology, Memory and Aging Center, University of California, San Francisco, San Francisco, California [35, 448]

Michael V. Seiden, MD, PhD

Chief Medical Officer, McKesson Specialty Health, The Woodlands, Texas [117]

Julian L. Seifter, MD

Associate Professor of Medicine, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [343]

David C. Seldin, MD, PhD

Professor, Departments of Medicine and Microbiology; Chief, Section of Hematology-Oncology; Director, Amyloidosis Center, Boston University School of Medicine; Boston Medical Center, Boston, Massachusetts [137]

Ankoor Shah, MD

Assistant Professor, Department of Medicine, Division of Rheumatology and Immunology, Duke University Medical Center, Durham, North Carolina [380]

Steven D. Shapiro, MD

Jack D. Myers Professor and Chair, Department of Medicine, University of Pittsburgh, Pittsburgh, Pennsylvania [314]

Erica S. Shenoy, MD, PhD

Instructor in Medicine, Harvard Medical School; Assistant Chief, Infection Control Unit, Massachusetts General Hospital, Boston, Massachusetts [170]

Kanade Shinkai, MD, PhD

Assistant Professor, Department of Dermatology, University of California, San Francisco, San Francisco, California [74]

William Silen, MD

Johnson and Johnson Professor Emeritus of Surgery, Harvard Medical School, Aurburndale, Massachusetts [20]

Edwin K. Silverman, MD, PhD

Professor of Medicine, Harvard Medical School; Chief, Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts [314]

Karl Skorecki, MD, FRCP(C), FASN

Annie Chutick Professor in Medicine (Nephrology); Director, Rappaport Research Institute, Technion-Israel Institute of Technology; Director of Medical and Research Development, Rambam Health Care Campus, Haifa, Israel [85e, 335]

Wade S. Smith, MD, PhD

Professor of Neurology, Daryl R. Gress Endowed Chair of Neurocritical Care and Stroke; Director, University of California, San Francisco Neurovascular Service, San Francisco, California [330, 446]

Elizabeth Smyth, MB BAO, MSc

Department of Gastrointestinal Oncology, Royal Marsden NHS Foundation Trust, London and Sutton, United Kingdom [112]

Kelly A. Soderberg, PhD, MPH

Associate Director, Duke Center for HIV/AIDS Vaccine Immunology-Immunogen Discovery, Duke Human Vaccine Institute, Duke University, Durham, North Carolina [372e]

Scott D. Solomon, MD

Professor, Harvard Medical School; Director, Noninvasive Cardiology, Brigham and Women's Hospital, Boston, Massachusetts [270e, 271e]

Julian Solway, MD

Walter L. Palmer Distinguished Service Professor of Medicine and Pediatrics; Associate Dean for Translational Medicine, Biological Sciences Division; Vice Chair for Research, Department of Medicine; Chair, Committee on Molecular Medicine, University of Chicago, Chicago, Illinois [306e, 318]

Michael F. Sorrell, MD

Robert L. Grissom Professor of Medicine, Department of Internal Medicine, University of Nebraska Medical Center, Omaha, Nebraska [363]

Eric J. Sorscher, MD

Professor, Departments of Medicine and Genetics, Gwaltney Chair for Medical Research; Director, Gregory Fleming James Cystic Fibrosis Research Center, University of Alabama at Birmingham, Birmingham, Alabama [313]

Frank E. Speizer, MD

E. H. Kass Distinguished Professor of Medicine, Harvard Medical School; Channing Division of Network Medicine, Department of Medicine, Brigham and Women's Hospital; Professor of Environmental Science, Department of Environmental Health, Harvard School of Public Health, Boston, Massachusetts [311]

Brad Spellberg, MD

Professor of Medicine; Associate Medical Director for Inpatient Services, Harbor-UCLA Medical Center and Los Angeles Biomedical Research Institute, Torrance, California [242]

Nancy B. Spinner, PhD, FACMG

Professor of Pathology and Laboratory Medicine, Perelman School of Medicine, University of Pennsylvania; Chief, Division of Genomic Diagnostics, Children's Hospital of Philadelphia, Philadelphia, Pennsylvania [83e]

Jerry L. Spivak, MD

Professor of Medicine and Oncology, Hematology Division, Johns Hopkins University School of Medicine, Baltimore, Maryland [131]

David D. Spragg, MD

Associate Professor, Department of Medicine, Johns Hopkins University; Director, Electrophysiology Laboratory, Johns Hopkins Bayview Medical Center, Baltimore, Maryland [273e-275]

E. William St. Clair, MD

Professor of Medicine and Immunology, Department of Medicine, Duke University Medical Center, Durham, North Carolina [380]

Allen C. Steere, MD

Professor of Medicine, Harvard Medical School; Massachusetts General Hospital, Boston, Massachusetts [210]

Robert S. Stern, MD

Carl J. Herzog Professor of Dermatology, Harvard Medical School; Chair, Department of Dermatology, Beth Israel Deaconess Medical Center, Boston, Massachusetts [74]

Dennis L. Stevens, MD, PhD

Professor of Medicine, University of Washington School of Medicine, Seattle, Washington [156, 179]

Lynne Warner Stevenson, MD

Professor of Medicine, Harvard Medical School; Director, Heart Failure Program, Brigham and Women's Hospital, Boston, Massachusetts [287]

William G. Stevenson, MD

Brigham and Women's Hospital; Cardiovascular Division, Department of Medicine, Harvard Medical School, Boston, Massachusetts [276, 277]

John H. Stone, MD, MPH

Professor of Medicine, Harvard Medical School; Director, Clinical Rheumatology, Massachusetts General Hospital, Boston, Massachusetts [391e]

Stephanie Studenski, MD, MPH

Director, Longitudinal Studies Section, Intramural Research Program, National Institute on Aging, National Institutes of Health, Baltimore, Maryland [11]

Lewis Sudarsky, MD

Associate Professor of Neurology, Harvard Medical School; Director of Movement Disorders, Brigham and Women's Hospital, Boston, Massachusetts [32]

Donna C. Sullivan, PhD

Professor, Department of Medicine, Division of Infectious Diseases, University of Mississippi Medical School, Jackson, Mississippi [238]

Shyam Sundar, MD, FRCP, FNA

Professor of Medicine, Institute of Medical Sciences, Banaras Hindu University, Varanasi, India [251]

Neeraj K. Surana, MD, PhD

Instructor in Pediatrics, Harvard Medical School; Assistant in Medicine, Boston Children's Hospital, Boston, Massachusetts [144]

Paolo M. Suter, MD, MS

Professor, Clinic and Policlinic of Internal Medicine, University Hospital, Zurich, Switzerland [96e]

Richard M. Suzman, PhD

Director, Behavioral and Social Research Program, National Institute on Aging, National Institutes of Health, Bethesda, Maryland [93e]

Robert A. Swerlick, MD

Alicia Leizman Stonecipher Professor and Chair of Dermatology, Emory University School of Medicine, Atlanta, Georgia [76e]

Homayoun Tabandeh, MD

Retina-Vitreous Associates Medical Group, Los Angeles, California [40e]

Geoffrey Tabin, MD

John and Marva Warnock Presidential Professor, University of Utah School of Medicine; Director, International Ophthalmology Division, John A. Moran Eye Center; Director, Himalayan Cataract Project, Salt Lake City, Utah [476e]

Maria Carmela Tartaglia, MD

Assistant Professor, Tanz Centre for Research in Neurodegenerative Diseases, University of Toronto, Toronto, Ontario, Canada [37e]

Joel D. Taurog, MD

Professor of Internal Medicine, Rheumatic Diseases Division, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas [384]

Ayalew Tefferi, MD

Professor of Medicine and Hematology, Mayo Clinic, Rochester, Minnesota [135e]

Stephen C. Textor, MD

Professor of Medicine, Division of Nephrology and Hypertension, Mayo Clinic, Rochester, Minnesota [299, 341]

Rajesh V. Thakker, MD, FMedSci, FR

May Professor of Medicine, Academic Endocrine Unit, University of Oxford; O.C.D.E.M., Churchill Hospital, Headington, Oxford, United Kingdom [408]

C. Louise Thwaites, MD, MBBS

Oxford University Clinical Research Unit, Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam [177]

Zelig A. Tochner, MD

Professor of Radiation Oncology, University of Pennsylvania School of Medicine; Medical Director, Proton Therapy Center, Philadelphia, Pennsylvania [263e]

Gordon F. Tomaselli, MD

Michel Mirowski, MD Professor of Cardiology; Professor of Medicine and Cellular and Molecular Medicine; Chief, Division of Cardiology, Johns Hopkins University, Baltimore, Maryland [273e-275]

Karina A. Top, MD, MS

Assistant Professor of Pediatrics, Dalhousie University, Halifax, Nova Scotia, Canada [185]

Mark Topazian, MD

Professor of Medicine, Mayo Clinic, Rochester, Minnesota [345, 346e]

Barbara W. Trautner, MD, PhD

Assistant Professor, Section of Infectious Diseases, Department of Medicine, Baylor College of Medicine; Houston VA Health Services Research and Development Center of Excellence, Houston, Texas [162]

Jeffrey M. Trent, PhD, FACMG

President and Research Director, Translational Genomics Research Institute, Phoenix, Arizona; Van Andel Research Institute, Grand Rapids, Michigan [101e]

Elbert P. Trulock, III, MD

Rosemary and I. Jerome Fance Professor in Pulmonary Medicine, Washington University School of Medicine, St. Louis, Missouri [320e]

Kenneth L. Tyler, MD

Reuler-Lewin Family Professor and Chair of Neurology; Professor of Medicine, Immunology, and Microbiology, University of Colorado School of Medicine, Aurora, Colorado; Neurologist, Denver Veterans Affairs Medical Center, Denver, Colorado [164]

Athanasios G. Tzioufas, MD

Professor, Department of Pathophysiology, School of Medicine, National University of Athens, Athens, Greece [383]

Walter J. Urba, MD, PhD

Director of Research, Earle A. Chiles Research Institute, Providence Cancer Center, Portland, Oregon [105]

Jos W. M. van der Meer, MD, PhD

Professor of Medicine; Head, Department of General Internal Medicine, Radboud University Nijmegen Medical Centre, Nijmegen, The Netherlands [26, 464e]

Edouard G. Vannier, PharmD, PhD

Assistant Professor, Division of Geographic Medicine and Infectious Diseases, Department of Medicine, Tufts Medical Center and Tufts University School of Medicine, Boston, Massachusetts [249]

Gauri R. Varadhachary, MD

Professor, Department of Gastrointestinal Medical Oncology, The University of Texas M.D. Anderson Cancer Center, Houston, Texas [120e]

John Varga, MD

John Hughes Professor of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois [382]

Christy A. Varughese, PharmD

Infectious Disease Specialist, Department of Pharmacy, Massachusetts General Hospital, Boston, Massachusetts [170]

Panayiotis G. Vlachoyiannopoulos, MD

Professor of Medicine-Immunology, Department of Pathophysiology, Medical School, National University of Athens, Athens, Greece [379]

Bert Vogelstein, MD

Investigator, Howard Hughes Medical Institute; Director, Ludwig Center at the Sidney Kimmel Comprehensive Cancer Center; Clayton Professor of Oncology and Pathology; Johns Hopkins Medical Institutions, Baltimore, Maryland [101e]

Everett E. Vokes, MD

John E. Ulmann Professor; Chairman, Department of Medicine; Physician-in-Chief, University of Chicago Medical Center, Chicago, Illinois [106]

Tamara J. Vokes, MD

Professor, Department of Medicine, Section of Endocrinology, University of Chicago, Chicago, Illinois [426e]

Jiri F. P. Wagenaar, MD, PhD

Senior Scientist, WHO/FAO/OIE and National Leptospirosis Reference Centre, KIT Biomedical Research, KIT (Royal Tropical Institute), Amsterdam, The Netherlands [208]

Sushrut S. Waikar, MD, MPH

Associate Professor, Harvard Medical School; Director, Renal Ambulatory Services, Brigham and Women's Hospital, Boston, Massachusetts [334]

Matthew K. Waldor, MD, PhD

Edward H. Kass Professor of Medicine, Channing Laboratory, Brigham and Women's Hospital; Harvard Medical School and Howard Hughes Medical Institute, Boston, Massachusetts [193]

David H. Walker, MD

The Carmage and Martha Walls Distinguished University Chair in Tropical Diseases; Professor and Chairman, Department of Pathology; Executive Director, Center for Biodefense and Emerging Infectious Diseases, University of Texas Medical Branch, Galveston, Texas [211]

Mark F. Walker, MD

Associate Professor, Neurology, Case Western Reserve University; Cleveland VA Medical Center, Cleveland, Ohio [28]

Fred Wang, MD

Professor of Medicine, Harvard Medical School and Brigham and Women's Hospital, Boston, Massachusetts [214e, 220e]

John W. Warren, MD

Professor of Medicine, University of Maryland School of Medicine, Baltimore, Maryland [60e]

Aaron B. Waxman, MD, PhD, FACP, FCCP

Associate Professor of Medicine, Harvard Medical School; Executive Director, Center for Pulmonary-Heart Diseases, Brigham and Women's Hospital Heart and Vascular Center, Boston, Massachusetts [304]

Michael E. Wechsler, MD, MMSc

Professor of Medicine; Director, Asthma Program, National Jewish Health, Denver, Colorado [310]

Anthony P. Weetman, MD, DSc

University of Sheffield, School of Medicine Sheffield, United Kingdom [405]

Robert A. Weinstein, MD

The C. Anderson Hedberg, MD Professor of Internal Medicine, Rush Medical College; Chief Academic Officer, Cook County Health and Hospitals System, Chicago, Illinois [168]

Jeffrey I. Weitz, MD, FRCP(C), FACP

Professor of Medicine and Biochemistry, McMaster University; Executive Director, Thrombosis and Atherosclerosis Research Institute, Hamilton, Ontario, Canada [143]

Peter F. Weller, MD

Chief, Infectious Disease Division; Chief, Allergy and Inflammation Division; Beth Israel Deaconess Medical Center, Boston, Massachusetts [254-258, 260]

Andrew Wellman, MD, PhD

Assistant Professor of Medicine, Division of Sleep Medicine, Harvard Medical School; Brigham and Women's Hospital, Boston, Massachusetts [319]

Patrick Y. Wen, MD

Professor of Neurology, Harvard Medical School; Director, Center for Neuro-Oncology, Dana-Farber Cancer Institute; Director, Division of Neuro-Oncology, Department of Neurology, Brigham and Women's Hospital; Dana-Farber Cancer Institute, Boston, Massachusetts [118]

Michael R. Wessels, MD

John F. Enders Professor of Pediatrics; Professor of Medicine, Harvard Medical School; Chief, Division of Infectious Diseases, Boston Children's Hospital, Boston, Massachusetts [173]

L. Joseph Wheat, MD

President and Medical Director, MiraVista Diagnostics, LLC, Indianapolis, Indiana [236]

A. Clinton White, Jr., MD

Paul R. Stalnaker Distinguished Professor; Director, Infectious Disease Division, Department of Internal Medicine, University of Texas Medical Branch, Galveston, Texas [260]

Nicholas J. White, DSc, MD, FRCP, F Med Sci, FRS

Professor of Tropical Medicine, Faculty of Tropical Medicine, Mahidol University, Mahidol-Oxford Research Unit, Bangkok, Thailand [248, 250e]

Richard J. Whitley, MD

Distinguished Professor of Pediatrics; Loeb Eminent Scholar Chair in Pediatrics; Professor of Microbiology, Medicine and Neurosurgery, The University of Alabama at Birmingham, Birmingham, Alabama [217]

Bruce U. Wintroub, MD

Professor and Chair, Department of Dermatology, University of California, San Francisco, San Francisco, California [74]

Andrea S. Wolf, MD, MPH

Assistant Professor, and Director, Women's Lung Cancer Program, Mt. Sinai Medical Center, New York, New York [482e]

Allan W. Wolkoff, MD

The Herman Lopata Chair in Liver Disease Research; Professor of Medicine and Anatomy and Structural Biology; Associate Chair of Medicine for Research; Chief, Division of Gastroenterology and Liver Diseases; Director, Marion Bessin Liver Research Center, Albert Einstein College of Medicine and Montefiore Medical Center, Bronx, New York [359]

John B. Wong, MD

Professor of Medicine, Tufts University School of Medicine; Chief, Division of Clinical Decision Making, Department of Medicine, Tufts Medical Center, Boston, Massachusetts [3]

Louis Michel Wong Kee Song, MD

Associate Professor, Division of Gastroenterology and Hepatology, Mayo Clinic College of Medicine, Rochester, Minnesota [345, 346e]

Robert L. Wortmann, MD, FACP, MACR

Professor Emeritus, Department of Medicine, Geisel School of Medicine at Dartmouth, Lebanon, New Hampshire [431e]

Shirley H. Wray, MD, PhD, FRCP

Professor of Neurology, Harvard Medical School; Master Clinician, Department of Neurology, Massachusetts General Hospital, Boston, Massachusetts [41e]

Richard G. Wunderink, MD

Professor, Pulmonary and Critical Care, Northwestern University Feinberg School of Medicine, Chicago, Illinois [153]

Kim B. Yancey, MD

Professor and Chair, Department of Dermatology, University of Texas Southwestern Medical Center in Dallas, Dallas, Texas [70, 73]

Janet A. Yellowitz, DMD, MPH

Associate Professor; Director, Geriatric Dentistry, University of Maryland Dental School, Baltimore, Maryland [46e]

Lam Minh Yen, MD

Director, Tetanus Intensive Care Unit, Hospital for Tropical Diseases, Ho Chi Minh City, Vietnam [177]

Maria A. Yialamas, MD

Assistant Professor of Medicine, Harvard Medical School; Associate Program Director, Internal Medicine Residency, Brigham and Women's Hospital, Boston, Massachusetts [481e, 483e]

Neal S. Young, MD

Chief, Hematology Branch, National Heart, Lung and Blood Institute; Director, NIH Center for Human Immunology, Autoimmunity and Inflammation, National Institutes of Health, Bethesda, Maryland [130]

Victor L. Yu, MD

Professor of Medicine, Department of Medicine, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania [184]

Jing Zhou, MD, PhD, FASN

Director, Laboratory of Molecular Genetics and Developmental Biology of Disease, Renal Division; Director, Center for Polycystic Kidney Disease Research, Brigham and Women's Hospital; Harvard Medical School, Boston, Massachusetts [339]

Werner Zimmerli, MD

Professor of Medicine, Basel University; Interdisciplinary Unit of Orthopaedic Infection, Kantonspital Baselland, Liestal, Switzerland [158]

Laura A. Zimmerman, MPH

Epidemiologist, Centers for Disease Control and Prevention, Atlanta, Georgia [230e]

The Editors are pleased to present the 19th edition of *Harrison's Principles of Internal Medicine*. Since the first edition was published 65 years ago, virtually every area of medicine and medical education has evolved remarkably, and many new fields have emerged.

While retaining the founding goals of *Harrison's*, this edition has been modified extensively in light of the varied needs of the book's readers and the diverse methods and formats by which information is now acquired and applied. The focus of medical education worldwide is shifting from the classic structure/function/disease approach to an integrated, often case-based approach in which basic and population sciences are specifically linked to the practical diagnosis and management of disease. Many of the updates and changes described here have been undertaken with the modern educational and clinical environments in mind.

This new edition offers a thoroughly updated presentation of the classic pathophysiologic basis of clinical medicine and details the cutting-edge methods and tools that are now available for the assessment of symptoms and the effective management of diseases in the modern patient-care environment. The text is supplemented by germane new photographs, radiographs, illustrations, atlases, patient-care algorithms, tables, and practical demonstrative videos.

In the interest of producing the most practical format possible for the 19th edition, a new system of referencing has been used. Detailed bibliographic listings, with summaries of articles' relevance to practice, appear in the online edition, replacing the general and limited collection of Suggested Readings that appeared in the prior print editions.

The 19th edition of *Harrison's* is designed for accessibility and flexibility. The print textbook is available in two volumes. Volume 1 focuses on the foundations of medicine and the understanding and assessment of cardinal disease manifestations; Volume 2 focuses on specific diseases, by system. This functional division will be helpful to students who are mastering the basis of clinical medicine and to clinicians who are more focused on gaining an advanced understanding of mechanisms and patient care in specific diseases. In terms of digital media, *Harrison's* is now available as an eBook on multiple platforms, as an enhanced "app" developed especially for tablet and smartphone devices that offer high-definition resolution of multimedia content and interactive features, and as an updated online edition. All of these options provide access to our numerous e-chapters as well as to videos and atlases. Additional resources include the *Harrison's Self-Assessment and Board Review*, a useful study guide based on information in the 19th edition, and the *Harrison's Manual of Medicine*, a pocket version of *Harrison's Principles of Internal Medicine*. A new *Harrison's* collection of case vignettes emphasizing differential diagnostic considerations in the assessment of cardinal manifestations will also be available.

Advances in medical science have been spectacular since *Harrison's* was first published in 1949. At that time, peptic ulcer disease was thought to be caused by stress, nearly every tumor that was not resected resulted in death, rheumatic heart disease was widely prevalent, and hepatitis B and HIV infection were unknown. In the intervening years, both the infectious cause of and the cure for peptic ulcer disease were identified; advances in diagnosis and treatment made it possible to cure two-thirds of cancers; rheumatic heart disease virtually disappeared; atherosclerotic coronary artery disease waxed and then—at least in part through management of modifiable risk factors—began to wane; hepatitis B and its consequences, cirrhosis and hepatocellular carcinoma, became preventable by a vaccine; and HIV, first viewed as a uniformly fatal worldwide scourge, became a treatable chronic disease. Notably, emerging and reemerging diseases have presented significant challenges to medical research and practice, while a new understanding of systems-wide concepts such as the microbiome offers exciting new possibilities for understanding and managing health and disease in ways never before possible.

Of particular note in this 19th edition are critical updates in the classic chapter on HIV/AIDS, which offers both a clinically pragmatic

focus and a comprehensive and analytical approach to pathogenesis. The updates cover the latest treatment protocols and address the issue of combination prevention modalities, making the chapter the most up-to-date and comprehensive treatise on HIV disease available.

Several other chapters likewise reflect the rapid pace of advancement in the field of immune-related diseases and their treatment. In this regard, Chapter 372e, "Introduction to the Immune System," serves as a mini-textbook of immunology for use in immunology courses. In addition, a new chapter on IgG4-mediated disease summarizes an important and newly recognized constellation of entities.

Readers will find expanded coverage of the neurodegenerative diseases, highlighting advances in their classification and management and delineating the new understanding of mechanisms responsible for the deposition and spread of pathogenic protein aggregates in these disorders. The chapter on chronic hepatitis discusses in detail the dramatic new discoveries in the use of direct-acting antiviral agents for the treatment of hepatitis C virus disease; these agents are responsible for some of the most exciting therapeutic advances in medicine today.

The rapidly expanding application of genetic knowledge to medicine is covered in many chapters, including a new chapter on microbial genomics and infectious diseases and substantially updated chapters on the human microbiome and chromosomal genetic disorders. Other new chapters address timely topics such as the impact of climate change on disease, infections in U.S. veterans returning from foreign wars, and advances in contraception and the treatment of infertility. Another topic of increasing interest, the impact of aging on health and disease, is addressed by several chapters, including a newly authored chapter on the biology of aging. A new chapter on men's health complements the updated chapter on women's health. New chapters also address diverse topics including the emerging field of tissue engineering, the examination of the comatose patient, the management of heart failure, the major characteristics of helminths and helminthic infections, specific cardiac valvular disorders, venous and lymphatic diseases of the extremities, renovascular disease, late complications of diabetes, chronic myeloid leukemia, heat-related illnesses, fatigue, polyglandular failure syndromes, and nonalcoholic fatty liver disease and nonalcoholic steatohepatitis.

Supplementing new content and updates on diseases and patient care, new videos in this edition cover sleep disorders, tissue engineering, noninvasive cardiac imaging, examination of the comatose patient, and myasthenia gravis and other addresses of the neuromuscular junction. New atlases for this edition address noninvasive imaging, percutaneous revascularization, and gastrointestinal endoscopy.

We have many people to thank for their efforts in producing this book. First, the authors have done a superb job of producing authoritative chapters that synthesize vast amounts of scientific and clinical data to create state-of-the-art descriptions of medical disorders encompassed by internal medicine. In today's information-rich, rapidly evolving environment, they have ensured that this information is current. Helpful suggestions and critical input have been provided by a number of colleagues; particularly notable was the advice of Chung Owyang on the Gastroenterology Section. We are most grateful to our colleagues in each of our editorial offices who have kept track of the work in its various phases and facilitated communication with the authors, with the McGraw-Hill Education staff, and among the editors: Patricia Conrad, Patricia L. Duffey, Gregory K. Folkers, Julie B. McCoy, Elizabeth Robbins, Anita Rodriguez, and Stephanie Tribuna.

The staff at McGraw-Hill Education has been a constant source of support and expertise. James Shanahan, Associate Publisher for McGraw-Hill Education's Professional Publishing Division, has been a superb and insightful partner to the editors, guiding the development of the book and

xxxviii its related products in new formats. Kim Davis, as Associate Managing Editor, has adeptly ensured that the complex production of this multi-authored textbook proceeded smoothly and efficiently. Dominik Pucek oversaw the production of the new procedural videos and Priscilla Beer expertly oversaw the production of our extensive DVD content. Jeffrey Herzich ably served as production manager for this new edition.

We are privileged to have compiled this 19th edition and are enthusiastic about all that it offers our readers. We learned much in the process of editing *Harrison's* and hope that you will find this edition a uniquely valuable educational resource.

THE EDITORS

1

The Practice of Medicine

The Editors

THE PHYSICIAN IN THE TWENTY-FIRST CENTURY

No greater opportunity, responsibility, or obligation can fall to the lot of a human being than to become a physician. In the care of the suffering, [the physician] needs technical skill, scientific knowledge, and human understanding.... Tact, sympathy, and understanding are expected of the physician, for the patient is no mere collection of symptoms, signs, disordered functions, damaged organs, and disturbed emotions. [The patient] is human, fearful, and hopeful, seeking relief, help, and reassurance.

—Harrison's Principles of Internal Medicine, 1950

The practice of medicine has changed in significant ways since the first edition of this book appeared more than 60 years ago. The advent of molecular genetics, molecular and systems biology, and molecular pathophysiology; sophisticated new imaging techniques; and advances in bioinformatics and information technology have contributed to an explosion of scientific information that has fundamentally changed the way physicians define, diagnose, treat, and attempt to prevent disease. This growth of scientific knowledge is ongoing and accelerating.

The widespread use of electronic medical records and the Internet have altered the way doctors practice medicine and access and exchange information (Fig. 1-1). As today's physicians strive to integrate copious amounts of scientific knowledge into everyday practice, it is critically important that they remember two things: first, that the ultimate goal of medicine is to prevent disease and treat patients; and second, that despite more than 60 years of scientific advances since the first edition of this text, cultivation of the intimate relationship between physician and patient still lies at the heart of successful patient care.

THE SCIENCE AND ART OF MEDICINE

Deductive reasoning and applied technology form the foundation for the solution to many clinical problems. Spectacular advances in biochemistry, cell biology, and genomics, coupled with newly developed imaging techniques, allow access to the innermost parts of the cell and provide a window into the most remote recesses of the body. Revelations about the nature of genes and single cells have opened a portal for formulating a new molecular basis for the physiology of systems. Increasingly, physicians are learning how subtle changes in many different genes can affect the function of cells and organisms. Researchers are deciphering the complex mechanisms by which genes are regulated. Clinicians have developed a new appreciation of the role of stem cells in normal tissue function; in the development of cancer, degenerative diseases, and other disorders; and in the treatment of certain diseases. Entirely new areas of research, including studies of the human microbiome, have become important in understanding both health and disease. The knowledge gleaned from the *science of medicine* continues to enhance physicians' understanding of complex disease processes and provide new approaches to treatment and prevention. Yet skill in the most sophisticated applications of laboratory technology and in the use of the latest therapeutic modality alone does not make a good physician.

When a patient poses challenging clinical problems, an effective physician must be able to identify the crucial elements in a complex history and physical examination; order the appropriate laboratory, imaging, and diagnostic tests; and extract the key results from densely populated computer screens to determine whether to treat or to "watch." As the number of tests increases, so does the likelihood that some incidental finding, completely unrelated to the clinical problem at hand, will be uncovered. Deciding whether a clinical clue is worth pursuing or should be dismissed as a "red herring" and weighing

whether a proposed test, preventive measure, or treatment entails a greater risk than the disease itself are essential judgments that a skilled clinician must make many times each day. This combination of medical knowledge, intuition, experience, and judgment defines the *art of medicine*, which is as necessary to the practice of medicine as is a sound scientific base.

CLINICAL SKILLS

History-Taking The written history of an illness should include all the facts of medical significance in the life of the patient. Recent events should be given the most attention. Patients should, at some early point, have the opportunity to tell their own story of the illness without frequent interruption and, when appropriate, should receive expressions of interest, encouragement, and empathy from the physician. Any event related by a patient, however trivial or seemingly irrelevant, may provide the key to solving the medical problem. In general, only patients who feel comfortable with the physician will offer complete information; thus putting the patient at ease to the greatest extent possible contributes substantially to obtaining an adequate history.

An informative history is more than an orderly listing of symptoms. By listening to patients and noting the way in which they describe their symptoms, physicians can gain valuable insight. Inflections of voice, facial expression, gestures, and attitude (i.e., "body language") may offer important clues to patients' perception of their symptoms. Because patients vary in their medical sophistication and ability to recall facts, the reported medical history should be corroborated whenever possible. The social history also can provide important insights into the types of diseases that should be considered. The family history not only identifies rare Mendelian disorders within a family but often reveals risk factors for common disorders, such as coronary heart disease, hypertension, and asthma. A thorough family history may require input from multiple relatives to ensure completeness and accuracy; once recorded, it can be updated readily. The process of history-taking provides an opportunity to observe the patient's behavior and to watch for features to be pursued more thoroughly during the physical examination.

The very act of eliciting the history provides the physician with an opportunity to establish or enhance the unique bond that forms the basis for the ideal patient-physician relationship. This process helps the physician develop an appreciation of the patient's view of the illness, the patient's expectations of the physician and the health care system, and the financial and social implications of the illness for the patient. Although current health care settings may impose time constraints on patient visits, it is important not to rush the history-taking. A hurried approach may lead patients to believe that what they are relating is not of importance to the physician, and thus they may withhold relevant information. The confidentiality of the patient-physician relationship cannot be overemphasized.

Physical Examination The purpose of the physical examination is to identify physical signs of disease. The significance of these objective indications of disease is enhanced when they confirm a functional or structural change already suggested by the patient's history. At times, however, physical signs may be the only evidence of disease.

The physical examination should be methodical and thorough, with consideration given to the patient's comfort and modesty. Although attention is often directed by the history to the diseased organ or part of the body, the examination of a new patient must extend from head to toe in an objective search for abnormalities. Unless the physical examination is systematic and is performed consistently from patient to patient, important segments may be omitted inadvertently. The results of the examination, like the details of the history, should be recorded at the time they are elicited—not hours later, when they are subject to the distortions of memory. Skill in physical diagnosis is acquired with experience, but it is not merely technique that determines success in eliciting signs of disease. The detection of a few

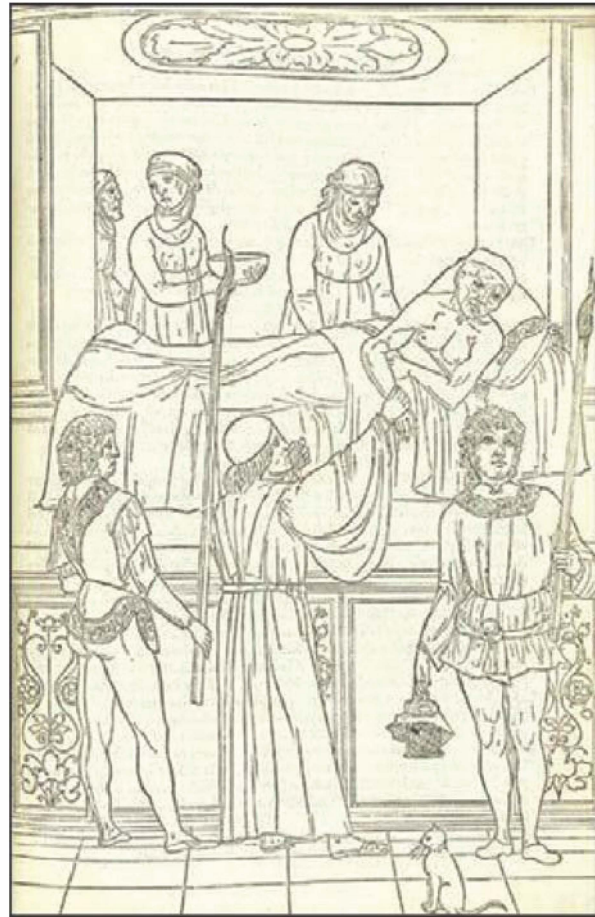
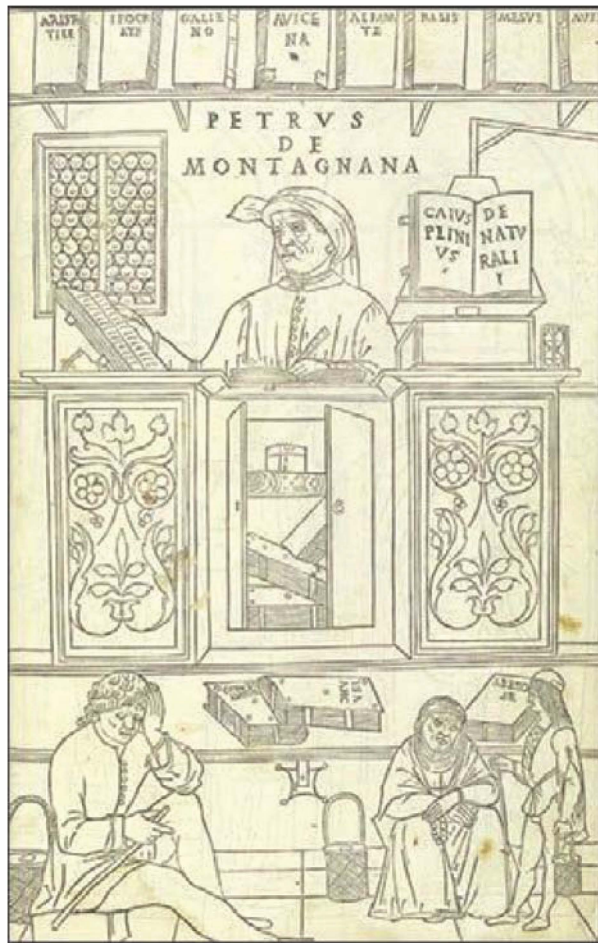


FIGURE 1-1 Woodcuts from Johannes de Ketham's *Fasciculus Medicinae*, the first illustrated medical text ever printed, show methods of information access and exchange in medical practice during the early Renaissance. Initially published in 1491 for use by medical students and practitioners, *Fasciculus Medicinae* appeared in six editions over the next 25 years. *Left:* Petrus de Montagnana, a well-known physician and teacher at the University of Padua and author of an anthology of instructive case studies, consults medical texts dating from antiquity up to the early Renaissance. *Right:* A patient with plague is attended by a physician and his attendants. (Courtesy, U.S. National Library of Medicine.)

scattered petechiae, a faint diastolic murmur, or a small mass in the abdomen is not a question of keener eyes and ears or more sensitive fingers but of a mind alert to those findings. Because physical findings can change with time, the physical examination should be repeated as frequently as the clinical situation warrants.

Given the many highly sensitive diagnostic tests now available (particularly imaging techniques), it may be tempting to place less emphasis on the physical examination. Indeed, many patients are seen by consultants after a series of diagnostic tests have been performed and the results are known. This fact should not deter the physician from performing a thorough physical examination since important clinical findings may have escaped detection by the barrage of prior diagnostic tests. The act of examining (touching) the patient also offers an opportunity for communication and may have reassuring effects that foster the patient-physician relationship.

Diagnostic Studies Physicians rely increasingly on a wide array of laboratory tests to solve clinical problems. However, accumulated laboratory data do not relieve the physician from the responsibility of carefully observing, examining, and studying the patient. It is also essential to appreciate the limitations of diagnostic tests. By virtue of their impersonal quality, complexity, and apparent precision, they often gain an aura of certainty regardless of the fallibility of the tests themselves, the instruments used in the tests, and the individuals performing or interpreting the tests. Physicians must weigh the expense involved in laboratory procedures against the value of the information these procedures are likely to provide.

Single laboratory tests are rarely ordered. Instead, physicians generally request “batteries” of multiple tests, which often prove useful.

For example, abnormalities of hepatic function may provide the clue to nonspecific symptoms such as generalized weakness and increased fatigability, suggesting a diagnosis of chronic liver disease. Sometimes a single abnormality, such as an elevated serum calcium level, points to a particular disease, such as hyperparathyroidism or an underlying malignancy.

The thoughtful use of screening tests (e.g., measurement of low-density lipoprotein cholesterol) may be of great value. A group of laboratory values can conveniently be obtained with a single specimen at relatively low cost. Screening tests are most informative when they are directed toward common diseases or disorders and when their results indicate whether other useful—but often costly—tests or interventions are needed. On the one hand, biochemical measurements, together with simple laboratory determinations such as blood count, urinalysis, and erythrocyte sedimentation rate, often provide a major clue to the presence of a pathologic process. On the other hand, the physician must learn to evaluate occasional screening-test abnormalities that do not necessarily connote significant disease. An in-depth workup after the report of an isolated laboratory abnormality in a person who is otherwise well is almost invariably wasteful and unproductive. Because so many tests are performed routinely for screening purposes, it is not unusual for one or two values to be slightly abnormal. Nevertheless, even if there is no reason to suspect an underlying illness, tests yielding abnormal results ordinarily are repeated to rule out laboratory error. If an abnormality is confirmed, it is important to consider its potential significance in the context of the patient's condition and other test results.

The development of technically improved imaging studies with greater sensitivity and specificity proceeds apace. These tests provide remarkably detailed anatomic information that can be a pivotal factor

in medical decision-making. Ultrasonography, a variety of isotopic scans, CT, MRI, and positron emission tomography have supplanted older, more invasive approaches and opened new diagnostic vistas. In light of their capabilities and the rapidity with which they can lead to a diagnosis, it is tempting to order a battery of imaging studies. All physicians have had experiences in which imaging studies revealed findings that led to an unexpected diagnosis. Nonetheless, patients must endure each of these tests, and the added cost of unnecessary testing is substantial. Furthermore, investigation of an unexpected abnormal finding may be associated with risk and/or expense and may lead to the diagnosis of an irrelevant or incidental problem. A skilled physician must learn to use these powerful diagnostic tools judiciously, always considering whether the results will alter management and benefit the patient.

PRINCIPLES OF PATIENT CARE

Evidence-Based Medicine *Evidence-based medicine* refers to the making of clinical decisions that are formally supported by data, preferably data derived from prospectively designed, randomized, controlled clinical trials. This approach is in sharp contrast to anecdotal experience, which is often biased. Unless they are attuned to the importance of using larger, more objective studies for making decisions, even the most experienced physicians can be influenced to an undue extent by recent encounters with selected patients. Evidence-based medicine has become an increasingly important part of routine medical practice and has led to the publication of many practice guidelines.

Practice Guidelines Many professional organizations and government agencies have developed formal clinical-practice guidelines to aid physicians and other caregivers in making diagnostic and therapeutic decisions that are evidence-based, cost-effective, and most appropriate to a particular patient and clinical situation. As the evidence base of medicine increases, guidelines can provide a useful framework for managing patients with particular diagnoses or symptoms. Clinical guidelines can protect patients—particularly those with inadequate health care benefits—from receiving substandard care. These guidelines also can protect conscientious caregivers from inappropriate charges of malpractice and society from the excessive costs associated with the overuse of medical resources. There are, however, caveats associated with clinical-practice guidelines since they tend to oversimplify the complexities of medicine. Furthermore, groups with different perspectives may develop divergent recommendations regarding issues as basic as the need for screening of women in their forties by mammography or of men over age 50 by serum prostate-specific antigen (PSA) assay. Finally, guidelines, as the term implies, do not—and cannot be expected to—account for the uniqueness of each individual and his or her illness. The physician's challenge is to integrate into clinical practice the useful recommendations offered by experts without accepting them blindly or being inappropriately constrained by them.

Medical Decision-Making Medical decision-making is an important responsibility of the physician and occurs at each stage of the diagnostic and therapeutic process. The decision-making process involves the ordering of additional tests, requests for consultations, and decisions about treatment and predictions concerning prognosis. This process requires an in-depth understanding of the pathophysiology and natural history of disease. As discussed above, medical decision-making should be evidence-based so that patients derive full benefit from the available scientific knowledge. Formulating a differential diagnosis requires not only a broad knowledge base but also the ability to assess the relative probabilities of various diseases. Application of the scientific method, including hypothesis formulation and data collection, is essential to the process of accepting or rejecting a particular diagnosis. Analysis of the differential diagnosis is an iterative process. As new information or test results are acquired, the group of disease processes being considered can be contracted or expanded appropriately.

Despite the importance of evidence-based medicine, much medical decision-making relies on good clinical judgment, an attribute that is difficult to quantify or even to assess qualitatively. Physicians must use

their knowledge and experience as a basis for weighing known factors, along with the inevitable uncertainties, and then making a sound judgment; this synthesis of information is particularly important when a relevant evidence base is not available. Several quantitative tools may be invaluable in synthesizing the available information, including diagnostic tests, Bayes' theorem, and multivariate statistical models. *Diagnostic tests* serve to reduce uncertainty about an individual's diagnosis or prognosis and help the physician decide how best to manage that individual's condition. The battery of diagnostic tests complements the history and the physical examination. The accuracy of a particular test is ascertained by determining its sensitivity (true-positive rate) and specificity (true-negative rate) as well as the predictive value of a positive and a negative result. *Bayes' theorem* uses information on a test's sensitivity and specificity, in conjunction with the pretest probability of a diagnosis, to determine mathematically the posttest probability of the diagnosis. More complex clinical problems can be approached with *multivariate statistical models*, which generate highly accurate information even when multiple factors are acting individually or together to affect disease risk, progression, or response to treatment. Studies comparing the performance of statistical models with that of expert clinicians have documented equivalent accuracy, although the models tend to be more consistent. Thus, multivariate statistical models may be particularly helpful to less experienced clinicians. **See Chap. 3 for a more thorough discussion of decision-making in clinical medicine.**

Electronic Medical Records Both the growing reliance on computers and the strength of information technology now play central roles in medicine. Laboratory data are accessed almost universally through computers. Many medical centers now have electronic medical records, computerized order entry, and bar-coded tracking of medications. Some of these systems are interactive, sending reminders or warning of potential medical errors.

Electronic medical records offer rapid access to information that is invaluable in enhancing health care quality and patient safety, including relevant data, historical and clinical information, imaging studies, laboratory results, and medication records. These data can be used to monitor and reduce unnecessary variations in care and to provide real-time information about processes of care and clinical outcomes. Ideally, patient records are easily transferred across the health care system. However, technologic limitations and concerns about privacy and cost continue to limit broad-based use of electronic health records in many clinical settings.

As valuable as it is, information technology is merely a tool and can never replace the clinical decisions that are best made by the physician. Clinical knowledge and an understanding of a patient's needs, supplemented by quantitative tools, still represent the best approach to decision-making in the practice of medicine.

Evaluation of Outcomes Clinicians generally use *objective* and readily measurable parameters to judge the outcome of a therapeutic intervention. These measures may oversimplify the complexity of a clinical condition as patients often present with a major clinical problem in the context of multiple complicating background illnesses. For example, a patient may present with chest pain and cardiac ischemia, but with a background of chronic obstructive pulmonary disease and renal insufficiency. For this reason, outcome measures such as mortality, length of hospital stay, or readmission rates are typically risk-adjusted. An important point is that patients usually seek medical attention for *subjective* reasons; they wish to obtain relief from pain, to preserve or regain function, and to enjoy life. The components of a patient's health status or quality of life can include bodily comfort, capacity for physical activity, personal and professional function, sexual function, cognitive function, and overall perception of health. Each of these important areas can be assessed through structured interviews or specially designed questionnaires. Such assessments provide useful parameters by which a physician can judge patients' subjective views of their disabilities and responses to treatment, particularly in chronic illness. The practice of medicine requires consideration and integration of both objective and subjective outcomes.

Women's Health and Disease Although past epidemiologic studies and clinical trials have often focused predominantly on men, more recent studies have included more women, and some, like the Women's Health Initiative, have exclusively addressed women's health issues. Significant sex-based differences exist in diseases that afflict both men and women. Much is still to be learned in this arena, and ongoing studies should enhance physicians' understanding of the mechanisms underlying these differences in the course and outcome of certain diseases. **For a more complete discussion of women's health, see Chap. 6e.**

Care of the Elderly The relative proportion of elderly individuals in the populations of developed nations has grown considerably over the past few decades and will continue to grow. The practice of medicine is greatly influenced by the health care needs of this growing demographic group. The physician must understand and appreciate the decline in physiologic reserve associated with aging; the differences in appropriate doses, clearance, and responses to medications; the diminished responses of the elderly to vaccinations such as those against influenza; the different manifestations of common diseases among the elderly; and the disorders that occur commonly with aging, such as depression, dementia, frailty, urinary incontinence, and fractures. **For a more complete discussion of medical care for the elderly, see Chap. 11 and Part 5, Chaps. 93e and 94e.**

Errors in the Delivery of Health Care A 1999 report from the Institute of Medicine called for an ambitious agenda to reduce medical error rates and improve patient safety by designing and implementing fundamental changes in health care systems. Adverse drug reactions occur in at least 5% of hospitalized patients, and the incidence increases with the use of a large number of drugs. Whatever the clinical situation, it is the physician's responsibility to use powerful therapeutic measures wisely, with due regard for their beneficial actions, potential dangers, and cost. It is the responsibility of hospitals and health care organizations to develop systems to reduce risk and ensure patient safety. Medication errors can be reduced through the use of ordering systems that rely on electronic processes or, when electronic options are not available, that eliminate misreading of handwriting. Implementation of infection control systems, enforcement of hand-washing protocols, and careful oversight of antibiotic use can minimize the complications of nosocomial infections. Central-line infection rates have been dramatically reduced at many centers by careful adherence of trained personnel to standardized protocols for introducing and maintaining central lines. Rates of surgical infection and wrong-site surgery can likewise be reduced by the use of standardized protocols and checklists. Falls by patients can be minimized by judicious use of sedatives and appropriate assistance with bed-to-chair and bed-to-bathroom transitions. Taken together, these and other measures are saving thousands of lives each year.

The Physician's Role in Informed Consent The fundamental principles of medical ethics require physicians to act in the patient's best interest and to respect the patient's autonomy. These requirements are particularly relevant to the issue of informed consent. Patients are required to sign a consent form for essentially any diagnostic or therapeutic procedure. Most patients possess only limited medical knowledge and must rely on their physicians for advice. Communicating in a clear and understandable manner, physicians must fully discuss the alternatives for care and explain the risks, benefits, and likely consequences of each alternative. In every case, the physician is responsible for ensuring that the patient thoroughly understands these risks and benefits; encouraging questions is an important part of this process. This is the very definition of *informed consent*. Full, clear explanation and discussion of the proposed procedures and treatment can greatly mitigate the fear of the unknown that commonly accompanies hospitalization. Excellent communication can also help alleviate misunderstandings in situations where complications of intervention occur. Often the patient's understanding is enhanced by repeatedly discussing the issues in an unthreatening and supportive way, answering new questions that occur to the patient as they arise.

Special care should be taken to ensure that a physician seeking a patient's informed consent has no real or apparent conflict of interest involving personal gain.

The Approach to Grave Prognoses and Death No circumstance is more distressing than the diagnosis of an incurable disease, particularly when premature death is inevitable. What should the patient and family be told? What measures should be taken to maintain life? What can be done to maintain the quality of life?

Honesty is absolutely essential in the face of a terminal illness. The patient must be given an opportunity to talk with the physician and ask questions. A wise and insightful physician uses such open communication as the basis for assessing what the patient wants to know and when he or she wants to know it. On the basis of the patient's responses, the physician can assess the right tempo for sharing information. Ultimately, the patient must understand the expected course of the disease so that appropriate plans and preparations can be made. The patient should participate in decision-making with an understanding of the goal of treatment (palliation) and its likely effects. The patient's religious beliefs must be taken into consideration. Some patients may find it easier to share their feelings about death with their physician, who is likely to be more objective and less emotional, than with family members.

The physician should provide or arrange for emotional, physical, and spiritual support and must be compassionate, unhurried, and open. In many instances, there is much to be gained by the laying on of hands. Pain should be controlled adequately, human dignity maintained, and isolation from family and close friends avoided. These aspects of care tend to be overlooked in hospitals, where the intrusion of life-sustaining equipment can detract from attention to the whole person and encourage concentration instead on the life-threatening disease, against which the battle ultimately will be lost in any case. In the face of terminal illness, the goal of medicine must shift from *cure* to *care* in the broadest sense of the term. *Primum succurrere*, first hasten to help, is a guiding principle. In offering care to a dying patient, a physician must be prepared to provide information to family members and deal with their grief and sometimes their feelings of guilt or even anger. It is important for the doctor to assure the family that everything reasonable has been done. A substantial problem in these discussions is that the physician often does not know how to gauge the prognosis. In addition, various members of the health care team may offer different opinions. Good communication among providers is essential so that consistent information is provided to patients. This is especially important when the best path forward is uncertain. Advice from experts in palliative and terminal care should be sought whenever necessary to ensure that clinicians are not providing patients with unrealistic expectations. **For a more complete discussion of end-of-life care, see Chap. 10.**

THE PATIENT-PHYSICIAN RELATIONSHIP

The significance of the intimate personal relationship between physician and patient cannot be too strongly emphasized, for in an extraordinarily large number of cases both the diagnosis and treatment are directly dependent on it. One of the essential qualities of the clinician is interest in humanity, for the secret of the care of the patient is in caring for the patient.

—Francis W. Peabody, October 21, 1925,
Lecture at Harvard Medical School

Physicians must never forget that patients are individual human beings with problems that all too often transcend their physical complaints. They are not "cases" or "admissions" or "diseases." Patients do not fail treatments; treatments fail to benefit patients. This point is particularly important in this era of high technology in clinical medicine. Most patients are anxious and fearful. Physicians should instill confidence and offer reassurance but must never come across as arrogant or patronizing. A professional attitude, coupled with warmth and openness, can do much to alleviate anxiety and to encourage patients to share all aspects of their medical history. Empathy and compassion are the essential features of a caring physician. The physician needs to consider the setting in which an illness occurs—in terms not only of patients themselves but also of their familial, social, and cultural backgrounds. The ideal patient-physician relationship is based on thorough knowledge of the patient, mutual trust, and the ability to communicate.

The Dichotomy of Inpatient and Outpatient Internal Medicine The hospital environment has changed dramatically over the last few decades. Emergency departments and critical care units have evolved to identify and manage critically ill patients, allowing them to survive formerly fatal diseases. At the same time, there is increasing pressure to reduce the length of stay in the hospital and to manage complex disorders in the outpatient setting. This transition has been driven not only by efforts to reduce costs but also by the availability of new outpatient technologies, such as imaging and percutaneous infusion catheters for long-term antibiotics or nutrition, minimally invasive surgical procedures, and evidence that outcomes often are improved by minimizing inpatient hospitalization.

In these circumstances, two important issues arise as physicians cope with the complexities of providing care for hospitalized patients. On the one hand, highly specialized health professionals are essential to the provision of optimal acute care in the hospital; on the other, these professionals—with their diverse training, skills, responsibilities, experiences, languages, and “cultures”—need to work as a team.

In addition to traditional medical beds, hospitals now encompass multiple distinct levels of care, such as the emergency department, procedure rooms, overnight observation units, critical care units, and palliative care units. A consequence of this differentiation has been the emergence of new trends, including specialties (e.g., emergency medicine and end-of-life care) and the provision of in-hospital care by hospitalists and intensivists. Most *hospitalists* are board-certified internists who bear primary responsibility for the care of hospitalized patients and whose work is limited entirely to the hospital setting. The shortened length of hospital stay that is now standard means that most patients receive only acute care while hospitalized; the increased complexities of inpatient medicine make the presence of a generalist with specific training, skills, and experience in the hospital environment extremely beneficial. *Intensivists* are board-certified physicians who are further certified in critical care medicine and who direct and provide care for very ill patients in critical care units. Clearly, then, an important challenge in internal medicine today is to ensure the continuity of communication and information flow between a patient’s primary care doctor and these physicians who are in charge of the patient’s hospital care. Maintaining these channels of communication is frequently complicated by patient “handoffs”—i.e., from the outpatient to the inpatient environment, from the critical care unit to a general medicine floor, and from the hospital to the outpatient environment. The involvement of many care providers in conjunction with these transitions can threaten the traditional one-to-one relationship between patient and primary care physician. Of course, patients can benefit greatly from effective collaboration among a number of health care professionals; however, *it is the duty of the patient’s principal or primary physician to provide cohesive guidance through an illness.* To meet this challenge, primary care physicians must be familiar with the techniques, skills, and objectives of specialist physicians and allied health professionals who care for their patients in the hospital. In addition, primary care doctors must ensure that their patients will benefit from scientific advances and from the expertise of specialists when they are needed both in and out of the hospital. Primary care physicians can also explain the role of these specialists to reassure patients that they are in the hands of the physicians best trained to manage an acute illness. However, the primary care physician should retain ultimate responsibility for making major decisions about diagnosis and treatment and should assure patients and their families that decisions are being made in consultation with these specialists by a physician who has an overall and complete perspective on the case.

A key factor in mitigating the problems associated with multiple care providers is a commitment to interprofessional teamwork. Despite the diversity in training, skills, and responsibilities among health care professionals, common values need to be reinforced if patient care is not to be adversely affected. This component of effective medical care is widely recognized, and several medical schools have integrated interprofessional teamwork into their curricula. The evolving concept of the “medical home” incorporates team-based primary care with linked subspecialty care in a cohesive environment that ensures smooth transitions of care cost-effectively.

Appreciation of the Patient’s Hospital Experience The hospital is an intimidating environment for most individuals. Hospitalized patients find themselves surrounded by air jets, buttons, and glaring lights; invaded by tubes and wires; and beset by the numerous members of the health care team—hospitalists, specialists, nurses, nurses’ aides, physicians’ assistants, social workers, technologists, physical therapists, medical students, house officers, attending and consulting physicians, and many others. They may be transported to special laboratories and imaging facilities replete with blinking lights, strange sounds, and unfamiliar personnel; they may be left unattended at times; and they may be obligated to share a room with other patients who have their own health problems. It is little wonder that a patient’s sense of reality may be compromised. Physicians who appreciate the hospital experience from the patient’s perspective and who make an effort to develop a strong relationship within which they can guide the patient through this experience may make a stressful situation more tolerable.

Trends in the Delivery of Health Care: A Challenge to the Humane Physician Many trends in the delivery of health care tend to make medical care impersonal. These trends, some of which have been mentioned already, include (1) vigorous efforts to reduce the escalating costs of health care; (2) the growing number of managed-care programs, which are intended to reduce costs but in which the patient may have little choice in selecting a physician or in seeing that physician consistently; (3) increasing reliance on technological advances and computerization for many aspects of diagnosis and treatment; and (4) the need for numerous physicians to be involved in the care of most patients who are seriously ill.

In light of these changes in the medical care system, it is a major challenge for physicians to maintain the *humane* aspects of medical care. The American Board of Internal Medicine, working together with the American College of Physicians–American Society of Internal Medicine and the European Federation of Internal Medicine, has published a *Charter on Medical Professionalism* that underscores three main principles in physicians’ contract with society: (1) the primacy of patient welfare, (2) patient autonomy, and (3) social justice. While medical schools appropriately place substantial emphasis on professionalism, a physician’s personal attributes, including integrity, respect, and compassion, also are extremely important. Availability to the patient, expression of sincere concern, willingness to take the time to explain all aspects of the illness, and a nonjudgmental attitude when dealing with patients whose cultures, lifestyles, attitudes, and values differ from those of the physician are just a few of the characteristics of a humane physician. Every physician will, at times, be challenged by patients who evoke strongly negative or positive emotional responses. Physicians should be alert to their own reactions to such patients and situations and should consciously monitor and control their behavior so that the patient’s best interest remains the principal motivation for their actions at all times.

An important aspect of patient care involves an appreciation of the patient’s “quality of life,” a subjective assessment of what each patient values most. This assessment requires detailed, sometimes intimate knowledge of the patient, which usually can be obtained only through deliberate, unhurried, and often repeated conversations. Time pressures will always threaten these interactions, but they should not diminish the importance of understanding and seeking to fulfill the priorities of the patient.

EXPANDING FRONTIERS IN MEDICAL PRACTICE

The Era of “Omics”: Genomics, Epigenomics, Proteomics, Microbiomics, Metagenomics, Metabolomics, Exposomics . . . In the spring of 2003, announcement of the complete sequencing of the human genome officially ushered in the genomic era. However, even before that landmark accomplishment, the practice of medicine had been evolving as a result of the insights into both the human genome and the genomes of a wide variety of microbes. The clinical implications of these insights are illustrated by the complete genome sequencing of H1N1 influenza virus in 2009 and the rapid identification of H1N1 influenza as a potentially fatal pandemic illness, with swift development and dissemination of an effective protective vaccine. Today, gene expression profiles are being

used to guide therapy and inform prognosis for a number of diseases, the use of genotyping is providing a new means to assess the risk of certain diseases as well as variations in response to a number of drugs, and physicians are better understanding the role of certain genes in the causality of common conditions such as obesity and allergies. Despite these advances, the use of complex genomics in the diagnosis, prevention, and treatment of disease is still in its early stages. The task of physicians is complicated by the fact that phenotypes generally are determined not by genes alone but by the interplay of genetic and environmental factors. Indeed, researchers have just begun to scratch the surface of the potential applications of genomics in the practice of medicine.

Rapid progress also is being made in other areas of molecular medicine. *Epigenomics* is the study of alterations in chromatin and histone proteins and methylation of DNA sequences that influence gene expression. Every cell of the body has identical DNA sequences; the diverse phenotypes a person's cells manifest are the result of epigenetic regulation of gene expression. Epigenetic alterations are associated with a number of cancers and other diseases. *Proteomics*, the study of the entire library of proteins made in a cell or organ and its complex relationship to disease, is enhancing the repertoire of the 23,000 genes in the human genome through alternate splicing, post-translational processing, and posttranslational modifications that often have unique functional consequences. The presence or absence of particular proteins in the circulation or in cells is being explored for diagnostic and disease-screening applications. *Microbiomics* is the study of the resident microbes in humans and other mammals. The human haploid genome has ~20,000 genes, while the microbes residing on and in the human body comprise over 3–4 million genes; the contributions of these resident microbes are likely to be of great significance with regard to health status. In fact, research is demonstrating that the microbes inhabiting human mucosal and skin surfaces play a critical role in maturation of the immune system, in metabolic balance, and in disease susceptibility. A variety of environmental factors, including the use and overuse of antibiotics, have been tied experimentally to substantial increases in disorders such as obesity, metabolic syndrome, atherosclerosis, and immune-mediated diseases in both adults and children. *Metagenomics*, of which microbiomics is a part, is the genomic study of environmental species that have the potential to influence human biology directly or indirectly. An example is the study of exposures to microorganisms in farm environments that may be responsible for the lower incidence of asthma among children raised on farms. *Metabolomics* is the study of the range of metabolites in cells or organs and the ways they are altered in disease states. The aging process itself may leave telltale metabolic footprints that allow the prediction (and possibly the prevention) of organ dysfunction and disease. It seems likely that disease-associated patterns will be sought in lipids, carbohydrates, membranes, mitochondria, and other vital components of cells and tissues. Finally, *exposomics* refers to efforts to catalogue and capture environmental exposures such as smoking, sunlight, diet, exercise, education, and violence, which together have an enormous impact on health. All of this new information represents a challenge to the traditional reductionist approach to medical thinking. The variability of results in different patients, together with the large number of variables that can be assessed, creates difficulties in identifying pre-clinical disease and defining disease states unequivocally. Accordingly, the tools of *systems biology* and *network medicine* are being applied to the enormous body of information now obtainable for every patient and may eventually provide new approaches to classifying disease. **For a more complete discussion of a complex systems approach to human disease, see Chap. 87e.**

The rapidity of these advances may seem overwhelming to practicing physicians. However, physicians have an important role to play in ensuring that these powerful technologies and sources of new information are applied with sensitivity and intelligence to the patient. Since “omics” are evolving so rapidly, physicians and other health care professionals must continue to educate themselves so that they can apply this new knowledge to the benefit of their patients' health and well-being. Genetic testing requires wise counsel based on an understanding of the value and limitations of the tests as well as the implications of

their results for specific individuals. **For a more complete discussion of genetic testing, see Chap. 84.**

The Globalization of Medicine Physicians should be cognizant of diseases and health care services beyond local boundaries. Global travel has implications for disease spread, and it is not uncommon for diseases endemic to certain regions to be seen in other regions after a patient has traveled to and returned from those regions. In addition, factors such as wars, the migration of refugees, and climate change are contributing to changing disease profiles worldwide. Patients have broader access to unique expertise or clinical trials at distant medical centers, and the cost of travel may be offset by the quality of care at those distant locations. As much as any other factor influencing global aspects of medicine, the Internet has transformed the transfer of medical information throughout the world. This change has been accompanied by the transfer of technological skills through telemedicine and international consultation—for example, regarding radiologic images and pathologic specimens. **For a complete discussion of global issues, see Chap. 2.**

Medicine on the Internet On the whole, the Internet has had a very positive effect on the practice of medicine; through personal computers, a wide range of information is available to physicians and patients almost instantaneously at any time and from anywhere in the world. This medium holds enormous potential for the delivery of current information, practice guidelines, state-of-the-art conferences, journal content, textbooks (including this text), and direct communications with other physicians and specialists, expanding the depth and breadth of information available to the physician regarding the diagnosis and care of patients. Medical journals are now accessible online, providing rapid sources of new information. By bringing them into direct and timely contact with the latest developments in medical care, this medium also serves to lessen the information gap that has hampered physicians and health care providers in remote areas.

Patients, too, are turning to the Internet in increasing numbers to acquire information about their illnesses and therapies and to join Internet-based support groups. Patients often arrive at a clinic visit with sophisticated information about their illnesses. In this regard, physicians are challenged in a positive way to keep abreast of the latest relevant information while serving as an “editor” as patients navigate this seemingly endless source of information, the accuracy and validity of which are not uniform.

A critically important caveat is that virtually anything can be published on the Internet, with easy circumvention of the peer-review process that is an essential feature of academic publications. Both physicians and patients who search the Internet for medical information must be aware of this danger. Notwithstanding this limitation, appropriate use of the Internet is revolutionizing information access for physicians and patients and in this regard represents a remarkable resource that was not available to practitioners a generation ago.

Public Expectations and Accountability The general public's level of knowledge and sophistication regarding health issues has grown rapidly over the last few decades. As a result, expectations of the health care system in general and of physicians in particular have risen. Physicians are expected to master rapidly advancing fields (the *science* of medicine) while considering their patients' unique needs (the *art* of medicine). Thus, physicians are held accountable not only for the technical aspects of the care they provide but also for their patients' satisfaction with the delivery and costs of care.

In many parts of the world, physicians increasingly are expected to account for the way in which they practice medicine by meeting certain standards prescribed by federal and local governments. The hospitalization of patients whose health care costs are reimbursed by the government and other third parties is subjected to utilization review. Thus, a physician must defend the cause for and duration of a patient's hospitalization if it falls outside certain “average” standards. Authorization for reimbursement increasingly is based on documentation of the nature and complexity of an illness, as reflected by recorded elements of the history and physical examination. A growing “pay-for-performance” movement seeks to link reimbursement to quality of

care. The goal of this movement is to improve standards of health care and contain spiraling health care costs. In many parts of the United States, managed (capitated) care contracts with insurers have replaced traditional fee-for-service care, placing the onus of managing the cost of all care directly on the providers and increasing the emphasis on preventive strategies. In addition, physicians are expected to give evidence of their current competence through mandatory continuing education, patient record audits, maintenance of certification, and relicensing.

Medical Ethics and New Technologies The rapid pace of technological advance has profound implications for medical applications that go far beyond the traditional goals of disease prevention, treatment, and cure. Cloning, genetic engineering, gene therapy, human-computer interfaces, nanotechnology, and use of designer drugs have the potential to modify inherited predispositions to disease, select desired characteristics in embryos, augment “normal” human performance, replace failing tissues, and substantially prolong life span. Given their unique training, physicians have a responsibility to help shape the debate on the appropriate uses of and limits placed on these new techniques and to consider carefully the ethical issues associated with the implementation of such interventions.

The Physician as Perpetual Student From the time doctors graduate from medical school, it becomes all too apparent that their lot is that of the “perpetual student” and that the mosaic of their knowledge and experiences is eternally unfinished. This realization is at the same time exhilarating and anxiety-provoking. It is exhilarating because doctors can apply constantly expanding knowledge to the treatment of their patients; it is anxiety-provoking because doctors realize that they will never know as much as they want or need to know. Ideally, doctors will translate the latter feeling into energy through which they can continue to improve themselves and reach their potential as physicians. It is the physician’s responsibility to pursue new knowledge continually by reading, attending conferences and courses, and consulting colleagues and the Internet. This is often a difficult task for a busy practitioner; however, a commitment to continued learning is an integral part of being a physician and must be given the highest priority.

The Physician as Citizen Being a physician is a privilege. The capacity to apply one’s skills for the benefit of one’s fellow human beings is a noble calling. The doctor-patient relationship is inherently unbalanced in the distribution of power. In light of their influence, physicians must always be aware of the potential impact of what they do and say and must always strive to strip away individual biases and preferences to find what is best for the patient. To the extent possible, physicians should also act within their communities to promote health and alleviate suffering. Meeting these goals begins by setting a healthy example and continues in taking action to deliver needed care even when personal financial compensation may not be available.

A goal for medicine and its practitioners is to strive to provide the means by which the poor can cease to be unwell.

Learning Medicine It has been a century since the publication of the Flexner Report, a seminal study that transformed medical education and emphasized the scientific foundations of medicine as well as the acquisition of clinical skills. In an era of burgeoning information and access to medical simulation and informatics, many schools are implementing new curricula that emphasize lifelong learning and the acquisition of competencies in teamwork, communication skills, system-based practice, and professionalism. These and other features of the medical school curriculum provide the foundation for many of the themes highlighted in this chapter and are expected to allow physicians to progress, with experience and learning over time, from competency to proficiency to mastery.

At a time when the amount of information that must be mastered to practice medicine continues to expand, increasing pressures both within and outside of medicine have led to the implementation of restrictions on the amount of time a physician-in-training can spend in the hospital. Because the benefits associated with continuity of medical care and observation of a patient’s progress over time were thought

to be outstripped by the stresses imposed on trainees by long hours and by the fatigue-related errors they made in caring for patients, strict limits were set on the number of patients that trainees could be responsible for at one time, the number of new patients they could evaluate in a day on call, and the number of hours they could spend in the hospital. In 1980, residents in medicine worked in the hospital more than 90 hours per week on average. In 1989, their hours were restricted to no more than 80 per week. Resident physicians’ hours further decreased by ~10% between 1996 and 2008, and in 2010 the Accreditation Council for Graduate Medical Education further restricted (i.e., to 16 hours per shift) consecutive in-hospital duty hours for first-year residents. The impact of these changes is still being assessed, but the evidence that medical errors have decreased as a consequence is sparse. An unavoidable by-product of fewer hours at work is an increase in the number of “handoffs” of patient responsibility from one physician to another. These transfers often involve a transition from a physician who knows the patient well, having evaluated that individual on admission, to a physician who knows the patient less well. It is imperative that these transitions of responsibility be handled with care and thoroughness, with all relevant information exchanged and acknowledged.

Research, Teaching, and the Practice of Medicine The word *doctor* is derived from the Latin *docere*, “to teach.” As teachers, physicians should share information and medical knowledge with colleagues, students of medicine and related professions, and their patients. The practice of medicine is dependent on the sum total of medical knowledge, which in turn is based on an unending chain of scientific discovery, clinical observation, analysis, and interpretation. Advances in medicine depend on the acquisition of new information through research, and improved medical care requires the transmission of that information. As part of their broader societal responsibilities, physicians should encourage patients to participate in ethical and properly approved clinical investigations if these studies do not impose undue hazard, discomfort, or inconvenience. However, physicians engaged in clinical research must be alert to potential conflicts of interest between their research goals and their obligations to individual patients. The best interests of the patient must always take priority.

To wrest from nature the secrets which have perplexed philosophers in all ages, to track to their sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of disease—these are our ambitions.

—William Osler, 1849–1919

2

Global Issues in Medicine

Paul Farmer, Joseph Rhatigan

WHY GLOBAL HEALTH?

Global health is not a discipline; it is, rather, a collection of problems. Some scholars have defined global health as the field of study and practice concerned with improving the health of all people and achieving health equity worldwide, with an emphasis on addressing transnational problems. No single review can do much more than identify the leading problems in applying evidence-based medicine in settings of great poverty or across national boundaries. However, this is a moment of opportunity: only recently, persistent epidemics, improved metrics, and growing interest have been matched by an unprecedented investment in addressing the health problems of poor people in the developing world. To ensure that this opportunity is not wasted, the facts need to be laid out for specialists and laypeople alike. This chapter introduces the major international bodies that address health problems; identifies the more significant barriers to improving the health of people who to date have not, by and large, had access

to modern medicine; and summarizes population-based data on the most common health problems faced by people living in poverty. Examining specific problems—notably HIV/AIDS (**Chap. 226**) but also tuberculosis (TB, **Chap. 202**), malaria (**Chap. 248**), and key “non-communicable” chronic diseases (NCDs)—helps sharpen the discussion of barriers to prevention, diagnosis, and care as well as the means of overcoming them. This chapter closes by discussing global health equity, drawing on notions of social justice that once were central to international public health but had fallen out of favor during the last decades of the twentieth century.

A BRIEF HISTORY OF GLOBAL HEALTH INSTITUTIONS

Concern about health across national boundaries dates back many centuries, predating the Black Plague and other pandemics. One of the first organizations founded explicitly to tackle cross-border health issues was the Pan American Sanitary Bureau, which was formed in 1902 by 11 countries in the Americas. The primary goal of what later became the Pan American Health Organization was the control of infectious diseases across the Americas. Of special concern was yellow fever, which had been running a deadly course through much of South and Central America and halted the construction of the Panama Canal. In 1948, the United Nations formed the first truly global health institution: the World Health Organization (WHO). In 1958, under the aegis of the WHO and in line with a long-standing focus on communicable diseases that cross borders, leaders in global health initiated the effort that led to what some see as the greatest success in international health: the eradication of smallpox. Naysayers were surprised when the smallpox eradication campaign, which engaged public health officials throughout the world, proved successful in 1979 despite the ongoing Cold War.

At the International Conference on Primary Health Care in Alma-Ata (in what is now Kazakhstan) in 1978, public health officials from around the world agreed on a commitment to “Health for All by the Year 2000,” a goal to be achieved by providing universal access to primary health care worldwide. Critics argued that the attainment of this goal by the proposed date was impossible. In the ensuing years, a strategy for the provision of selective primary health care emerged that included four inexpensive interventions collectively known as GOBI: growth monitoring, oral rehydration, breast-feeding, and immunizations for diphtheria, whooping cough, tetanus, polio, TB, and measles. GOBI later was expanded to GOBI-FFF, which also included female education, food, and family planning. Some public health figures saw GOBI-FFF as an interim strategy to achieve “health for all,” but others criticized it as a retreat from the bolder commitments of Alma-Ata.

The influence of the WHO waned during the 1980s. In the early 1990s, many observers argued that, with its vastly superior financial resources and its close—if unequal—relationships with the governments of poor countries, the World Bank had eclipsed the WHO as the most important multilateral institution working in the area of health. One of the stated goals of the World Bank was to help poor countries identify “cost-effective” interventions worthy of public funding and international support. At the same time, the World Bank encouraged many of those nations to reduce public expenditures in health and education in order to stimulate economic growth as part of (later discredited) structural adjustment programs whose restrictions were imposed as a condition for access to credit and assistance through international financial institutions such as the World Bank and the International Monetary Fund. There was a resurgence of many diseases, including malaria, trypanosomiasis, and schistosomiasis, in Africa. TB, an eminently curable disease, remained the world’s leading infectious killer of adults. Half a million women per year died in childbirth during the last decade of the twentieth century, and few of the world’s largest philanthropic or funding institutions focused on global health equity.

HIV/AIDS, first described in 1981, precipitated a change. In the United States, the advent of this newly described infectious killer marked the culmination of a series of events that discredited talk of “closing the book” on infectious diseases. In Africa, which would emerge as the global epicenter of the pandemic, HIV disease strained TB control programs, and malaria continued to take as many lives as

ever. At the dawn of the twenty-first century, these three diseases alone killed nearly 6 million people each year. New research, new policies, and new funding mechanisms were called for. The past decade has seen the rise of important multilateral global health financing institutions such as the Global Fund to Fight AIDS, Tuberculosis, and Malaria; bilateral efforts such as the U.S. President’s Emergency Plan for AIDS Relief (PEPFAR); and private philanthropic organizations such as the Bill & Melinda Gates Foundation. With its 193 member states and 147 country offices, the WHO remains important in matters relating to the cross-border spread of infectious diseases and other health threats. In the aftermath of the epidemic of severe acute respiratory syndrome in 2003, the WHO’s International Health Regulations—which provide a legal foundation for that organization’s direct investigation into a wide range of global health problems, including pandemic influenza, in any member state—were strengthened and brought into force in May 2007.

Even as attention to and resources for health problems in poor countries grow, the lack of coherence in and among global health institutions may undermine efforts to forge a more comprehensive and effective response. The WHO remains underfunded despite the ever-growing need to engage a wider and more complex range of health issues. In another instance of the paradoxical impact of success, the rapid growth of the Gates Foundation, which is one of the most important developments in the history of global health, has led some foundations to question the wisdom of continuing to invest their more modest resources in this field. This indeed may be what some have called “the golden age of global health,” but leaders of major organizations such as the WHO, the Global Fund, the United Nations Children’s Fund (UNICEF), the Joint United Nations Programme on HIV/AIDS (UNAIDS), PEPFAR, and the Gates Foundation must work together to design an effective architecture that will make the most of opportunities to link new resources for and commitments to global health equity with the emerging understanding of disease burden and unmet need. To this end, new and old players in global health must invest heavily in *discovery* (relevant basic science), *development* of new tools (preventive, diagnostic, and therapeutic), and modes of *delivery* that will ensure the equitable provision of health products and services to all who need them.

THE ECONOMICS OF GLOBAL HEALTH

Political and economic concerns have often guided global health interventions. As mentioned, early efforts to control yellow fever were tied to the completion of the Panama Canal. However, the precise nature of the link between economics and health remains a matter for debate. Some economists and demographers argue that improving the health status of populations must begin with economic development; others maintain that addressing ill health is the starting point for development in poor countries. In either case, investment in health care, especially the control of communicable diseases, should lead to increased productivity. The question is where to find the necessary resources to start the predicted “virtuous cycle.”

During the past two decades, spending on health in poor countries has increased dramatically. According to a study from the Institute for Health Metrics and Evaluation (IHME) at the University of Washington, total development assistance for health worldwide grew to \$28.2 billion in 2010—up from \$5.6 billion in 1990. In 2010, the leading contributors included U.S. bilateral agencies such as PEPFAR, the Global Fund, nongovernmental organizations (NGOs), the WHO, the World Bank, and the Gates Foundation. It appears, however, that total development assistance for health plateaued in 2010, and it is unclear whether growth will continue in the upcoming decade.

To reach the United Nations Millennium Development Goals, which include targets for poverty reduction, universal primary education, and gender equality, spending in the health sector must be increased above the 2010 levels. To determine by how much and for how long, it is imperative to improve the ability to assess the global burden of disease and to plan interventions that more precisely match need.

MORTALITY AND THE GLOBAL BURDEN OF DISEASE

Refining metrics is an important task for global health: only recently have there been solid assessments of the global burden of disease. The first study to look seriously at this issue, conducted in 1990, laid the foundation for the first report on *Disease Control Priorities in Developing Countries* and for the World Bank's 1993 World Development Report *Investing in Health*. Those efforts represented a major advance in the understanding of health status in developing countries. *Investing in Health* has been especially influential: it familiarized a broad audience with cost-effectiveness analysis for specific health interventions and with the notion of disability-adjusted life years (DALYs). The DALY, which has become a standard measure of the impact of a specific health condition on a population, combines absolute years of life lost and years lost due to disability for incident cases of a condition. (See [Fig. 2-1](#) and [Table 2-1](#) for an analysis of the global disease burden by DALYs.)

In 2012, the IHME and partner institutions began publishing results from the Global Burden of Diseases, Injuries, and Risk Factors Study 2010 (GBD 2010). GBD 2010 is the most comprehensive effort to date to produce longitudinal, globally complete, and comparable estimates of the burden of diseases, injuries, and risk factors. This report reflects the expansion of the available data on health in the poorest countries and of the capacity to quantify the impact of specific conditions on a population. It measures current levels and recent trends in all major diseases, injuries, and risk factors among 21 regions and for 20 age groups and both sexes. The GBD 2010 team revised and improved the health-state severity weight system, collated published data, and used household surveys to enhance the breadth and accuracy of disease burden data. As analytic methods and data quality improve, important trends can be identified in a comparison of global disease burden estimates from 1990 to 2010.

GLOBAL MORTALITY

Of the 52.8 million deaths worldwide in 2010, 24.6% (13 million) were due to communicable diseases, maternal and perinatal conditions, and nutritional deficiencies—a marked decrease compared with figures for 1990, when these conditions accounted for 34% of global mortality. Among the fraction of all deaths related to communicable diseases, maternal and perinatal conditions, and nutritional deficiencies, 76% occurred in sub-Saharan Africa and southern Asia. While the proportion of deaths due to these conditions has decreased significantly in the past decade, there has been a dramatic rise in the number of deaths from NCDs, which constituted the top five causes of death in 2010. The leading cause of death among adults in 2010 was ischemic heart disease, accounting for 7.3 million deaths (13.8% of total deaths) worldwide. In high-income countries ischemic heart disease accounted for 17.9% of total deaths, and in developing (low- and middle-income) countries it accounted for 10.1%. It is noteworthy that ischemic heart disease was responsible for just 2.6% of total deaths in sub-Saharan Africa ([Table 2-2](#)). In second place—causing 11.1% of global mortality—was cerebrovascular disease, which accounted for 9.9% of deaths in high-income countries, 10.5% in developing countries, and 4.0% in sub-Saharan Africa. Although the third leading cause of death in high-income countries was lung cancer (accounting for 5.6% of all deaths), this condition did not figure among the top 10 causes in low- and middle-income countries. Among the 10 leading causes of death in sub-Saharan Africa, 6 were infectious diseases, with malaria and HIV/AIDS ranking as the dominant contributors to disease burden. In high-income countries, however, only one infectious disease—lower respiratory infection—ranked among the top 10 causes of death.

The GBD 2010 found that the worldwide mortality figure among children <5 years of age dropped from 16.39 million in 1970 to 11.9 million in 1990 and to 6.8 million in 2010—a decrease that surpassed predictions. Of childhood deaths in 2010, 3.1 million (40%) occurred in the neonatal period. About one-third of deaths among children <5 years old occurred in southern Asia and almost one-half in sub-Saharan Africa; <1% occurred in high-income countries.

The global burden of death due to HIV/AIDS and malaria was on an upward slope until 2004; significant improvements have since been documented. Global deaths from HIV infection fell from 1.7 million

in 2006 to 1.5 million in 2010, while malaria deaths dropped from 1.2 million to 0.98 million over the same period. Despite these improvements, malaria and HIV/AIDS continue to be major burdens in particular regions, with global implications. Although it has a minor impact on mortality outside sub-Saharan Africa and Southeast Asia, malaria is the eleventh leading cause of death worldwide. HIV infection ranked thirty-third in global DALYs in 1990 but was the fifth leading cause of disease burden in 2010, with sub-Saharan Africa bearing the vast majority of this burden ([Fig. 2-1](#)).

The world's population is living longer: global life expectancy has increased significantly over the past 40 years from 58.8 years in 1970 to 70.4 years in 2010. This demographic change, accompanied by the fact that the prevalence of NCDs increases with age, is dramatically shifting the burden of disease toward NCDs, which have surpassed communicable, maternal, nutritional, and neonatal causes. By 2010, 65.5% of total deaths at all ages and 54% of all DALYs were due to NCDs. Increasingly, the global burden of disease comprises conditions and injuries that cause disability rather than death.

Worldwide, although both life expectancy and years of life lived in good health have risen, years of life lived with disability have also increased. Despite the higher prevalence of diseases common in older populations (e.g., dementia and musculoskeletal disease) in developed and high-income countries, best estimates from 2010 reveal that disability resulting from cardiovascular diseases, chronic respiratory diseases, and the long-term impact of communicable diseases was greater in low- and middle-income countries. In most developing countries, people lived shorter lives and experienced disability and poor health for a greater proportion of their lives. Indeed, 50% of the global burden of disease occurred in southern Asia and sub-Saharan Africa, which together account for only 35% of the world's population.

HEALTH AND WEALTH

Clear disparities in burden of disease (both communicable and noncommunicable) across country income levels are strong indicators that poverty and health are inherently linked. Poverty remains one of the most important root causes of poor health worldwide, and the global burden of poverty continues to be high. Among the 6.7 billion people alive in 2008, 19% (1.29 billion) lived on less than \$1.25 a day—one standard measurement of extreme poverty—and another 1.18 billion lived on \$1.25 to \$2 a day. Approximately 600 million children—more than 30% of those in low-income countries—lived in extreme poverty in 2005. Comparison of national health indicators with gross domestic product per capita among nations shows a clear relationship between higher gross domestic product and better health, with only a few outliers. Numerous studies have also documented the link between poverty and health within nations as well as across them.

RISK FACTORS FOR DISEASE BURDEN

The GBD 2010 study found that the three leading risk factors for global disease burden in 2010 were (in order of frequency) high blood pressure, tobacco smoking (including secondhand smoke), and alcohol use—a substantial change from 1990, when childhood undernutrition was ranked first. Though ranking eighth in 2010, childhood undernutrition remains the leading risk factor for death worldwide among children <5 years of age. In an era that has seen obesity become a major health concern in many developed countries—and the sixth leading risk factor worldwide—the persistence of undernutrition is surely cause for great consternation. Low body weight is still the dominant risk factor for disease burden in sub-Saharan Africa. Inability to feed the hungry reflects many years of failed development projects and must be addressed as a problem of the highest priority. Indeed, no health care initiative, however generously funded, will be effective without adequate nutrition.

In a 2006 publication that examined how specific diseases and injuries are affected by environmental risk, the WHO estimated that roughly one-quarter of the total global burden of disease, one-third of the global disease burden among children, and 23% of all deaths were due to modifiable environmental factors. Many of these factors lead to deaths from infectious diseases; others lead to deaths