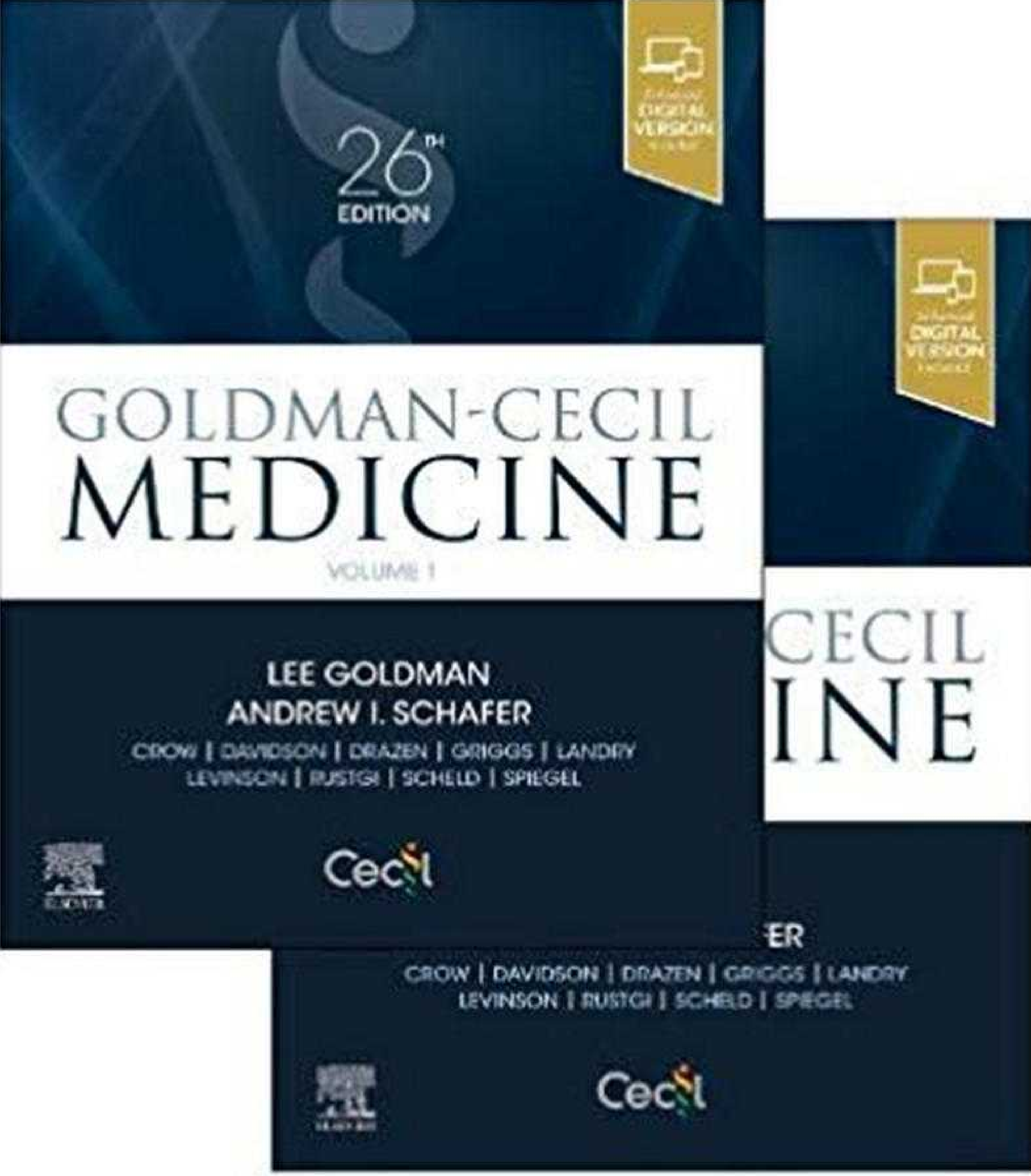

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26TH EDITION

GOLDMAN-CECIL MEDICINE

VOLUME 1

LEE GOLDMAN
ANDREW I. SCHAFER
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Organized and Edited by:

Min Thant Thaw

GOLDMAN-CECIL MEDICINE

26TH EDITION

Volume 1

EDITED BY
LEE GOLDMAN, MD
Harold and Margaret Hatch Professor
Chief Executive, Columbia University Irving Medical Center
Dean of the Faculties of Health Sciences and Medicine
Columbia University
New York, New York

ANDREW I. SCHAFER, MD
Professor of Medicine
Director, Richard T. Silver Center for Myeloproliferative Neoplasms
Weill Cornell Medical College
New York, New York

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Elsevier
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David Atkins – Chapter 12
John O'Shea – Chapter 33
Leslie Biesecker – Chapter 36
Amy Klion – Chapter 161
Donna Krasnewich & Ellen Sidransky – Chapter 197
Lynnette Nieman – Chapter 208, 214, 218
Richard Siegel & Daniel Kastner – Chapter 245
Roland Sutter – Chapter 276
Paul Mead – Chapter 296
Joseph Kovacs – Chapter 321
Louis Kirchhoff – Chapter 326
Theodore Nash – Chapter 330
Neal Young – Chapter 347
Jeffrey Cohen – Chapter 351

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Content Development Manager: Laura Schmidt
Publishing Services Manager: Catherine Jackson
Senior Project Manager: Daniel Fitzgerald
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ASSOCIATE EDITORS

Mary K. Crow, MD
Joseph P. Routh Professor of Rheumatic Diseases in Medicine
Weill Cornell Medical College
Physician-in-Chief and Benjamin M. Rosen Chair in Immunology and Inflammation Research
Hospital for Special Surgery
New York, New York

Nancy E. Davidson, MD
Professor of Medicine and Raisbeck Endowed Chair
President
Seattle Cancer Care Alliance
Senior Vice President and Director, Clinical Research Division
Fred Hutchinson Cancer Research Center
Chief
Division of Medical Oncology
University of Washington School of Medicine
Seattle, Washington

Jeffrey M. Drazen, MD
Distinguished Parker B. Francis Professor of Medicine
Harvard Medical School
Senior Physician
Department of Medicine
Brigham and Women's Hospital
Boston, Massachusetts

Robert C. Griggs, MD
Professor of Neurology, Medicine, Pediatrics, Pathology & Laboratory Medicine
University of Rochester School of Medicine & Dentistry
Rochester, New York

Donald W. Landry, MD, PhD
Samuel Bard Professor and Chair
Department of Medicine
Columbia University Vagelos College of Physicians and Surgeons
Physician-in-Chief
Columbia University Irving Medical Center
New York, New York

Wendy Levinson, MD
Professor of Medicine
Chair Emeritus
Department of Medicine
University of Toronto
Toronto, Ontario, Canada

Anil K. Rustgi, MD
Irving Professor of Medicine
Director
Herbert Irving Comprehensive Cancer Center
Chief
NewYork-Presbyterian Hospital/Columbia University Irving Medical Center Cancer Service
Columbia University Vagelos College of Physicians and Surgeons
New York, New York

W. Michael Scheld, MD
Bayer-Gerald L. Mandell Professor of Infectious Diseases
Professor of Medicine
Clinical Professor of Neurosurgery
David A. Harrison Distinguished Educator
University of Virginia Health System
Charlottesville, Virginia

Allen M. Spiegel, MD
Dean Emeritus
Professor of Medicine
Albert Einstein College of Medicine
Bronx, New York

PREFACE

In the more than 90 years since the first edition of the *Cecil Textbook of Medicine* was published, almost everything we know about internal medicine has changed. Progress in medical science is now occurring at an ever-accelerating pace, and it is doing so within the framework of transformational changes in clinical practice and the delivery of health care at individual, social, and global levels. This textbook and its associated electronic products incorporate the latest medical knowledge in multiple formats that should appeal to students and seasoned practitioners regardless of how they prefer to access this rapidly changing information.

Even as *Cecil*'s specific information has changed, however, we have remained true to the tradition of a comprehensive textbook of medicine that carefully explains the *why* (the underlying genetics, genomics, and pathobiology of disease) and the *how* (now expected to be evidence-based from randomized controlled trials and meta-analyses). Descriptions of physiology and pathophysiology include the latest genetic advances in a practical format that strives to be useful to the nonexpert so that care can truly be as precise and personalized as possible.

Medicine has entered an era when the acuity of illness and the limited time available to evaluate a patient have diminished the ability of physicians to satisfy their intellectual curiosity. As a result, the acquisition of information, quite easily achieved in this era, is often confused with knowledge. We have attempted to address this dilemma with a textbook that not only informs but also stimulates new questions and gives a glimpse of the future path to new knowledge. Grade A evidence is specifically highlighted in the text and referenced at the end of each chapter. In addition to the information provided in the textbook, the *Cecil* website supplies expanded content and functionality. In many cases, the full articles referenced in each chapter can be accessed from the *Cecil* website. The website is also continuously updated to incorporate subsequent Grade A information, other evidence, and new discoveries.

The sections for each organ system begin with a chapter that summarizes an approach to patients with key symptoms, signs, or laboratory abnormalities associated with dysfunction of that organ system. As summarized in E-Table 1-1, the text specifically provides clear, concise information regarding how a physician should approach more than 100 common symptoms, signs, and laboratory abnormalities, usually with a flow diagram, a table, or both for easy reference. In this way, *Cecil* remains a comprehensive text to guide diagnosis and therapy, not only for patients with suspected or known diseases but also for patients who may have undiagnosed symptoms or signs that require an initial evaluation.

Just as each edition brings new authors, it also reminds us of our gratitude to past editors and authors. Previous editors of *Cecil* include a short but remarkably distinguished group of leaders of American medicine: Russell Cecil, Paul Beeson, Walsh McDermott, James Wyngaarden, Lloyd H. Smith, Jr., Fred Plum, J. Claude Bennett, and Dennis Ausiello. As we welcome a new associate editor—Nancy Davidson—we also express our appreciation to James Doroshow and other associate editors from the previous editions on whose foundation we have built. Our returning associate editors—Mary K. Crow, Jeffrey M. Drazen, Robert C. Griggs, Donald W. Landry, Wendy Levinson, Anil Rustgi, W. Michael Scheld, and Allen M. Spiegel—continue to make critical contributions to the selection of authors and the review and approval of all manuscripts. The editors, however, are fully responsible for the book as well as the integration among chapters.

The tradition of *Cecil* is that all chapters are written by distinguished experts in each field. Two of those authors, Frank A. Lederle, author of the chapter on "Diseases of the Aorta," and Ronald Victor, author of the chapter on "Arterial Hypertension," passed away after submitting their chapters, and we mourn their passing.

We are also most grateful for the editorial assistance in New York of Timothy Gahr, Maribel Lim, Eva Allen, and Magdalena Fuentes. These individuals and others in our offices have shown extraordinary dedication and equanimity in working with authors and editors to manage the unending flow of manuscripts, figures, and permissions.

This edition of *Goldman-Cecil Medicine* includes many new authors. We would also like to thank outgoing authors, who often provided figures that are included in this edition as well as tables that have been included or modified for this edition. Furthermore, because of the templated format and extensive editing that are characteristic of *Goldman-Cecil Medicine*, some new chapters incorporate principles, concepts, and organizational aspects from those prior chapters, often revised extensively prior to publication. Among prior authors who deserve our appreciation, in the numerical order of their chapters, are Victoria M. Taylor, Steven A. Schroeder, Thomas B. Newman, Charles E. McCulloch, Thomas H. Lee, F. Daniel Duffy, Lawrence S. Neinstein, Steven E. Hyman, Grant W. Cannon, Cem Gabay, Carlo Patrono, Jack Hirsh, Adam Perlman, Sandesh C.S. Nagamani, Paweł Stankiewicz, James R. Lupski, Sekar Kathiresan, David Altshuler, Göran K. Hansson, Anders Hamsten, L. David Hillis, Bruce W. Lytle, William C. Little, Donna Mancini, Yoshifumi Naka, Dennis E. Niewoehner, Frank J. Accurso, Emanuel P. Rivers, Marsha D. Ford, Geoffrey K. Isbister, Itzchak Slotki, Mark L. Zeidel, David H. Kim, Perry J. Pickhardt, Martin J. Blaser, Stephen Crane Hauser, H. Franklin Bunn, Gordon D. Ginder, Martin H. Steinberg, Aśok C. Antony, Ayalew Tefferi, Michael Glogauer, Marc E. Rothenberg, William L. Nichols, Lawrence T. Goodnough, Adrian R. Black, Kenneth H. Cowan, Susan O'Brien, Elias Jabbour, Marshall R. Posner, Charles D. Blanke, Douglas O. Faigel, David Spriggs, John D. Hainsworth, F. Anthony Greco, Clay F. Semenkovich, Stephen G. Kaler, Bruce R. Bacon, Bruce R. Bistrian, Stephen A. McClave, Mark E. Molitch, Matthew Kim, Paul W. Ladenson, Kenneth R. Hande, Robert W. Rebar, Deborah Grady, Elizabeth Barrett-Connor, Samuel A. Wells, Jr., Stephen I. Wasserman, Larry Borish, Suneel S. Apte, Joel A. Block, Carla Scanzello, Robert M. Bennett, Ilseung Cho, S. Ragnar Norrby, Lionel A. Mandell, Donald E. Low, Kenneth L. Gage, Atis Muehlenbachs, Stuart Levin, Kamaljit Singh, Richard L. Guerrant, Dirk M. Elston, Larry J. Anderson, Martin Weisse, Mark Papania, Letha M. Healey, Tamsin A. Knox, Christine Wanke, Kristina Crothers, Alison Morris, Toby A. Maurer, Thomas S. Uldrick, Robert Yarchoan, Robert Colebunders, Ralph F. Józefowicz, Michael Aminoff, Eelco F.M. Wijdicks, Myron Yanoff, Douglas Cameron, David H. Chu, James C. Shaw, Neil J. Korman, and Ronald J. Elin. We also thank Michael G. House, who contributed to the chapter on "Diseases of the Gallbladder and Bile Ducts," and Anna Louise Beavis, who contributed to the chapter on "Gynecologic Cancers." Chapters written by public employees reflect recommendations and conclusions of the authors and do not necessarily reflect the official position of the entity for which they work.

At Elsevier, we are most indebted to Dolores Meloni and Laura Schmidt, and also thank Lucia Gunzel, Dan Fitzgerald, and Maggie Reid, who have been critical to the planning and production.

We have been exposed to remarkable physicians in our lifetimes and would like to acknowledge the mentorship and support of several of those who exemplify this paradigm—Eugene Braunwald, the late Lloyd H. Smith, Jr., Frank Gardner, and William Castle. Finally, we would like to thank the Goldman family—Jill, Jeff, Abigail, Mira, Samuel, Daniel, Morgan, Robyn, Tobin, Dashel, and Alden—and the Schafer family—Pauline, Eric, Melissa, Nathaniel, Caroline, Pam, John, Evan, Samantha, Kate, Sean, Patrick, and Meghan—for their understanding of the time and focus required to edit a book that attempts to sustain the tradition of our predecessors and to meet the needs of today's physician.

LEE GOLDMAN, MD
ANDREW I. SCHAFER, MD

CONTRIBUTORS

Charles S. Abrams, MD
Francis C. Wood Professor of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Thrombocytopenia

Ronald S. Adler, MD, PhD
Professor of Radiology, New York University School of Medicine; NYU Langone Health, New York, New York
Imaging Studies in the Rheumatic Diseases

Cem Akin, MD, PhD
Professor of Medicine, Internal Medicine, University of Michigan Medical School, Ann Arbor, Michigan
Mastocytosis

Allen J. Aksamit, Jr., MD
Professor of Neurology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Acute Viral Encephalitis

Qais Al-Awqati, MB ChB
Robert F. Loeb Professor, Medicine, and Physiology & Cellular Biophysics, Columbia University Vagelos College of Physicians & Surgeons, New York, New York
Structure and Function of the Kidneys; Disorders of Sodium and Water

Ban Mishu Allos, MD
Associate Professor of Medicine, Division of Infectious Diseases, Vanderbilt University School of Medicine, Nashville, Tennessee
Campylobacter *Infections*

Jeffrey L. Anderson, MD
Professor of Medicine, Division of Cardiovascular Medicine, University of Utah School of Medicine; Distinguished Clinical and Research Physician, Intermountain Medical Center Heart Institute, Salt Lake City, Utah
ST Elevation Acute Myocardial Infarction and Complications of Myocardial Infarction

Derek C. Angus, MD, MPH
Professor and Mitchell P. Fink Endowed Chair, Department of Critical Care Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
Approach to the Patient with Shock

Gerald B. Appel, MD
Professor of Medicine and Director, Glomerular Center, Columbia University Irving Medical Center, New York, New York
Glomerular Disorders and Nephrotic Syndromes

Frederick R. Appelbaum, MD
Professor of Medicine, University of Washington School of Medicine; Executive Senior VP and Deputy Director, Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, Washington
The Acute Leukemias

James O. Armitage, MD
Professor of Internal Medicine, University of Nebraska Medical Center College of Medicine, Omaha, Nebraska
Non-Hodgkin Lymphomas

Deborah K. Armstrong, MD
Professor of Gynecology and Obstetrics, Johns Hopkins University School of Medicine, Baltimore, Maryland
Gynecologic Cancers

M. Amin Arnaout, MD
Professor of Medicine, Chief Emeritus, Division of Nephrology, Department of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts
Cystic Kidney Diseases

Robert M. Arnold, MD
Distinguished Service Professor, Chief, Section of Palliative Care and Medical Ethics, University of Pittsburgh School of Medicine; Chief Medical Officer, UPMC Palliative and Supportive Institute, UPMC Health Plan, Pittsburgh, Pennsylvania
Palliative Care

David Atkins, MD, MPH
Director, Health Services Research and Development, Office of Research and Development, Dept. of Veterans Affairs (10P9H), Washington, D.C.
The Periodic Health Examination

John P. Atkinson, MD
Professor of Medicine, Division of Rheumatology, Washington University School of Medicine in St. Louis, St. Louis, Missouri
Complement System in Disease

John Z. Ayanian, MD, MPP
Alice Hamilton Professor of Medicine; Director, Institute for Healthcare Policy and Innovation, University of Michigan Medical School, Ann Arbor, Michigan
Disparities in Health and Health Care

Larry M. Baddour, MD
Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Infective Endocarditis

Grover C. Bagby, MD
Professor of Medicine, Molecular and Medical Genetics, Oregon Health & Science University, Portland, Oregon
Aplastic Anemia and Related Bone Marrow Failure States

Barbara J. Bain, MBBS
Professor in Diagnostic Haematology, Haematology, St Mary's Hospital Campus of Imperial College London, London, United Kingdom
The Peripheral Blood Smear

Dean F. Bajorin, MD
Attending Physician and Member, Memorial Sloan Kettering Cancer Center; Professor of Medicine, Weill Cornell Medical College, New York, New York
Tumors of the Kidney, Bladder, Ureters, and Renal Pelvis

Robert W. Baloh, MD
Professor of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California
Neuro-Ophthalmology; Smell and Taste; Hearing and Equilibrium

CONTRIBUTORS

Charles R.M. Bangham, BM BCh
Professor of Medicine, Faculty of Medicine, Imperial College London School of Medicine, London, United Kingdom
Retroviruses Other Than Human Immunodeficiency Virus

Jonathan Barasch, MD, PhD
Samuel W Lambert Professor of Medicine, Professor of Pathology and Cell Biology, Columbia University Vagelos College of Physicians & Surgeons, New York, New York
Structure and Function of the Kidneys

Richard L. Barbano, MD, PhD
Professor of Neurology and Chief of the Movement Disorders Division, University of Rochester School of Medicine & Dentistry, Rochester, New York
Mechanical and Other Lesions of the Spine, Nerve Roots, and Spinal Cord

Bruce Barrett, MD, PhD
Professor, Department of Family Medicine and Community Health, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin
The Common Cold

John R. Bartholomew, MD
Professor of Medicine and Section Head Vascular Medicine, Cleveland Clinic Lerner College of Medicine, Cleveland, Ohio
Other Peripheral Arterial Diseases

J.D. Bartleson, MD
Professor of Neurology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Mechanical and Other Lesions of the Spine, Nerve Roots, and Spinal Cord

Mary Barton, MD, MPP
Vice President, Performance Measurement, National Committee for Quality Assurance, Washington, D.C.
The Periodic Health Examination

Robert C. Basner, MD
Professor of Medicine, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Sleep Disorders

Anne R. Bass, MD
Professor of Clinical Medicine, Weill Cornell Medical College; Attending Physician, Hospital for Special Surgery, New York, New York
Immunomodulatory Drugs

Stephen G. Baum, MD
Professor of Medicine and of Microbiology and Immunology, Albert Einstein College of Medicine, Bronx, New York
Mycoplasma *Infections*

Julie E. Bauman, MD, MPH
Professor of Medicine, University of Arizona Cancer Center, Tucson, Arizona
Head and Neck Cancer

Daniel G. Bausch, MD, MPH&TM
Director, United Kingdom Public Health Rapid Support Team, Public Health England/London School of Hygiene and Tropical Medicine, London, United Kingdom
Viral Hemorrhagic Fevers

Arnold S. Bayer, MD
Distinguished Professor of Medicine, David Geffen School of Medicine at UCLA; Senior Investigator-LA Biomedical Research Institute At Harbor-UCLA, Los Angeles, California
Infective Endocarditis

Hasan Bazari, MD
Associate Professor of Medicine, Massachusetts General Hospital and Harvard Medical School, Boston, Massachusetts
Approach to the Patient with Renal Disease

Jeffrey J. Bazarian, MD, MPH
Professor of Emergency Medicine, University of Rochester School of Medicine & Dentistry, Rochester, New York
Traumatic Brain Injury and Spinal Cord Injury

John H. Beigel, MD
Associate Director for Clinical Research, Division of Microbiology and Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
Antiviral Therapy (Non-HIV)

Elisabeth H. Bel, MD, PhD
Professor and Head of the Department of Respiratory Medicine, Amsterdam University Medical Center, University of Amsterdam, The Netherlands
Asthma

George A. Beller, MD
Emeritus Professor of Cardiology, Department of Medicine, University of Virginia Health System, Charlottesville, Virginia
Noninvasive Cardiac Imaging

Joseph R. Berger, MD
Professor of Neurology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Cytomegalovirus, Epstein-Barr Virus, and Slow Virus Infections of the Central Nervous System; Brain Abscess and Parameningeal Infections

Paul D. Berk, MD
Professor of Medicine, Columbia University Vagelos College of Physicians & Surgeons, New York, New York
Approach to the Patient with Jaundice or Abnormal Liver Tests

Nancy Berliner, MD
H. Franklin Bunn Professor of Medicine; Chief, Division of Hematology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts
Leukocytosis and Leukopenia; Histiocytoses

James L. Bernat, MD
Professor of Neurology and Medicine, Geisel School of Medicine at Dartmouth, Hanover, New Hampshire and Dartmouth-Hitchcock Medical Center, Lebanon, New Hampshire
Coma, Vegetative State, and Brain Death

Philip J. Bierman, MD
Professor of Internal Medicine, University of Nebraska Medical Center College of Medicine, Omaha, Nebraska
Non-Hodgkin Lymphomas

Leslie G. Biesecker, MD
Chief, Medical Genomics and Metabolic Genetics Branch, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland
Clinical Genomics—Genome Structure and Variation

Michael R. Bishop, MD
Professor of Medicine and Director of the Cellular Therapy Program, Section of Hematology and Oncology, University of Chicago Pritzker School of Medicine, Chicago, Illinois
Hematopoietic Stem Cell Transplantation

Joseph J. Biundo, MD
Clinical Professor of Medicine, Tulane Medical Center, New Orleans, Louisiana
Bursitis, Tendinitis, and Other Periarticular Disorders and Sports Medicine

Joel N. Blankson, MD, PhD
Professor of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland
Immunopathogenesis of Human Immunodeficiency Virus Infection

William A. Blattner, MD
Chief Executive Officer, Salt Run Global Health and Research, Saint Augustine, Florida
Retroviruses Other Than Human Immunodeficiency Virus

Thomas P. Bleck, MD
Professor of Neurology, Northwestern University Feinberg School of Medicine; Professor Emeritus of Neurological Sciences, Neurosurgery, Medicine, and Anesthesiology, Rush Medical College, Chicago, Illinois
Arboviruses Affecting the Central Nervous System

Karen C. Bloch, MD, MPH
Associate Professor of Medicine (Infectious Diseases) and Health Policy, Vanderbilt University School of Medicine, Nashville, Tennessee
Tularemia and Other Francisella *Infections*

Henk J. Blom, PhD
Professor of Biochemistry of Inherited Metabolic Disease, Department of Clinical Genetics, Center for Lysosomal and Metabolic Diseases, Erasmus MC, Rotterdam, The Netherlands
Homocystinuria and Hyperhomocysteinemia

Olaf A. Bodamer, MD, PhD
Park Gerald Chair of Genetics and Genomics, Department of Medicine, Boston Children's Hospital and Harvard Medical School, Boston, Massachusetts
Approach to Inborn Errors of Metabolism

William E. Boden, MD
Professor of Medicine, Boston University School of Medicine; Lecturer in Medicine, Harvard Medical School; Scientific Director, Clinical Trials Network, Department of Medicine, VA Boston Healthcare System, Boston, Massachusetts
Angina Pectoris and Stable Ischemic Heart Disease

Guy Boivin, MD
Professor of Microbiology, Immunology and Infectiology, CHU de Québec-Laval University, Quebec City, Quebec, Canada
Cytomegalovirus

Jean Bolognia, MD
Professor of Dermatology, Yale University School of Medicine, New Haven, Connecticut
Infections, Hyperpigmentation and Hypopigmentation, Regional Dermatology, and Distinctive Lesions in Black Skin

William Bonnez, MD
Professor Emeritus of Medicine, University of Rochester School of Medicine & Dentistry, Rochester, New York
Papillomavirus

Robert A. Bonomo, MD
Professor of Medicine, Case Western Reserve University School of Medicine; Chief of Medicine, Cleveland VA Hospital, Cleveland, Ohio
Diseases Caused by Acinetobacter *and* Stenotrophomonas *Species*

Sarah L. Booth, PhD
Professor of Nutrition, Tufts University; Director, USDA Human Nutrition Research Center on Aging; Director, Vitamin K Laboratory, USDA Human Nutrition Research Center on Aging, Boston, Massachusetts
Vitamins, Trace Minerals, and Other Micronutrients

Patrick J. Bosque, MD
Associate Professor of Neurology, University of Colorado School of Medicine; Chief, Neurology Division, Department of Medicine, Denver Health Medical Center, Denver, Colorado
Prion Diseases

Lucy Breakwell, PhD, MSc
Epidemiologist, Global Immunization Division, Centers for Disease Control and Prevention, Atlanta, Georgia
Diphtheria and Other Corynebacterium *Infections*

David J. Brenner, PhD, DSc
Higgins Professor of Radiation Biophysics, Center for Radiological Research, Columbia University Irving Medical Center, New York, New York
Radiation Injury

Laurent Brochard, MD
Keenan Chair in Critical Care and Respiratory Medicine and Professor of Medicine and Interdepartmental Division Director for Critical Care, University of Toronto Faculty of Medicine; Division of Critical Care, Saint Michael's Hospital, Toronto, Ontario, Canada
Mechanical Ventilation

Itzhak Brook, MD
Professor of Pediatrics, Georgetown University School of Medicine, Washington, D.C.
Diseases Caused by Non–Spore-Forming Anaerobic Bacteria; Actinomycosis

Enrico Brunetti, MD
Associate Professor, Department of Clinical, Surgical, Diagnostic and Pediatric Sciences and Staff Physician, Department of Infectious and Tropical Diseases, San Matteo Hospital Foundation, University of Pavia, Pavia, Italy
Cestodes

Amy E. Bryant, PhD
Associate Professor of Medicine, University of Washington School of Medicine, Seattle, Washington and Research Career Scientist, Infectious Diseases Section, VA Medical Center, Boise, Idaho
Nonpneumococcal Streptococcal Infections and Rheumatic Fever

David M. Buchner, MD, MPH
Professor Emeritus, Department of Kinesiology & Community Health, University of Illinois Urbana Champaign, Champaign, Illinois
Physical Activity

Pierre A. Buffet, MD, PhD
Professor of Cell Biology, Faculty of Medicine, Paris University and Consultant Physician, Institut Pasteur Medical Center, Paris, France
Leishmaniasis

David A. Bushinsky, MD
John J. Kuiper Distinguished Professor of Medicine and of Pharmacology and Physiology, University of Rochester School of Medicine & Dentistry, Rochester, New York
Nephrolithiasis

Vivian P. Bykerk, MD
Associate Professor of Medicine, Weill Cornell Medical College; Associate Attending Physician, Hospital for Special Surgery, New York, New York
Approach to the Patient with Rheumatic Disease

John C. Byrd, MD
Distinguished University Professor, Ohio State University, Columbus, Ohio
Chronic Lymphocytic Leukemia

Peter A. Calabresi, MD
Professor of Neurology and Neuroscience, Director of the Richard T Johnson Division of Neuroimmunology and Neuroinfectious Diseases; Director of the Multiple Sclerosis Center, Johns Hopkins University School of Medicine, Baltimore, Maryland
Multiple Sclerosis and Demyelinating Conditions of the Central Nervous System

David P. Calfee, MD, MS
Professor of Medicine and of Health Policy & Research, Weill Cornell Medical College; Chief Hospital Epidemiologist, NewYork-Presbyterian Hospital/Weill Cornell, New York, New York
Prevention and Control of Health Care–Associated Infections

Clara Camaschella, MD
Professor of Medicine, Division of Genetics and Cell Biology, San Raffaele Scientific Institute, Milano, Italy
Microcytic and Hypochromic Anemias

Michael Camilleri, MD
Atherton and Winifred W. Bean Professor of Medicine, Pharmacology, and Physiology, Mayo Clinic College of Medicine and Science; Consultant, Division of Gastroenterology and Hepatology, Department of Medicine, Mayo Clinic, Rochester, Minnesota
Disorders of Gastrointestinal Motility

Maria Domenica Cappellini, MD
Professor of Internal Medicine, Department of Clinical Sciences and Community Health, University of Milan; and Ca' Granda Foundation-Policlinico Hospital, Milan, Italy
The Thalassemias

Blase A. Carabello, MD
Professor of Cardiovascular Sciences and Chief, Division of Cardiology, East Carolina University Brody School of Medicine, Greenville, North Carolina
Valvular Heart Disease

Edgar M. Carvalho, MD, PhD
Professor of Medicine, Federal University of Bahia, Oswaldo Cruz Foundation (Fiocruz), Instituto de Pesquisa Gonçalo Moniz (IGM), Salvador-Bahia, Brazil
Trematode Infections

William H. Catherino, MD, PhD
Professor and Chair-Research Division, Department of Obstetrics and Gynecology, Uniformed Services University of the Health Sciences, Bethesda, Maryland
Ovaries and Pubertal Development; Reproductive Endocrinology and Infertility

Jane A. Cauley, DrPH
Distinguished Professor of Epidemiology, Graduate School of Public Health, University of Pittsburgh, Pittsburgh, Pennsylvania
Epidemiology of Aging: Implications of an Aging Society

Naga P. Chalasani, MD
David W. Crabb Professor and Director, Division of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana
Alcoholic and Nonalcoholic Steatohepatitis

Henry F. Chambers, MD
Professor of Medicine and Director, Clinical Research Services, Clinical Translational Science Institute, University of California, San Francisco, School of Medicine, San Francisco, California
Staphylococcal Infections

Larry W. Chang, MD, MPH
Associate Professor of Medicine, Epidemiology, and International Health, Johns Hopkins University School of Medicine and Bloomberg School of Public Health, Baltimore, Maryland
Epidemiology and Diagnosis of Human Immunodeficiency Virus Infection and Acquired Immunodeficiency Syndrome

Lin H. Chen, MD
Associate Professor of Medicine, Harvard Medical School, Boston, Massachusetts and Director of the Travel Medicine Center, Division of Infectious Diseases and Travel Medicine, Mount Auburn Hospital, Cambridge, Massachusetts
Approach to the Patient before and after Travel

Sharon C-A Chen, MB, PhD
Professor of Medicine, University of Sydney and Centre for Infectious Diseases and Microbiology, ICPMR and Westmead Hospital, New South Wales, Australia
Cryptococcosis

William P. Cheshire, Jr., MD
Professor of Neurology, Mayo Clinic College of Medicine and Science, Jacksonville, Florida
Autonomic Disorders and Their Management

Arun Chockalingam, PhD
Professor of Epidemiology, Medicine and Global Health, Dalla Lana School of Public Health, University of Toronto, Toronto, Ontario, Canada
Global Health

David C. Christiani, MD
Professor of Medicine, Harvard Medical School; Physician, Pulmonary and Critical Care, Massachusetts General Hospital; Elkan Blout Professor of Environmental Genetics, Environmental Health, Harvard School of Public Health, Boston, Massachusetts
Physical and Chemical Injuries of the Lung

Edward Chu, MD, MMS
Professor and Chief, Division of Hematology-Oncology, Deputy Director, UPMC Hillman Cancer Center, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania
Neoplasms of the Small and Large Intestine

Theodore J. Cieslak, MD, MPH
Associate Professor of Epidemiology, Co-Medical Director, Nebraska Biocontainment Unit, College of Public Health, University of Nebraska, Omaha, Nebraska
Bioterrorism

George A. Cioffi, MD
Edward S. Harkness Professor and Chair, Jean and Richard Deems Professor of Ophthalmology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Diseases of the Visual System

Carolyn M. Clancy, MD
Clinical Associate Professor of Internal Medicine, George Washington University School of Medicine; Assistant Deputy Undersecretary for Health, Quality, Safety and Value, Veterans Administration, Washington, D.C.
Measuring Health and Health Care

Heather E. Clauss, MD
Associate Professor of Medicine, Section of Infectious Diseases, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania
Listeriosis

Daniel J. Clauw, MD
Professor of Anesthesiology, Medicine (Rheumatology) and Psychiatry, Director, Chronic Pain and Fatigue Research Center, University of Michigan Medical School, Ann Arbor, Michigan
Fibromyalgia, Chronic Fatigue Syndrome, and Myofascial Pain

David R. Clemmons, MD
Kenan Professor of Medicine, University of North Carolina School of Medicine; Attending Physician, Medicine, UNC Hospitals, Chapel Hill, North Carolina
Approach to the Patient with Endocrine Disease

David Cohen, MD
Professor of Medicine, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Treatment of Irreversible Renal Failure

Jeffrey Cohen, MD
Chief, Laboratory of Infectious Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
Varicella-Zoster Virus (Chickenpox, Shingles)

Myron S. Cohen, MD
Yeargan-Bates Eminent Professor of Medicine, Microbiology and Epidemiology, Associate Vice Chancellor for Global Health; Director, Institute of Global Health and Infectious Diseases, University of North Carolina School of Medicine, Chapel Hill, North Carolina
Approach to the Patient with a Sexually Transmitted Infection; Prevention of Human Immunodeficiency Virus Infection

Steven P. Cohen, MD
Professor of Anesthesiology & Critical Care Medicine, Neurology and Physical Medicine & Rehabilitation and Chief, Pain Medicine Division, Johns Hopkins School of Medicine; Director of Pain Research and Professor of Anesthesiology and Physical Medicine & Rehabilitation, Walter Reed National Military Medical Center, Uniformed Services University of the Health Sciences, Baltimore, Maryland
Pain

Steven L. Cohn, MD
Professor Emeritus, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida; Clinical Professor of Medicine Emeritus, SUNY Downstate, Brooklyn, New York
Preoperative Evaluation

Joseph M. Connors, MD
Emeritus Professor, BC Cancer Centre for Lymphoid Cancer and the University of British Columbia, Vancouver, British Columbia, Canada
Hodgkin Lymphoma

Deborah J. Cook, MD, MSc
Professor of Medicine, Clinical Epidemiology & Biostatistics, McMaster University Michael G. DeGroote School of Medicine, Hamilton, Ontario, Canada
Approach to the Patient in a Critical Care Setting

David S. Cooper, MD
Professor of Medicine, Division of Endocrinology and Metabolism, The Johns Hopkins University School of Medicine, Baltimore, Maryland
Thyroid

Joseph Craft, MD
Paul B. Beeson Professor of Medicine and Professor of Immunobiology, Departments of Internal Medicine and Immunobiology, Yale University, New Haven, Connecticut
The Adaptive Immune System

Jill P. Crandall, MD
Professor of Medicine and Chief, Division of Endocrinology, Albert Einstein College of Medicine, Bronx, New York
Diabetes Mellitus

Simon L. Croft, PhD
Professor of Parasitology, Faculty of Infectious and Tropical Diseases, London School of Hygiene & Tropical Medicine, London, United Kingdom
Leishmaniasis

Mary K. Crow, MD
Joseph P. Routh Professor of Rheumatic Diseases in Medicine, Weill Cornell Medical College; Physician-in-Chief and Benjamin M. Rosen Chair in Immunology and Inflammation Research, Hospital for Special Surgery, New York, New York
The Innate Immune System; Approach to the Patient with Rheumatic Disease; Systemic Lupus Erythematosus

John A. Crump, MB ChB, MD, DTM&H
McKinlay Professor of Global Health, Centre for International Health, University of Otago, Dunedin, Otago; Adjunct Professor of Medicine, Pathology, and Global Health, Division of Infectious Diseases and International Health, Duke University Medical Center, Durham, North Carolina
Salmonella *Infections (Including Enteric Fever)*

Merit E. Cudkowicz, MD
Professor of Neurology, Harvard Medical School and Chair of Neurology, Massachusetts General Hospital, Boston, Massachusetts
Amyotrophic Lateral Sclerosis and Other Motor Neuron Diseases

Mark R. Cullen, MD
Professor of Medicine, Stanford University School of Medicine, Stanford, California
Principles of Occupational and Environmental Medicine

Charlotte Cunningham-Rundles, MD, PhD
David S Gottesman Professor of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York
Primary Immunodeficiency Diseases

Inger K. Damon, MD, PhD
Director, Division of High Consequence Pathogens and Pathology, Centers for Disease Control and Prevention, Atlanta, Georgia
Smallpox, Monkeypox, and Other Poxvirus Infections

Troy E. Daniels, DDS, MS
Professor Emeritus of Oral Pathology & Pathology, University of California, San Francisco, School of Medicine, San Francisco, California
Diseases of the Mouth and Salivary Glands

Richard Dart, MD, PhD
Professor of Emergency Medicine, University of Colorado School of Medicine and Director, Rocky Mountain Poison and Drug Center, Denver Health and Hospital Authority, Denver, Colorado
Envenomation, Bites, and Stings

Nancy E. Davidson, MD
Professor of Medicine and Raisbeck Endowed Chair; President, Seattle Cancer Care Alliance; Senior Vice President and Director, Clinical Research Division, Fred Hutchinson Cancer Research Center; Chief, Division of Medical Oncology, University of Washington School of Medicine, Seattle, Washington
Breast Cancer and Benign Breast Disorders

Lisa M. DeAngelis, MD
Lillian Rojtman Chair in Honor of Jerome B Posner, Acting Physician-in-Chief, Memorial Hospital, Chair, Department of Neurology, Memorial Sloan-Kettering Cancer Center, New York, New York
Tumors of the Central Nervous System

Malcolm M. DeCamp, MD
Professor of Surgery and Chair, Division of Cardiothoracic Surgery, K. Craig Kent Chair in Strategic Leadership, University of Wisconsin School of Medicine and Public Health, Madison, Wisconsin
Interventional and Surgical Approaches to Lung Disease

Carlos Del Rio, MD
Hubert Professor and Chair, Hubert Department of Global Health, Rollins School of Public Health of Emory University; Professor, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia
Prevention of Human Immunodeficiency Virus Infection

Gabriele C. DeLuca, MD, DPhil
Associate Professor, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, Oxfordshire, United Kingdom
Approach to the Patient with Neurologic Disease

David W. Denning, MBBS
Professor of Infectious Diseases in Global Health and Director of the National Aspergillosis Centre, University of Manchester and Wythenshawe Hospital, Manchester, United Kingdom
Systemic Antifungal Agents

Patricia A. Deuster, PhD, MPH
Professor and Director, Department of Military and Emergency Medicine, Director, Consortium for Health and Military Performance, Uniformed Services University, Bethesda, Maryland
Rhabdomyolysis

Robert B. Diasio, MD
William J and Charles H Mayo Professor of Molecular Pharmacology and Experimental Therapeutics, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Principles of Drug Therapy

David J. Diemert, MD
Associate Professor, Departments of Medicine and Microbiology, Immunology and Tropical Medicine, George Washington University School of Medicine and Health Sciences, Washington, D.C.
Nematode Infections

Kathleen B. Digre, MD
Professor of Neurology and Ophthalmology, University of Utah School of Medicine, Salt Lake City, Utah
Headaches and Other Head Pain

James. H. Doroshow, MD
Deputy Director for Clinical and Translational Research, Director, Division of Cancer Treatment and Diagnosis, National Cancer Institute, National Institutes of Health, Bethesda, Maryland
Approach to the Patient with Cancer

John M. Douglas, Jr., MD
Executive Director, Tri-County Health Department, Greenwood Village, Colorado
Papillomavirus

Jeffrey M. Drazen, MD
Distinguished Parker B. Francis Professor of Medicine, Harvard Medical School and Senior Physician, Department of Medicine, Brigham and Women's Hospital, Boston, Massachusetts
Asthma

Dimitri Drekonja, MD, MS
Associate Professor of Medicine, University of Minnesota and Chief, Infectious Diseases Section, Minneapolis VA Health Care System, Minneapolis, Minnesota
Approach to the Patient with Urinary Tract Infection

Stephen C. Dreskin, MD, PhD
Professor of Medicine and Immunology, University of Colorado School of Medicine, Aurora, Colorado
Urticaria and Angioedema

W. Lawrence Drew, MD, PhD
Professor Emeritus of Laboratory Medicine and Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Cytomegalovirus

George L. Drusano, MD
Professor of Medicine and Director, Institute for Therapeutic Innovation, University of Florida College of Medicine, Orlando, Florida
Antibacterial Chemotherapy

Thomas D. DuBose, Jr., MD
Professor Emeritus of Medicine, Wake Forest School of Medicine, Winston-Salem, North Carolina; Visiting Professor of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
Vascular Disorders of the Kidney

J. Stephen Dumler, MD
Professor and Chairperson, Joint Departments of Pathology, Uniformed Services University, Walter Reed National Military Medical Center, and Joint Pathology Center, Bethesda, Maryland
Zoonoses

Herbert L. DuPont, MD
Professor of Infectious Diseases, University of Texas School of Public Health, Mary W. Kelsey Chair, University of Texas McGovern Medical School, Houston, Texas
Approach to the Patient with Suspected Enteric Infection

Madeleine Duvic, MD
Professor and Deputy Chairman, Department of Dermatology, University Texas MD Anderson Cancer Center, Houston, Texas
Urticaria, Drug Hypersensitivity Rashes, Nodules and Tumors, and Atrophic Diseases

Kathryn M. Edwards, MD
Sarah H. Sell and Cornelius Vanderbilt Chair in Pediatrics, Vanderbilt University School of Medicine, Nashville, Tennessee
Parainfluenza Viral Disease

N. Lawrence Edwards, MD
Professor and Vice Chairman, Department of Medicine, University of Florida College of Medicine; Chief, Section of Rheumatology Medicine, Malcolm Randall Veterans Administration Medical Center, Gainesville, Florida
Crystal Deposition Diseases

Lawrence H. Einhorn, MD
Distinguished Professor of Medicine, Indiana University School of Medicine, Indianapolis, Indiana
Testicular Cancer

George M. Eliopoulos, MD
Professor of Medicine, Harvard Medical School; Physician, Beth Israel Deaconess Medical Center, Boston, Massachusetts
Principles of Anti-Infective Therapy

Perry M. Elliott, MBBS, MD
Professor of Cardiovascular Medicine, Institute of Cardiovascular Science, University College London & St. Bartholomew's Hospital, London, United Kingdom
Diseases of the Myocardium and Endocardium

Jerrold J. Ellner, MD
Professor of Medicine, Rutgers-New Jersey Medical School; Director of Research Innovations, Center for Emerging Pathogens, Newark, New Jersey
Tuberculosis

Ezekiel J. Emanuel, MD, PhD
Vice Provost for Global Initiatives, Office of the Provost; Chair, Department of Medical Ethics and Health Policy, University of Pennsylvania, Philadelphia, Pennsylvania
Bioethics in the Practice of Medicine

Joel D. Ernst, MD
Professor and Chief, Division of Experimental Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Leprosy (Hansen Disease)

Gregory T. Everson, MD
Professor of Medicine, University of Colorado Denver; Director of Hepatology, Hepatology and Transplant Center, University of Colorado Hospital, Aurora, Colorado
Hepatic Failure and Liver Transplantation

Amelia Evoli, MD
Associate Professor of Neurology, Institute of Neurology, Catholic University, Roma, Italy
Disorders of Neuromuscular Transmission

Matthew E. Falagas, MD, MSc, DSc
Director, Alfa Institute of Biomedical Sciences and Chief, Department of Medicine, Henry Dunant Hospital Center, Athens, Greece; Adjunct Associate Professor of Medicine, Tufts University School of Medicine, Boston, Massachusetts
Pseudomonas *and Related Gram-Negative Bacillary Infections*

Gary W. Falk, MD, MS
Professor of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Diseases of the Esophagus

James C. Fang, MD
Professor of Medicine, University of Utah School of Medicine; Executive Director, Cardiovascular Service Line, University of Utah Health Sciences, Salt Lake City, Utah
ST Elevation Acute Myocardial Infarction and Complications of Myocardial Infarction

Gene Feder, MBBS, MD
Professor, Centre for Academic Primary Care, Population Health Sciences, Bristol Medical School, University of Bristol; General Practitioner, Helios Medical Centre, Bristol, United Kingdom
Intimate Partner Violence

David J. Feller-Kopman, MD
Professor of Medicine, Anesthesiology, Otolaryngology-Head & Neck Surgery and Director, Bronchoscopy & Interventional Pulmonology, Johns Hopkins University School of Medicine, Baltimore, Maryland
Interventional and Surgical Approaches to Lung Disease

Thomas McDonald File, Jr., MD, MSc
Professor and Chair, Infectious Disease Section, Northeast Ohio Medical University, Rootstown, Ohio; Chair, Infectious Disease Division, Summa Health, Akron, Ohio
Streptococcus Pneumoniae *Infections*

Gary S. Firestein, MD
Professor of Medicine, Dean, and Associate Vice Chancellor of Clinical and Translational Research, University of California, San Diego, School of Medicine, La Jolla, California
Mechanisms of Inflammation and Tissue Repair

Glenn I. Fishman, MD
William Goldring Professor of Medicine and Director, Leon H. Charney Division of Cardiology, New York University School of Medicine, New York, New York
Principles of Electrophysiology

Lee A. Fleisher, MD
Robert D. Dripps Professor and Chair, Anesthesiology and Critical Care; Professor of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Overview of Anesthesia

Paul W. Flint, MD
Professor and Chair of Otolaryngology-Head & Neck Surgery, Oregon Health & Science University, Portland, Oregon
Throat Disorders

Evan L. Fogel, MD, MSc
Professor of Medicine, Indiana University School of Medicine, Indianapolis, Indiana
Diseases of the Gallbladder and Bile Ducts

Chris E. Forsmark, MD
Professor of Medicine, University of Florida College of Medicine, Gainesville, Florida
Pancreatitis

Pierre-Edouard Fournier, MD, PhD
Professor of Medical Bacteriology-Virology and Hygiene, Faculté de Médecine, Aix-Marseille Université and Institut Hospitalo-Universitaire Méditerranée-Infection, Marseille, France
Rickettsial Infections

Vance G. Fowler, Jr., MD, MHS
Professor of Medicine and of Molecular Genetics and Microbiology, Duke University School of Medicine, Durham, North Carolina
Infective Endocarditis

Manuel A. Franco, MD, PhD
Professor, Instituto de Genética Humana, Facultad de Medicina, Pontificia Universidad Javeriana, Bogotá, Colombia
Rotaviruses, Noroviruses, and Other Gastrointestinal Viruses

David O. Freedman, MD
Professor Emeritus of Infectious Diseases, University of Alabama at Birmingham School of Medicine; Medical Director, Shoreland Travax, Birmingham, Alabama
Approach to the Patient before and after Travel

Martyn A. French, MB ChB, MD
Emeritus Professor in Clinical Immunology, University of Western Australia Medical School and School of Biomedical Sciences, Faculty of Health and Medical Sciences, Perth, Australia
Immune Reconstitution Inflammatory Syndrome in HIV/AIDS

Karen M. Freund, MD, MPH
Professor of Medicine and Vice Chair for Faculty Affairs and Quality Improvement, Tufts University School of Medicine, Boston, Massachusetts
Approach to Women's Health

John N. Galgiani, MD
Professor of Medicine and Director, Valley Fever Center for Excellence, University of Arizona College of Medicine; Chief Medical Officer, Valley Fever Solutions, Tucson, Arizona
Endemic Mycoses

Patrick G. Gallagher, MD
Professor of Pediatrics, Pathology and Genetics, Yale University School of Medicine, New Haven, Connecticut
Hemolytic Anemias: Red Blood Cell Membrane and Metabolic Defects

Leonard Ganz, MD
Director of Cardiac Electrophysiology, Heart and Vascular Center, Heritage Valley Health System, Beaver, Pennsylvania
Electrocardiography

Hasan Garan, MD, MS
Dickinson W. Richards, Jr. Professor of Medicine, Director, Cardiac Electrophysiology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Ventricular Arrhythmias

Guadalupe Garcia-Tsao, MD
Professor of Medicine, Yale University School of Medicine, New Haven, Connecticut; Chief of Digestive Diseases, School of Medicine, VA-CT Healthcare System, West Haven, Connecticut
Cirrhosis and Its Sequelae

William M. Geisler, MD, MPH
Professor of Medicine, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama
Diseases Caused by Chlamydiae

Tony P. George, MD
Professor of Psychiatry and Director, Division of Brain and Therapeutics, University of Toronto; Chief, Addictions Division, Centre for Addiction and Mental Health, Toronto, Ontario, Canada
Nicotine and Tobacco

Lior Gepstein, MD, PhD
Sohnis Family Professor in Medicine, Technion - Israel Institute of Technology; Director, Cardiology Department, Rambam Health Care Campus, Haifa, Israel
Regenerative Medicine, Cell, and Gene Therapies

Susan I. Gerber, MD
Chief, Respiratory Viruses Branch, Division of Viral Diseases, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia
Coronaviruses

Dale N. Gerding, MD
Professor (retired) of Medicine, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois; Research Physician, Medicine, Edward Hines Jr. VA Hospital, Hines, Illinois
Clostridial Infections

Morie A. Gertz, MD
Roland Seidler Jr. Professor of the Art of Medicine and Chair Emeritus, Internal Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Amyloidosis

Khalil G. Ghanem, MD, PhD
Associate Professor of Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland
Granuloma Inguinale (Donovanosis); Syphilis; Nonsyphilitic Treponematoses

Christopher J. Gill, MD, MS
Associate Professor of Global Health, Boston University School of Public Health, Boston, Massachusetts
Whooping Cough and Other Bordetella *Infections*

Jeffrey S. Ginsberg, MD
Professor of Medicine, McMaster University Michael G. DeGroote School of Medicine, Hamilton, Ontario, Canada
Venous Thrombosis and Embolism

Geoffrey S. Ginsburg, MD, PhD
Professor of Medicine and Pathology and Director, Duke Center for Applied Genomics & Precision Medicine, Duke University, Durham, North Carolina
Applications of Molecular Technologies to Clinical Medicine

Marshall J. Glesby, MD, PhD
Professor of Medicine, Weill Cornell Medical College, New York, New York
Systemic Manifestations of HIV/AIDS

John W. Gnann, Jr., MD
Professor of Medicine, Medical University of South Carolina, Charleston, South Carolina
Mumps; Herpes Simplex Virus Infections

Matthew R. Golden, MD, MPH
Professor of Medicine, University of Washington School of Medicine; Director, HIV/STD Program, Public Health - Seattle & King County, Seattle, Washington
Neisseria Gonorrhoeae *Infections*

David L. Goldman, MD
Associate Professor of Pediatrics, Microbiology and Immunology, Children's Hospital at Montefiore/Albert Einstein College of Medicine, Bronx, New York
Mycoplasma *Infections*

Lee Goldman, MD
Harold and Margaret Hatch Professor, Chief Executive, Columbia University Irving Medical Center, Dean of the Faculties of Health Sciences and Medicine, Columbia University, New York, New York
Approach to Medicine, the Patient, and the Medical Profession: Medicine as a Learned and Humane Profession; Approach to the Patient with Possible Cardiovascular Disease

Larry B. Goldstein, MD
Ruth L Works Professor and Chairman, Department of Neurology, University of Kentucky College of Medicine; Co-Director, Kentucky Neuroscience Institute, Lexington, Kentucky
Approach to Cerebrovascular Diseases; Ischemic Cerebrovascular Disease

Richard M. Gore, MD
Professor of Radiology, University of Chicago Pritzker School of Medicine; Chief, Section of Gastrointestinal Radiology, NorthShore University HealthSystem, Evanston, Illinois
Diagnostic Imaging Procedures in Gastroenterology

Jason Gotlib, MD, MS
Professor of Medicine, Stanford University School of Medicine, Stanford Cancer Institute, Stanford, California
Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis

Eduardo Gotuzzo, MD
Professor Emeritus, Alexander von Humboldt Tropical Medicine Institute, Universidad Peruana Cayetano Heredia; Principal Professor of Medicine and Tropical Diseases, National Hospital Cayetano Heredia, Lima, Peru
Cholera and Other Vibrio *Infections; Trematode Infections*

Leslie C. Grammer, MD
Professor of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois
Drug Allergy

Hartmut Grasemann, MD, PhD
Professor of Pediatrics, The Hospital for Sick Children and University of Toronto, Toronto, Ontario, Canada
Cystic Fibrosis

M. Lindsay Grayson, MBBS, MD, MS
Professor of Medicine, University of Melbourne, Director, Infectious Diseases & Microbiology, Austin Health, Melbourne, Victoria, Australia
Principles of Anti-Infective Therapy

Harry B. Greenberg, MD
Professor of Medicine and of Microbiology and Immunology, Stanford University School of Medicine, Stanford, California
Rotaviruses, Noroviruses, and Other Gastrointestinal Viruses

Steven A. Greenberg, MD
Professor of Neurology, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts
Inflammatory Myopathies

David M. Greer, MD, MA
Professor and Chair of Neurology, Boston University School of Medicine, Boston, Massachusetts
Coma, Vegetative State, and Brain Death

Robert C. Griggs, MD
Professor of Neurology, Medicine, Pediatrics, Pathology & Laboratory Medicine, University of Rochester School of Medicine & Dentistry, Rochester, New York
Approach to the Patient with Neurologic Disease

Lev M. Grinberg, MD, PhD
Professor and Chair, Department of Pathology, Ural State Medical University, Ekaterinburg, Russia
Anthrax

Daniel Grossman, MD
Professor of Obstetrics, Gynecology and Reproductive Sciences, University of California, San Francisco, School of Medicine, San Francisco, California
Contraception

Lisa M. Guay-Woodford, MD
Richard L. Hudson Professor of Pediatrics, George Washington University School of Medicine and Health Science and Director, Center for Translational Research, Children's National Medical Center, Washington D.C.
Hereditary Nephropathies and Developmental Abnormalities of the Urinary Tract

Roy M. Gulick, MD, MPH
Professor of Medicine, Weill Cornell Medical School; Attending Physician, NewYork-Presbyterian Hospital, New York, New York
Antiretroviral Therapy for Human Immunodeficiency Virus and Acquired Immunodeficiency Syndrome

Rajesh Gupta, MD, MEd
Associate Professor of Medicine, University of Toronto; General Internist, Medicine, St. Michael's Hospital, Toronto, Ontario, Canada
Medical Consultation in Psychiatry

Colleen Hadigan, MD, MPH
Staff Clinician, National Institutes of Health, Laboratory of Immunoregulation, NIAID, Bethesda, Maryland
Microbial Complications in Patients Infected with Human Immunodeficiency Virus

Melissa M. Hagman, MD
Associate Professor of Medicine, Program Director, Internal Medicine Residency-Boise, University of Washington, Boise, Idaho
Nonpneumococcal Streptococcal Infections and Rheumatic Fever

Klaus D. Hagspiel, MD
Professor of Radiology, Medicine (Cardiology) and Pediatrics; Chief, Division of Noninvasive Cardiovascular Imaging, Department of Radiology and Medical Imaging, University of Virginia School of Medicine, Charlottesville, Virginia
Noninvasive Cardiac Imaging

H. Hunter Handsfield, MD
Professor of Medicine Emeritus, University of Washington School of Medicine, Seattle, Washington
Neisseria Gonorrhoeae *Infections*

Raymond C. Harris, MD
Anne and Roscoe R. Robinson Chair and Professor of Medicine and Associate Chair, Division of Nephrology, Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee
Diabetes and the Kidney

Frederick G. Hayden, MD
Stuart S. Richardson Professor Emeritus of Clinical Virology and Professor Emeritus of Medicine, Department of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
Influenza

Frederick M. Hecht, MD
Professor of Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Complementary, Alternative, and Integrative Medicine

Douglas C. Heimburger, MD, MS
Professor of Medicine, Vanderbilt University School of Medicine; Associate Director for Education & Training, Vanderbilt Institute for Global Health, Vanderbilt University, Nashville, Tennessee
Nutrition's Interface with Health and Disease

Donald D. Hensrud, MD, MPH
Associate Professor of Preventive Medicine and Nutrition, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Nutrition's Interface with Health and Disease

Erik L. Hewlett, MD
Professor of Medicine, Microbiology, Immunology and Cancer Biology, University of Virginia School of Medicine, Charlottesville, Virginia
Whooping Cough and Other Bordetella *Infections*

Richard J. Hift, MMed(Med), PhD
Professor of Medicine, University of KwaZulu-Natal, Durban, KwaZulu-Natal, South Africa
The Porphyrias

David R. Hill, MD, DTM&H
Professor of Medical Sciences, Director, Global Public Health, Quinnipiac University Frank H Netter MD School of Medicine, Hamden, Connecticut
Giardiasis

Nicholas S. Hill, MD
Professor of Medicine, Tufts University School of Medicine; Chief, Division of Pulmonary, Critical Care and Sleep Medicine, Tufts Medical Center, Boston, Massachusetts
Respiratory Monitoring in Critical Care

Christopher D. Hillyer, MD
President and Chief Executive Officer, New York Blood Center; Professor of Medicine, Weill Cornell Medical College, New York, New York
Transfusion Medicine

Brian D. Hoit, MD
Professor of Medicine, Physiology and Biophysics, Case Western Reserve University School of Medicine; Director of Echocardiography, Harrington Heart & Vascular Center, University Hospital Cleveland Medical Center, Cleveland, Ohio
Pericardial Diseases

Steven M. Holland, MD
Director, Division of Intramural Research, Chief, Immunopathogenesis Section, National Institute of Allergy and Infectious Diseases, NIH, Bethesda, Maryland
The Nontuberculous Mycobacteria

Steven M. Hollenberg, MD
Professor of Medicine, Cooper Medical School of Rowan University; Director, Coronary Care Unit, Cooper University Hospital, Camden, New Jersey
Cardiogenic Shock

Edward W. Hook, III, MD
Professor of Medicine and Director, Division of Infectious Diseases, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama
Granuloma Inguinale (Donovanosis); Syphilis; Nonsyphilitic Treponematoses

Jo Howard, MB BChir
Consultant Haematologist and Lead Clinician, Haematology, Guy's and St Thomas' National Health Service Foundation Trust; Honorary Reader, King's College London, London, United Kingdom
Sickle Cell Disease and Other Hemoglobinopathies

David J. Hunter, MBBS, MPH, ScD
Richard Doll Professor of Epidemiology and Medicine, Nuffield Department of Population Health, University of Oxford, Oxford, United Kingdom
Epidemiology of Cancer

Khalid Hussain, MB ChB, MD, MSc
Professor of Pediatrics, Weill Cornell Medicine-Qatar; Division Chief-Endocrinology, Vice Chair for Research, Program Director-Research, Sidra Medicine, OPC, Doha, Qatar
Hypoglycemia and Pancreatic Islet Cell Disorders

Michael C. Iannuzzi, MD, MBA
Professor and Chairman, Department of Internal Medicine, Northwell-Staten Island University Hospital and Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, New York
Sarcoidosis

Robert D. Inman, MD
Professor of Medicine and Immunology, University of Toronto and Kremil Research Institute, University Health Network, Toronto, Ontario, Canada
The Spondyloarthropathies

Sharon K. Inouye, MD, MPH
Professor of Medicine, Harvard Medical School; Director, Aging Brain Center, Marcus Institute for Aging Research-Hebrew SeniorLife, Boston, Massachusetts
Neuropsychiatric Aspects of Aging; Delirium in the Older Patient

Michael G. Ison, MD, MS
Professor of Medicine (Infectious Diseases) and Surgery (Organ Transplantation), Northwestern University Feinberg School of Medicine, Chicago, Illinois
Influenza; Adenovirus Diseases

Karen R. Jacobson, MD, MPH
Assistant Professor of Medicine, Medical Director, Boston Tuberculosis Clinic, Boston University School of Medicine, Boston, Massachusetts
Tuberculosis

Michael R. Jaff, DO
Professor of Medicine, Harvard Medical School, Boston, Massachusetts; President, Newton-Wellesley Hospital, Newton, Massachusetts
Other Peripheral Arterial Diseases

Joanna C. Jen, MD, PhD
Professor of Neurology, David Geffen School of Medicine at UCLA, Los Angeles, California
Neuro-Ophthalmology; Smell and Taste; Hearing and Equilibrium

Dennis M. Jensen, MD
Professor of Medicine, David Geffen School of Medicine at UCLA; Staff Physician, Medicine-GI, VA Greater Los Angeles Healthcare System; Director, Human Studies Core & GI Hemostasis Research Unit, CURE Digestive Diseases Research Center, Los Angeles, California
Gastrointestinal Hemorrhage

Michael D. Jensen, MD
Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Obesity

Robert T. Jensen, MD
Chief, Cell Biology Section, Digestive Diseases Branch, National Institute of Diabetes and Digestive and Kidney Diseases, National Institutes of Health, Bethesda, Maryland
Neuroendocrine Tumors

Alain Joffe, MD, MPH
Retired. Most recently, Associate Professor of Pediatrics, Johns Hopkins University School of Medicine and Director, Student Health and Wellness Center, Johns Hopkins University, Baltimore, Maryland
Adolescent Medicine

Stuart Johnson, MD
Professor of Medicine/Infectious Disease, Loyola University Chicago Stritch School of Medicine, Maywood, Illinois; Physician Researcher, Research Service, Hines VA Hospital, Hines, Illinois
Clostridial Infections

Robin L. Jones, MD, BSc, MB
Consultant Medical Oncologist, Royal Marsden Hospital and Institute of Cancer Research, London, United Kingdom
Malignant Tumors of Bone, Sarcomas, and Other Soft Tissue Neoplasms

Sian Jones, MD
Associate Professor of Clinical Medicine, Weill Cornell Medical College, New York, New York
Systemic Manifestations of HIV/AIDS

Jacqueline Jonklaas, MD, PhD
Professor of Medicine, Georgetown University School of Medicine, Washington, D.C.
Thyroid

Richard C. Jordan, DDS, PhD
Professor of Pathology, Oral Pathology & Radiation Oncology, University of California, San Francisco, School of Medicine, San Francisco, California
Diseases of the Mouth and Salivary Glands

Charles J. Kahi, MD, MS
Professor of Clinical Medicine, Indiana University School of Medicine; GI Section Chief, Richard L. Roudebush VAMC, Indianapolis, Indiana
Vascular Diseases of the Gastrointestinal Tract

Moses R. Kamya, MB ChB, MMed, MPH, PhD
Professor of Medicine, Makerere University School of Medicine, Kampala, Uganda
Malaria

Louise W. Kao, MD
Associate Professor of Clinical Emergency Medicine and Director, Medical Toxicology Fellowship Program, Indiana University School of Medicine, Indianapolis, Indiana
Chronic Poisoning: Trace Metals and Others

Steven A. Kaplan, MD
Professor of Urology, Icahn School of Medicine at Mount Sinai; Director, Men's Health Program, Mount Sinai Health System, New York, New York
Benign Prostatic Hyperplasia and Prostatitis

Daniel L. Kastner, MD, PhD
Scientific Director, Division of Intramural Research, National Human Genome Research Institute, National Institutes of Health, Bethesda, Maryland
The Systemic Autoinflammatory Diseases

David A. Katzka, MD
Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Diseases of the Esophagus

Debra K. Katzman, MD
Professor of Pediatrics, The Hospital for Sick Children and University of Toronto; Senior Associate Scientist, Research Institute; Director, Health Science Research, Faculty of Medicine, University of Toronto, Toronto, Ontario, Canada
Adolescent Medicine

Carol A. Kauffman, MD
Professor of Internal Medicine and Chief, Infectious Diseases, Veterans Affairs Ann Arbor Healthcare System, University of Michigan Medical School, Ann Arbor, Michigan
Endemic Mycoses; Cryptococcosis; Candidiasis

Kenneth Kaushansky, MD
Professor of Medicine, Senior Vice President for Health Sciences, and Dean, Stony Brook University School of Medicine, Stony Brook, New York
Hematopoiesis and Hematopoietic Growth Factors

Keith S. Kaye, MD, MPH
Professor of Medicine, University of Michigan Medical School, Ann Arbor, Michigan
Diseases Caused by Acinetobacter *and* Stenotrophomonas *Species*

Armand Keating, MD
Professor of Medicine and Professor, Institute of Biomaterials and Biomedical Engineering, University of Toronto, Toronto, Canada
Hematopoietic Stem Cell Transplantation

Robin K. Kelley, MD
Associate Professor of Clinical Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Liver and Biliary Tract Cancers

Morton J. Kern, MD
Professor of Medicine and Associate Chief of Cardiology, University of California, Irvine, Orange, California; Chief of Medicine, Long Beach Veterans Health Care System, Long Beach, California
Catheterization and Angiography

Gerald T. Keusch, MD
Professor of Medicine, Boston University School of Medicine, Boston, Massachusetts
Shigellosis

Fadlo R. Khuri, MD
President and Professor of Hematology and Medical Oncology, American University of Beirut; Adjunct Professor of Medicine, Pharmacology and Otolaryngology, Emory University School of Medicine, Atlanta, Georgia
Lung Cancer and Other Pulmonary Neoplasms

Louis V. Kirchhoff, MD, MPH
Professor of Internal Medicine (Infectious Diseases), Psychiatry, and Epidemiology, University of Iowa Carver College of Medicine and College of Public Health, Iowa City, Iowa
Chagas Disease

Ajay J. Kirtane, MD
Associate Professor of Medicine, Columbia University Vagelos College of Physicians and Surgeons; Chief Academic Officer, Center for Interventional Vascular Therapy; Director, Columbia University Irving Medical Center Cardiac Catheterization Laboratories, New York New York
Catheterization and Angiography

Amy D. Klion, MD
Senior Clinical Investigator, Laboratory of Parasitic Diseases, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
Eosinophilic Syndromes

David S. Knopman, MD
Professor of Neurology, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Regional Cerebral Dysfunction: Higher Mental Functions; Cognitive Impairment and Dementia

Christine J. Ko, MD
Professor of Dermatology and Pathology, Yale University School of Medicine, New Haven, Connecticut
Approach to Skin Diseases

Dimitrios P. Kontoyiannis, MD, ScD
Texas 4000 Distinguished Endowed Professor For Cancer Research, Deputy Head, Division of Internal Medicine, University of Texas MD Anderson Cancer Center, Houston, Texas
Mucormycosis; Mycetoma and Dematiaceous Fungal Infections

Barbara S. Koppel, MD
Chief of Neurology, Metropolitan Hospital, New York, New York and Professor of Clinical Neurology, New York Medical College, Valhalla, New York
Nutritional and Alcohol-Related Neurologic Disorders

Kevin M. Korenblat, MD
Professor of Medicine, Washington University School of Medicine in St. Louis, St. Louis, Missouri
Approach to the Patient with Jaundice or Abnormal Liver Tests

Bruce R. Korf, MD, PhD
Professor of Genetics, University of Alabama at Birmingham and Chief Genomics Officer, UAB Medicine, Birmingham, Alabama
Principles of Genetics

Mark G. Kortepeter, MD, MPH
Professor of Epidemiology, College of Public Health, University of Nebraska, Omaha, Nebraska; Adjunct Professor of Preventive Medicine and Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland
Bioterrorism

Shyamasundaran Kottilil, MD, PhD
Professor of Medicine and Associate Chief of Infectious Diseases at the Institute of Human Virology, University of Maryland School of Medicine, Baltimore, Maryland
Antiviral Therapy (Non-HIV)

Joseph A. Kovacs, MD
Senior Investigator, Critical Care Medicine Department, National Institutes of Health Clinical Center, Bethesda, Maryland
Pneumocystis *Pneumonia*

Thomas O. Kovacs, MD
Professor of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California
Gastrointestinal Hemorrhage

Kris V. Kowdley, MD
Director, Liver Care Network and Organ Care Research, Swedish Medical Center; Clinical Professor of Medicine, Washington State University, Elson S. Floyd College of Medicine, Seattle, Washington
Iron Overload (Hemochromatosis)

Monica Kraft, MD
Robert and Irene Flinn Professor and Chair, Department of Medicine, Deputy Director, Asthma and Airway Disease Research Center, University of Arizona Health Sciences, Tucson, Arizona
Approach to the Patient with Respiratory Disease

Christopher M. Kramer, MD
Ruth C. Heede Professor of Cardiology and Professor of Radiology, University of Virginia School of Medicine, Charlottesville, Virginia
Noninvasive Cardiac Imaging

Donna M. Krasnewich, MD, PhD
Program Director, NIGMS, National Institutes of Health, Bethesda, Maryland
Lysosomal Storage Diseases

Alexander Kratz, MD, PhD, MPH
Professor of Clinical Pathology and Cell Biology, Columbia University Vagelos College of Physicians and Surgeons; Director, Automated Core Laboratory and Point of Care Testing Service, Columbia University Irving Medical Center and NewYork-Presbyterian Hospital, New York, New York
Reference Intervals and Laboratory Values

Virginia Byers Kraus, MD, PhD
Professor of Medicine, Adjunct Professor of Pathology and Orthopaedic Surgery, Duke University School of Medicine, Duke Molecular Physiology Institute, Durham, North Carolina
Osteoarthritis

William E. Kraus, MD
Richard and Pat Johnson Distinguished University Professor, Duke University School of Medicine, Durham, North Carolina
Physical Activity

Peter J. Krause, MD
Senior Research Scientist, Yale University School of Public Health, Yale University School of Medicine, New Haven, Connecticut
Babesiosis and Other Protozoan Diseases

Daniela Kroshinsky, MD, MPH
Associate Professor of Dermatology, Massachusetts General Hospital, Harvard Medical School, Boston, Massachusetts
Macular, Papular, Purpuric, Vesicobullous, and Pustular Diseases

John F. Kuemmerle, MD
Charles M. Caravati Professor of Medicine, Chair, Division of Gastroenterology, Hepatology and Nutrition, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia
Inflammatory and Anatomic Diseases of the Intestine, Peritoneum, Mesentery, and Omentum

Ernst J. Kuipers, MD, PhD
Professor of Medicine, Erasmus MC University Medical Center, Rotterdam, Netherlands
Acid Peptic Disease

Daniel Laheru, MD
Ian T. MacMillan Professorship in Clinical Pancreatic Research, Johns Hopkins University School of Medicine, Baltimore, Maryland
Pancreatic Cancer

Donald W. Landry, MD, PhD
Samuel Bard Professor and Chair, Department of Medicine, Columbia University Vagelos College of Physicians and Surgeons and Physician-in-Chief, Columbia University Irving Medical Center, New York, New York
Approach to the Patient with Renal Disease

Anthony E. Lang, MD
Jack Clark Chair in Parkinson's Disease Research and Director, Division of Neurology, University of Toronto; Director, Morton and Gloria Shulman Movement Disorders Clinic and Edmond J Safra Program in Parkinson's Disease, University Health Network, Toronto Western Hospital, Toronto, Ontario, Canada
Parkinsonism; Other Movement Disorders

Richard A. Lange, MD, MBA
Rick and Ginger Francis Endowed Professor and President, Texas Tech University Health Sciences Center, El Paso; Dean, Paul L. Foster School of Medicine, El Paso, Texas
Acute Coronary Syndrome: Unstable Angina and Non–ST Elevation Myocardial Infarction

Frank A. Lederle, MD†
Formerly Professor of Medicine, University of Minnesota School of Medicine; Director of the Minneapolis Veterans Administration Center for Epidemiological and Clinical Research, Minneapolis, Minnesota
Diseases of the Aorta

William M. Lee, MD
Meredith Mosle Chair in Liver Disease and Professor of Internal Medicine, University of Texas Southwestern Medical Center at Dallas, Dallas, Texas
Toxin- and Drug-Induced Liver Disease

James E. Leggett, MD
Department of Medical Education, Providence Portland Medical Center; Associate Professor of Medicine Emeritus, Division of Infectious Diseases, Oregon Health & Science University, Portland, Oregon
Approach to Fever or Suspected Infection in the Normal Host

Glenn N. Levine, MD
Professor of Medicine, Baylor College of Medicine; Director, Cardiac Care Unit, Michael E. DeBakey VA Medical Center, Houston, Texas
Antithrombotic and Antiplatelet Therapy

Marc S. Levine, MD
Emeritus Professor of Radiology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Diagnostic Imaging Procedures in Gastroenterology

Stephanie M. Levine, MD
Professor of Medicine, University of Texas Health San Antonio, San Antonio, Texas
Alveolar Filling Disorders

Gary R. Lichtenstein, MD
Professor of Medicine, University of Pennsylvania Perelman School of Medicine; Director, Center for Inflammatory Bowel Disease, Department of Medicine, Hospital of the University of Pennsylvania, Philadelphia, Pennsylvania
Inflammatory Bowel Disease

Jeffrey M. Liebmann, MD
Shirlee and Bernard Brown Professor and Vice Chair, Department of Ophthalmology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Diseases of the Visual System

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†Deceased.

Henry W. Lim, MD
Chairman and C.S. Livingood Chair Emeritus of Dermatology, Henry Ford Hospital; Senior Vice President for Academic Affairs, Henry Ford Health System, Detroit, Michigan
Eczemas, Photodermatoses, Papulosquamous (Including Fungal) Diseases, and Figurate Erythemas

Aldo A.M. Lima, MD, PhD
Professor, Institute of Biomedicine, Federal University of Ceara, Fortaleza, Ceará, Brazil
Cryptosporidiosis; Trematode Infections

Geoffrey S.F. Lin, MD, PhD
Professor of Neurology, Johns Hopkins University School of Medicine, Baltimore, Maryland
Traumatic Brain Injury and Spinal Cord Injury

Mark S. Link, MD
Professor of Medicine, University of Texas Southwestern Medical Center, Dallas, Texas
Electrocardiography

Donald M. Lloyd-Jones, MD, ScM
Chair and Eileen M. Foell Professor of Preventive Medicine, Senior Associate Dean for Clinical & Translational Research, Northwestern University Feinberg School of Medicine, Chicago, Illinois
Epidemiology of Cardiovascular Disease

Bennett Lorber, MD, DSc
Thomas M. Durant Professor of Medicine and Professor of Microbiology and Immunology, Lewis Katz School of Medicine at Temple University, Philadelphia, Pennsylvania
Listeriosis

Arnold Louie, MD
Professor of Medicine, Molecular Genetics and Microbiology and Associate Director, Institute for Therapeutic Innovation, University of Florida College of Medicine, Orlando, Florida
Antibacterial Chemotherapy

Daniel R. Lucey, MD, MPH
Adjunct Professor, Department of Medicine/Infectious Diseases, Georgetown University Medical Center, Washington, D.C.
Anthrax

Jeffrey M. Lyness, MD
Professor of Psychiatry & Neurology and Senior Associate Dean for Academic Affairs, University of Rochester School of Medicine & Dentistry, Rochester, New York
Psychiatric Disorders in Medical Practice

C. Ronald MacKenzie, MD
C. Ronald MacKenzie Chair in Ethics and Medicine, Hospital for Special Surgery; Professor of Clinical Medicine and Medical Ethics, Weill Cornell Medical College, New York, New York
Surgical Treatment of Joint Diseases

Harriet L. MacMillan, CM, MD, MSc
Chedoke Health Chair in Child Psychiatry and Professor of Psychiatry & Behavioural Neurosciences and of Pediatrics, Offord Centre for Child Studies, McMaster University Michael G. DeGroote School of Medicine, Hamilton, Ontario, Canada
Intimate Partner Violence

Robert D. Madoff, MD
Professor of Surgery, University of Minnesota, Minneapolis, Minnesota
Diseases of the Rectum and Anus

Frank Maldarelli, MD, PhD
Head, Clinical Retrovirology Section, HIV Dynamics and Replication Program, NCI-Frederick, Frederick, Maryland
Biology of Human Immunodeficiency Viruses

Atul Malhotra, MD
Kenneth M. Moser Professor of Medicine, Chief of Pulmonary and Critical Care Medicine, Director of Sleep Medicine, University of California, San Diego, School of Medicine, La Jolla, California
Disorders of Ventilatory Control

Mark J. Manary, MD
Helene B. Roberson Professor of Pediatrics, Washington University School of Medicine in St. Louis, St. Louis, Missouri; Senior Lecturer, Department of Community Health, University of Malawi College of Medicine, Blantyre, Malawi
Protein-Energy Malnutrition

Peter Manu, MD
Professor of Medicine and Psychiatry, Donald and Barbara Zucker School of Medicine at Hofstra/Northwell, Hempstead, New York; Director of Medical Services, South Oaks Hospital, Amityville, New York
Medical Consultation in Psychiatry

Luis A. Marcos, MD, MPH
Associate Professor of Clinical Medicine, School of Medicine, Stony Brook University, Stony Brook, New York
Trematode Infections

Ariane J. Marelli, MD, MPH
Professor of Medicine and Director, McGill Adult Unit for Congenital Heart Disease, McGill University Health Centre, Montreal, Quebec, Canada
Congenital Heart Disease in Adults

Xavier Mariette, MD, PhD
Professor of Rheumatology, Université Paris-Sud, AP-HP, Le Kremlin Bicêtre, France
Sjögren Syndrome

Andrew R. Marks, MD
Wu Professor and Chair, Department of Physiology and Cellular Biophysics, Director, Helen and Clyde Wu Center for Molecular Cardiology, Columbia University Vagelos College of Physicians & Surgeons, New York, New York
Cardiac and Circulatory Function

Kieren A. Marr, MD
Professor of Medicine and Oncology and Director, Transplant and Oncology Infectious Diseases, John Hopkins University School of Medicine, Baltimore, Maryland
Approach to Fever and Suspected Infection in the Immunocompromised Host

Thomas J. Marrie, MD
Professor of Medicine and Dean Emeritus, Faculty of Medicine, Dalhousie University, Halifax, Nova Scotia, Canada
Legionella *Infections*

Paul Martin, MD
Professor of Medicine and Chief, Division of Gastroenterology and Hepatology, University of Miami Miller School of Medicine, Miami, Florida
Approach to the Patient with Liver Disease

Fernando J. Martinez, MD, MS
Bruce Webster Professor of Internal Medicine and Chief, Division of Pulmonary and Critical Care Medicine, Weill Cornell Medical College, New York, New York
Interstitial Lung Disease

Joel B. Mason, MD
Professor of Medicine and Nutrition, Tufts University School of Medicine; Director, Vitamins & Carcinogenesis Laboratory, U.S.D.A. Human Nutrition Research Center at Tufts University, Boston, Massachusetts
Vitamins, Trace Minerals, and Other Micronutrients

Henry Masur, MD
Chief, Critical Care Medicine Department, Clinical Center, National Institutes of Health, Bethesda, Maryland
Microbial Complications in Patients Infected with Human Immunodeficiency Virus

Amy J. Mathers, MD
Associate Professor of Medicine and Pathology, Associate Director of Clinical Microbiology, Medical Director Antimicrobial Stewardship, University of Virginia School of Medicine, Charlottesville, Virginia
Infections Due to Other Members of the Enterobacteriaceae, Including Management of Multidrug-Resistant Strains

Eric L. Matteson, MD, MPH
Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Infections of Bursae, Joints, and Bones

Michael A. Matthay, MD
Professor of Medicine and Anesthesia, University of California, San Francisco, San Francisco, California
Acute Respiratory Failure

Emeran A. Mayer, MD
Professor of Medicine and Psychiatry, Executive Director G. Oppenheimer Center for Neurobiology of Stress and Resilience, David Geffen School of Medicine at UCLA, Los Angeles, California
Functional Gastrointestinal Disorders: Irritable Bowel Syndrome, Dyspepsia, Esophageal Chest Pain, and Heartburn

Stephan A. Mayer, MD
William T. Gossett Endowed Chair of Neurology, Henry Ford Health System, Professor of Neurology, Wayne State University School of Medicine, Detroit, Michigan
Hemorrhagic Cerebrovascular Disease

F. Dennis McCool, MD
Professor of Medicine, Warren Alpert Medical School of Brown University, Providence, Rhode Island; Memorial Hospital of Rhode Island, Pawtucket, Rhode Island
Diseases of the Diaphragm, Chest Wall, Pleura, and Mediastinum

Iain McInnes, PhD
Professor of Experimental Medicine and Director, Institute of Infection, Immunity and Inflammation, University of Glasgow, Glasgow, United Kingdom
Rheumatoid Arthritis

William J. McKenna, MD
Emeritus Professor of Cardiology, Institute of Cardiovascular Science, University College London, London, United Kingdom
Diseases of the Myocardium and Endocardium

Vallerie McLaughlin, MD
Professor of Medicine, University of Michigan Medical School; Director, Pulmonary Hypertension Program, Ann Arbor, Michigan
Pulmonary Hypertension

John J.V. McMurray, BSc, MB ChB, MD
Professor of Medical Cardiology, British Heart Foundation Cardiovascular Research Centre, University of Glasgow; Honorary Consultant Cardiologist, Queen Elizabeth University Hospital Glasgow, Glasgow, Scotland, United Kingdom
Heart Failure: Management and Prognosis

Kenneth R. McQuaid, MD
Professor of Clinical Medicine and Vice-Chair, Department of Medicine, University of California, San Francisco, School of Medicine; Chief of Gastroenterology and of the Medical Service, San Francisco Veterans, Affairs Medical Center, San Francisco, California
Approach to the Patient with Gastrointestinal Disease

Paul S. Mead, MD, MPH
Chief, Bacterial Diseases Branch, Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado
Plague and Other Yersinia Infections

Robert T. Means, Jr., MD
Professor of Internal Medicine, East Tennessee State University James H. Quillen College of Medicine, Johnson City, Tennessee
Approach to the Anemias

Graeme Meintjes, MB ChB, MPH, PhD
Professor of Medicine, University of Cape Town, Cape Town, South Africa
Immune Reconstitution Inflammatory Syndrome in HIV/AIDS

Genevieve B. Melton-Meaux, MD, PhD
Professor of Surgery, University of Minnesota Medical School, Minneapolis, Minnesota
Diseases of the Rectum and Anus

Samuel T. Merrick, MD
Professor of Clinical Medicine, Weill Cornell Medical College, New York, New York
Systemic Manifestations of HIV/AIDS

Marc Michel, MD
Professor and Head of the Unit of Internal Medicine, Henri Mondor University Hospital, Assistance Publique Hopitaux de Paris, Université Paris-Est Créteil, Creteil, France
Autoimmune and Intravascular Hemolytic Anemias

Jonathan W. Mink, MD, PhD
Professor of Neurology, University of Rochester School of Medicine & Dentistry, Rochester, New York
Congenital, Developmental, and Neurocutaneous Disorders

William E. Mitch, MD
Professor of Medicine, Baylor College of Medicine, Houston, Texas
Chronic Kidney Disease

Bruce A. Molitoris, MD
Distinguished Professor of Medicine, Indiana University School of Medicine, Indianapolis, Indiana
Acute Kidney Injury

José G. Montoya, MD
Professor of Medicine, Division of Infectious Diseases and Geographic Medicine, Stanford University School of Medicine, Stanford, California; Director, Palo Alto Medical Foundation Toxoplasma Serology Laboratory, National Reference Center for the Study and Diagnosis of Toxoplasmosis, Palo Alto, California
Toxoplasmosis

Ernest Moy, MD, MPH
Executive Director, Office of Health Equity, Veterans Health Administration, Washington, D.C.
Measuring Health and Health Care

Debabrata Mukherjee, MD, MS
Professor and Chairman, Department of Internal Medicine, Chief, Cardiovascular Medicine, Texas Tech University Health Sciences Center, El Paso, Texas
Acute Coronary Syndrome: Unstable Angina and Non–ST Elevation Myocardial Infarction

Andrew H. Murr, MD
Professor and Chairman, Department of Otolaryngology-Head and Neck Surgery, University of California, San Francisco, School of Medicine, San Francisco, California
Approach to the Patient with Nose, Sinus, and Ear Disorders

Daniel M. Musher, MD
Distinguished Service Professor of Medicine and Professor of Molecular Virology and Microbiology, Baylor College of Medicine; Staff Physician, Infectious Disease Section, Michael E. DeBakey VA Medical Center, Houston, Texas
Overview of Pneumonia

Robert J. Myerburg, MD
Professor of Medicine and Physiology, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida
Approach to Cardiac Arrest and Life-Threatening Arrhythmias

Kari C. Nadeau, MD, PhD
Naddisy Family Foundation Professor of Allergy and Director, Sean N. Parker Center for Allergy and Asthma Research at Stanford University, Stanford, California
Approach to the Patient with Allergic or Immunologic Disease

Stanley J. Naides, MD
President, Stanley J. Naides, M.D., P.C., Dana Point, California
Arboviruses Causing Fever and Rash Syndromes

Theodore E. Nash, MD
Principal Investigator, Clinical Parasitology Section, National Institutes of Allergy and Infectious Diseases, National Institutes of Health, Bethesda, Maryland
Giardiasis

Avindra Nath, MD
Chief, Section of Infections of the Nervous System, National Institutes of Neurological Diseases and Stroke, National Institutes of Health, Bethesda, Maryland
Cytomegalovirus, Epstein-Barr Virus, and Slow Virus Infections of the Central Nervous System; Meningitis: Bacterial, Viral, and Other; Brain Abscess and Parameningeal Infections

Genevieve Neal-Perry, MD, PhD
Professor of Obstetrics and Gynecology and Director of the Reproductive Endocrinology and Infertility Center, University of Washington School of Medicine, Seattle, Washington
Menopause

Anne T. Neff, MD
Professor of Medicine, Hematology/Medical Oncology, Cleveland Clinic Lerner College of Medicine; Staff Physician, Cleveland Clinic Foundation, Cleveland, Ohio
Von Willebrand Disease and Hemorrhagic Abnormalities of Platelet and Vascular Function

Eric G. Neilson, MD
Vice President for Medical Affairs and Lewis Landsberg Dean and Professor of Medicine and of Cell and Developmental Biology, Northwestern University Feinberg School of Medicine, Chicago, Illinois
Tubulointerstitial Diseases

Christina A. Nelson, MD, MPH
Medical Officer, Bacterial Diseases Branch, Division of Vector-Borne Diseases, Centers for Disease Control and Prevention, Fort Collins, Colorado
Plague and Other Yersinia *Infections*

Lewis S. Nelson, MD
Professor and Chair, Department of Emergency Medicine; Director, Division of Medical Toxicology, Rutgers New Jersey Medical School, Newark, New Jersey
Acute Poisoning

Eric J. Nestler, MD, PhD
Nash Family Professor of Neuroscience, Director, Friedman Brain Institute, Icahn School of Medicine at Mount Sinai, New York, New York
Biology of Addiction

Anne B. Newman, MD, MPH
Distinguished Professor and Chair, Department of Epidemiology, Katherine M. Detre Endowed Chair of Population Health Sciences; Director, Center for Aging and Population Health, Professor of Medicine, and Clinical and Translational Science Graduate School of Public Health, University of Pittsburgh; Clinical Director, Aging Institute of UPMC and Pitt, Pittsburgh, Pennsylvania
Epidemiology of Aging: Implications of an Aging Society

Lindsay E. Nicolle, MD
Professor Emeritus, Department of Internal Medicine, University of Manitoba, Winnipeg, Manitoba, Canada
Approach to the Patient with Urinary Tract Infection

Lynnette K. Nieman, MD
Senior Investigator, Diabetes, Endocrinology and Obesity Branch, NIDDK/NIH, Bethesda, Maryland
Approach to the Patient with Endocrine Disease; Adrenal Cortex; Polyglandular Disorders

Gaetane Nocturne, MD, PhD
Associate Professor of Rheumatology, Université Paris-Sud, AP-HP, Le Kremlin Bicêtre, France
Sjögren Syndrome

Christopher M. O'Connor, MD
Adjunct Professor of Medicine, Duke University School of Medicine, Durham, North Carolina; CEO, Inova Heart and Vascular Institute, Fairfax, Virginia
Heart Failure: Pathophysiology and Diagnosis

Francis G. O'Connor, MD, MPH
Professor and Medical Director, Consortium for Health and Military Performance, Uniformed Services University of the Health Sciences, Bethesda, Maryland
Disorders Due to Heat and Cold; Rhabdomyolysis

Patrick G. O'Connor, MD, MPH
Dan Adams and Amanda Adams Professor and Chief, General Internal Medicine, Yale University School of Medicine, New Haven, Connecticut
Alcohol Use Disorders

James R. O'Dell, MD
Bruce Professor and Vice Chair of Internal Medicine, University of Nebraska Medical Center College of Medicine; Chief of Rheumatology, Medicine, Omaha VA, Omaha, Nebraska
Rheumatoid Arthritis

Anne E. O'Donnell, MD
The Nehemiah and Naomi Cohen Chair in Pulmonary Disease Research, Chief, Division of Pulmonary, Critical Care and Sleep Medicine, Georgetown University Medical Center, Washington, D.C.
Bronchiectasis, Atelectasis, Cysts, and Localized Lung Disorders

Jae K. Oh, MD
Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota; Director, Heart Vascular Stroke Institute, Samsung Medical Center, Seoul, Gangnam, South Korea
Pericardial Diseases

Pablo C. Okhuysen, MD
Professor of Infectious Diseases, Infection Control and Employee Health, University of Texas MD Anderson Cancer Center; Adjunct Professor of Infectious Diseases, Baylor College of Medicine; Adjunct Professor of Epidemiology, Human Genetics and Environmental Health, University of Texas School of Public Health; Adjunct Professor of Infectious Diseases, McGovern Medical School at the University of Texas Health Science Center at Houston, Houston, Texas
Approach to the Patient with Suspected Enteric Infection

Michael S. Okun, MD
Professor and Chair of Neurology, Fixel Institute for Neurological Diseases, University of Florida College of Medicine, Gainesville, Florida
Parkinsonism; Other Movement Disorders

Jeffrey E. Olgin, MD
Gallo-Chatterjee Distinguished Professor and Chief of Cardiology, University of California, San Francisco, School of Medicine, San Francisco, California
Approach to the Patient with Suspected Arrhythmia

Nancy J. Olsen, MD
Professor of Medicine, Penn State Milton S. Hershey Medical Center, Hershey, Pennsylvania
Biologic Agents and Signaling Inhibitors

Walter A. Orenstein, MD, DSc
Professor of Medicine, Pediatrics, Epidemiology & Global Health, Emory University School of Medicine; Associate Director, Emory Vaccine Center, Atlanta, Georgia
Immunization

John J. O'Shea, MD
Scientific Director, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland
Biologic Agents and Signaling Inhibitors

Douglas R. Osmon, MD
Professor of Medicine, Mayo Clinic College of Medicine and Science; Consultant, Division Infectious Disease, Mayo Clinic, Rochester, Minnesota
Infections of Bursae, Joints, and Bones

Catherine M. Otto, MD
J. Ward Kennedy-Hamilton Endowed Chair in Cardiology and Professor of Medicine, University of Washington School of Medicine; Director, Heart Valve Clinic, Associate Director, Echocardiography, University of Washington Medical Center, Seattle, Washington
Echocardiography

Martin G. Ottolini, MD
Professor of Pediatrics and Director, Capstone Student Research Program, Uniformed Services University of the Health Sciences; Consultant, Pediatric Infectious Diseases, Pediatrics, Walter Reed National Military Medical Center, Bethesda, Maryland
Measles

Peter G. Pappas, MD
Professor of Medicine, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama
Candidiasis; Mycetoma and Dematiaceous Fungal Infections

Ben Ho Park, MD, PhD
The Donna S. Hall Professor of Medicine, Vanderbilt University School of Medicine; Co-Leader Breast Cancer Research; Director of Precision Oncology; Associate Director for Translational Research, Vanderbilt-Ingram Cancer Center, Nashville, Tennessee
Cancer Biology and Genetics

Pankaj Jay Pasricha, MD
Professor of Medicine and Neuroscience, Johns Hopkins University School of Medicine, Baltimore, Maryland
Gastrointestinal Endoscopy

Manisha Patel, MD, MS
Measles, Mumps, Rubella, Herpesvirus, and Domestic Polio Epidemiology Team Lead, National Center for Immunization and Respiratory Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia
Mumps

Robin Patel, MD
Elizabeth P. and Robert E. Allen Professor of Individualized Medicine and Professor of Medicine and of Microbiology; Chair, Division of Clinical Microbiology; Consultant, Divisions of Clinical Microbiology and Infectious Diseases; Director, Infectious Diseases Research Laboratory, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Introduction to Microbial Disease: Pathophysiology and Diagnostics

David L. Paterson, MBBS, PhD
Professor of Medicine and Director, Centre for Clinical Research, University of Queensland, Herston, Queensland; Consultant Infectious Diseases Physician, Department of Infectious Diseases, Royal Brisbane and Women's Hospital, Brisbane, Australia
Infections Due to Other Members of the Enterobacteriaceae, Including Management of Multidrug-Resistant Strains

Jean-Michel Pawlotsky, MD, PhD
Professor, Department of Virology, Henri Mondor University Hospital, Creteil, France
Acute Viral Hepatitis; Chronic Viral and Autoimmune Hepatitis

Thomas H. Payne, MD
Professor of Medicine, University of Washington School of Medicine; Medical Director, Information Technology Services, UW Medicine, Seattle, Washington
Statistical Interpretation of Data and Using Data for Clinical Decisions

Richard D. Pearson, MD
Professor Emeritus of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
Antiparasitic Therapy

Trish M. Perl, MD, MSc
Jay Sanford Professor of Medicine and Chief of Infectious Diseases and Geographic Medicine, University of Texas Southwestern Medical Center Dallas, Texas
Enterococcal Infections

Michael A. Pesce, PhD
Professor Emeritus of Pathology and Cell Biology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Reference Intervals and Laboratory Values

Brett W. Petersen, MD, MPH
Epidemiology Team Lead, Poxvirus and Rabies Branch, Centers for Disease Control and Prevention, Atlanta, Georgia
Smallpox, Monkeypox, and Other Poxvirus Infections

William A. Petri, Jr., MD, PhD
Wade Hampton Frost Professor of Epidemiology and Vice Chair for Research, Department of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
Relapsing Fever and Other Borrelia *Infections; African Sleeping Sickness; Amebiasis*

Marc A. Pfeffer, MD, PhD
Dzau Professor of Medicine, Harvard Medical School; Senior Physician, Brigham and Women's Hospital, Boston, Massachusetts
Heart Failure: Management and Prognosis

David S. Pisetsky, MD, PhD
Professor of Medicine and Immunology, Duke University School of Medicine, Chief, Rheumatology, VA Medical Center, Durham, North Carolina
Laboratory Testing in the Rheumatic Diseases

Frank Powell, PhD
Professor of Medicine, University of California, San Diego, School of Medicine, La Jolla, California
Disorders of Ventilatory Control

Reed E. Pyeritz, MD, PhD
Professor of Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Inherited Diseases of Connective Tissue

Thomas C. Quinn, MD, MSc
Professor of Medicine and Pathology, Director, Center for Global Health, Johns Hopkins University School of Medicine; Associate Director, National Institute of Allergy and Infectious Diseases, National Institutes of Health, Baltimore, Maryland
Epidemiology and Diagnosis of Human Immunodeficiency Virus Infection and Acquired Immunodeficiency Syndrome

Jai Radhakrishnan, MD, MS
Professor of Medicine, Columbia University Vagelos College of Physicians and Surgeons; Clinical Chief, Division of Nephrology, Columbia University Irving Medical Center, New York, New York
Glomerular Disorders and Nephrotic Syndromes

Jerald Radich, MD
Associate Professor of Medical Oncology, Clinical Research Division, Fred Hutchinson Cancer Research Center and University of Washington School of Medicine, Seattle, Washington
Chronic Myeloid Leukemia

Petros I. Rafailidis, MD, PhD, MSc
Assistant Professor Internal Medicine-Infectious Diseases, Democritus University of Thrace; Beta University Department of Internal Medicine, University General Hospital of Greece, Alexandroupolis, Greece; Senior Researcher, Alfa Institute of Biomedical Sciences, Athens, Greece
Pseudomonas *and Related Gram-Negative Bacillary Infections*

Ganesh Raghu, MD
Professor of Medicine and Laboratory Medicine (adjunct), University of Washington School of Medicine; Director, Center for Interstitial Lung Diseases, UW Medicine; Co-Director, Scleroderma Clinic, University of Washington Medical Center, Seattle, Washington
Interstitial Lung Disease

Margaret V. Ragni, MD, MPH
Professor of Medicine, and Clinical Translational Science, University of Pittsburgh School of Medicine; Director, Hemophilia Center of Western Pennsylvania, Pittsburgh, Pennsylvania
Hemorrhagic Disorders: Coagulation Factor Deficiencies

Srinivasa N. Raja, MD
Professor of Anesthesiology, Critical Care Medicine, and Neurology; Director of Pain Research, Division of Pain Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland
Pain

S. Vincent Rajkumar, MD
Edward W. and Betty Knight Scripps Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Plasma Cell Disorders

James D. Ralston, MD, MPH
Senior Investigator, Kaiser Permanente Washington Health Research Institute, Seattle, Washington
Comprehensive Chronic Disease Management

Stuart H. Ralston, MB ChB
Professor of Rheumatology, University of Edinburgh, Edinburgh, United Kingdom
Paget Disease of Bone

Didier Raoult, MD, PhD
Professor, Aix-Marseille Université, Faculté de Médecine, Chief, Institut Hospitalo-Universitaire Méditerranée-Infection, Marseille, France
Bartonella *Infections; Rickettsial Infections*

Adam J. Ratner, MD, MPH
Associate Professor of Pediatrics and Microbiology and Chief, Division of Pediatric Infectious Diseases, New York University School of Medicine, New York, New York
Haemophilus *and* Moraxella *Infections*

Annette C. Reboli, MD
Dean and Professor of Medicine, Cooper Medical School of Rowan University and Cooper University Hospital, Camden, New Jersey
Erysipelothrix *Infections*

K. Rajender Reddy, MD
Ruimy Family President's Distinguished Professor of Internal Medicine, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Bacterial, Parasitic, Fungal, and Granulomatous Liver Diseases

Donald A. Redelmeier, MD
Professor of Medicine, University of Toronto; Canada Research Chair, Medical Decision Science; Senior Scientist, Evaluative Clinical Sciences, Sunnybrook Research Institute; Staff Physician, Sunnybrook Health Sciences Centre, Toronto, Ontario, Canada
Postoperative Care and Complications

Susan E. Reef, MD
Medical Epidemiologist, Global Immunization Division, Centers for Disease Control and Prevention, Atlanta, Georgia
Rubella (German Measles)

John Reilly, MD
Richard D. Krugman Endowed Chair and Dean, School of Medicine, and Vice Chancellor for Health Affairs, University of Colorado School of Medicine, Aurora, Colorado
Chronic Obstructive Pulmonary Disease

Megan E. Reller, MD, PhD
Associate Professor of Medicine, Duke University School of Medicine, Durham, North Carolina
Zoonoses

Neil M. Resnick, MD
Thomas Detre Professor of Medicine and Chief, Division of Geriatric Medicine and Gerontology, University of Pittsburgh Medical Center, Pittsburgh, Pennsylvania
Urinary Incontinence

David B. Reuben, MD
Archstone Professor and Chief, Division of Geriatrics, David Geffen School of Medicine at UCLA, Los Angeles, California
Geriatric Assessment

Jennifer G. Robinson, MD, MPH
Professor of Epidemiology and Medicine, Director, Prevention Intervention Center, Department of Epidemiology, University of Iowa Carver College of Medicine, Iowa City, Iowa
Disorders of Lipid Metabolism

Inez Rogatsky, PhD
Professor of Microbiology and Immunology, Weill Cornell Medical College; Senior Scientist, Arthritis and Tissue Degeneration Program, Hospital for Special Surgery, New York, New York
Immunomodulatory Drugs

Joseph G. Rogers, MD
Professor of Medicine, Duke University School of Medicine, Durham, North Carolina
Heart Failure: Pathophysiology and Diagnosis

Jean-Marc Rolain, PharmD, PhD
Professor, Aix-Marseille Université and Institut Hospitalo-Universitaire Méditerranée Infection, Marseille, France
Bartonella *Infections*

Barrett J. Rollins, MD, PhD
Linde Family Professor of Medicine, Dana-Farber Cancer Institute, Brigham & Women's Hospital and Harvard Medical School, Boston, Massachusetts
Histiocytoses

José R. Romero, MD
Horace C. Cabe Professor of Infectious Diseases, Department of Pediatrics, University of Arkansas for Medical Sciences; Director, Pediatric Infectious Diseases Section, Arkansas Children's Hospital; Director, Clinical Trials Research, Arkansas Children's Research Institute, Little Rock, Arkansas
Enteroviruses

Karen Rosene-Montella, MD
President, Karen Rosene, LLC; Senior Consultant the Levinson Institute; Professor Emerita of Medicine, Warren Alpert Medical School at Brown University, Providence, Rhode Island
Common Medical Problems in Pregnancy

Philip J. Rosenthal, MD
Professor of Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Malaria

James A. Russell, MD
Professor of Medicine, University of British Columbia, Vancouver, British Columbia
Shock Syndromes Related to Sepsis

Anil K. Rustgi, MD
Irving Professor of Medicine, Director, Herbert Irving Comprehensive Cancer Center; Chief, NewYork-Presbyterian Hospital/Columbia University Irving Medical Center Cancer Service, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Neoplasms of the Esophagus and Stomach

Daniel E. Rusyniak, MD
Professor of Emergency Medicine, Indiana University School of Medicine, Indianapolis, Indiana
Chronic Poisoning: Trace Metals and Others

George Sakoulas, MD
Associate Adjunct Professor, Division of Host-Microbe Systems & Therapeutics, University of California, San Diego, School of Medicine, La Jolla, California; Infectious Disease Consultant, Sharp Healthcare, San Diego, California
Staphylococcal Infections

Robert A. Salata, MD
STERIS Chair of Excellence in Medicine, Professor and Chairman, Department of Medicine, Case Western Reserve University School of Medicine; Physician-in-Chief, Master Clinician in Infectious Diseases, University Hospitals Cleveland Medical Center, Cleveland, Ohio
Brucellosis

Jane E. Salmon, MD
Collette Kean Research Chair, Hospital for Special Surgery; Professor of Medicine, Weill Cornell Medical College, New York, New York
Mechanisms of Immune-Mediated Tissue Injury

Edsel Maurice T. Salvana, MD, DTM&H
Associate Professor of Medicine and Director, Institute of Molecular Biology and Biotechnology, National Institutes of Health, University of the Philippines College of Medicine, Manila, Philippines
Brucellosis

Nanette Santoro, MD
Professor and E. Stewart Taylor Chair, Department of Obstetrics and Gynecology, University of Colorado School of Medicine, Aurora, Colorado
Menopause

Renato M. Santos, MD
Assistant Professor of Medicine, Emory University School of Medicine, Emory Heart and Vascular Center, John's Creek, Georgia
Vascular Disorders of the Kidney

Peter A. Santucci, MD
Professor of Medicine, Loyola University Medical Center, Maywood, Illinois
Electrophysiologic Interventional Procedures and Surgery

Patrice Savard, MD, MSc
Assistant Professor of Microbiology and Immunology, Université de Montréal; Director, Unité de Prévention, Centre Hospitalier de l'Université de Montréal, Québec, Canada
Enterococcal Infections

Michael N. Sawka, PhD
Professor, School of Biological Sciences, Georgia Institute of Technology, Atlanta, Georgia
Disorders Due to Heat and Cold

Paul D. Scanlon, MD
Professor of Medicine, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Respiratory Testing and Function

Andrew I. Schafer, MD
Professor of Medicine, Director, Richard T. Silver Center for Myeloproliferative Neoplasms, Weill Cornell Medical College, New York, New York
Approach to Medicine, the Patient, and the Medical Profession: Medicine as a Learned and Humane Profession; Thrombotic Disorders: Hypercoagulable States; Approach to the Patient with Bleeding and Thrombosis; Hemorrhagic Disorders: Disseminated Intravascular Coagulation, Liver Failure, and Vitamin K Deficiency

William Schaffner, MD
Professor of Preventive Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee
Tularemia and Other Francisella *Infections*

W. Michael Scheld, MD
Bayer-Gerald L. Mandell Professor of Infectious Diseases; Professor of Medicine; Clinical Professor of Neurosurgery; David A. Harrison Distinguished Educator, University of Virginia Health System, Charlottesville, Virginia
Introduction to Microbial Disease: Pathophysiology and Diagnostics

Manuel Schiff, MD, PhD
Associate Professor of Pediatrics and Head of Metabolic Unit, Reference Center for Inborn Errors of Metabolism, Robert Debré University Hospital, Paris, France
Homocystinuria and Hyperhomocysteinemia

Michael L. Schilsky, MD
Professor of Medicine and Surgery, Yale University School of Medicine, New Haven, Connecticut
Wilson Disease

Robert T. Schooley, MD
Professor of Medicine, University of California, San Diego, School of Medicine, San Diego, California
Epstein-Barr Virus Infection

David L. Schriger, MD, MPH
Professor of Emergency Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California
Approach to the Patient with Abnormal Vital Signs

Lynn M. Schuchter, MD
Professor of Medicine, C. Willard Robinson Professor and Chair of the Division of Hematology-Oncology, University of Pennsylvania Perelman School of Medicine, Philadelphia, Pennsylvania
Melanoma and Nonmelanoma Skin Cancers

Sam Schulman, MD, PhD
Professor of Medicine, McMaster University Michael G. DeGroote School of Medicine, Hamilton, Ontario, Canada
Antithrombotic and Antiplatelet Therapy

Lawrence B. Schwartz, MD, PhD
Charles and Evelyn Thomas Professor of Medicine, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia
Systemic Anaphylaxis, Food Allergy, and Insect Sting Allergy

Carlos Seas, MD, MSc
Associate Professor of Medicine, Universidad Peruana Cayetano Heredia; Vice Director, Alexander von Humboldt Tropical Medicine Institute, Attending Physician, Infectious and Tropical Medicine, Hospital Nacional Cayetano Heredia, Lima, Peru
Cholera and Other Vibrio *Infections*

Steven A. Seifert, MD
Professor of Emergency Medicine, University of New Mexico School of Medicine; Medical Director, New Mexico Poison and Drug Information Center, Albuquerque, New Mexico
Envenomation, Bites, and Stings

Julian Lawrence Seifter, MD
James G. Haidas Distinguished Chair in Medicine, Brigham and Women's Hospital and Harvard Medical School, Boston, Massachusetts
Potassium Disorders; Acid-Base Disorders

Duygu Selcen, MD
Professor of Neurology and Pediatrics, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Muscle Diseases

Carol E. Semrad, MD
Professor of Medicine, University of Chicago Pritzker School of Medicine, Chicago, Illinois
Approach to the Patient with Diarrhea and Malabsorption

Harry Shamoon, MD
Professor of Medicine and Senior Associate Dean for Clinical & Translational Research, Albert Einstein College of Medicine; Director, Harold and Muriel Block Institute for Clinical and Translational Research at Einstein and Montefiore, Bronx, New York
Diabetes Mellitus

Pamela J. Shaw, DBE, MBBS, MD
Professor of Neurology, Sheffield Institute for Translational Neuroscience, University of Sheffield, Sheffield, United Kingdom
Amyotrophic Lateral Sclerosis and Other Motor Neuron Diseases

Beth H. Shaz, MD
Chief Medical and Scientific Officer, New York Blood Center; Adjunct Assistant Professor, Department of Pathology and Cell Biology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Transfusion Medicine

Robert L. Sheridan, MD
Professor of Surgery, Harvard Medical School and Massachusetts General Hospital, COL (ret), U.S. Army, Boston, Massachusetts
Medical Aspects of Trauma and Burns

Stuart Sherman, MD
Glen A. Lehman Professor of Gastroenterology and Professor of Medicine and Radiology; Clinical Director of Gastroenterology and Hepatology, Indiana University School of Medicine, Indianapolis, Indiana
Diseases of the Gallbladder and Bile Ducts

Wun-Ju Shieh, MD, MPH, PhD
Deputy Chief/Medical Officer, Infectious Diseases Pathology Branch, Centers for Disease Control and Prevention, Atlanta, Georgia
Leptospirosis

Michael E. Shy, MD
Professor of Neurology and Pediatrics, University of Iowa Carver College of Medicine, Iowa City, Iowa
Peripheral Neuropathies

Ellen Sidransky, MD
Chief, Section of Molecular Neurogenetics, Medical Genetics Branch, NHGRI, National Institutes of Health, Bethesda, Maryland
Lysosomal Storage Diseases

Richard M. Siegel, MD, PhD
Clinical Director and Chief, Autoimmunity Branch, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, Maryland
The Systemic Autoinflammatory Diseases

Costi D. Sifri, MD
Professor of Medicine and Medical Director, Immunocompromised Infectious Diseases Program, University of Virginia Health System, Charlottesville, Virginia
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Robert F. Siliciano, MD, PhD
Professor of Medicine, Johns Hopkins University School of Medicine; Investigator, Howard Hughes Medical Institute, Baltimore, Maryland
Immunopathogenesis of Human Immunodeficiency Virus Infection

Michael S. Simberkoff, MD
Professor of Medicine, New York University School of Medicine and Chief of Staff, VA New York Harbor Healthcare System, New York, New York
Haemophilus *and* Moraxella *Infections*

David L. Simel, MD, MHS
Professor of Medicine, Duke University School of Medicine; Chief of Medical Service, Durham Veterans Affairs Medical Center, Durham, North Carolina
Approach to the Patient: History and Physical Examination

Karl Skorecki, MD
Professor and Dean, Azriel Faculty of Medicine, Bar-Ilan University, Ramat Gan, Israel
Regenerative Medicine, Cell, and Gene Therapies

Arthur S. Slutsky, CM, MD
Professor of Medicine, Director, Interdepartmental Division of Critical Care Medicine, University of Toronto; Vice President (Research), St Michael's Hospital; Keenan Research Centre, Li Ka Shing Knowledge Institute, Toronto, Ontario, Canada
Mechanical Ventilation

Eric J. Small, MD
Professor of Medicine, Deputy Director and Chief Scientific Officer, UCSF Helen Diller Family Comprehensive Cancer Center, University of California, San Francisco, School of Medicine, San Francisco, California
Prostate Cancer

Gerald W. Smetana, MD
Professor of Medicine, Harvard Medical School and Physician, Division of General Medicine and Primary Care, Beth Israel Deaconess Medical Center, Boston, Massachusetts
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Gordon Smith, MD
Professor and Chair of Neurology, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia
Peripheral Neuropathies

Frederick S. Southwick, MD
Professor of Medicine, University of Florida College of Medicine, Gainesville, Florida
Nocardiosis

Allen M. Spiegel, MD
Dean Emeritus and Professor of Medicine, Albert Einstein College of Medicine, Bronx, New York
Principles of Endocrinology; Polyglandular Disorders

Robert Spiera, MD
Professor of Clinical Medicine, Weill Cornell Medical College; Director, Scleroderma, Vasculitis, & Myositis Center, Hospital for Special Surgery, New York, New York
Giant Cell Arteritis and Polymyalgia Rheumatica

Stanley M. Spinola, MD
Professor of Medicine, Microbiology and Immunology, Pathology and Laboratory Medicine and Chair, Microbiology and Immunology, Indiana University School of Medicine, Indianapolis, Indiana
Chancroid

Sally P. Stabler, MD
Professor of Medicine and Cleo Scott & Mitchell Vincent Allen Chair in Hematology Research, University of Colorado School of Medicine, Aurora, Colorado
Megaloblastic Anemias

Stephanie M. Stanford, PhD
Assistant Professor of Medicine, University of California, San Diego, School of Medicine, La Jolla, California
Mechanisms of Inflammation and Tissue Repair

Paul Stark, MD
Professor Emeritus of Radiology, University of California, San Diego, School of Medicine; Chief of Cardiothoracic Radiology, VA San Diego Healthcare System, La Jolla, California
Imaging in Pulmonary Disease

David P. Steensma, MD
Associate Professor of Medicine, Harvard Medical School and Physician, Dana-Farber Cancer Institute, Boston, Massachusetts
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Theodore S. Steiner, MD
Professor and Associate Head, Division of Infectious Diseases, University of British Columbia, Vancouver, British Columbia, Canada
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David S. Stephens, MD
Stephen W. Schwarzmann Distinguished Professor of Medicine and Chair, Department of Medicine, Emory University School of Medicine, Atlanta, Georgia
Neisseria Meningitidis *Infections*

David A. Stevens, MD
Professor of Medicine, Stanford University School of Medicine, Stanford, California; President and Principal Investigator, Infectious Diseases Research Laboratory, California Institute for Medical Research, San Jose, California
Systemic Antifungal Agents

Dennis L. Stevens, PhD, MD
Professor of Medicine, University of Washington School of Medicine, Seattle, Washington; Research & Development Service, Veterans Affairs Medical Center, Boise, Idaho
Nonpneumococcal Streptococcal Infections and Rheumatic Fever

James K. Stoller, MD, MS
Professor and Chairman, Education Institute, Jean Wall Bennett Professor of Medicine, Samson Global Leadership Endowed Chair, Cleveland Clinic Lerner College of Medicine, Cleveland Clinic, Cleveland, Ohio
Respiratory Monitoring in Critical Care

John H. Stone, MD, MPH
Professor of Medicine, Harvard Medical School, Director, Clinical Rheumatology, Massachusetts General Hospital, Boston, Massachusetts
The Systemic Vasculitides

Richard M. Stone, MD
Professor of Medicine, Harvard Medical School; Chief of the Medical Staff, Dana-Farber Cancer Institute, Boston, Massachusetts
Myelodysplastic Syndromes

Raymond A. Strikas, MD, MPH
Medical Officer, Immunization Services Division, Centers for Disease Control and Prevention, Atlanta, Georgia
Immunization

Edwin P. Su, MD
Associate Professor of Clinical Orthopaedics, Weill Cornell Medical College; Associate Attending Orthopaedic Surgeon, Hospital for Special Surgery, New York, New York
Surgical Treatment of Joint Diseases

Roland W. Sutter, MD, MPH&TM
Special Adviser to Director, Polio Eradication Department, World Health Organization, Geneva, Switzerland
Diphtheria and Other Corynebacterium *Infections*

Ronald S. Swerdloff, MD
Professor of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California; Chief, Division of Endocrinology, Metabolism and Nutrition, Harbor-UCLA Medical Center, Senior Investigator, Los Angeles Biomedical Research Institute, Torrance, California
The Testis and Male Hypogonadism, Infertility, and Sexual Dysfunction

Heidi Swygard, MD, MPH
Professor of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina
Approach to the Patient with a Sexually Transmitted Infection

Megan Sykes, MD
Michael J. Friedlander Professor of Medicine, Director, Columbia Center for Translational Immunology, Columbia University Vagelos College of Physicians and Surgeons, New York, New York
Transplantation Immunology

H. Keipp Talbot, MD, MPH
Associate Professor of Medicine, Vanderbilt University School of Medicine, Nashville, Tennessee
Respiratory Syncytial Virus

Marian Tanofsky-Kraff, PhD
Professor of Medical and Clinical Psychology and of Medicine, Uniformed Services University of the Health Sciences, Bethesda, Maryland
Eating Disorders

Susan M. Tarlo, MBBS
Professor of Medicine, University of Toronto; Respiratory Physician, University Health Network, Toronto, Ontario, Canada
Occupational Lung Disease

Paul S. Teirstein, MD
Chief of Cardiology; Director, Interventional Cardiology, Scripps Clinic, La Jolla, California
Interventional and Surgical Treatment of Coronary Artery Disease

Sam R. Telford, III, ScD
Professor of Infectious Disease and Global Health, Tufts University School of Veterinary Medicine, North Grafton, Massachusetts
Babesiosis and Other Protozoan Diseases

Rajesh V. Thakker, MD
May Professor of Medicine, Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom
The Parathyroid Glands, Hypercalcemia, and Hypocalcemia

Judith Therrien, MD
Professor of Medicine, Jewish General Hospital, Montreal, Quebec, Canada
Congenital Heart Disease in Adults

George R. Thompson, III, MD
Associate Professor of Clinical Medicine, University of California, Davis School of Medicine, Davis, California
Endemic Mycoses

Antonella Tosti, MD
Fredric Brandt Endowed Professor of Dermatology, Dr. Phillip Frost Department of Dermatology and Cutaneous Surgery, University of Miami Miller School of Medicine, Miami, Florida
Diseases of Hair and Nails

Indi Trehan, MD, MPH, DTM&H
Associate Professor of Pediatrics, Washington University School of Medicine in St. Louis, St. Louis, Missouri; Executive Director and Medical Director, Lao Friends Hospital for Children, Luang Prabang, Lao People's Democratic Republic
Protein-Energy Malnutrition

Ronald B. Turner, MD
Professor of Pediatrics, University of Virginia School of Medicine, Charlottesville, Virginia
The Common Cold

Anthony Michael Valeri, MD
Associate Professor of Medicine, Vagelos College of Physicians and Surgeons; Medical Director, Hemodialysis, Columbia University Irving Medical Center, New York, New York
Treatment of Irreversible Renal Failure

John Varga, MD
John and Nancy Hughes Distinguished Professor of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois
Systemic Sclerosis (Scleroderma)

Bradley V. Vaughn, MD
Professor of Neurology, University of North Carolina, Chapel Hill, North Carolina
Sleep Disorders

Alan P. Venook, MD
Professor of Clinical Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Liver and Biliary Tract Cancers

Joseph G. Verbalis, MD
Professor of Medicine, Georgetown University; Chief, Endocrinology and Metabolism, Georgetown University Hospital, Washington, D.C.
Posterior Pituitary

Ronald G. Victor, MD[†]
Formerly Burns & Allen Professor of Medicine, Smidt Heart Institute, Cedars-Sinai Medical Center, Los Angeles, California
Arterial Hypertension

Angela Vincent, MBBS, MSc
Emeritus Professor, Nuffield Department of Clinical Neurosciences, University of Oxford, Oxford, United Kingdom
Disorders of Neuromuscular Transmission

Tonia L. Vincent, PhD
Professor of Musculoskeletal Biology, Arthritis Research UK Senior Fellow and Consultant Rheumatologist; Director, Arthritis Research UK Centre for Osteoarthritis Pathogenesis, University of Oxford, Oxford, England
Osteoarthritis

Robert M. Wachter, MD
Holly Smith Professor and Chairman, Department of Medicine, University of California, San Francisco, School of Medicine, San Francisco, California
Quality, Safety, and Value

Edward H. Wagner, MD, MPH
Director Emeritus, MacColl Center for Health Care Innovation, Group Health Research Institute, Seattle, Washington
Comprehensive Chronic Disease Management

Edward E. Walsh, MD
Professor of Medicine, University of Rochester School of Medicine & Dentistry; Unit Chief, Infectious Diseases, Rochester General Hospital, Rochester, New York
Respiratory Syncytial Virus

Thomas J. Walsh, MD
Professor of Medicine, Pediatrics, Microbiology & Immunology and Chief, Infectious Diseases Translational Research Laboratory, Weill Cornell Medical College, New York, New York; Adjunct Professor of Pathology, Johns Hopkins University School of Medicine; Adjunct Professor of Medicine, University of Maryland School of Medicine, Baltimore, Maryland
Aspergillosis

Jeremy D. Walston, MD
Raymond and Anna Lublin Professor of Geriatric Medicine, Johns Hopkins University School of Medicine, Baltimore, Maryland
Common Clinical Sequelae of Aging

[†] Deceased.

Roland B. Walter, MD, PhD, MS
Associate Professor of Medicine, University of Washington School of Medicine and Associate Member, Clinical Research Division, Fred Hutchinson Cancer Research Center, Seattle, Washington
The Acute Leukemias

Christina Wang, MD
Professor of Medicine, David Geffen School of Medicine at UCLA, Los Angeles, California; Clinical and Translational Science Institute, Los Angeles Biomedical Research Institute and Division of Endocrinology, Department of Medicine, Harbor-UCLA Medical Center, Torrance, California
The Testis and Male Hypogonadism, Infertility, and Sexual Dysfunction

Lorraine B. Ware, MD
Professor of Medicine, Pathology, Microbiology, and Immunology, Vanderbilt University School of Medicine, Nashville, Tennessee
Acute Respiratory Failure

Cirle A. Warren, MD
Associate Professor of Medicine, University of Virginia School of Medicine, Charlottesville, Virginia
Cryptosporidiosis

John T. Watson, MD, MSc
Respiratory Viruses Branch, Division of Viral Diseases, Centers for Disease Control and Prevention, Atlanta, Georgia
Coronaviruses

Thomas J. Weber, MD
Associate Professor of Medicine, Duke University School of Medicine, Durham, North Carolina
Approach to the Patient with Metabolic Bone Disease; Osteoporosis

Geoffrey A. Weinberg, MD
Professor of Pediatrics, University of Rochester School of Medicine & Dentistry; Director, Clinical Pediatric Infectious Diseases & Pediatric HIV Program, Golisano Children's Hospital, University of Rochester Medical Center, Rochester, New York
Parainfluenza Viral Disease

David A. Weinstein, MD, MMSc
Professor of Pediatrics, University of Connecticut School of Medicine, Farmington, Connecticut; Director, Glycogen Storage Disease Program, Connecticut Children's Medical Center, Hartford, Connecticut
Glycogen Storage Diseases

Robert S. Weinstein, MD
Professor of Medicine, University of Arkansas for Medical Sciences; Staff Endocrinologist, Central Arkansas Veterans Health Care System, Little Rock, Arkansas
Osteomalacia and Rickets

Roger D. Weiss, MD
Professor of Psychiatry, Harvard Medical School, Boston, Massachusetts; Chief, Division of Alcohol and Drug Abuse, McLean Hospital, Belmont, Massachusetts
Drugs of Abuse

Roy E. Weiss, MD, PhD
Kathleen & Stanley Glaser Distinguished Chair and Chairman, Department of Medicine, University of Miami Miller School of Medicine, Miami, Florida; Esformes Professor Emeritus, Department of Medicine, University of Chicago Pritzker School of Medicine, Chicago, Illinois
Neuroendocrinology and the Neuroendocrine System; Anterior Pituitary

Jeffrey I. Weitz, MD
Professor of Medicine & Biochemistry, McMaster University Michael G. DeGroote School of Medicine; Executive Director, Thrombosis & Atherosclerosis Research Institute, Hamilton, Ontario, Canada
Venous Thrombosis and Embolism

Richard P. Wenzel, MD, MSc
Professor and Former Chairman, Internal Medicine, Medical College of Virginia, Virginia Commonwealth University, Richmond, Virginia
Acute Bronchitis and Tracheitis

Victoria P. Werth, MD
Professor of Dermatology, University of Pennsylvania Perelman School of Medicine; Chief of Dermatology, Corporal Michael J. Crescenz VAMC, Philadelphia, Pennsylvania
Principles of Therapy of Skin Diseases

Sterling G. West, MD
Professor of Medicine, University of Colorado School of Medicine, Aurora, Colorado
Systemic Diseases in Which Arthritis Is a Feature

A. Clinton White, Jr., MD
Professor of Internal Medicine, University of Texas Medical Branch, Galveston, Texas
Cestodes

Christopher J. White, MD
Chairman and Professor of Medicine, Ochsner Clinical School of the University of Queensland, Ochsner Medical Institutions, New Orleans, Louisiana
Atherosclerotic Peripheral Arterial Disease

Julian White, MBBS, MD
Professor and Head, Toxinology Department, Women's & Children's Hospital, North Adelaide, South Australia, Australia
Envenomation, Bites, and Stings

Perrin C. White, MD
Professor of Pediatrics, University of Texas Southwestern Medical Center; Chief of Endocrinology, Children's Medical Center, Dallas, Texas
Sexual Development and Identity

Richard J. Whitley, MD
Distinguished Professor of Pediatrics, Loeb Eminent Scholar Chair in Pediatrics, Professor of Microbiology, Medicine, and Neurosurgery, Pediatrics, University of Alabama at Birmingham School of Medicine, Birmingham, Alabama
Herpes Simplex Virus Infections

Michael P. Whyte, MD
Professor of Medicine, Pediatrics, and Genetics, Washington University School of Medicine in St. Louis; Medical-Scientific Director, Center for Metabolic Bone Disease and Molecular Research, Shriners Hospital for Children, St. Louis, Missouri
Osteonecrosis, Osteosclerosis/Hyperostosis, and Other Disorders of Bone

Samuel Wiebe, MD, MSc
Professor of Clinical Neurosciences, Community Health Sciences and Pediatrics, University of Calgary Cumming School of Medicine, Calgary, Alberta, Canada
The Epilepsies

Jeanine P. Wiener-Kronish, MD
Henry Isaiah Dorr Professor of Research and Teaching in Anaesthesia, Department of Anesthesia, Critical Care and Pain Medicine, Harvard Medical School; Anesthestist-in-Chief, Massachusetts General Hospital, Boston, Massachusetts
Overview of Anesthesia

David J. Wilber, MD
George M Eisenberg Professor of Medicine, Loyola University Chicago Stritch School of Medicine; Director, Division of Cardiology, Loyola University Medical Center, Maywood, Illinois
Electrophysiologic Interventional Procedures and Surgery

Beverly Winikoff, MD, MPH
President, Gynuity Health Projects; Professor of Clinical Population and Family Health, Population and Family Health, Columbia University Mailman School of Public Health, New York, New York
Contraception

Jane N. Winter, MD
Professor of Medicine, Robert H Lurie Comprehensive Cancer Center and the Department of Medicine, Northwestern University Feinberg School of Medicine, Chicago, Illinois
Approach to the Patient with Lymphadenopathy and Splenomegaly

Edward M. Wolin, MD
Professor of Medicine, Albert Einstein College of Medicine; Director, Neuroendocrine Tumor Program, Department of Medical Oncology, Montefiore Einstein Center for Cancer Care, Bronx, New York
Neuroendocrine Tumors

Gary P. Wormser, MD
Professor of Medicine and of Microbiology and Immunology and Pharmacology, New York Medical College; Chief, Division of Infectious Diseases, Valhalla, New York
Lyme Disease

Neal S. Young, MD
Chief, Hematology Branch, NHLBI, National Heart, Lung, and Blood Institute, Bethesda, Maryland
Parvovirus

Vincent B. Young, MD, PhD
William Henry Fitzbutler Professor of Internal Medicine/Infectious Diseases, Professor of Microbiology & Immunology, University of Michigan Medical School, Ann Arbor, Michigan
The Human Microbiome

William F. Young, Jr., MD, MSc
Professor of Medicine, Tyson Family Endocrinology Clinical Professor, Mayo Clinic College of Medicine and Science, Rochester, Minnesota
Adrenal Medulla, Catecholamines, and Pheochromocytoma

Alan S.L. Yu, MB BChir
Harry Statland and Solon Summerfield Professor, University of Kansas Medical Center; Director, The Kidney Institute, University of Kansas Medical Center, Kansas City, Kansas
Disorders of Magnesium and Phosphorus

Anita K. M. Zaidi, MBBS, SM
Director, Enteric and Diarrheal Diseases; and Vaccine Development and Surveillance, Bill and Melinda Gates Foundation, Seattle, Washington
Shigellosis

Sherif Zaki, MD, PhD
Chief, Infectious Diseases Pathology Branch, Centers for Disease Control and Prevention, Atlanta, Georgia
Leptospirosis

Thomas R. Ziegler, MD
Department of Medicine, Division of Endocrinology, Metabolism and Lipids, Emory University School of Medicine, Atlanta, Georgia
Malnutrition: Assessment and Support

Peter Zimetbaum, MD
Richard and Susan Smith Professor of Cardiovascular Medicine, Harvard Medical School; Associate Chief and Director of Clinical Cardiology, Medicine, Beth Israel Deaconess Medical Center, Boston, Massachusetts
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1

APPROACH TO MEDICINE, THE PATIENT, AND THE MEDICAL PROFESSION: MEDICINE AS A LEARNED AND HUMANE PROFESSION

LEE GOLDMAN AND ANDREW I. SCHAFER

APPROACH TO MEDICINE

Medicine is a profession that incorporates science and the scientific method with the art of being a physician. The art of tending to the sick is as old as humanity itself. Even in modern times, the art of caring and comforting, guided by millennia of common sense as well as a more recent, systematic approach to medical ethics (Chapter 2), remains the cornerstone of medicine. Without these humanistic qualities, the application of the modern science of medicine is suboptimal, ineffective, or even detrimental.

The caregivers of ancient times and premodern cultures tried a variety of interventions to help the afflicted. Some of their potions contained what are now known to be active ingredients that form the basis for proven medications (Chapter 26). Others (Chapter 34) have persisted into the present era despite a lack of convincing evidence. Modern medicine should not dismiss the possibility that these unproven approaches may be helpful; instead, it should adopt a guiding principle that all interventions, whether traditional or newly developed, can be tested vigorously, with the expectation that any beneficial effects can be explored further to determine their scientific basis.

When compared with its long and generally distinguished history of caring and comforting, the scientific basis of medicine is remarkably recent. Other than an understanding of human anatomy and the later description, albeit widely contested at the time, of the normal physiology of the circulatory system, almost all of modern medicine is based on discoveries made within the past 150 years, during which human life expectancy has more than doubled.[1] Until the late 19th century, the paucity of medical knowledge was also exemplified best by hospitals and hospital care. Although hospitals provided caring that all but well-to-do people might not be able to obtain elsewhere, there is little if any evidence that hospitals improved health outcomes. The term *hospitalism* referred not to expertise in hospital care but rather to the aggregate of iatrogenic and nosocomial afflictions that were induced by the hospital stay itself.

The essential humanistic qualities of caring and comforting can achieve full benefit only if they are coupled with an understanding of how medical science can and should be applied to patients with known or suspected diseases. Without this knowledge, comforting may be inappropriate or misleading, and caring may be ineffective or counterproductive if it inhibits a sick person from obtaining appropriate, scientific medical care. *Goldman-Cecil Medicine* focuses on the discipline of *internal medicine,* from which neurology and dermatology, which are also covered in substantial detail in this text, are relatively recent evolutionary branches. The term *internal medicine,* which is often misunderstood by the lay public, was developed in 19th-century Germany. *Inneren medizin* was to be distinguished from clinical medicine because it emphasized the physiology and chemistry of disease, not just the patterns or progression of clinical manifestations. *Goldman-Cecil Medicine* follows this tradition by showing how pathophysiologic abnormalities cause symptoms and signs and by emphasizing how therapies can modify the underlying pathophysiology and improve the patient's well-being.

Modern medicine has moved rapidly past organ physiology to an increasingly detailed understanding of cellular, subcellular, and genetic mechanisms. For example, the understanding of microbial pathogenesis and many inflammatory diseases (Chapter 241) is now guided by a detailed understanding of the human immune system and its response to foreign antigens (Chapters 39 to 44). Advances in our understanding of the human microbiome raise the possibility that our complex interactions with microbes, which outnumber our cells by a factor of 10, will help explain conditions ranging from inflammatory bowel disease (Chapter 132) to obesity (Chapter 207).

Health, disease, and an individual's interaction with the environment are also substantially determined by genetics. In addition to many conditions that may be determined by a single gene, medical science increasingly understands the complex interactions that underlie multigenic traits (Chapter 36). The decoding of the human genome holds the promise that personalized health care increasingly can be targeted according to an individual's genetic profile, in terms of screening and presymptomatic disease management, as well as in terms of specific medications, their complex interactions, and their adjusted dosing schedules.[2]

Knowledge of the structure and physical forms of proteins helps explain abnormalities as diverse as sickle cell anemia (Chapter 154) and prion-related diseases (Chapter 387). Proteomics, which is the study of normal and abnormal protein expression of genes, also holds extraordinary promise for developing drug targets for more specific and effective therapies.

Gene therapy is currently approved by the U.S. Food and Drug Administration (FDA) for only a few diseases—Leber congenital amaurosis (Chapter 395), retinal dystrophy, and hemophilia (Chapter 165)—but many more are in development and clinical testing. Cell therapy is now beginning to provide vehicles for the delivery of cells engineered to address a patient's particular chimeric antigen receptor (CAR),[3] and CAR-T cell therapy is now FDA-approved for non-Hodgkin lymphoma (Chapter 176) and acute lymphoblastic leukemia (Chapter 173). Regenerative medicine to help heal injured or diseased organs and tissues is in its infancy, but cultured chondrocytes are now FDA-approved to repair cartilaginous defects of the femoral condyle and the knee. Immune checkpoint inhibitors have revolutionized the approach to cancer, especially melanoma (Chapter 193).[4] In the future, immunotherapy will likely find applications not only for malignancies but also for the treatment of refractory infectious diseases, autoimmunity, and allergy.[5]

Concurrent with these advances in fundamental human biology has been a dramatic shift in methods for evaluating the application of scientific advances to the individual patient and to populations. The randomized controlled trial, sometimes with thousands of patients at multiple institutions, has replaced anecdote as the preferred method for measuring the benefits and optimal uses of diagnostic and therapeutic interventions (Chapter 8).

And now, even the well-established randomized controlled trial model is being challenged. To reduce costs as well as overcome inefficiencies, redundancies, and the late failure of many clinical trials (at the phase 3 stage) inherent in classical randomized controlled trials, technologic advances are enabling new methods, tools, and approaches to bring clinical trials into the 21st century. These methods include: disease modeling and simulation; alternative trial methods such as response-adaptive randomized designs (Chapter 8); novel objective outcome measures, and engagement of clinical trial "participants" (rather than "human subjects") to expand the pool of patients willing to be involved in clinical research.

As studies progress from those that show biologic effect, to those that elucidate dosing schedules and toxicity, and finally to those that assess true clinical benefit, the metrics of measuring outcome has also improved from subjective impressions of physicians or patients to reliable and valid measures of morbidity, quality of life, functional status, and other patient-oriented outcomes (Chapter 9). These marked improvements in the scientific methodology of clinical investigation have expedited extraordinary changes in clinical practice, such as recanalization therapy for acute myocardial infarction (Chapter 64), and have shown that reliance on intermediate outcomes, such as a reduction in asymptomatic ventricular arrhythmias with certain drugs, may unexpectedly increase rather than decrease mortality. Just as physicians in the 21st century must understand advances in fundamental biology, similar understanding of the fundamentals of clinical study design as it applies to diagnostic and therapeutic interventions is important. Studies can be designed to show benefit or to show noninferiority, and newer pragmatic designs (Chapter 8) help with the study of topics that would be challenging using traditional approaches.

An understanding of human genetics can also help stratify and refine the approach to clinical trials by helping researchers select fewer patients with a more homogeneous disease pattern to study the efficacy of an intervention. Such an approach has been especially relevant in cancer, where tumors with certain genetic mutations can respond to a drug specifically designed for that target, whereas other tumors with similar microscopic but different genomic characteristics will not.[6] Genomic, transcriptomic, epigenomic, proteomic, metabolomic, and other "omic" technologies provide a more holistic view of the molecular makeup of a normal or abnormal organism, tissue, or cell. Systems biology, which is the integration of all these techniques, can enable the development of new predictive, preventive, and personalized approaches to disease.

Sophisticated computerized analyses of radiographs and retinal images[7] are also poised to revolutionize the interpretation of these images much as computerized electrocardiographic interpretation (Chapter 48) changed clinical cardiology. Electronic medical records also can detect patterns of drug side

ABSTRACT

The medical profession incorporates both the science of medicine as well as the art of being a physician. Physicians cannot help patients unless they are well-grounded in the latest information about medical diagnosis and therapy, which increasingly is based on randomized clinical trials as well as specific information about the genetics and genomics of individual patients. However, this scientific expertise must also be applied in the context of understanding the patient as an individual person. In applying both scientific knowledge and medical professionalism, the physician must also recognize the importance of social justice as well as how to advocate for and help each individual patient in the context of broader societal issues.

KEYWORDS

medical professionalism
scientific medicine
evidence-based medicine
approach to the patient
signs and symptoms

effects or interactions that can then guide molecular analyses that confirm new risks or even genetic diseases.[8] Although it is too soon to know whether patients would routinely benefit from sequencing and analysis of their exome or full genome, such information is increasingly becoming affordable and more accurate, with potential usefulness for identifying mendelian disease patterns[9] and informing reproductive planning to avoid autosomal recessive diseases. Despite much hope, however, genetic profiling has had very limited positive impact on drug selection and dosing.

This explosion in medical knowledge has led to increasing specialization and subspecialization, defined initially by organ system and more recently by locus of principal activity (inpatient vs. outpatient), reliance on manual skills (proceduralist vs. nonproceduralist), or participation in research. Nevertheless, it is becoming increasingly clear that the same fundamental molecular and genetic mechanisms are broadly applicable across all organ systems and that the scientific methodologies of randomized trials and careful clinical observation span all aspects of medicine.

The advent of modern approaches to managing data now provides the rationale for the use of health information technology. Computerized health records, oftentimes shared with patients in a portable format, can avoid duplication of tests, assure that care is coordinated among the patient's various health care providers, and increase the value of health care.[10] Real-time electronic records can also be used to alert physicians about patients whose vital signs (Chapter 7) might warrant urgent evaluation to avoid more serious clinical decompensation. However, a current downside is that for every hour physicians provide direct clinical face time to patients in the office, nearly two additional hours may be spent on electronic health records and desk work within the work day.[11]

Extraordinary advances in the science and practice of medicine, which have continued to accelerate with each recent edition of this textbook, have transformed the global burden of disease. Life expectancies for men and women have been increasing, a greater proportion of deaths are occurring among people older than age 70 years, and far fewer children are dying before the age of 5 years. In the United States, however, overall life expectancy has surprisingly declined in the last several years. Explanations include obesity-related diseases[12] as well as so-called deaths of despair owing to alcohol, drugs, and suicide.[13] Nevertheless, huge regional disparities remain, and disability from conditions such as substance abuse, mental health disorders, injuries, diabetes, musculoskeletal disease, and chronic respiratory disease have become increasingly important issues for all health systems.

APPROACH TO THE PATIENT

Patients commonly have complaints (symptoms), but at least one third of these symptoms will not be readily explainable by any detectable abnormalities on examination (signs) or on laboratory testing. Even in our modern era of advanced diagnostic testing, the history and physical examination are estimated to contribute at least 75% of the information that informs the evaluation of symptoms, and symptoms that are not explained on initial comprehensive evaluation rarely are manifestations of a serious underlying disease. Conversely, asymptomatic patients may have signs or laboratory abnormalities, and laboratory abnormalities can occur in the absence of symptoms or signs.

Symptoms and signs commonly define *syndromes,* which may be the common final pathway of a wide range of pathophysiologic alterations. The fundamental basis of internal medicine is that diagnosis should elucidate the pathophysiologic explanation for symptoms and signs so that therapy may improve the underlying abnormality, not just attempt to suppress the abnormal symptoms or signs.

When patients seek care from physicians, they may have manifestations or exacerbations of known conditions, or they may have symptoms and signs that suggest malfunction of a particular organ system. Sometimes the pattern of symptoms and signs is highly suggestive or even pathognomonic for a particular disease process. In these situations, in which the physician is focusing on a particular disease, *Goldman-Cecil Medicine* provides scholarly yet practical approaches to the epidemiology, pathobiology, clinical manifestations, diagnosis, treatment, prevention, and prognosis of entities such as acute myocardial infarction (Chapter 64), chronic obstructive lung disease (Chapter 82), inflammatory bowel disease (Chapter 132), gallstones (Chapter 146), rheumatoid arthritis (Chapter 248), hypothyroidism (Chapter 213), and tuberculosis (Chapter 308), as well as newly described disorders such as emerging zoonoses, small fiber neuropathies, nephrogenic systemic fibrosis, mitochondrial diseases, autoinflammatory diseases, and clonal disorders of indeterminate potential.

Many patients, however, have undiagnosed symptoms, signs, or laboratory abnormalities that cannot be immediately ascribed to a particular disease or cause. Whether the initial manifestation is chest pain (Chapter 45), diarrhea (Chapter 131), neck or back pain (Chapter 372), or a variety of more than 100 common symptoms, signs, or laboratory abnormalities, *Goldman-Cecil Medicine* provides tables, figures, and entire chapters to guide the approach to diagnosis and therapy (see E-Table 1-1 or table on inside back cover). By virtue of this dual approach to known disease as well as to undiagnosed abnormalities, this textbook, similar to the modern practice of medicine, applies directly to patients regardless of their mode of manifestation or degree of previous evaluation.

The patient-physician interaction proceeds through many phases of clinical reasoning and decision making. The interaction begins with an elucidation of complaints or concerns, followed by inquiries or evaluations to address these concerns in increasingly precise ways. The process commonly requires a careful history or physical examination, ordering of diagnostic tests, integration of clinical findings with test results, understanding of the risks and benefits of the possible courses of action, and careful consultation with the patient and family to develop future plans. Physicians can increasingly call on a growing literature of evidence-based medicine to guide the process so that benefit is maximized while respecting individual variations in different patients. Throughout *Goldman-Cecil Medicine,* the best current evidence is highlighted with specific grade A references that can be accessed directly in the electronic version.

The increasing availability of evidence from randomized trials to guide the approach to diagnosis and therapy should not be equated with "cookbook" medicine.[14] Evidence and the guidelines that are derived from it emphasize proven approaches for patients with specific characteristics. Substantial clinical judgment is required to determine whether the evidence and guidelines apply to individual patients and to recognize the occasional exceptions. Even more judgment is required in the many situations in which evidence is absent or inconclusive. Evidence must also be tempered by patients' preferences, although it is a physician's responsibility to emphasize evidence when presenting alternative options to the patient. The adherence of a patient to a specific regimen is likely to be enhanced if the patient also understands the rationale and evidence behind the recommended option.

To care for a patient as an individual, the physician must understand the patient as a person. This fundamental precept of doctoring includes an understanding of the patient's social situation, family issues, financial concerns, and preferences for different types of care and outcomes, ranging from maximum prolongation of life to the relief of pain and suffering (Chapters 2 and 3). If the physician does not appreciate and address these issues, the science of medicine cannot be applied appropriately, and even the most knowledgeable physician will fail to achieve the desired outcomes.

Even as physicians become increasingly aware of new discoveries, patients can obtain their own information from a variety of sources, some of which are of questionable reliability. The increasing use of alternative and complementary therapies (Chapter 34) is an example of patients' frequent dissatisfaction with prescribed medical therapy. Physicians should keep an open mind regarding unproven options but must advise their patients carefully if such options may carry any degree of potential risk, including the risk that they may be relied on to substitute for proven approaches. It is crucial for the physician to have an open dialogue with the patient and family regarding the full range of options that either may consider.

Another manifestation of problematic interactions and care is medical malpractice litigation, which commonly is a result of both suboptimal medical care and suboptimal communication (Chapter 10). Of note is that about 1% of all physicians account for 32% of paid malpractice claims nationally,[15] thereby suggesting that individual physician characteristics are important and addressable contributors.

The physician does not exist in a vacuum, but rather as part of a complicated and extensive system of medical care and public health. In premodern times and even today in some developing countries, basic hygiene, clean water, and adequate nutrition have been the most important ways to promote health and reduce disease. In developed countries, adoption of healthy lifestyles, including better diet (Chapter 202) and appropriate exercise (Chapter 13), is the cornerstone to reducing the epidemics of obesity (Chapter 207), coronary disease (Chapter 46), and diabetes (Chapter 216). Public health interventions to provide immunizations (Chapter 15) and to reduce injuries and the use of tobacco (Chapter 29), illicit drugs (Chapter 31), and excess alcohol (Chapter 30) can collectively produce more health benefits than nearly any other imaginable health intervention.

E-TABLE 1-1 GUIDE TO THE APPROACH TO COMMON SYMPTOMS, SIGNS, AND LABORATORY ABNORMALITIES

	CHAPTER	SPECIFIC TABLES OR FIGURES
SYMPTOMS		
Constitutional		
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Fatigue	258	E-Table 258-1
Poor appetite	123	Table 123-1
Weight loss	123, 206	Figure 123-4; Tables 123-4, 206-1, 206-2
Obesity	207	Figure 207-1
Snoring, sleep disturbances	377	Table 377-6
Head, Eyes, Ears, Nose, Throat		
Headache	370	Tables 370-1, 370-2
Visual loss, transient	395, 396	Tables 395-2, 396-1
Ear pain	398	Table 398-3
Hearing loss	400	Figure 400-1
Ringing in ears (tinnitus)	400	Figure 400-2
Vertigo	400	Figure 400-3
Nasal congestion, rhinitis, or sneezing	398	
Loss of smell or taste	399	Table 399-1
Dry mouth	397	Table 397-7
Sore throat	401	Figure 401-2; Table 401-1
Hoarseness	401	
Cardiopulmonary		
Chest pain	45, 128	Tables 45-2, 128-5, 128-6
Bronchitis	90	
Shortness of breath	45, 77	Figure 77-3
Palpitations	45, 56	Figure 56-1; Tables 45-4, 56-5
Dizziness	45, 56, 400	Figure 56-1; Table 400-1
Syncope	56	Figure 56-1; Tables 56-1, 56-2, 56-4
Cardiac arrest	57	Figures 57-2, 57-3
Cough	77	Figure 77-1; Tables 77-2, 77-3
Hemoptysis	77	Tables 77-6, 77-7
Gastrointestinal		
Nausea and vomiting	123	Figure 123-5; Table 123-5
Dysphagia, odynophagia	123, 129	Table 123-1
Hematemesis	126, 144	Figure 126-3; Table 126-1
Heartburn/dyspepsia	123, 128 to 130	Figures 123-6, 129-2; Tables 128-3, 128-4, 130-1
Abdominal pain		
Acute	123, 133	Figures 123-1, 123-2; Tables 123-2, 123-3, 133-1
Chronic	123, 128	Figure 123-3; Tables 123-2, 129-1
Diarrhea	128, 131	Figures 128-1, 131-1 to 131-4
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Dysuria	268, 269	Tables 268-3, 268-5, 269-2
Frequency	268	Table 268-3
Incontinence	23	Tables 23-1 to 23-3
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Erectile dysfunction	221	Figure 221-10
Male infertility	221	Figures 221-8, 221-9; Table 221-7
Scrotal mass	190	Figure 190-1
Genital ulcers or warts	269	Table 269-1

E-TABLE 1-1 GUIDE TO THE APPROACH TO COMMON SYMPTOMS, SIGNS, AND LABORATORY ABNORMALITIES—cont'd

	CHAPTER	SPECIFIC TABLES OR FIGURES
Musculoskeletal		
Neck or back pain	372	Figures 372-4, 372-5, 372-6; Tables 372-3 to 372-5
Painful joints	241	Figure 241-1; Tables 241-1, 241-3
Extremities		
Swollen feet, ankles, or legs		
Bilateral	45	Figure 45-8
Unilateral	74	Figure 74-2; Table 74-2
Claudication	71	Table 71-3
Acute limb ischemia	71	Figure 71-4; Table 71-2
Neurologic		
Weakness	368, 392 to 394	Tables 368-1, 392-2, 393-2, 393-4
Sensory loss	368, 392	Figure 392-1; Tables 392-1, 392-3 to 392-5
Memory loss	374	Figures 374-1, 374-2; Tables 374-1 to 374-6
Abnormal gait	368	Table 368-2
Seizures	375	Tables 375-1 to 375-6
Integumentary		
Abnormal bleeding	162	Table 162-1
Rash	407, 412	Figure 407-1; Tables 407-1 to 407-6, 412-5
Hives	237, 411	Figure 237-2; Tables 237-1, 411-1, 411-2
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BUN = blood urea nitrogen; ECG = electrocardiogram; PT = prothrombin time; PTT = partial thromboplastin time.

TABLE 1-1 PROFESSIONAL RESPONSIBILITIES

Commitment to:
- Professional competence
- Honesty with patients
- Patient confidentiality
- Maintaining appropriate relations with patients
- Improving the quality of care
- Improving access to care
- Just distribution of finite resources
- Scientific knowledge
- Maintaining trust by managing conflicts of interest
- Professional responsibilities

From Brennan T, Blank L, Cohen J, et al. Medical professionalism in the new millennium: a physician charter. *Ann Intern Med.* 2002;1136:243-246.

APPROACH TO THE MEDICAL PROFESSION

Medical professionalism should emphasize three fundamental principles: the primacy of patient welfare, patient autonomy, and social justice.[16] As modern medicine brings a plethora of diagnostic and therapeutic options, the interactions of the physician with the patient and society become more complex and potentially fraught with ethical dilemmas (Chapter 2). To help provide a moral compass that is not only grounded in tradition but also adaptable to modern times, the primacy of patient welfare emphasizes the fundamental principle of a profession. The physician's altruism, which begets the patient's trust, must be impervious to the economic, bureaucratic, and political challenges that are faced by the physician and the patient (Chapter 4).

The principle of patient autonomy asserts that physicians make recommendations but patients make the final decisions. The physician is an expert advisor who must inform and empower the patient to base decisions on scientific data and how these data can and should be integrated with a patient's preferences.

The importance of social justice symbolizes that the patient-physician interaction does not exist in a vacuum. The physician has a responsibility to the individual patient and to broader society to promote access, to eliminate disparities in health and health care, and to bring science to even the most contentious political issues. For example, research into the relationship of firearms to rates of murder and suicide[17] can be useful for preventive medicine and public policy regardless of an individual's position on background checks and licensing for gun owners.

To promote these fundamental principles, a series of professional responsibilities (Table 1-1) represents practical, daily traits that benefit the physician's own patients and society as a whole. Physicians who use these and other attributes to improve their patients' satisfaction with care are not only promoting professionalism but also reducing their own risk for liability and malpractice. By comparison, the recent emphasis on maintenance of certification requirements is of uncertain benefit for improving patient outcomes.

An interesting new aspect of professionalism is the increasing reliance on team approaches to medical care, as exemplified by physicians whose roles are defined by the location of their practice—historically in the intensive care unit or emergency department and more recently on the inpatient general hospital floor. Quality care requires coordination and effective communication across inpatient and outpatient sites among physicians who themselves now typically work defined hours. This transition from reliance on a single, always available physician to a team, ideally with a designated coordinator, places new challenges on physicians, the medical care system, and the medical profession.

An ongoing challenge for a profession that values dedication, attention to detail, and selflessness is the risk of burnout, which is characterized by emotional exhaustion and depersonalization. Both individual-focused and structural or organizational modifications in the work environment can result in clinically meaningful reductions in physician burnout.[18]

The changing medical care environment is placing increasing emphasis on standards, outcomes, and accountability. As purchasers of insurance become more cognizant of value rather than just cost (Chapter 10), outcomes ranging from rates of screening mammography (Chapter 188) to mortality rates with coronary artery bypass graft surgery (Chapter 65) become metrics by which rational choices can be made. Clinical guidelines and critical pathways derived from randomized controlled trials and evidence-based medicine can potentially lead to more cost-effective care and better outcomes.

These major changes in many Western health care systems bring with them many major risks and concerns. If the concept of limited choice among physicians and health care providers is based on objective measures of quality and outcome, channeling of patients to better providers is one reasonable definition of better selection and enlightened competition. If the limiting of options is based overwhelmingly on cost rather than measures of quality, outcomes, and patient satisfaction, physicians and their patients can be seriously disadvantaged.

Another risk is that the same genetic information that could lead to more effective, personalized medicine will be used against the very people whom it is supposed to benefit—by creating a stigma, raising health insurance costs, or even making someone uninsurable. The ethical approach to medicine (Chapter 2), genetics (Chapter 35), and genetic counseling provides means to protect against this adverse effect of scientific progress.

In this new environment, the physician often has a dual responsibility: to the health care system as an expert who helps create standards, measures of outcome, clinical guidelines, and mechanisms to ensure high-quality, cost-effective care; and to individual patients who entrust their well-being to that physician to promote their best interests within the reasonable limits of the system. A health insurance system that emphasizes cost-effective care, that gives physicians and health care providers responsibility for the health of a population and the resources required to achieve these goals, that must exist in a competitive environment in which patients can choose alternatives if they are not satisfied with their care, and that places increasing emphasis on health education and prevention can have many positive effects. In this environment, however, physicians must beware of overt and subtle pressures that could entice them to underserve patients and abrogate their professional responsibilities by putting personal financial reward ahead of their patients' welfare. The physician's responsibility to represent the patient's best interests and avoid financial conflicts by doing too little in the newer systems of capitated care provides different specific challenges but an analogous moral dilemma to the historical American system in which the physician could be rewarded financially for doing too much.

In the current health care environment, all physicians and trainees must redouble their commitment to professionalism. At the same time, the challenge to the individual physician to retain and expand the scientific knowledge base and process the vast array of new information is daunting. In this spirit of a profession based on science and caring, *Goldman-Cecil Medicine* seeks to be a comprehensive approach to modern internal medicine.

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BIOETHICS IN THE PRACTICE OF MEDICINE

EZEKIEL J. EMANUEL

It commonly is argued that the bioethical dilemmas physicians face today result primarily from modern advances in medical technology. The rise of antibiotics, transplantation, intensive care units, genetics, implantable devices, and other technologies have created novel bioethical concerns. In reality, however, concerns about ethical issues are as old as the practice of medicine itself. The Hippocratic Oath, composed sometime around 400 BC, attests to the need even of ancient Greek physicians for advice on how to address the many bioethical dilemmas that they confronted. The Oath addresses issues of confidentiality, abortion, euthanasia, sexual relations between physicians and patients, divided loyalties, and, at least implicitly, charity care and executions. Whether we agree with the advice it dispensed or not, the mere existence of the Oath serves as a reminder that bioethical conundrums are inherent to medical practice. Technology may make these issues more common and change the context in which they arise, but many, if not most, bioethical issues that physicians regularly confront are timeless.

During their training, many physicians are taught that four main principles can be invoked to address bioethical dilemmas: autonomy, nonmaleficence,

ABSTRACT

It commonly is argued that the bioethical dilemmas physicians face today result primarily from modern advances in medical technology. In reality, however, concerns about ethical issues are as old as the practice of medicine itself. The Hippocratic Oath, composed sometime around 400 BC, attests to the need even of ancient Greek physicians for advice on how to address the many bioethical dilemmas that they confronted. Technology may make these issues more common and change the context in which they arise, but many, if not most, bioethical issues that physicians regularly confront are timeless. A multitude of bioethical dilemmas arise in medical practice each year, including issues of genetics, conscientious objection by providers, and termination of care. In clinical practice, the most common issues revolve around informed consent, termination of life-sustaining treatments, euthanasia and physician-assisted suicide, and conflicts of interest.

KEYWORDS

bioethics
informed consent
life-sustaining treatment
euthanasia
physician-assisted suicide
conflict of interest

beneficence, and justice. Autonomy is the idea that people should have the right and freedom to choose, pursue, and revise their own life plans. Nonmaleficence is the idea that people should not be knowingly harmed or injured. This principle is encapsulated in the oft-repeated phrase that a physician must "first do no harm"—*primum non nocere.* Interestingly, this phrase is not found in the Hippocratic Oath; the only related, but still not identical, Hippocratic phrase is "at least, do not harm." Beneficence refers to the positive actions that a physician should undertake to promote the well-being of his or her patients. In clinical practice, this obligation usually arises from the implicit and explicit commitments and promises central to the physician-patient relationship. Finally, the principle of justice is defined by the fair distribution of benefits and burdens that result from a clinical interaction.

Although helpful in providing an initial framework, these principles are too broad to have more than limited value. The principles are also frequently underdeveloped and likely to conflict with each other, thereby resulting in bioethical dilemmas. The principles themselves do not offer guidance on how they should be balanced or specified to resolve dilemmas. Given that they are focused on physician-patient encounters, the principles are also unhelpful when considering bioethical issues at the system or institutional level, such as the allocation of scarce vaccines or transplant organs. Finally, these four principles are not comprehensive. Other fundamental ethical principles and values—such as priority to the worst off, duties to future generations, and professional integrity—are important in bioethics but not fully encapsulated by these four principles.

There is no formula that can magically determine how to solve bioethical dilemmas. Instead, medical professionals should follow an orderly analytic process. First, practitioners need to obtain the facts relevant to the situation. Second, they must delineate the fundamental bioethical issue. Third, they must identify all the crucial principles and values that relate to, and potentially conflict with, the case. Fourth, because many ethical dilemmas have been previously analyzed and subjected to empirical study, practitioners should examine the relevant literature so they may potentially identify new values, understand existing principles, reformulate the issue at hand, and see if there is an accepted resolution. Fifth, with this information, the practitioner must distinguish clearly unethical practices from a range of ethically permissible actions. Finally, it is important not only to come to a resolution but also to state clearly the justification for such decisions. Although unanimous decisions are ideal, the reality remains that such consensus may be elusive. Reasonable physicians must therefore take care to explain what principles and interpretations they relied upon to resolve ethical dilemmas.

A multitude of bioethical dilemmas arise in medical practice each year, including issues of genetics, conscientious objection by providers, and termination of care. In clinical practice, the most common issues revolve around informed consent, termination of life-sustaining treatments, euthanasia and physician-assisted suicide, and conflicts of interest.

PHYSICIAN-PATIENT RELATIONSHIP: INFORMED CONSENT

History

The requirement of informed consent dates as far back as Plato. The first recorded legal case on informed consent took place in England in 1767 when a patient complained that he had not given his consent for two surgeons to refracture his leg after it had healed improperly. An 18th-century English court ultimately ruled that obtaining a patient's consent prior to a procedure was the "rule of the profession" and thus a legal obligation of surgeons. Failure to obtain consent, the court declared, was inexcusable. In more contemporary times, a landmark 1957 U.S. court ruling stated that physicians have a positive legal obligation to disclose information about risks, benefits, and alternative treatments to patients; this decision popularized the term *informed consent.*

Definition and Justification

Informed consent is a person's autonomous authorization to permit a physician—or other health care professional—to undertake diagnostic or therapeutic interventions for himself or herself. The patient understands that he or she is taking responsibility for the decision while empowering someone else, the physician, to implement it. However, agreement to a course of medical treatment does not necessarily qualify as informed consent.

The four fundamental requirements for valid informed consent are: mental capacity, disclosure, understanding, and voluntariness. First, informed consent assumes that people have the mental capacity to make decisions; disease, development, or medications can compromise patients' mental capacity to provide informed consent. Adults are presumed to have the legal competence to make medical decisions, and whether an adult is incompetent to make medical decisions is a legal determination. Practically, physicians usually decide whether patients are competent based on whether they can understand the information disclosed, appreciate its significance for their own situation, and use logical and consistent thought processes in decision making. Incompetence in medical decision making does not mean a person is incompetent in all types of decision making and vice versa. Second, crucial information relevant to the decision must be disclosed, usually by the physician, to the patient. Third, the patient should understand the information and its implications for his or her interests and life goals. Finally, the patient's decision must be made voluntarily, i.e., without coercion or manipulation by the physician.

It is a mistake to view informed consent as a one-time event, such as the signing of a form. Informed consent is viewed more accurately as a process that evolves throughout the course of a patient's diagnosis and subsequent treatment.

Typically, a patient's autonomy is the value invoked to justify informed consent. Other values, such as bodily integrity and beneficence, have also been cited, especially in early legal rulings.

Empirical Data

Extensive research on informed consent shows that physicians frequently do not communicate all the relevant information needed for patients to make an informed decision in clinical settings. The more complex the medical decisions, the more likely it is that physicians will obtain all the elements of informed consent.

Interestingly, data suggest that disclosure, both in informed consent documents and in discussion, is better in research than clinical settings. Greater disclosure in the research setting may be the result of the research-specific requirement of having a written informed consent document reviewed by an independent committee, such as an institutional review board or a research ethics committee.

Patients frequently fail to recall crucial information disclosed during the process of obtaining informed consent, although they usually think they have sufficient information to make a decision. Whether patients fail to recall key information because they are overwhelmed by the information or because they find much of it not salient to their decision is unclear. The issue therefore lies more in determining what patients understand at the point of decision making, rather than what they recall later. For common medical interventions, such as elective surgery, the ideal informed consent would include the risks and benefits as quantified in randomized controlled trials, relevant data on the surgeon, the institution's clinical outcomes for the procedure, and a list of acceptable alternatives.[1]

Studies aimed at improving informed consent in clinical settings suggest that interactive media, such as videos and interactive computer software, can improve patients' understanding of such competing alternatives.■ A review of 115 studies on shared decision making found that, compared with those receiving usual care, patients who used a decision aid had greater knowledge of the evidence, felt more clear about what mattered to them, had more accurate understanding of risks and benefits, and participated more in the decision-making process. These decision aids can be especially important in preference-sensitive conditions—situations with several treatment options and important tradeoffs that are dependent on a patient's values, such as decisions about prostatectomy for early stage prostate cancer. Computer and web-based decision aides are now available for over 200 common conditions and procedures.

A more modern challenge in obtaining informed consent is the introduction of electronic methods into the process, including smartphone applications in acute situations such as ischemic stroke.■ Digital models for informed consent often are not user-friendly for older patients, and evidence suggests that most people do not read click-through agreements on computers and mobile devices. Concern also exists that it may be challenging to obtain true voluntary choice without being able to assess the body language, tone, and emotion that can be observed during a person-to-person interaction.[2]

One of the most important results of empirical research on informed consent is that there is a gap between a desire for information and a desire for actual decision making. Many studies show that although most patients want information, far fewer actually want to make decisions about their own care. In one study, for example, only one third of patients desired decision-making authority, and patients' decision-making preferences were not correlated with their information-seeking preferences (which were high). Patients' preferences for decision-making authority generally increase with higher educational levels and decline with age. Most importantly, the more serious the illness, the more likely patients are to prefer that physicians make the decisions. Several studies

TABLE 2-1 FUNDAMENTAL ELEMENTS FOR DISCLOSURE TO PATIENTS

Diagnosis and prognosis
Nature of proposed intervention
Reasonable alternative interventions
Risks associated with each alternative intervention
Benefits associated with each alternative intervention
Probable outcomes of each alternative intervention

suggest that patients who have less of a desire to make their own decisions generally are more satisfied with how the decisions are ultimately made.

Practical Considerations

Implementing informed consent raises questions about the extent to which information should be disclosed and how to disclose it. Physicians should disclose at least six fundamental elements of information to patients: (1) diagnosis and prognosis; (2) nature of the proposed intervention; (3) alternative interventions, including no treatment; (4) risks associated with each alternative; (5) benefits of each alternative; and (6) likely outcomes of these alternatives (Table 2-1). Because risk is usually a physician's principal concern, physicians also should disclose (1) the nature of the risks, (2) their magnitude, (3) the probability that each risk will occur, and (4) when the consequence might occur. Increasingly, these disclosures should include data both from clinical trials and from the institution and physician performing the test and treatments. In general, all serious risks, such as death, paralysis, stroke, infections, or chronic pain, even if rare, should be disclosed, as should common risks.

The key challenge in providing this information is doing so within reasonable time constraints and without overwhelming the patient with unnecessarily complex or technical details. Fortunately, time constraints can be somewhat ameliorated by using interactive electronic media that allow patients to view information on their own schedules while facilitating the transfer of basic information.

The question of how much physicians should disclose has been approached differently state-by-state. Generally, states have adopted one of two divergent legal standards. The *physician* or *customary* standard, adapted from malpractice law, states that the physician should disclose all information "which a reasonable medical practitioner would make under the same or similar circumstances." Conversely, the *reasonable person* or *lay-oriented* standard states that physicians should disclose all information that a "reasonable person in the patient's circumstances would find material" to the medical decision. The physician standard is factual and can be determined empirically, but the patient-oriented standard, which is meant to engage physicians with patients, is hypothetical. Currently, each standard is used by about half of the United States. In 2015, the United Kingdom's Supreme Court ruled that the standard for what information a physician should disclose should not be determined by what a reasonable physician would do, but rather by what a reasonable patient would want.

The requirement of informed consent has no exceptions. In emergency situations, consent can be assumed under the belief that patients' interests are in survival and retaining maximal mental and physical functioning; as a result, reasonable persons would want treatment. In some circumstances, physicians may believe the process of informed consent could pose a serious psychological threat. In rare cases, the "therapeutic privilege" of promoting a patient's well-being trumps autonomy, but physicians should be wary of invoking this exception too readily.

If patients are deemed mentally incompetent to make medical decisions, family members—beginning with spouse, children, parents, siblings, then more distant relatives—usually are selected as surrogates or proxies, although there may be concerns about conflicting interests or knowledge of the patient's wishes. In the relatively rare circumstance in which a patient has formally designated a proxy, that person has decision-making authority.

The *substituted judgment* standard states that the proxy should choose what the patient would choose if he or she were competent. The *best interests* standard states that the proxy should choose what is best for the patient. However, it is often not clear what the patient would have decided, because the situation was not discussed with the patient and he or she left no living will. Similarly, what is considered "best" for a patient can be controversial because of tradeoffs between quality of life and pure survival. These problems are complicated by the poor ability of many proxies to predict a patient's quality of life; proxies also tend to underestimate patients' future functional status and satisfaction. Similarly, a proxy's predictions on a mentally incapacitated patient's life-sustaining preferences are often inaccurate. In cases in which the patient is diagnosed with dementia, families tend to agree with patients on decisions regarding life-sustaining treatment two thirds of the time, better but not much better than the 50% agreement based on chance alone. Such confusion on how to decide for incapacitated patients can create conflicts among family members or between the family and medical providers. In such circumstances, an ethics consultation may be helpful.

TERMINATION OF MEDICAL INTERVENTIONS

History

Since the origins of medicine, withholding medical treatment from terminally ill patients while still providing palliative care, thereby allowing "nature to take its course," has been deemed ethical.[3] Hippocrates argued that physicians should "refuse to treat those [patients] who are overmastered by their disease." In the 19th century, prominent American physicians advocated withholding cathartic and emetic "treatments" from the terminally ill. In 1900, the editors of *The Lancet* argued that physicians should intervene to ease the pain of death and that they did not have an obligation to prolong a clearly terminal life. The contemporary debate on terminating care began in 1976 with the *Quinlan* case, in which the New Jersey Supreme Court ruled that patients had a right to refuse life-sustaining interventions on the basis of a right to privacy, and that the family could exercise that right for a patient in a persistent vegetative state.

Definition and Justification

It generally is agreed that all patients have a right to refuse medical interventions. Ethically, this right is based on the patient's right to autonomy and is implied by the doctrine of informed consent. Legally, state courts have cited the right to privacy, the right to bodily integrity, and common law to justify the right to refuse medical treatment. In the 1990 *Cruzan* case, and in the subsequent physician-assisted suicide cases, the U.S. Supreme Court affirmed that there is a "constitutionally protected right to refuse lifesaving hydration and nutrition." The Court stated that "[A] liberty interest [based on the 14th Amendment] in refusing unwanted medical treatment may be inferred from our prior decisions." All patients have both a constitutional and an ethical right to refuse medical interventions. These rulings were the basis of consistent state and federal court rulings in the *Schiavo* case to permit the husband to terminate artificial nutrition and hydration for his terminally ill wife in a vegetative state (Chapter 376).

Empirical Data

Data show that termination of medical treatments is now the norm, and the trend has shifted toward stopping medical interventions based on the preferences of patients and their surrogate decision makers. Over 85% of Americans and 90% of decedents in intensive care units do not receive cardiopulmonary resuscitation. Of decedents in intensive care units, more than 85% die after the withholding or withdrawal of medical treatments, with an average of 2.6 interventions being withheld or withdrawn per decedent.

Despite extensive public support for use of advance care directives and the passage of the Patient Self-Determination Act mandating that health care institutions inform patients of their right to complete such documents, less than 40% of Americans appear to have completed any written form of end-of-life decisions. Among Americans ages 75 and older, 1 in 5 have neither written nor talked with someone about their wishes for medical treatment at the end of their lives. Data suggest that although over 40% of patients required active decision making about terminating medical treatments in their final days, more than 70% lacked actual decision-making capacity, thereby emphasizing the importance of completing advance directives.

Efforts to improve completion of advance care directives have generated mixed results. In La Crosse County, Wisconsin, for example, after health care organizations in the county added an "Advance Directive" section to their electronic medical records, 90% of decedents had some type of advance directive. Unfortunately, even successful pilot efforts like La Crosse County's have not been adopted or easily scaled. A persistent problem has been that even when patients complete advance care directives, the documents frequently are not readily available, physicians do not know they exist, or they tend to be too general or vague to guide decisions. The increasing use of electronic health records should make it possible for advance directives to be available whenever and wherever the patient presents to a health care provider. Although electronic health records will help in making existing advance directives available, they will not solve the problem of actually having a conversation between the physician and the patient about advance care planning. Starting that conversation still seems to be a persistent barrier.

Just as proxies are poor at predicting patients' wishes, data show that physicians are even worse at determining patients' preferences for life-sustaining treatments. In one study, for example, 30% of family conferences between clinicians and surrogates did not discuss preferences for end-of-life decision making for patients who were at high risk of death.[4] In many cases, life-sustaining treatments are continued even when patients or their proxies desire them to be stopped. Conversely, many physicians discontinue or never begin interventions unilaterally without the knowledge or consent of patients or their surrogate decision makers. These discrepancies emphasize the importance of engaging patients early on in their care about treatment preferences.

Practical Considerations

Many practical considerations are applicable to enacting the right to terminate medical treatment (Table 2-2). First, patients have a right to refuse any and all medical interventions.

The question of what medical interventions can be terminated—or not started—is a recurrent topic of debate among physicians and other health care providers. Initiation of cardiopulmonary resuscitation was the focus of early court cases. Courts have made clear that any treatment prescribed by a physician and administered by a health care provider can be stopped if it is more harmful than beneficial.[5] The issue is not whether the treatment is ordinary, extraordinary, or heroic, or whether it is high-technology or low-technology. Treatments that can be stopped include not only ventilators, artificial nutrition, and hydration, but also dialysis, pacemakers, ventricular assist devices, antibiotics, and any medication.

Second, there is no ethical or legal difference between withholding an intervention and withdrawing it. If a respirator or other treatment is started because physicians are uncertain whether a patient would have wanted it, they always can stop it later when information clarifies the patient's wishes. Although physicians and nurses might find stopping a treatment to be more difficult psychologically, withdrawal is ethically and legally permitted—and required—when it is consonant with the patient's wishes.

Third, competent patients have the exclusive right to make decisions about terminating their own care. If there is a conflict between a competent patient and his or her family, the patient's wishes are to be followed. It is the patient's right to refuse treatment, not the family's right. For mentally incompetent patients, the situation is more complex. If the patients left clear indications of their wishes, whether as explicit oral statements or as written advance care directives, these wishes should be followed. Physicians should not be overly concerned about the precise form patients use to express their wishes; because patients have a constitutional right to refuse treatment, the real concern is whether the wishes are clear and relevant to the situation. If an incompetent patient did not leave explicit indications of his or her wishes or designate a proxy decision maker, the physician should identify a surrogate decision maker and rely on the decision maker's wishes. Some state courts have restricted what treatments a proxy decision-maker can terminate, thereby requiring the incompetent patient to have given very specific instructions about the particular treatments he or she does not want to receive and the conditions under which care should be withheld or withdrawn. This requirement severely limits the authority and power of proxy decision makers.

Fourth, the right to refuse medical treatment does not translate into a right to demand any treatment, especially treatments that have no pathophysiologic rationale, have already failed, or are known to be harmful. Futility has become a justification to permit physicians unilaterally to withhold or withdraw treatments despite the family's requests for treatment. Some states, such as Texas, have enacted futility laws, which prescribe procedures by which physicians can invoke futility either to transfer a patient or to terminate interventions. However, the principle of futility is not easy to implement in medical practice. Initially, some commentators advocated that an intervention was futile when the probability of success was 1% or lower. Although this threshold seems to be based on empirical data, it is a covert value judgment. Because the declaration of futility is meant to justify unilateral determinations by physicians, it generally has been viewed as an inappropriate assertion that undermines physician-patient communication and violates the principle of shared decision making. Similar to the distinction between ordinary and extraordinary care, futility is increasingly viewed as more obfuscating than clarifying and is therefore being invoked much less often.

For example, a recent California case involved a 13-year-old girl who suffered a cardiac arrest during a tonsillectomy and adenoidectomy and who was subsequently declared brain dead. Her family refused to accept the determination of death and sued. After several legal appeals, courts agreed that she was dead. Her body was nevertheless given on a respirator to the county coroner, who then transferred the body to the parents. The parents kept the body and authorized that a tracheostomy and a feeding tube be inserted. The court ruled that neither physicians nor a medical facility had any obligation to provide treatments to a dead body, even if the parents asserted, contrary to medical experts, that the patient was not dead.

TABLE 2-2 PRACTICAL CONSIDERATIONS IN TERMINATION OF MEDICAL TREATMENTS

PRACTICAL QUESTION	ANSWER
Is there a legal right to refuse medical interventions?	Yes. The U.S. Supreme Court declared that competent people have a constitutionally protected right to refuse unwanted medical treatments based on the 14th Amendment.
What interventions can be legally and ethically terminated?	Any and all interventions (including respirators, antibiotics, pacemakers, ventricular assist devices, intravenous or enteral nutrition and hydration) can be legally and ethically terminated.
Is there a difference between withholding life-sustaining interventions and withdrawing them?	No. The consensus is that there is no important legal or ethical difference between withholding and withdrawing medical interventions. Stopping a treatment once begun is just as ethical as never having started it.
Whose view about terminating life-sustaining interventions prevails if there is a conflict between the patient and family?	The views of a competent adult patient prevail. It is the patient's body and life.
Who decides about terminating life-sustaining interventions if the patient is incompetent?	If the patient appointed a proxy or surrogate decision maker when competent, that person is legally empowered to make decisions about terminating care. If no proxy was appointed, there is a legally designated hierarchy, usually (1) spouse, (2) adult children, (3) parents, (4) siblings, and (5) available relatives.
Are advance care directives legally enforceable?	Yes. As a clear expression of the patient's wishes, they are a constitutionally protected method for patients to exercise their right to refuse medical treatments. In almost all states, clear and explicit oral statements are legally and ethically sufficient for decisions about withholding or withdrawing medical interventions.

ASSISTED SUICIDE AND EUTHANASIA

History

As far back as the time of Hippocrates, euthanasia and physician-assisted suicide were controversial issues. In 1905, a bill was introduced into the Ohio legislature to legalize euthanasia; it was defeated. In the mid-1930s, similar bills were introduced and defeated in the British Parliament and the Nebraska legislature. As of January 2017, physician-assisted suicide—but not euthanasia—has been made legal in Oregon, Washington, California, Colorado, Vermont, and Washington, D.C. In Montana, the Supreme Court did not recognize a constitutional right to physician-assisted suicide, but it ruled that the law permitting the termination of life-sustaining treatment protected physicians from prosecution if they helped hasten the death of a consenting, rational, terminally ill patient. Of note, however, is that the American College of Physicians does not currently support the legalization of physician-assisted suicide.[6] Both euthanasia and physician-assisted suicide are legal in the Netherlands, Belgium, and Luxembourg, and physician-assisted suicide is legal in Switzerland.

Definition and Justification

The terms *euthanasia* and *physician-assisted suicide* require careful definition (Table 2-3). So-called passive and indirect euthanasia are misnomers and not actual instances of euthanasia; rather, they are ethical and legal ways to terminate care.

TABLE 2-3 DEFINITIONS OF ASSISTED SUICIDE AND EUTHANASIA

TERM	DEFINITION
Voluntary active euthanasia	Intentional administration of medications or other interventions to cause the patient's death with the patient's informed consent
Involuntary active euthanasia	Intentional administration of medications or other interventions to cause the patient's death when the patient was competent to consent but did not consent (e.g., the patient may not have been asked)
Nonvoluntary active euthanasia	Intentional administration of medications or other interventions to cause the patient's death when the patient was incompetent and was mentally incapable of consenting (e.g., the patient might have been in a coma)
Passive euthanasia	Withholding or withdrawal of life-sustaining medical treatments from a patient to let him or her die (termination of life-sustaining treatments)—a poor term that should not be used
Indirect euthanasia	Administration of narcotics or other medications to relieve pain with the incidental consequence of causing sufficient respiratory depression to result in the patient's death
Physician-assisted suicide	A physician provides prescription medications or other interventions to a patient with the understanding that the patient can use them to commit suicide

There are four arguments against permitting euthanasia and physician-assisted suicide. First, Kant and Mill, the philosophical champions of individual autonomy, believed that autonomy itself did not allow a person voluntarily to end conditions that made them autonomous. As a result, both philosophers were against voluntary enslavement and suicide. They therefore argued that the exercise of autonomy cannot include the ending of life, which would mean ending the possibility of exercising autonomy. Second, many dying patients may experience pain and suffering as the result of not receiving appropriate care. It is therefore possible that adequate care and pain management (Chapter 27) might relieve suffering without the need for euthanasia or physician-assisted suicide (Chapter 3). Although some patients may experience uncontrolled pain despite optimal end-of-life care, relatively few give pain as the justification for seeking euthanasia or physician-assisted suicide. Third, there is a clear ethical distinction between intentionally ending a life and terminating life-sustaining treatments. Both the motivations and physical acts are different. Injecting a life-ending medication, or providing a prescription for one, is not the same as removing or refraining from introducing an invasive medical intervention. Finally, permitting euthanasia and physician-assisted suicide may introduce adverse consequences. There are disturbing reports of involuntary euthanasia in the Netherlands and Belgium, and many worry about coercion of expensive or burdensome patients to accept euthanasia or physician-assisted suicide. Permitting euthanasia and physician-assisted suicide is likely to lead to further intrusions of lawyers, courts, and legislatures into the physician-patient relationship.

There are four parallel arguments for permitting euthanasia and physician-assisted suicide. First, it is argued that autonomy justifies euthanasia and physician-assisted suicide. To respect autonomy requires permitting individuals to decide when and how it is better to end their lives. Second, beneficence—furthering the well-being of individuals—supports permitting euthanasia and physician-assisted suicide. In some cases, living can create more pain and suffering than death; ending a painful life relieves more suffering and produces a net good for the patient. Just the reassurance of having the option of euthanasia or physician-assisted suicide, even if not used, can provide "psychological insurance" and be beneficial to people. Third, euthanasia and physician-assisted suicide are no different from termination of life-sustaining treatments that are recognized as ethically justified. In both cases, the patient consents to die; in both cases, the physician intends to end the patient's life and takes some action to end the patient's life; and in both cases, the final result is the same: the patient's death. With no difference in the patient's consent, the physician's intention, or the final result, there can be no difference in the ethical justification. Fourth, the supposed slippery slope that would result from permitting euthanasia and physician-assisted suicide is unlikely. The idea that permitting euthanasia and physician-assisted suicide would undermine the physician-patient relationship or lead to forced euthanasia is completely speculative and not borne out by the available data.

In its 1997 decisions, the U.S. Supreme Court stated that there is no constitutional right to euthanasia and physician-assisted suicide, but that there also is no constitutional prohibition against states legalizing these interventions. Consequently, five states and the District of Columbia (see above) have constitutionally legalized physician-assisted suicide, and others may do so either by legislation or ballot measure.

Empirical Data

Attitudes and practices related to euthanasia and physician-assisted suicide have been studied extensively.[7] Two thirds of Americans say there are some situations in which a patient should be allowed to die, but 30% say that medical professionals should always do everything possible to save a patient's life. About 60% of adults think that these interventions are moral for a person who has an incurable disease and is suffering great pain with no hope of improvement. However, public support dramatically decreases to below 40% for patients who are ready to die because living is a burden or for patients who are burdensome to their families. Overall, public support for physician-assisted suicide in the United States remains just below 50%.

Physicians tend to be much less supportive of euthanasia and physician-assisted suicide than the public, with oncologists, palliative care physicians, and geriatricians among the least supportive. Among American and British physicians, the majority opposes legalizing either practice.

Approximately 25% of American physicians have received requests for euthanasia or physician-assisted suicide, including about 50% of oncologists. Studies also indicate that less than 5% of American physicians have performed euthanasia or physician-assisted suicide. Surveys of oncologists indicate that about 4% have performed euthanasia and about 11% have performed physician-assisted suicide during their careers.

Safeguards for euthanasia and physician-assisted suicide are frequently violated. For example, one study found 54% of euthanasia requests came from the family. In about 40% of euthanasia and 20% of physician-assisted suicide cases, the patient was depressed; in only half of the cases was the request repeated, irrespective of treatment.

Oregon has legally permitted physician-assisted suicide for the longest of any U.S. jurisdiction. Data show that over 70% of patients receiving physician-assisted suicide had cancer. Other characteristics strongly linked to requesting physician-assisted suicide included age over 65 years, white race, more formal education, and having medical insurance.

Importantly, use of physician-assisted suicide is rare. Over 20 years, less than 0.4% of all dying patients died by physician-assisted suicide.[8] In the Netherlands and Belgium, where both euthanasia and physician-assisted suicide are legal, less than 2% of all deaths are by these measures, with 0.4 to 1.8% of all deaths as the result of euthanasia without the patient's consent.[9]

Counterintuitively, in all jurisdictions where it has been studied, pain is not the primary motivation for requesting euthanasia or physician-assisted suicide. In Oregon, loss of autonomy, dignity, and fear of being a burden are cited by patients as the predominant motives. In addition, psychological distress, especially depression and hopelessness, seem to be more important than pain. Interviews with physicians and with patients with amyotrophic lateral sclerosis, cancer, or infection with human immunodeficiency virus show that pain is not associated with interest in euthanasia or physician-assisted suicide; instead, depression and hopelessness are the strongest predictors of interest. These findings raise important issues about the involvement of mental health experts in attempts to determine whether psychiatric treatment would change a patient's views.[10]

Finally, data from the Netherlands and the United States suggest that there are significant problems in performing euthanasia and physician-assisted suicide. Dutch researchers reported that physician-assisted suicide causes complications in 7% of cases. Furthermore, the patients did not die, awoke from coma, or vomited up the medication in 15% of cases. Ultimately, in nearly 20% of physician-assisted suicide cases, the physician ended up injecting the patient with life-ending medication, converting physician-assisted suicide to euthanasia. These data raise serious questions about how to address complications of physician-assisted suicide when euthanasia is illegal or unacceptable.

Practical Considerations

There is widespread agreement that if euthanasia and physician-assisted suicide are used, they should be considered only after all reasonable attempts at physical and psychological palliation have failed. A consensus—with slight differences—among American states and European countries has emerged on safeguards. These safeguards include: (1) the patient must be competent and must request euthanasia or physician-assisted suicide repeatedly and voluntarily; (2) in the Netherlands and other European countries, the patient must have unbearable pain or other suffering that cannot be relieved by optimal palliative interventions; by comparison, there is no requirement for suffering in the United States, but the patient must be terminally ill; (3) there should be a waiting period to ensure that the patient's desire for euthanasia or physician-assisted suicide is stable and sincere; and (4) the physician should obtain a second opinion from an independent physician. Although there have been some prosecutions in the United States, there have been no convictions—except for Dr. Kevorkian—when physicians and others have participated in euthanasia and physician-assisted suicide.

FINANCIAL CONFLICTS OF INTEREST

History

Worrying about how payment structures and fees compromise the integrity of medical decision making is not new. In 1899, a physician reported that more than 60% of surgeons in Chicago were willing to provide a 50% commission to physicians for referring cases. He subsequently argued that in some cases, this fee splitting led to unnecessary surgical procedures. A 1912 study by the American Medical Association confirmed that fee splitting was a common practice and it added to the list of physicians' financial conflicts of interest acts, which included selling patented medicines and patenting surgical instruments. In the 1990s, the ethics of pharmaceutical and biotech companies paying clinical researchers and physicians again raised the issue of financial conflicts of interest.

Definition and Justification

A conflict of interest occurs when a physician's secondary interests, such as making money, risks compromising or undermining a physician's primary interest, especially promoting a patient's well-being. Physicians also have other primary interests: (1) to advance biomedical research, (2) to educate future physicians, and, more controversially, (3) to promote public health (Table 2-4). Physicians also have other, secondary interests, such as earning income, raising a family, contributing to the profession, and pursuing avocational interests, such as hobbies. These secondary interests are not evil; typically, they are legitimate, even admirable. A conflict of interest occurs when one of these secondary interests could compromise pursuit of a primary interest, especially the patient's well-being.

Conflicts of interest are problematic because they can, or at least appear to, compromise the integrity of physicians' judgment, the patient's well-being, or research. Conflicts of interest can induce a physician to do something—perform a procedure, fail to order a test, or distort data—that may not be in a patient's best interest. These conflicts can undermine the trust of both the patient and the public, not only in an individual physician but also in the medical profession at large.

Sometimes a distinction may be claimed between actual and potential conflicts of interest, suggesting that a conflict exists only when a physician's judgment is actually distorted or undermined. This concept is wrong. An actual conflict of interest occurs when a reasonable person could suspect that the physician's judgment could have been altered by the secondary interest. Appearances can be damaging, because it is difficult for patients and the public to determine what motives influence a physician's decision and it often is impossible to know whether judgment actually has been distorted. Financial conflicts of interest are of particular concern, not because they are worse than other types of conflicts, but rather because they are more pervasive, identifiable, and regulated compared with other conflicts. Since ancient times, the ethical norm on conflicts has been clear: the physician's primary obligation is to the patient's well-being, and a physician's personal financial well-being comes second and should never compromise this duty.

TABLE 2-4 PRIMARY INTERESTS OF PHYSICIANS

Promotion of the health and well-being of their patients
Advancement of biomedical knowledge through research
Education of future physicians and health care providers
Promotion of public health

Empirical Data

Financial conflicts are not rare, but they are frequently under-reported. The more imaging facilities and specialty referrals a practice has, the greater the utilization of medical services and the higher the health care spending—often without any clear benefit to the patients. In Florida, nearly 40% of physicians are owners of freestanding facilities to which they refer patients. In one study, 4 to 4.5 times more imaging examinations were ordered by self-referring physicians than by physicians who referred patients to radiologists. Similarly, patients referred to joint-venture physical therapy facilities have an average of 16 visits compared with 11 at non–joint-venture facilities. A recent study of urologists found that those who had integrated radiation facilities into their practices increased their radiation use by 2.5 times compared with urologists who did not have financial relationships with radiation facilities.

Similarly, multiple studies have shown that interaction with pharmaceutical representatives can lead to prescribing of new drugs, nonrational prescribing, and decreased use of generic drugs by physicians. Industry funding for continuing medical education payment for travel to educational symposia increases prescribing of the sponsor's drug. A study of 1,400 FDA advisory committee members found that 13% had some financial interest in a drug company whose product was being reviewed by that committee; these members had a 63% chance of voting for its approval, and an 84% chance of doing so if they sat on advisory boards for that company. A separate study found that 80% of U.S.-based hematologist-oncologists who use Twitter, often to tweet about pharmaceutical products, have at least one financial conflict of interest, with median payments of over $1000.[11]

Regarding researcher conflicts of interest, the available data suggest that corporate funding does not appear to compromise the design and methodology of clinical research; in fact, commercially funded research may be methodologically more rigorous than government- or foundation-supported research. Conversely, data suggest that financial interests do distort researchers' interpretation of data. The most important impact of financial interests, however, appears to be on dissemination of research studies. Growing evidence suggests the suppression or selective publication of data unfavorable to corporate sponsors but the repeated publication of favorable results.

Practical Considerations

First, financial conflicts of interest are inherent in any profession in which the professional earns income from rendering a service. Second, conflicts come in many different forms, from legitimate payment for services rendered and ownership of medical laboratories and facilities, to drug company dinners, payment for attendance at pharmaceutical meetings, and consultation with companies.

Third, in considering how to manage conflicts, it is important to note that people are poor judges of their own potential conflicts. Individuals often cannot distinguish the various influences that guide their judgments, do not think of themselves as inherently bad, and do not imagine that payment shapes their judgments. Physicians tend to be defensive about charges of conflicts of interest. In addition, conflicts tend to act insidiously, subtly changing practice patterns so that they then become what appear to be justifiable norms.

Fourth, rules—whether laws, regulations, or professional standards—to regulate conflicts of interest are based on two considerations: (1) the likelihood that payment or other secondary interests would create a conflict, with greater financial interest tending to increase the risk of compromised judgment, and (2) the magnitude of the potential harm if judgment is compromised. Rules tend to be of three types: (1) disclosure of conflicts, (2) management of conflicts, and (3) outright prohibition. Federal law bans certain types of self-referral of physicians in the Medicare program. The American Medical Association and the Pharmaceutical Research and Manufacturers of America have established joint rules that permit physicians to accept gifts of minimal value but "refuse substantial gifts from drug companies, such as the costs of travel, lodging, or other personal expenses…for attending conferences or meetings." Additionally, the Physician Payment Sunshine Act, which was passed in 2010 as part of the Affordable Care Act and went into effect in August 2013, requires that drug and device manufacturers report all payments and transfers of value given to physicians to the Centers for Medicare and Medicaid Services so that such information can be published on a searchable public website.

Fifth, there is much emphasis on disclosure of conflicts, with the implicit idea being that sunshine is the best disinfectant. Disclosure may be useful in publications for peers, but it is unclear whether this is a suitable safeguard in the clinical setting. Disclosure may instead make patients worry more. Patients may have no context in which to place the disclosure or to evaluate the physician's clinical recommendation, and they may have few other options in selecting a physician or getting care, especially in an acute situation. Furthermore, self-disclosure often is incomplete, even when required.

Finally, some conflicts can be avoided by a physician's own action. Physicians can refuse to engage in personal investments in medical facilities or to accept gifts from pharmaceutical companies at relatively little personal cost. In other circumstances, the conflicts may be institutionalized, and minimizing them can occur only by changing the way organizations structure reimbursement incentives. Capitation encourages physicians to limit medical services, and its potentially adverse effects are likely to be managed by institutional rules rather than by personal decisions.

FUTURE DIRECTIONS

In the near future, as genetics moves from the research to the clinical setting, practicing physicians are increasingly likely to encounter ethical issues surrounding genetic testing, counseling, and treatment. The use of genetic tests without the extensive counseling so common in research studies would alter the nature of the bioethical issues. Because these tests have serious implications for the patient and others, scrupulous attention to informed consent must occur. The bioethical issues raised by genetic tests for somatic cell changes, such as tests that occur commonly in cancer diagnosis and risk stratification, are no different from the issues raised with the use of any laboratory or radiographic test.

In some cases, ethics consultation services may be of assistance in resolving bioethical dilemmas, although current data suggest that consultation services are used mainly for problems that arise in individual cases and are not used for more institutional or policy problems.

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REVIEW QUESTIONS

Medical content: End-of-life care

1. A 26-year-old woman collapses in her apartment because of a cardiac arrest. Her husband calls 9-1-1 after discovering her unconscious. Paramedics take her to the hospital, where she is intubated, ventilated, and ultimately diagnosed as being in a persistent vegetative state. The husband, appointed by the court as his wife's legal guardian, moves to petition to remove the feeding tube. The woman's parents oppose the movement. The woman has no living will. Who has the legal right to make end-of-life decisions in this case?

A. The husband, as he is the legal guardian.
B. The parents, as they are next of kin.
C. The state, as the woman lacked a living will.
D. The physicians, as they are the ones who would actually terminate care.
E. The hospital's ethics committee.

Answer: A This patient was legally incompetent and therefore unable to make end-of-life care decisions. Health care surrogates are selected according to the following priority: guardian, spouse, adult son or daughter, parents, adult siblings, adult relative, close friend, guardian of the estate. Her husband was therefore lawfully appointed to be her guardian and proxy decision maker, as he has higher priority than the woman's parents. Despite the parents' objections, the husband has full legal authority to make the final decisions.

Medical content: Conflict of interest

2. A patient with a headache goes to see his primary care physician. The patient describes the pain as a dull throbbing, not particularly painful, and as having appeared 12 hours earlier after a poor night's sleep. The physician sits on an advisory board of a pharmaceutical company that makes pain relievers. Which of the following represents the *MOST* ethical course of action by the physician?

A. Offer to enroll the patient in the study on a new pain relief medication for migraines.
B. Order magnetic resonance imaging.
C. Prescribe the patient pain relievers from the company on whose board the physician sits.
D. Refer the patient to another provider, as the physician has too many conflicts of interest to be involved in this case.
E. Recommend the patient take an over-the-counter pain reliever, go home, and call back if pain persists or worsens.

Answer: E The patient's symptoms are neither severe nor life-threatening. Especially given the patient's poor sleep prior to the headache's onset, it is reasonable for the physician to only recommend over-the-counter pain relievers and follow-up should the pain persist. Enrolling the patient in the migraine study presents a conflict of interest because the physician would be compensated for such action, and it does not appear the patient actually suffers from migraines. Ordering a magnetic resonance imaging scan would be an example of unnecessary care simply to increase the physician's compensation. Prescribing medications from the company on which the physician sits on the board is also a conflict of interest, because such prescription pills are not needed. If the physician is cognizant of his potential conflicts of interest, he can still provide high-quality care without having to refer the patient to another provider.

3

PALLIATIVE CARE

ROBERT M. ARNOLD

By 2030, 20% of the U.S. population will be older than 65 years, and people older than 85 years constitute the fastest growing segment of the population. Owing to successes in public health and medicine, many of these people will live the last years of their lives with chronic medical conditions such as cirrhosis, end-stage kidney disease, heart failure, and dementia. Even human immunodeficiency virus (HIV) and many cancers, once considered terminal, have turned into chronic diseases.

The burden associated with these illnesses and their treatments is high. Chronically ill patients report multiple physical and psychological symptoms that lower their quality of life. The economic pressures associated with medical care adversely affect patients' socioeconomic status and cause family stress, especially among caregivers, who spend 20 or more hours a week helping their loved ones.

Palliative care, which was developed to decrease the burden associated with chronic illness, emphasizes patient- and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. Palliative care throughout the continuum of illness addresses physical, intellectual, emotional, social, and spiritual needs while facilitating the patient's autonomy, access to information, and choice.

Palliative care is both a subspeciality and a key component of good medicine. Specialty palliative care, delivered by an interdisciplinary team, is available concurrently with or independent of curative or life-prolonging care. Palliative and nonpalliative health care providers should collaborate and communicate about care needs while focusing on peace and dignity throughout the course of illness, during the dying process, and after death.

Given that most seriously ill patients are not seen by a palliative care subspecialist, every clinician should have basic competency in palliative care. For example, all primary care physicians should know the basic tenets of treating pain (Chapter 27) as well as how to discuss advance directives (Chapter 2) and give "bad" news. Specialties with a high prevalence of seriously ill patients, such as critical care and oncology, should have more advanced skills.[1] Interventions to promote both specialty and primary palliative care are associated with improvements in the patient's burden of symptoms and quality of life, although its effects on the caregiver are less consistent.

Five points deserve special emphasis. First, palliative care can be delivered at any time during the course of an illness and is often provided concomitantly with disease-focused, life-prolonging therapy. Waiting until a patient is dying to provide palliative care is a serious error. For example, most elderly patients with chronic incurable illnesses, who might benefit from palliative care, are in the last 10 years of their lives but do not consider themselves to be dying. If palliative care is to have an impact on patients' lives, it should be provided earlier in a patient's illness, in tandem with other treatments. Second, prediction is an inexact science. For most illnesses, including cancer, physicians have trouble accurately predicting whether a patient is in the last 6 months of life (E-Fig. 3-1). Third, palliative care primarily focuses on the illness's burden rather than treating the illness itself. Because these burdens can be physical, psychological, spiritual, or social, good palliative care requires a multidisciplinary approach. Fourth, palliative care takes the family unit as the central focus of care. Treatment plans must be developed for both the patient and the family. Fifth, palliative care recognizes that medical treatments are not uniformly successful and that patients die. At some point in a patient's illness, the treatments may cause more burden than benefit. Palliative care recognizes this reality and starts with a discussion of the patient's goals and the development of an individualized treatment plan.

Many people confuse palliative care with hospice—an understandable confusion because hospices epitomize the palliative care philosophy. The two, however, are different. In the United States, hospice provides palliative care, primarily at home, for patients who have a life expectancy of 6 months or less and who are willing to forgo life-prolonging treatments. However, the requirement that patients must have a life expectancy of 6 months or less limits hospice's availability, as does the requirement that patients give up expensive and potentially life-prolonging treatments. Moreover, because doctors often are unwilling to cease these treatments until very late in the disease course, so are most patients.

PALLIATIVE CARE DOMAINS

Palliative care is a philosophy of care with physical, psychological, spiritual, existential, social, and ethical domains. When caring for patients with chronic life-limiting illness, good palliative care requires that the following questions be addressed:

Is the Patient Physically Comfortable?

Across many chronic conditions, patients have a large number of inadequately treated physical symptoms (Table 3-1). The reasons are multifactorial and range from inadequate physician education, to societal beliefs regarding the inevitability of suffering in chronic illness, to public concerns regarding opioids, to the lack of evidence-based treatments in noncancer patients.

The first step to improve symptom management is a thorough assessment.[2] Standardized instruments such as the Brief Pain Inventory (Fig. 3-1) measure both the patient's symptoms and the effect of those symptoms on the patient's life. Use of standardized instruments (such as the Edmonton Symptom Assessment Scale[3] [E-Fig. 3-2]) assures that physicians will identify overlooked or underreported symptoms and, as a result, will enhance the satisfaction of both the patient and family.

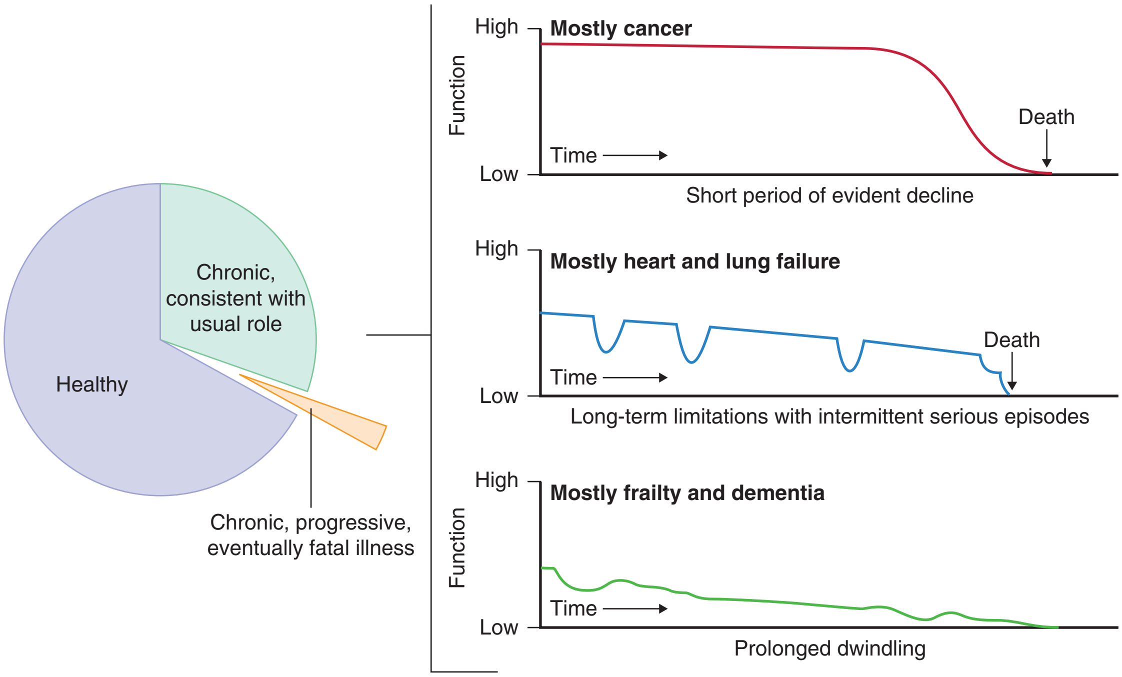
The evidence for the treatment of end-stage symptoms continues to improve. For example, palliative care can improve quality of life in patients with end-stage heart failure, who often require such help.[4] The use of nonsteroidal anti-inflammatory agents and opioids can result in effective pain management

ABSTRACT

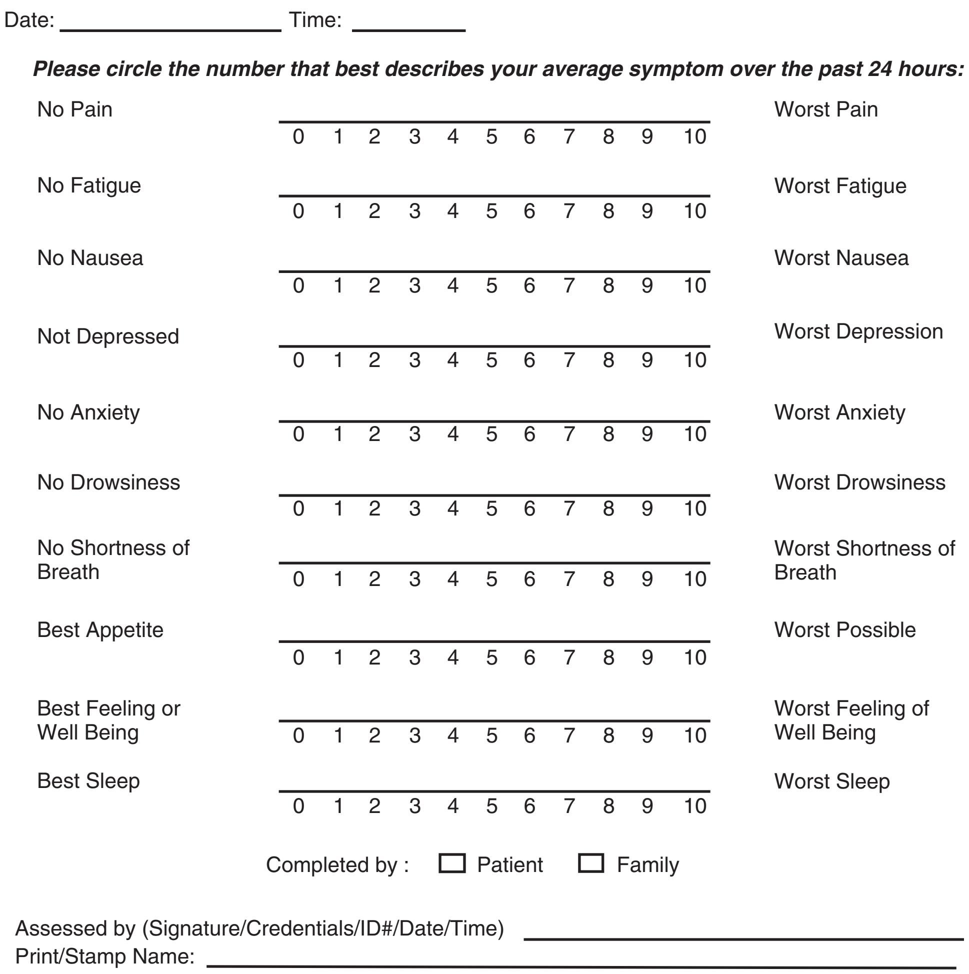
Palliative care, which was developed to decrease the burden associated with chronic illness, emphasizes patient- and family-centered care that optimizes quality of life by anticipating, preventing, and treating suffering. It is both a subspecialty and a key component of good medical care for seriously ill patients. Palliative care should be delivered throughout the course of a patient's illness—from diagnosis through death. The specialty involves a multidisciplinary group of clinicians who work with the patients' primary clinicians to provide an extra layer of support. When caring for patients with serious illness, good palliative care requires that the following questions be addressed: (1) is the patient's care consistent with his or her goals; (2) is the patient physically comfortable or psychologically suffering; and (3) is the family suffering.

KEYWORDS

palliative care
serious illness
end-of-life
supportive care
advance directives
living wills
quality of life



E-FIGURE 3-1. Different disease trajectories for different illnesses. (Permission obtained from RAND Corporation © Lynn J. Perspectives on care at the close of life. Serving patients who may die soon and their families: the role of hospice and other services. *JAMA.* 2001;285:925-932.)



Date: ____________________ Time: __________

Please circle the number that best describes your average symptom over the past 24 hours:

No Pain	0 1 2 3 4 5 6 7 8 9 10	Worst Pain
No Fatigue	0 1 2 3 4 5 6 7 8 9 10	Worst Fatigue
No Nausea	0 1 2 3 4 5 6 7 8 9 10	Worst Nausea
Not Depressed	0 1 2 3 4 5 6 7 8 9 10	Worst Depression
No Anxiety	0 1 2 3 4 5 6 7 8 9 10	Worst Anxiety
No Drowsiness	0 1 2 3 4 5 6 7 8 9 10	Worst Drowsiness
No Shortness of Breath	0 1 2 3 4 5 6 7 8 9 10	Worst Shortness of Breath
Best Appetite	0 1 2 3 4 5 6 7 8 9 10	Worst Possible
Best Feeling or Well Being	0 1 2 3 4 5 6 7 8 9 10	Worst Feeling of Well Being
Best Sleep	0 1 2 3 4 5 6 7 8 9 10	Worst Sleep

Completed by : ☐ Patient ☐ Family

Assessed by (Signature/Credentials/ID#/Date/Time) ______________________________
Print/Stamp Name: ______________________________

E-FIGURE 3-2. Edmonton Symptom Assessment System. (Hui D, Bruera E. The Edmonton Symptom Assessment System 25 years later: past, present, and future developments. *J Pain Symptom Manage.* 2017;53:630-643.)

TABLE 3-1 APPROACHES TO THE MANAGEMENT OF PHYSICAL AND PSYCHOLOGICAL SYMPTOMS

SYMPTOM	ASSESSMENT	TREATMENT
Pain	How severe is the symptom (as assessed with the use of validated instruments) and how does it interfere with the patient's life? What is the etiology of the pain? Is the pain assumed to be neuropathic or somatic? What has the patient used in the past (calculate previous days' equal analgesic dose)?	Prescribe medications to be administered on a standing or regular basis if pain is frequent. For mild pain: use acetaminophen or a nonsteroidal anti-inflammatory agent. For moderate pain: titrate short-acting opioids (see Table 27-4). For severe pain: rapidly titrate short-acting opioids until pain is relieved or intolerable side effects develop; start long-acting opiates once pain is controlled. Rescue doses: prescribe immediate-release opioids—10% of the 24-hour total opiate every hour (orally) or every 30 minutes (parenterally) as needed. Concomitant analgesics (e.g., corticosteroids, anticonvulsants, tricyclic antidepressants, and bisphosphonates) should be used when applicable (particularly for neuropathic pain). Consider alternative medicine and interventional treatments for pain.
Constipation	Is the patient taking opioids? Does the patient have a fecal impaction?	Prescribe laxatives for all patients on opiates. If ineffective, add drugs from multiple classes (e.g., stimulant, osmotic laxatives, and enemas). Prescribe methylnaltrexone if still constipated.
Shortness of breath	Ask the patient to assess the severity of the shortness of breath. Does the symptom have reversible causes?	Prescribe oxygen to treat hypoxia-induced dyspnea, but *not* if the patient is not hypoxic. Opioids relieve breathlessness without measurable reductions in respiratory rate or oxygen saturation; effective doses are often lower than those used to treat pain. Aerosolized opiates do not work. Fans or cool air may work through a branch of the trigeminal nerve. Use reassurance, relaxation, distraction, and massage therapy.
Fatigue	Is the patient too tired for activities of daily living? Is the fatigue secondary to depression? Is a disease process causing the symptom or is it secondary to reversible causes?	Provide cognitive education about conserving energy use. Treat underlying conditions appropriately.
Nausea	Which mechanism is causing the symptom (e.g., stimulation of the chemoreceptor trigger zone, gastric stimulation, delayed gastric emptying or "squashed stomach" syndrome, bowel obstruction, intracranial processes, or vestibular vertigo)? Is the patient constipated?	Prescribe an agent directed at the underlying cause (Chapter 123). If persistent, give antiemetic around the clock. Multiple agents directed at various receptors or mechanisms may be required.
Anorexia and cachexia	Is a disease process causing the symptom, or is it secondary to other symptoms (e.g., nausea and constipation) that can be treated? Is the patient troubled by the symptom or is the family worried about what not eating means?	A nutritionist may help find foods that are more appetizing (Chapter 202). Provide counseling about the prognostic implications of anorexia (Chapter 206).
Delirium	Is the cause reversible? Is the confusion acute, over hours to days? Does consciousness wax and wane? Is there a problem of attention? Does the patient have disorganized thinking? Does the patient have an altered level of consciousness—either agitated or drowsy?	Identify underlying causes and manage symptoms (Chapter 25). Recommend behavioral therapies, including avoidance of excess stimulation, frequent reorientation, and reassurance. Ensure presence of family caregivers and explain delirium to them. Prescribe haloperidol, risperidone, or olanzapine.
Depression	Over the last 2 weeks, have you been bothered (0) not at all, (1) several days, (2) more than half the days, (3) every day by: + Little interest or pleasure in doing things + Feeling down, depressed, or hopeless	Add the points for each answer. For a score >2, further evaluation is recommended, with consideration of supportive psychotherapy, cognitive approaches, behavioral techniques, pharmacologic therapies (see Table 369-5), or a combination of these interventions. Prescribe psychostimulants for rapid treatment of symptoms (within days) or selective serotonin reuptake inhibitors, which may require 3 to 4 weeks to take effect; tricyclic antidepressants are relatively contraindicated because of their side effects.
Anxiety (applicable also for family members)	Over the last 2 weeks, have you been bothered (0) not at all, (1) several days, (2) more than half the days, (3) every day by: + Feeling nervous, anxious, or on edge + Not being able to stop or control worrying	Add the points for each answer. A score of >2 should lead to a more in-depth evaluation (see Chapter 369) and consideration of supportive counseling and benzodiazepines (Table 369-9).
Spiritual distress	Are you at peace?	Inquire about spiritual support.

Modified from Morrison RS, Meier DE. Palliative care. *N Engl J Med.* 2004;350:2582-2590.

in more than 75% of patients with cancer. Advances such as intrathecal pumps and neurolytic blocks are helpful in the remaining 25% (Chapter 27). The use of oxygen is not helpful for refractory dyspnea except when hypoxia has been documented, whereas use of medications for depression often can be helpful (Chapter 369).

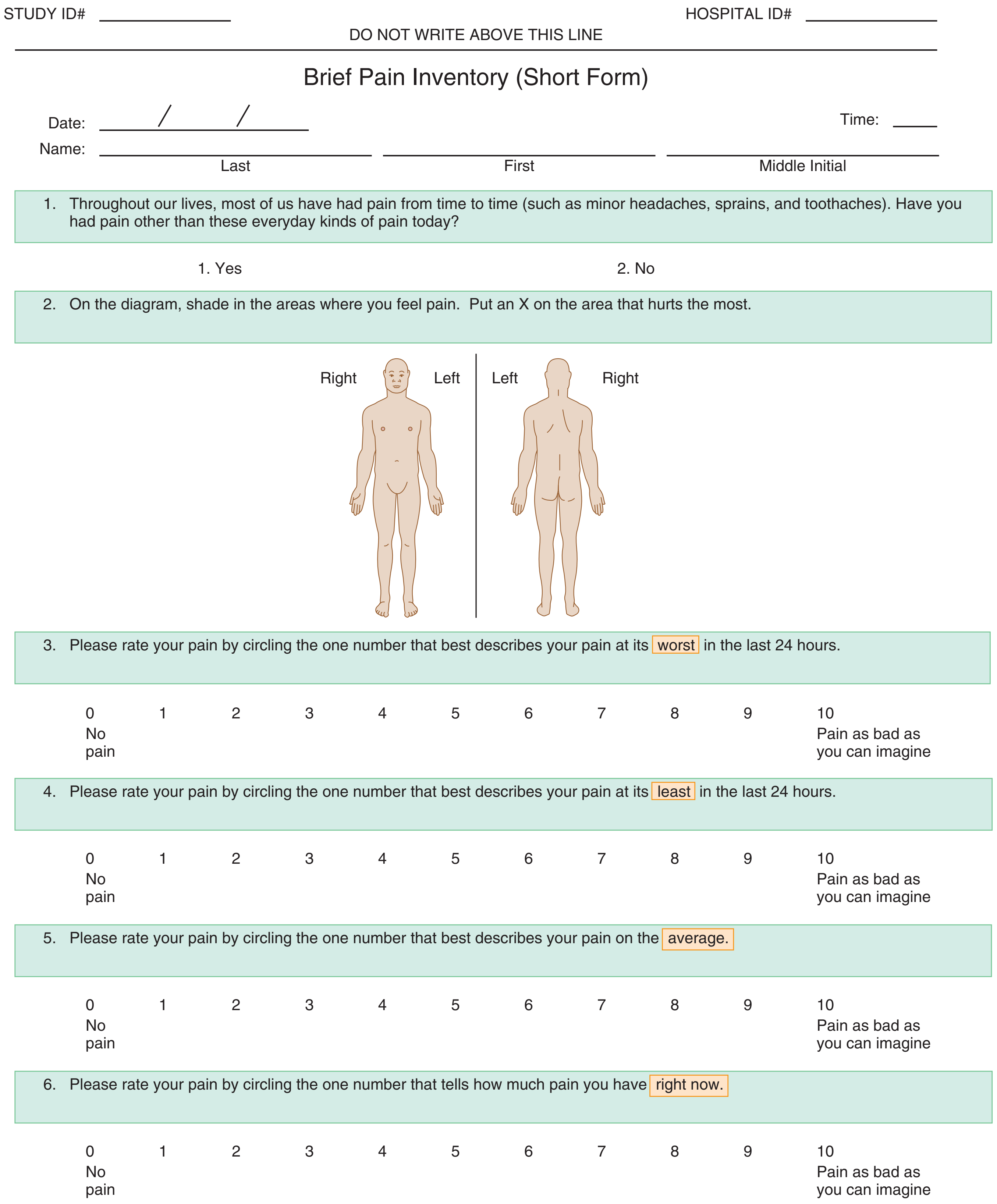
Is the Patient Psychologically Suffering?

Patients may be physically comfortable but still suffering. Psychological symptoms and syndromes such as depression, delirium, and anxiety are common in patients with life-limiting or chronic illnesses. It may be difficult to determine whether increased morbidity and mortality are caused by the physical effects of the illness or by the psychological effects of depression and anxiety on energy, appetite, or sleep. Screening questions focusing on mood (e.g., "Have you felt down, depressed, and hopeless most of the time for the past 2 weeks?") and anhedonism (e.g., "Have you found that little brings you pleasure or joy in the past 2 weeks?") have been shown to help in diagnosing depression in this population. Increasing data show that treatment of depression in chronic illness is possible and improves both morbidity and mortality.

For patients and families facing mortality, existential and spiritual concerns are common. Progressive illness often raises questions of love, legacy, loss, and meaning. A physician's role is not to answer these questions or to provide reassurance, but rather to understand concerns of the patient and family, how they are coping, and what resources might help. Spirituality often is a source of comfort, and physicians can ascertain a patient's beliefs using a brief instrument such as the FICA Spiritual Assessment Tool (Table 3-2). A single screening question such as "Are you at peace?" may identify patients who are in spiritual distress and facilitate referrals to chaplains.

Is the Family Suffering?

Families, defined broadly as those individuals who care most for the patient, are an important source of support for most patients. Families provide informal caregiving, often at the expense of their own physical, economic, and psychological health. Good palliative care requires an understanding of how the family is coping and a search for ways to provide family members with the social or clinical resources they need to improve their well-being. Comprehensive and



STUDY ID# ________ HOSPITAL ID# ________

DO NOT WRITE ABOVE THIS LINE

Brief Pain Inventory (Short Form)

Date: ____/____/____ Time: ____

Name: ____________ ____________ ____________

Last First Middle Initial

1. Throughout our lives, most of us have had pain from time to time (such as minor headaches, sprains, and toothaches). Have you had pain other than these everyday kinds of pain today?

1. Yes 2. No

2. On the diagram, shade in the areas where you feel pain. Put an X on the area that hurts the most.

3. Please rate your pain by circling the one number that best describes your pain at its **worst** in the last 24 hours.

0 No pain	1	2	3	4	5	6	7	8	9	10 Pain as bad as you can imagine

4. Please rate your pain by circling the one number that best describes your pain at its **least** in the last 24 hours.

0 No pain	1	2	3	4	5	6	7	8	9	10 Pain as bad as you can imagine

5. Please rate your pain by circling the one number that best describes your pain on the **average.**

0 No pain	1	2	3	4	5	6	7	8	9	10 Pain as bad as you can imagine

6. Please rate your pain by circling the one number that tells how much pain you have **right now.**

0 No pain	1	2	3	4	5	6	7	8	9	10 Pain as bad as you can imagine

FIGURE 3-1. Brief Pain Inventory (short form). (Copyright 1991. Charles S. Cleeland, PhD, Pain Research Group. All rights reserved.)

7. What treatments or medications are you receiving for your pain?

____

8. In the last 24 hours, how much relief have pain treatments or medications provided? Please circle the one percentage that most shows how much relief you have received.

0% No pain	10%	20%	30%	40%	50%	60%	70%	80%	90%	100% Complete relief

9. Circle one number that describes how, during the past 24 hours, pain has interfered with your:

A. General Activity

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

B. Mood

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

C. Walking Ability

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

D. Normal Work (includes both work outside the home and housework)

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

E. Relations with Other People

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

F. Sleep

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

G. Enjoyment of Life

0 Does not interfere	1	2	3	4	5	6	7	8	9	10 Completely interferes

FIGURE 3-1, cont'd.

individually targeted interventions can reduce caregivers' burdens, although the absolute benefits are relatively small.

Because patients in palliative care often die, the palliative care team must address bereavement and postdeath family suffering. Good communication and informational brochures in an intensive care unit can decrease family members' adverse psychological outcomes after death. A letter of condolence or a follow-up phone call to the next of kin after a patient's death is respectful and offers the opportunity to clarify questions about the patient's care. Some family members suffer from complicated grief—a recently described syndrome associated with separation and traumatic distress, with symptoms persisting for more than 6 months. Primary care physicians, who have ongoing relationships with the loved one, and hospices, which provide bereavement services for a year after the patient's death, have the opportunity to assess whether the grief symptoms persist or worsen.

Is the Patient's Care Consistent with the Patient's Goals?

The sine qua non for palliative care is ensuring that the treatment plan is consistent with the patient's values. Some patients prefer longevity over quality of life, but a large proportion of elderly, seriously ill patients are not focused on living as long as possible. Instead, they want to maintain a sense of control, relieve their symptoms, improve their quality of life, avoid being a burden on their families, and have a closer relationship with their loved ones.

Ensuring that treatment is consistent with a patient's goals requires good communication skills (Table 3-3). The approaches to giving bad news,

TABLE 3-2 FICA SPIRITUAL ASSESSMENT TOOL

F—What is your **faith**/religion? Do you consider yourself a religious or spiritual person? What do you believe in that gives meaning/importance to life?
I—**Importance** and **influence** of faith. Is your faith/religion important to you? How do your beliefs influence how you take care of yourself? What are your most important hopes? What role do your beliefs play in regaining your health? What makes life most worth living for you? How might your disease affect this?
C—Are you part of a religious or spiritual **community**? Is this of support to you, and how? Is there a person you really love or is very important to you? How is your family handling your illness? What are their reactions/expectations?
A—How would you like me to **address** these issues in your health care? What might be left undone if you were to die today? Given the severity or chronicity of your illness, what is most important for you to achieve? Would you like me to talk to someone about religious/spiritual matters?

From Puchalski C, Romer A. Taking a spiritual history. *J Palliat Med.* 2000;3:129-137.

TABLE 3-3 CORE COMMUNICATION SKILLS

RECOMMENDED SKILL	EXAMPLE
A. IDENTIFYING CONCERNS AND RECOGNIZING CUES	
Elicit Concerns	
Open-ended questions	“Is there anything you wanted to talk to me about today?”
Active listening	Allowing patient to speak without interruption; allowing pauses to encourage patient to speak
Recognize Cues	
Informational concerns	Patient: “I’m not sure about the treatment options”
Emotional concerns	Patient: “I’m worried about that”
B. RESPONDING TO INFORMATIONAL CONCERNS	
“Ask-tell-ask”	Topic: communicating information about cancer stage
Ask	“Have any of the other doctors talked about what stage this cancer is?”
Tell	“That’s right, this is a stage IV cancer, which is also called metastatic cancer…”
Ask	“Do you have questions about the staging?”
C. RESPONDING TO EMOTIONAL CONCERNS	
Nonverbal Empathy: S-O-L-E-R	
S	Face the patient **S**quarely
O	Adopt an **O**pen body posture
L	**L**ean toward the patient
E	Use **E**ye contact
R	Maintain a **R**elaxed body posture
Verbal Empathy: N-U-R-S-E	
N	**N**ame the emotion: “You seem worried”
U	**U**nderstand the emotion: “I see why you are concerned about this”
R	**R**espect the emotion: “You have shown a lot of strength”
S	**S**upport the patient: “I want you to know that I will still be your doctor whether you have chemotherapy or not”
E	**E**xplore the emotion: “Tell me more about what is worrying you”
D. DISCUSSING GOALS OF CARE	
R	**R**eframe that the status quo is not working: “I worry that more treatment will hurt you more than help”
E	**E**xpect emotion: “I can see this is not what you wanted to hear”
M	**M**ap the patient values: “Have you ever filled out a living will?” “Given the medical situation, what brings you joy and meaning?” “As you look at the future what do you want to avoid?”
A	**A**lign with the patient values: “What I am hearing you say is.…”
P	**P**ropose a plan

Adapted from Back AL, Arnold RM, Tulsky JA. *Discussing Prognosis.* Alexandria, VA: American Society of Clinical Oncology; 2008.

discussing goals of care, and talking about forgoing life-sustaining treatment have similar structures.[5] First, the patient needs to understand the basic facts about the diagnosis, possible treatments, and prognosis. The communication skill that helps physicians communicate information is *Ask-Tell-Ask*—exploring what the patient knows or wants to know, then explaining or answering questions, and then providing an opportunity for the patient to ask more. In the hospital, where discontinuity of care is common and misunderstandings frequent, it is important to determine what the patient knows before providing information so as to keep everyone well coordinated. When giving bad news, knowing what the patient knows allows the physician to anticipate the patient’s reaction. Finally, information must be titrated based on the patient’s preferences. Although most patients want to hear everything about their disease, a minority do not. There is no foolproof way to ascertain what any patient wants to know other than by asking.

When giving patients information, it is important to give small pieces of information, not use jargon, and to confirm that patients understand what they have been told.[6] Caregivers should focus on the key message the patient should hear (the headline) rather than overwhelming the patient with biomedical information. Giving information is like dosing a medication: one gives information, checks understanding, and then gives more information based on what the patient has heard.

After ensuring that the doctor and the patient have a shared understanding of the medical facts, the physician should engage in an open-ended conversation about the patient’s goals as the disease progresses. This strategy requires that the patient be asked about both hopes and fears. One might ask: “Given the medical situation, as you think about the future, what brings you joy and pleasure?” “If your time is limited, what are the things that are most important to achieve?” “What are your biggest fears or concerns?” “As you think about the future what do you want to avoid or not have the doctors do?” The clinician can use an understanding of these goals to make recommendations about which treatments to provide and which treatments would not be helpful. As a result, early palliative care can improve quality of life, mood, and even survival.

Physicians find talking about prognosis particularly difficult for two reasons: first, it is hard to foretell the future accurately; and second, they fear this information will “take away patients’ hope.” Thus, they often avoid talking to patients about these issues unless specifically asked. Although some patients do not want to hear prognostic information, for many patients, this information helps them plan their lives. Patients who are told that their disease is generally terminal are more likely to spend a longer period of time in hospice and avoid aggressive treatment at the end of life, without adverse psychological consequences. Furthermore, their families usually have fewer postdeath adverse psychological outcomes.

Given that one cannot guess how much information to provide, a physician can start these conversations by asking, “Are you the kind of person who wants to hear about what might happen in the future with your illness or would you rather take it day by day?” If the patient requests the latter, the physician can follow up by asking if there is someone else with whom he or she can talk about the prognosis. Second, before giving prognostic information, it is useful to inquire about the patient’s concerns in order to provide information in the most useful manner. Finally, it is appropriate when discussing prognostic information to acknowledge uncertainty: “The course of this cancer can be quite unpredictable, and physicians don’t have a crystal ball. I think you should be aware of the possibility that your health may deteriorate quickly, and you should plan accordingly. We probably are dealing with weeks to months, although some patients do better, and some do worse. Over time, the course may become clearer, and if you wish, I may be able to be a little more precise about what we are facing.”

The physician must discuss these topics in an empathic way. Palliative care conversations are as much about emotions as facts. Talking about disease progression or death may elicit negative emotions such as anxiety, sadness, or frustration. These emotions decrease a patient’s quality of life and interfere with the ability to hear factual information. Empathic responses strengthen the patient-physician relationship, increase the patient’s satisfaction, and make the patient more likely to disclose other concerns. The first step is recognizing when the patient is expressing emotions. Once the physician recognizes the emotion being expressed, he or she can respond empathically.

It is also important for physicians to recognize their own emotional reactions to these conversations. The physician's emotional reactions color impressions of the patient's prognosis, thereby making it hard to listen to the patient, and may influence the physician to hedge bad news. The physician should become aware of her or his own emotional reactions to ensure that the conversation focuses on the patient rather than the health care provider's needs.

In addition to good communication skills, palliative care requires a basic knowledge of medical ethics and the law. For example, patients have the moral and legal right to refuse any treatment, even if refusal results in their death. There is no legal difference between withholding and withdrawing life-sustaining treatment. In many states, physicians' aides can legally help in the dying process by clearly prescribed methods. When confronted with areas of ambiguity, the physician should know how to obtain either a palliative care or ethics consultation.

During the past 10 years, there has been a societal push to encourage patients to designate health care proxies and to create advance care planning documents, typified by the use of living wills.[7] These documents are meant to protect patients against unwanted treatments and to ensure that as they are dying, their wishes are followed. Unfortunately, there are few empirical data showing that these documents actually change practice. Still, discussions of the documents with health professionals and family members generally provoke important conversations about end-of-life care decisions and may help families confronted with difficult situations know they are respecting their loved one's wishes.[8]

Is the Patient Going to Die in the Location of Choice?

Most patients say that they want to die at home. Unfortunately, most patients die in institutions—either hospitals or nursing homes. Burdensome transitions decrease quality in end-of-life care. Good palliative care requires establishing a regular system of communication to minimize transitional errors. A social worker who knows about community resources is important in the development of a dispositional plan that respects the patient's goals.

Hospice programs are an important way to allow patients to die at home. In the United States, *hospice* refers to a specific, government-regulated form of end-of-life care, available under Medicare since 1982 but subsequently adopted by Medicaid and many other third-party insurers. Hospice care typically is given at home, a nursing home, or specialized acute care unit. Care is provided by an interdisciplinary team, which usually includes a physician, nurse, social worker, chaplain, volunteers, bereavement coordinator, and home health aides, all of whom collaborate with the primary care physician, patient, and family. Bereavement services are offered to the family for a year after the death.

Hospices are paid on a per diem rate and are required to cover all the costs related to the patient's life-limiting illness. Because of this and the fact that their focus is on comfort rather than life prolongation, many hospices will not cover expensive treatments such as inotropic agents in heart failure or chemotherapy in cancer, even if they have a palliative effect. Not surprisingly, many hospices are experimenting with different service models that do not require patients to forgo possibly life-prolonging treatments, in an attempt to enroll patients earlier in the course of their illness and increase access to their services.

Hospice care for nursing home residents is associated with less aggressive care near death but an overall increase in Medicare expenditures.[9] By comparison, interdisciplinary palliative care for hospitalized adults with serious illness can reduce costs.[10]

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REVIEW QUESTIONS

1. A 75-year-old man with lung cancer is admitted to the hospital with severe shortness of breath. Work-up reveals no other cause of his shortness of breath other than lymphogenic spread of his cancer. His oxygen saturation is 94%. Which of the following treatments should be instituted for his dyspnea?

A. Morphine
B. Benzodiazepines
C. Oxygen
D. A and C
E. All the above

Answer: A In randomized controlled data, opioids have been shown to decrease dyspnea both in lung cancer patients and in patients with COPD. Oxygen is helpful only if the patient has hypoxia. Benzodiazepines have not been shown to decrease breathlessness.

2. Which of the following is NOT required for a patient to be in hospice?

A. The patient must be DNR.
B. The patient must have a life-limiting illness, which is likely to cause her death in 6 months.
C. The patient wishes to focus on quality of life rather than longevity of life.
D. If the patient lives at home, she must have a primary caregiver.

Answer: A The patient does not have to be DNR to be in hospice. The others are requirements of hospice.

3. Which of the following is true of depression in life-limiting illnesses?

A. It is a normal reaction when people have a life-limiting illness, and it should not be treated.
B. It cannot be improved because the treatments take too long to work in patients with serious illness.
C. Treatment of depression decreases both morbidity and mortality.
D. It requires a psychiatric consult because treatment is very complicated.

Answer: C Data show that the treatment of depression improves both quality of life and mortality.

4. Which of the following is true?

A. Telling patients that they have a terminal illness will result in their losing hope.
B. Telling patients they have a terminal illness has no impact on their desire for future treatment.
C. Telling patients that they have terminal illnesses is associated with their choosing hospice more frequently.
D. Patients have clearly stated that they do not want to be told that they have a terminal illness.

Answer: C Data suggest that telling patients that they have a life-limiting illness is associated with a lower likelihood of choosing aggressive care at the end of life and is not associated with poorer psychiatric outcomes.

5. Which of the following is NOT a key component of the definition of specialty palliative care?

A. The care is interdisciplinary.
B. The care focuses on physical, spiritual, and psychological components.
C. The care is inconsistent with life-prolonging treatment.
D. The care model includes the family.

Answer: C Specialty palliative care can be given while a patient is also receiving life-prolonging care. All the other answers are correct.

6. Pain is a common symptom in patients with cancer, and opiates are often required to control the pain. Patients who are taking oral opiates should also be assessed for which of the following problems?

A. Hypogonadism
B. Constipation
C. HIV infection
D. QT prolongation

Answer: B Constipation is a very common symptom of opiates and most patients on opiates need a laxative. On the other hand, hypogonadism is an uncommon side effect of opiates and should not routinely be screened for. QT prolongation is seen with methadone but not other opiates. HIV is not associated with oral opiate use.

4

DISPARITIES IN HEALTH AND HEALTH CARE

JOHN Z. AYANIAN

Disparities in health care and health are evident in all countries around the world. Health disparities often reflect a country's specific history, such as the legacy of conquest and colonization for American Indians and of slavery and segregation for African Americans. Socioeconomic disparities in health related to poverty or lack of education occur globally and can be reduced by better educational and economic opportunities and by effective health care systems and social services.

Most efforts to understand and reduce health disparities have focused on race, ethnicity, and socioeconomic status, and have sought to disentangle the relative impact of health care, health behaviors, and biologic, social, and environmental factors as contributors to these disparities. More recently, these efforts have expanded to assess a wider range of health disparities, including those faced by sexual minorities, people with disabilities, and people in disadvantaged urban or rural areas.

DEFINITIONS OF HEALTH DISPARITY AND HEALTH EQUITY

The U.S. Department of Health and Human Services defines a health disparity as a "health difference that is closely linked with economic, social, or environmental disadvantage." Conversely, health equity is defined as the "attainment of the highest level of health for all people."[1] These definitions build on U.S. National Academy of Medicine reports in which equitable health care was defined as "care that does not vary in quality due to personal characteristics, such as gender, ethnicity, geographic location, or socioeconomic status" and which identified racial and ethnic disparities in health care as an important contributor to disparities in health outcomes. However, not all differences in health care represent unacceptable disparities related to discrimination and unequal treatment of patients in the health care system. For example, differences may be related to clinical appropriateness or patients' preferences.

DEMOGRAPHIC CHANGES IN U.S. POPULATION

The racial and ethnic composition of the U.S. population has changed substantially over the past 50 years, growing from 193 million in 1965 to 324 million in 2015, with almost half of this growth related to nearly 60 million new immigrants. During these 50 years, the non-Hispanic white proportion of the U.S. population dropped from 84 to 62%, and the African American proportion rose slightly from 11 to 12%. In contrast, the Hispanic proportion grew substantially from 4 to 18%, and the Asian proportion increased from 1 to 6%. These trends are projected to continue through 2065, when the corresponding proportions of the U.S. population are projected to be 46% for non-Hispanic whites, 13% for African Americans, 24% for Hispanics, and 14% for Asians if current immigration patterns persist.

RACIAL AND ETHNIC DISPARITIES IN HEALTH OUTCOMES

Substantial differences in life expectancy between African Americans and white Americans have narrowed in the past 40 years as life expectancy has risen (Fig. 4-1). Notably, life expectancy is now about 3 years longer for Hispanic men and women relative to white men and women.

Heart disease and cancer are the two leading causes of death for all five racial and ethnic groups officially designated by the U.S. federal government, but age-adjusted death rates for specific causes vary substantially by race and ethnicity (Table 4-1). African Americans have the highest age-adjusted death rates, overall and due specifically to heart disease and to cancer, followed by non-Hispanic whites. African Americans also have the highest death rates from cerebrovascular disease, diabetes mellitus, and kidney disease, but lower-than-average death rates from chronic lung disease, poisoning, and suicide. Non-Hispanic whites, in contrast, have higher-than-average death rates from these latter three causes.

Hispanics have lower-than-average death rates from all causes except diabetes mellitus (see Table 4-1). American Indians have lower-than-average death rates from most causes except diabetes mellitus and poisoning, but they also

ABSTRACT

Life expectancy in the United States varies substantially by race, ethnicity, and socioeconomic status. Relative to other racial and ethnic groups, African Americans have the highest death rates overall and due to heart disease and cancer—the two most common causes of death in the United States. American adults with low incomes have substantially shorter life expectancy than more affluent adults, and the magnitude of this disparity differs widely among U.S. geographic areas. These differences arise from differences in health risk factors such as smoking and hypertension, as well as disparities in insurance coverage and access to care. The increasing diversity of the U.S. population has created new challenges and opportunities for health care providers and organizations to serve patients from diverse backgrounds. Trained interpreters improve care for patients with limited English proficiency, and coordinated care especially benefits disadvantaged patients by reducing fragmentation. Health care organizations should implement reporting systems to monitor disparities in the quality and outcomes of care, set measurable goals for reducing disparities, and encourage programs to meet these goals.

KEYWORDS

health care disparities
health disparities
health equity
race
ethnicity
socioeconomic factors

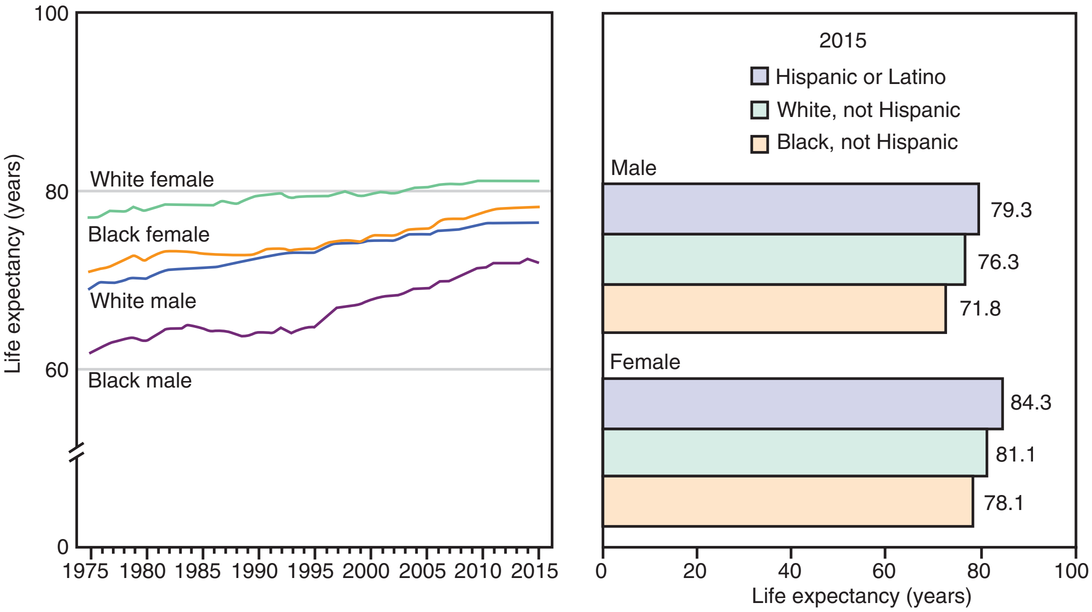

FIGURE 4-1. Life expectancy at birth. Note: Life expectancy data by Hispanic origin were available starting in 2006 and were corrected to address racial and ethnic misclassification. (Source: NCHS, *Health, United States, 2016,* Figure 6. Data from the National Vital Statistics System [NVSS].)

TABLE 4-1 AGE-ADJUSTED DEATH RATES FOR 10 LEADING CAUSES OF DEATH BY RACE/ETHNICITY IN UNITED STATES, 2015*

	ALL PERSONS	WHITE, NON-HISPANIC	AFRICAN AMERICAN	HISPANIC OR LATINO	ASIAN OR PACIFIC ISLANDER	AMERICAN INDIAN OR ALASKA NATIVE
All causes	733.1	753.2	851.9	525.3	394.8	596.9
Heart disease	168.5	171.9	205.1	116.9	86.5	118.5
Cancer	158.5	163.7	180.1	110.3	99.0	107.9
Chronic lung disease	41.6	46.9	28.9	17.7	12.2	30.9
Cerebrovascular disease	37.6	36.4	50.8	32.3	29.8	24.7
Alzheimer disease	29.4	30.8	26.6	24.2	14.7	15.4
Diabetes mellitus	21.3	18.9	37.0	25.2	15.7	34.2
Influenza & pneumonia	15.2	15.4	15.9	11.4	14.0	12.5
Poisoning	14.8	18.8	11.1	7.7	2.4	16.1
Kidney disease	13.4	12.2	25.4	11.4	8.3	12.2
Suicide	13.3	17.0	5.6	6.2	6.4	12.6

*Per 100,000 population, from *Health, United States, 2016: With Chartbook on Long-term Trends in Health.* Hyattsville, MD: National Center for Health Statistics; 2017:120-123.

have markedly elevated death rates from chronic liver disease (26.4 deaths per 100,000 vs. 10.8 among all persons). Asians and Pacific Islanders together have lower-than-average death rates from each of the 10 leading causes of death, including markedly lower rates for heart disease, cancer, chronic lung disease, Alzheimer disease, poisoning, and suicide.

Major health risk factors that contribute to morbidity and mortality among adults vary substantially by race, ethnicity, and level of education. African American adults have the highest age-adjusted prevalence of hypertension (43%; Chapter 70), which is a major contributor to their high rates of heart disease, cerebrovascular disease, and kidney disease; whereas the prevalence of hypertension is substantially lower among non-Hispanic whites (29%), Hispanics (28%), and Asians (27%). In contrast, the prevalence of diabetes mellitus is substantially higher among African Americans (18%), Mexican Americans (18%), and Asians (16%) than among non-Hispanic whites (10%).[2]

Smoking rates (Chapter 29) vary widely in the United States by race/ethnicity and sex. Rates are highest among non-Hispanic white men (21%), African American men (22%), and American Indian men (28%) and women (24%). Smoking rates are intermediate among non-Hispanic white women (19%), African American women (14%), Hispanic men (16%), and Asian men (15%), and they are lowest among Hispanic women (7%) and Asian women (5%).[3]

SOCIOECONOMIC DISPARITIES IN HEALTH OUTCOMES

Socioeconomic gradients in morbidity and mortality, which are a major component of health disparities, have widened in the United States in recent years. Adults with high incomes have experienced substantial gains in life expectancy related to their lower smoking rates and better control of hypertension, hyperlipidemia, and other chronic health conditions and risk factors. By comparison, adults with low incomes have experienced minimal gains overall.[4] Among middle-aged non-Hispanic white adults without postsecondary education, life expectancy has actually decreased since 1999 as a result of rising death rates from alcohol-related liver disease, drug overdoses, and suicide.[5]

U.S. smoking rates have declined substantially since 1974, with the steepest drop among college graduates (Fig. 4-2). Higher smoking rates among less educated adults remain a major contributor to socioeconomic disparities in morbidity and mortality. The temporal improvement in smoking rates overall has been offset by marked increases in age-adjusted death rates due to drug overdoses—particularly among non-Hispanic whites, who have had a threefold increase in this death rate from 1999 to 2015 primarily due to opioid overdoses (Fig. 4-3).[6]

The magnitude of socioeconomic disparities in mortality vary widely by geographic region within the United States. When considering life expectancy at age 40, for example, adults with incomes in the lowest quartile can expect to survive to age 81 years in New York City and several California cities, but only to age 77 years in some cities in Ohio, Indiana, and Michigan. These disparities in life expectancy are primarily related to regional differences in the prevalence of behavioral and metabolic risk factors, including smoking, limited physical activity, obesity, hypertension, and diabetes mellitus.[7]

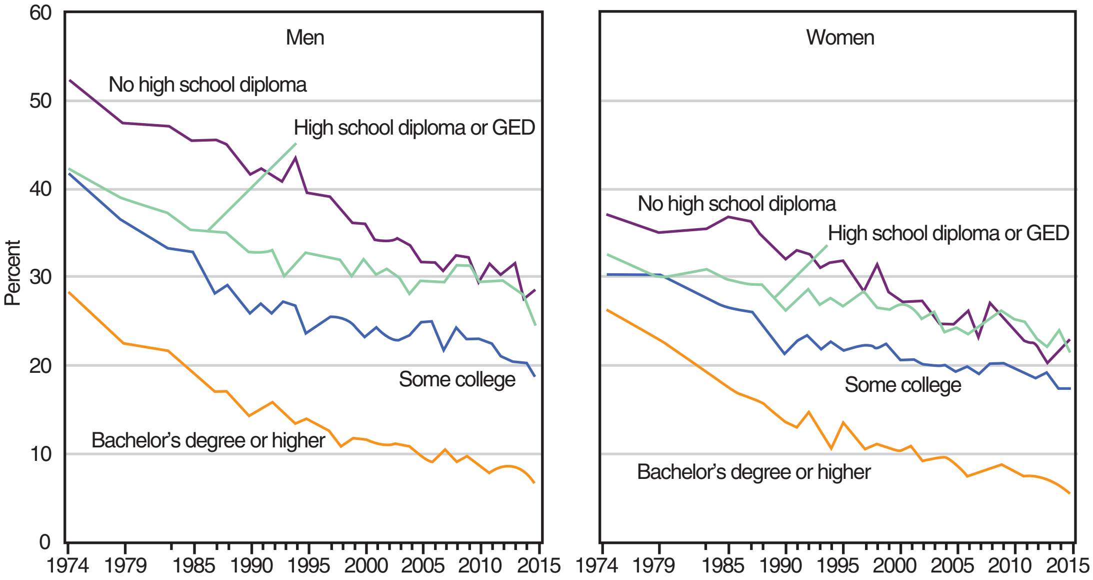

FIGURE 4-2. Current cigarette smoking: Adults aged 25+. Note: Smoked 100 cigarettes in their lifetime and now smoke every day or some days. (Source: NCHS, *Health, United States, 2016,* Figure 10 and Table 48. Data from the National Health Interview Survey [NHIS].)

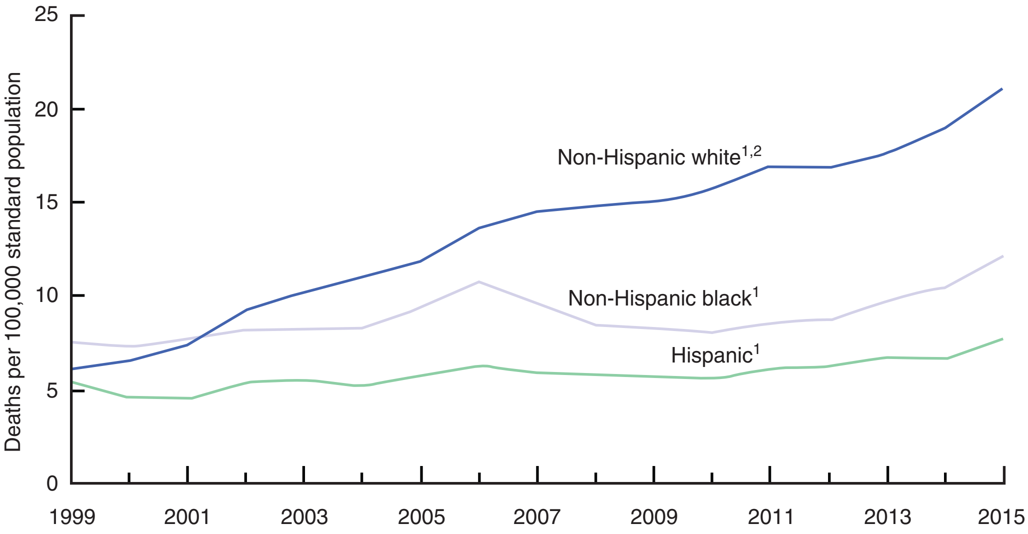

FIGURE 4-3. Age-adjusted drug overdose death rates, by race and ethnicity: United States, 1999-2015. [1]Significant increasing trend, $p < 0.005$. [2]Rate for non-Hispanic white persons was significantly higher than for non-Hispanic black and Hispanic persons, $p < 0.001$. Notes: Deaths are classified using the *International Classification of Diseases, Tenth Revision*. Drug overdose deaths are identified using underlying cause-of-death codes X40-X44, X60-X64, X85, and Y10-Y14. Deaths for Hispanic persons may be underreported by about 5%. Access data table for Figure 3 at: https://www.cdc.gov/nchs/data/databriefs/db273_table.pdf#3. (Source: Hedegaard H, Warner M, Miniño AM. *Drug overdose deaths in the United States, 1999–2015.* NCHS data brief, no 273. Hyattsville, MD: National Center for Health Statistics. 2017.)

INSURANCE COVERAGE AND ACCESS TO CARE

Health insurance coverage is an important contributor to racial, ethnic, and socioeconomic disparities in health care and health outcomes, especially for adults who are under age 65 years and do not have near-universal insurance coverage through Medicare as older adults do. Since the Affordable Care Act was enacted in 2010, 31 states have expanded Medicaid to non-elderly adults with annual incomes below 138% of the federal poverty level (<$16,400 for a single adult in 2017). In all states, adults with incomes of 100 to 400% of the federal poverty level (about $12,000-$48,000) have become eligible for subsidized private insurance.

With this expanded coverage, rates of uninsurance have declined substantially for poor and near-poor adults in all racial and ethnic groups since 2010 (Fig. 4-4), although they still remain substantially higher for Hispanic and African American adults (Fig. 4-5).

Health insurance is a primary determinant of access to care, because it reduces financial barriers to preventive services such as smoking cessation and cancer screening and to effective care for chronic health conditions such as hypertension, diabetes, and heart disease. Uninsured adults are three to five times more likely to delay or forego needed care or prescription medications because of cost than are adults with private insurance or Medicaid (Fig. 4-6). Gaining insurance coverage is associated with improved access to care and better health outcomes,[8] particularly for middle-aged adults with low incomes and chronic health conditions such as hypertension and diabetes mellitus.

QUALITY OF CARE

An extensive body of research has documented substantial racial and ethnic disparities in the quality of health care provided to patients with a wide range of major conditions, including heart disease, hypertension, diabetes mellitus, kidney disease, breast cancer, and colorectal cancer. Relative to non-Hispanic white adults, African American and Hispanic adults are much less likely to have good control of their hypertension or diabetes mellitus. These disparities are narrowed among Medicare enrollees nationally, and they have been eliminated in Medicare health maintenance organizations in the western United States. Over time, such improvements in the control of hypertension and diabetes mellitus may further reduce disparities in cardiovascular mortality for African Americans relative to other racial and ethnic groups.

Similar improvements have been noted in the quality of hospital care nationally for minority patients with acute myocardial infarction, heart failure, and pneumonia, for whom the quality of hospital care is now clinically equivalent by race and ethnicity. Most notably, substantial disparities in timely percutaneous coronary interventions (Chapter 63) and in rates of influenza and pneumococcal vaccination (Chapter 15) have been eliminated for African American and Hispanic patients relative to non-Hispanic white patients.

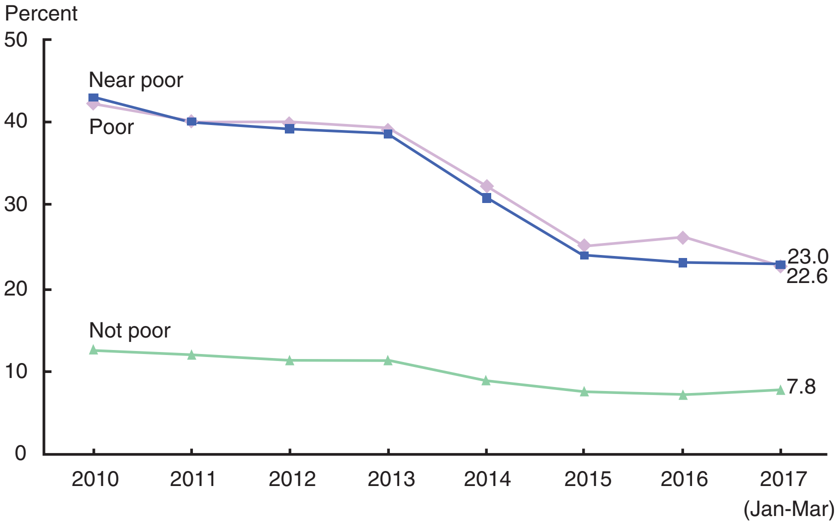

FIGURE 4-4. Percentage of adults aged 18-64 who were uninsured at the time of interview, by poverty status: United States, 2010-March 2017. Note: Data are based on household interviews of a sample of the civilian noninstitutionalized population. (Source: NCHS, National Health Interview Survey, 2010-2017, Family Core Component.)

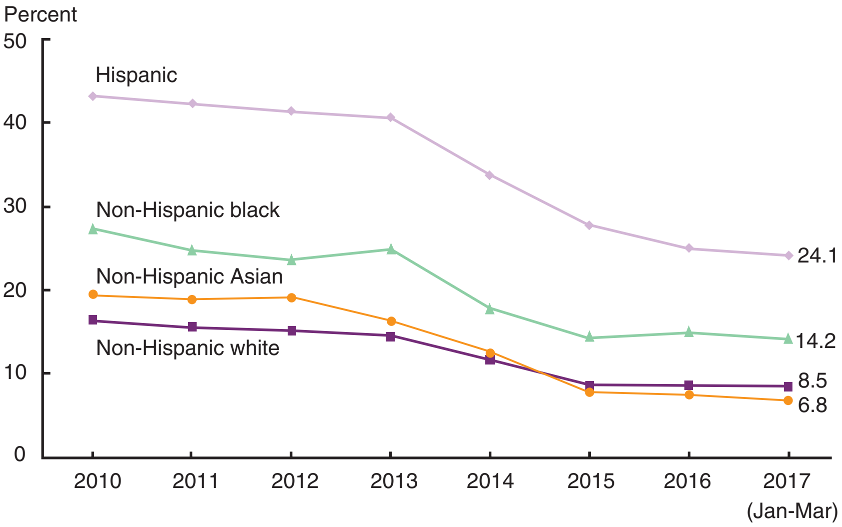

FIGURE 4-5. Percentage of adults aged 18-64 who were uninsured at the time of interview, by race and ethnicity: United States, 2010-March 2017. Note: Data are based on household interviews of a sample of the civilian noninstitutionalized population. (Source: NCHS, National Health Interview Survey, 2010-2017, Family Core Component.)

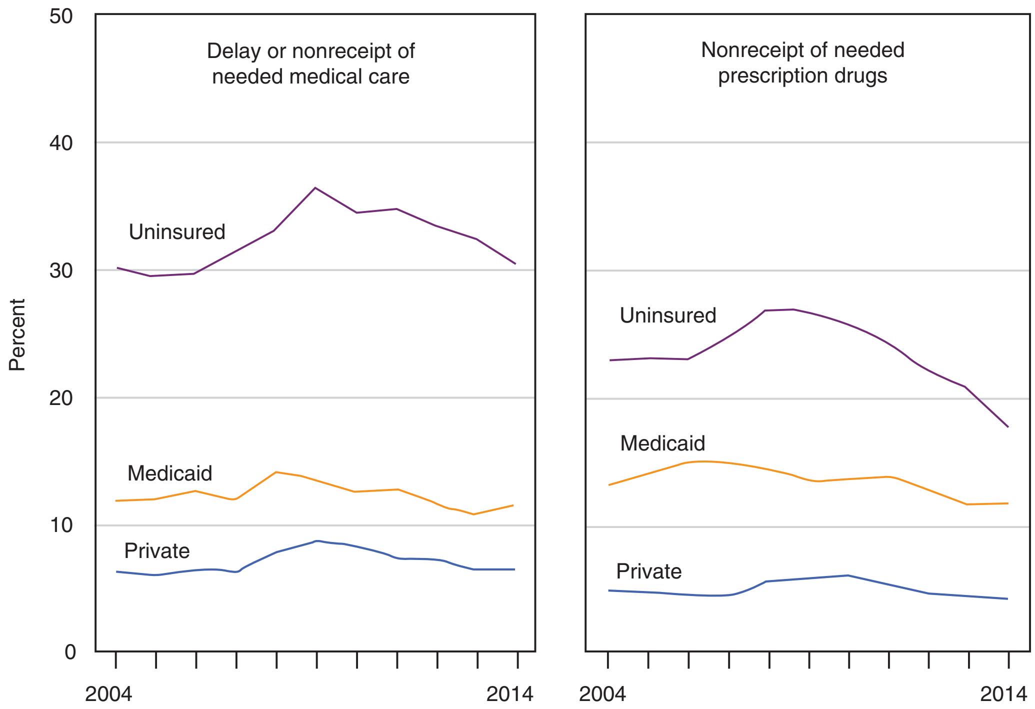

FIGURE 4-6. Difficulty accessing care: Adults aged 18-64. (Source: CDC/NCHS, Health, United States, 2015, Figure 12 and Table 63. Data from the National Health Interview Survey [NHIS].)

CLINICAL APPROACHES TO REDUCE DISPARITIES

The increasing diversity of the U.S. population has created new challenges and opportunities for health care providers and organizations to meet the needs of patients from diverse backgrounds, particularly immigrants. The federal Office of Minority Health has produced national standards for delivering culturally and linguistically appropriate health care, including the use of trained interpreters for patients with limited English proficiency. The principal standard is to "provide effective, equitable, understandable, and respectful quality care and services that are responsive to diverse cultural health beliefs and practices, preferred languages, health literacy, and other communication needs."[9] Physicians and other caregivers who have undergone educational programs in cultural competencies may provide better care to diverse populations.■ However, this training has not clearly improved patients' outcomes, such as reducing disparities in control of glycemia, blood pressure, or cholesterol for African Americans with diabetes mellitus.

Disparities in health care often arise from fragmented systems of care, particularly for conditions that require complex services, such as cancer, cardiovascular disease, end-stage renal disease, and organ transplantation. When care requires multiple specialists or sites of care, disparities also can be reduced by emphasizing patient-centered approaches that provide better coordinated care with enhanced support for patients from disadvantaged backgrounds, such as those who are uninsured or have less education or limited English proficiency. This support may include multidisciplinary team-based care and enhanced outreach to patients and their families via care coordinators, patient navigators, and community health workers.[10]

It is also essential for clinical leaders in health care organizations to implement reporting systems (e.g., through enhanced electronic health records) to identify and monitor disparities related to race, ethnicity, language, and socioeconomic factors. These systems can be used to set measurable goals for reducing disparities in the quality and outcomes of care, motivate quality improvement programs to address clinically important disparities, and assess progress toward achieving these goals.

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REVIEW QUESTIONS

1. Which U.S. racial/ethnic group has the highest age-adjusted death rates due to heart disease?

A. Non-Hispanic whites
B. African Americans
C. Hispanics
D. Asians and Pacific Islanders
E. American Indians and Alaska Natives

Answer: B African Americans have the highest U.S. death rates due to heart disease (Table 4-1). Major contributors to this increased risk include high rates of hypertension, diabetes, and smoking.

2. Which U.S. racial/ethnic group has the highest age-adjusted death rates due to opioid overdoses?

A. Non-Hispanic whites
B. African Americans
C. Hispanics
D. Asians and Pacific Islanders
E. American Indians and Alaska Natives

Answer: A Deaths due to drug overdoses have more than tripled since 1999 among non-Hispanic whites (Fig. 4-3). This marked increase is largely due to increased rates of opioid overdoses.

3. Which U.S. racial/ethnic group has the highest percentage of uninsured non-elderly adults?

A. Non-Hispanic whites
B. African Americans
C. Hispanics
D. Asians and Pacific Islanders
E. American Indians and Alaska Natives

Answer: C In 2017, 24% of non-elderly Hispanic adults were uninsured (Fig. 4-5). Hispanic adults are more likely to be undocumented or recent legal immigrants who are not eligible for expanded Medicaid coverage or subsidized private insurance under the Affordable Care Act. Low-income Hispanic adults are also more likely to reside in states such as Texas and Florida that have chosen not to expand Medicaid.

5

GLOBAL HEALTH

ARUN CHOCKALINGAM

Health is a human right, but more than 2 billion people live with a daily income of less than $2 and have no access to good health care. Health is determined by the context of people's lives. Individuals are unable to control many of the social determinants of health (Chapter 4), such as income, social status, education, physical environment, social support network, genetics, health services, and gender.

In the process of modernization from a less developed to a more developed nation, the epidemiological transition of modern sanitation, medications, and health care has drastically reduced infant and maternal mortality rates and extended average life expectancy. As a result, the world has progressed from the age of pestilence and famine, with a life expectancy between 20 and 40 years, to the age of receding pandemics, with a life expectancy of 30 to 50 years, and now to the current age of degenerative and man-made diseases, with a life expectancy of 60 years or more.

These trends, coupled with subsequent declines in fertility rates, have driven a *demographic transition* in which the major causes of death change from infectious diseases to chronic and degenerative diseases. As many countries around the world have undergone globalization, owing to their internal urbanization, modernization, and economic development, an increased proportion of their burden of morbidity and mortality is now due to chronic noncommunicable diseases, including cardiovascular,[1] cerebrovascular, and renovascular diseases[2] as well as cancer, diabetes, chronic respiratory diseases, and mental disorders (Table 5-1).

WHAT IS GLOBAL HEALTH?

The term *global health* is sometimes confused with public health, international health, tropical medicine, and population health. Global health, which is defined as the health of populations in a global context, transcends the perspectives and concerns of individual nations and crosses national borders. Global health depends on the public health efforts and institutions of all countries, including their strategies for improving health, both population-wide and for individuals. Global health depends on multiple factors, including social, political, environmental, and economic determinants of health. Although global health often focuses on improving the health of people who live in low- and middle-income countries, it also includes the health of any marginalized population in any country.

TABLE 5-1 EPIDEMIOLOGIC TRANSITION IN CARDIOVASCULAR DISEASES

STAGES OF DEVELOPMENT	LIFE EXPECTANCY	BURDEN OF CARDIOVASCULAR DISEASE DEATHS, % OF TOTAL DEATHS	PREDOMINANT CARDIOVASCULAR DISEASES AND RISK FACTORS	MODERN REGIONAL EXAMPLES
1. Age of pestilence and famine	20-40 years	5-10	Infections, rheumatic heart disease, and nutritional cardiomyopathies	Rural India, sub-Saharan Africa, South America
2. Age of receding pandemics	30-50 years	10-35	As above plus hypertensive heart disease and hemorrhagic strokes	China
3. Age of degenerative and man-made diseases	50->60 years	35-65	All forms of strokes; ischemic heart disease at young ages; increasing obesity and diabetes	Aboriginal communities, urban India, former socialist economies
3A. Age of delayed degenerative diseases	>60 years	<50	Stroke and ischemic heart disease at old age	Western Europe, North America, Australia, New Zealand
3B. Age of health regression and social upheaval	50-60 years	35-55	Re-emergence of deaths from rheumatic heart disease, infections, increased alcoholism and violence; increase in ischemic and hypertensive diseases in the young	Russia

During stages 1 to 3A, life expectancy increases, whereas life expectancy decreases in stage 3B compared with stage 3A and even stage 3.
Modified from Omran AR. The epidemiological transition: a theory of the epidemiology of population change. *The Milbank Quarterly.* 2005;83:731-757. Reprinted from *The Milbank Memorial Fund Quarterly.* 1971;49:509-538; and Yusuf S, Reddy S, Ounpuu S, et al. Global burden of cardiovascular diseases: part I: general considerations, the epidemiologic transition, risk factors, and impact of urbanization. *Circulation.* 2001;104:2746-2753.

ABSTRACT

Global health addresses the health of all population of all nations, including inequities between and within nations. While defining health, it is important to evaluate both morbidity and mortality. The estimated 55 million annual worldwide deaths are dominated by noncommunicable diseases, even in low- and middle-income countries where HIV/AIDS, tuberculosis, and malaria are still important causes of morbidity and mortality. In 2015, the United Nations adopted a set of sustainable development goals to end poverty, protect the planet, and reduce premature mortality from noncommunicable disease by one third by 2030. Universal health coverage is a key to realize global health and to bring global equity.

KEYWORDS

millennium development goals
global burden of diseases
low- and middle-income countries
sustainable development goals
universal health coverage

Global health requires using a wide range of institutions that collaborate in addressing all health issues. Global health also depends on the constructive use of evidence-based information to provide health and health equity, in part by strengthening primary health care and the health care delivery system.

Millennium Development Goals

In an attempt to address global inequity, the United Nations advanced eight millennium development goals with the objective of achieving these goals between 2000 and 2015. These eight goals incorporate 21 targets (E-Table 5-1), with a series of measurable health and economic indicators for each target. Although many of the targets have not yet been achieved, substantial progress has been made toward all targets.[3]

The millennium development goals emphasize that health and development are interconnected. To address global inequity, fundamental issues include reducing poverty, improving education, and empowering people. In addition to specific goals for reducing infant and child mortality, maternal mortality, and mortality owing to infectious diseases such as HIV/AIDS, malaria, and tuberculosis, the millennium development goals strongly encourage environmental sustainability and global partnership.

GLOBAL BURDEN OF DISEASES

The global burden of disease is measured in terms of total and cause-specific mortality and morbidity, as well as the national economic burden for health care. About 55 million people die from all causes annually, with about 25% of deaths due to communicable, maternal, neonatal, and nutritional disorders, 65% due to noncommunicable diseases, and 10% due to injuries (Table 5-2).[4] Although overall deaths between 1990 and 2010 increased by 13.5%, medical and public health advancements reduced deaths from communicable diseases by 17%, whereas deaths due to noncommunicable disease increased by 30% and deaths due to injury, including war-related deaths, increased by 24%.

Child mortality under the age of 5 years decreased by 52% between 1990 and 2015. Neonatal deaths and stillbirths also have fallen significantly.[5]

CHANGING PATTERNS OF DISEASES

Despite the general trends of declining morbidity and mortality from communicable diseases, parts of Africa, Asia, and Latin America are still facing the challenges of infectious diseases, such as HIV, malaria, and tuberculosis, even as their prevalence of chronic noncommunicable diseases has risen—a so-called *double burden.* Concerted global health efforts and public awareness, as well as investments by industrialized countries, multilateral agencies, and nongovernmental organizations, have resulted in significant progress against HIV/AIDS (Chapter 360). The worldwide mortality owing to HIV/AIDS and tuberculosis rose by 50% in 2010 compared with 1990 and then declined by 30% in 2015, but drug-resistant tuberculosis (Chapter 308) is an increasing worldwide challenge.[6]

Although malaria deaths have fallen worldwide over the last decade, malaria is a rising threat in parts of Southeast Asia—especially Cambodia, Myanmar, Thailand, and Vietnam—where drug resistance to antimalaria medications is problematic.

The age of the population is increasing all over the world, and so is the number of people living with consequences of diseases and injuries. Epidemiological shifts driven by socioeconomic change also contribute to the worldwide increase in years lived with disability as well as the rate of increase in years lived with disability.[7] Although some countries have recognized the problem of aging and developed programs to deal with its burden on health care resources, many countries are not prepared at all.[8]

Noncommunicable diseases account for nearly two thirds of the global burden of disease. Nearly 80% of all noncommunicable diseases related to death and disability occur in the low- and middle-income countries,[9] where they account for about 14 million deaths in people under age 60 years. The prevention and control of noncommunicable diseases should involve both upstream and downstream approaches, such as: social determinants; national and international policies regarding trade, agriculture, transportation, and environmental and other policies; health care, including accessibility, availability, and affordability; and settings, such as schools and worksites, where health promotion and disease prevention are targeted, as well as media by which health can be influenced.

Population growth and aging also have resulted in an increasing number of people living with atherosclerotic vascular disease worldwide, despite the decrease in the age-adjusted incidence of myocardial infarction and ischemic stroke in high-income regions. Rising levels of obesity (Chapter 207) and diabetes (Chapter 216) have reached epidemic proportions in many countries. Smoking (Chapter 29) rates are increasing in low-income countries, with the increase more than offsetting declines in high-income countries.[10] Hypertension (Chapter 70) has an estimated worldwide prevalence of 35 to 45% of the global population—more than 2 billion people over the age of 25

TABLE 5-2 GLOBAL DEATHS IN 1990 AND 2015 FOR ALL AGES AND BOTH SEXES COMBINED

	ALL AGES—DEATHS (THOUSANDS)		
CAUSES OF DEATH	**1990**	**2015**	**% CHANGE**
ALL CAUSES	46,511	55,793	+20
Communicable, Maternal, Neonatal, and Nutritional Disorders	15,859	11,264	–29
HIV/AIDS and tuberculosis	1770	2,305	+30
Diarrhea, lower respiratory infection, and other common IDs	7772	4,960	–36
Neglected tropical diseases and malaria	1211	843	–30
Maternal disorders	359	275	–23
Neonatal disorders	3081	2163	–30
Nutritional deficiencies	977	406	–58
Other communicable, maternal, neonatal, and nutritional disorders	690	311	–55
Noncommunicable Diseases	26,560	39,804	+50
Neoplasm	5779	8,765	+52
Cardiovascular and circulatory diseases	11,903	17,921	+51
Chronic respiratory diseases	3986	3,796	–5
Cirrhosis of the liver	778	1,292	+66
Digestive diseases (except cirrhosis)	973	1,203	+24
Neurologic disorders	595	2,259	+280
Mental and behavioral disorders	138	325	+136
Diabetes, urogenital, blood, and endocrine diseases	1544	3,409	+121
Musculoskeletal disorders	70	90	+29
Other noncommunicable diseases	794	745	–6
Injuries	4092	4,725	+16
Transport injuries	958	1,467	+53
Unintentional injuries other than transport injuries	2030	1,839	–9
Self-harm and interpersonal violence	1009	1,238	+23
Forces of nature, war, and legal intervention	95	183	+93

HIV/AIDS = human immunodeficiency virus infection/acquired immunodeficiency syndrome; ID = infectious disease.

Adapted from Lozano R, Naghavi M, Foreman K, et al. Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. *Lancet.* 2012;380:2095-2128; and GBD 2015 Mortality and Causes of Death Collaborators. Global, regional, and national life expectancy, all-cause mortality, and cause-specific mortality for 249 causes of death, 1980-2015: a systematic analysis for the Global Burden of Disease Study 2015. *Lancet.* 2016;388:1459-1544.

E-TABLE 5-1 MILLENNIUM DEVELOPMENT GOALS AND TARGETS (2000-2015)

GOAL 1: ERADICATE EXTREME POVERTY AND HUNGER
Target 1A: Halve, between 1990 and 2015, the proportion of people living on less than $1.25 a day. Target 1B: Achieve decent employment for women, men, and young people. Target 1C: Halve, between 1990 and 2015, the proportion of people who suffer from hunger.
GOAL 2: ACHIEVE UNIVERSAL PRIMARY EDUCATION
Target 2A: By 2015, all children (girls and boys) can complete a full course of primary schooling.
GOAL 3: PROMOTE GENDER EQUALITY AND EMPOWER WOMEN
Target 3A: Eliminate gender disparity in primary and secondary education preferably by 2005, and at all levels by 2015.
GOAL 4: REDUCE CHILD MORTALITY RATES
Target 4A: Reduce by two thirds, between 1990 and 2015, the under-five mortality rate.
GOAL 5: IMPROVE MATERNAL HEALTH
Target 5A: Reduce by three quarters, between 1990 and 2015, the maternal mortality ratio. Target 5B: Achieve, by 2015, universal access to reproductive health.
GOAL 6: COMBAT HIV/AIDS, MALARIA, AND OTHER DISEASES
Target 6A: Have halted by 2015 and begun to reverse the spread of HIV/AIDS. Target 6B: Achieve, by 2010, universal access to treatment for HIV/AIDS for all those who need it. Target 6C: Have halted by 2015 and begun to reverse the incidence of malaria and other major diseases.
GOAL 7: ENSURE ENVIRONMENTAL SUSTAINABILITY
Target 7A: Integrate the principles of sustainable development into country policies and programs; reverse loss of environmental resources. Target 7B: Reduce biodiversity loss, achieving, by 2010, a significant reduction in the rate of loss. Target 7C: Halve, by 2015, the proportion of the population without sustainable access to safe drinking water and basic sanitation. Target 7D: By 2020, to have achieved a significant improvement in the lives of at least 100 million slum-dwellers.
GOAL 8: DEVELOP A GLOBAL PARTNERSHIP FOR DEVELOPMENT
Target 8A: Develop further an open, rule-based, predictable, non-discriminatory trading and financial system. Target 8B: Address the special needs of the least developed countries. Target 8C: Address the special needs of landlocked developing countries and Small Island developing States. Target 8D: Deal comprehensively with the debt problems of developing countries through national and international measures in order to make debt sustainable in the long term. Target 8E: In cooperation with pharmaceutical companies, provide access to affordable, essential drugs in developing countries. Target 8F: In cooperation with the private sector, make available the benefits of new technologies, especially information and communications.

From United Nations Millennium Development Goals. http://www.un.org/millenniumgoals/poverty.shtml. 2008. Accessed May 10, 2019.

years.[11] The age-standardized prevalence of hypertension is highest in Africa, where it is about 45% for both sexes, and is lowest in the Americas, where it is about 35% for both sexes.[12] In all regions, men have a slightly higher prevalence of hypertension than do women. Despite significant efforts by global nongovernmental and multilateral organizations, including the World Health Organization, more than 50% of the world's population with hypertension does not even know their condition, and the percentage treated and controlled varies from less than 5% in Zambia to 66% in Canada.

The growing epidemic of noncommunicable diseases, including mental disorders, and the unfinished agenda of controlling infectious diseases (HIV/AIDS, malaria, tuberculosis, maternal and child health, and other infectious and parasitic diseases) poses a huge threat to the global population both in terms of human and fiscal losses. Noncommunicable diseases represent a growing economic threat across the globe and are becoming an acute problem in low- and middle-income countries (Table 5-3) in which they are estimated to account for nearly $500 billion per year.

Worldwide adoption of best practices could substantially reduce that economic burden. For example, population-based interventions to reduce tobacco and harmful alcohol use, as well as to improve unhealthy diets and increase physical activity, are estimated to cost less than $0.40 per person per year.

Although individual countries theoretically take responsibility for the health of their respective citizens, many low- and middle-income countries are unable to meet their domestic population's basic needs. The sum of public and private health care expenditure by countries based on their gross domestic product varies between 1.6% in South Sudan to 18% in the United States, with many high-income countries spending more than 10%. Thus, the worldwide solution requires a response of all of human society, including strategic domestic and international investments, both within countries and through multilateral agencies. This societal responsibility must be shared by the private sector, nongovernmental organizations, academia, professional societies, and the public themselves.

To meet these global needs, all 192 United Nations member states agreed to address their prevention and control worldwide, particularly in developing countries. The emphasis is on four major noncommunicable diseases (cardiovascular diseases, cancer, diabetes, and chronic respiratory diseases) and four key risk factors common to all four of these noncommunicable diseases (tobacco use, unhealthy diets, physical inactivity, and harmful use of alcohol). Since 2011, there has been considerable discussion about both mental health and musculoskeletal disorders, which also contribute to the global burden of noncommunicable diseases.[13] The World Health Organization developed a global monitoring framework to enable global tracking of progress in preventing and controlling these four major noncommunicable diseases and their key risk factors, aiming for a 25% reduction by 2025—with a slogan of *25 By 25*.

The United Nations also adopted a set of goals to end poverty, protect the planet, and ensure prosperity for all as part of a new sustainable development agenda called *Sustainable Development Goals (SDG) 2015-2030*.[14] The sustainable development goals aim to protect the world from dangers of environmental catastrophe and to protect the planetary life. The aims by 2030 are to reduce premature mortality from noncommunicable diseases by one third through prevention and treatment and to promote both mental health and well-being.

TABLE 5-3 WHO ESTIMATES, 2015: PROBABILITY OF DYING FROM ANY OF THE 4 MAJOR NONCOMMUNICABLE DISEASES (CARDIOVASCULAR DISEASES, CANCER, DIABETES OR CHRONIC RESPIRATORY DISEASES) BETWEEN THE AGES OF 30 AND 70

	LOW PROBABILITY 16% OR LESS		*HIGH PROBABILITY MORE THAN 25%*	
REGION	**COUNTRY**	**(%)**	**COUNTRY**	**(%)**
Africa	Algeria	15	Côte d'Ivoire	28
	Cabo Verde, Gabon	16	Sierra Leone	30
America	Canada	10	Trinidad and Tobago	26
	Chile, Costa Rica	11	Guyana	28
Eastern Mediterranean	Qatar	14	Sudan	26
	Iran	15	Afghanistan, Yemen	31
Europe	Iceland	8	Belarus, Kazakhstan, Russian Federation	29
	Italy, Sweden, Switzerland	9	Turkmenistan	35
South East Asia	Maldives	12	Democratic People's Republic of Korea	26
	Thailand	16	Indonesia	27
Western Pacific	Republic of Korea	8	Fiji	31
	Australia, Japan	9	Papua New Guinea	36

Adapted from World Health Statistics 2017: monitoring health for the SDGs. World Health Organization. https://reliefweb.int/sites/reliefweb.int/files/resources/9789241565486-eng.pdf. Accessed May 10, 2019.

Universal health coverage is a key global health transition for the future. Although many high-income countries have some form of universal health coverage and some upper middle-income countries have introduced basic universal health coverage, many lower-middle-income and low-income countries are just beginning to introduce universal health coverage. This transition, if successful, should bring global equity, save people from paying huge health care costs, and lead to better health outcomes.

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For the General References and other additional features, please visit Expert Consult at https://expertconsult.inkling.com.

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REVIEW QUESTIONS

1. Hypertension or high blood pressure is the major risk factor for heart disease, stroke, and kidney diseases worldwide. Which of the following statements is incorrect?

A. The prevalence of hypertension over the age of 25 varies between 35 and 45% globally.
B. Across all countries, men have a slightly higher prevalence of hypertension than do women.
C. The global hypertension control rate is about 60%.
D. Early diagnosis of hypertension leads to prevention of all forms of vascular complications.
E. According to the World Health Organization, population attributable deaths owing to hypertension are estimated to be about 7.5 million per year.

Answer: C The global control rate varies from less than 5% in Zambia to 66% in Canada and is very low overall worldwide. All other statements (Answers A, B, D and E) are correct.

2. Which of the following statements about global health is correct?

A. Global health is not the opposite of domestic health.
B. Global health must integrate both infectious diseases and noncommunicable diseases.
C. Public, private, and societal partnership is necessary to deliver effective global health.
D. Academia has a major role in promoting global health.
E. All of the above.

Answer: E Statement A is true since global health includes domestic health as well, particularly on the health of marginalized people in developed countries. Statement B is true, since the current health system must address all diseases, particularly when noncommunicable diseases account for 65% of all global causes of death. New evidence shows that one fifth of all cancers worldwide are caused by chronic infections produced by agents such as HIV, human papillomavirus, and hepatitis B virus. Infections and parasitic diseases also cause other noncommunicable diseases, such as rheumatic heart disease, Chagas disease, cardiomyopathy, and peptic ulcer. As HIV/AIDS survivors live longer, they also are exposed to lifestyle-related risk factors and noncommunicable diseases. Statement C is true. The economic burden of diseases is so large that public-private partnership is essential. Statement D is true. Academia should develop and supply needed knowledge and train the next generation of the global health work force.

6

APPROACH TO THE PATIENT: HISTORY AND PHYSICAL EXAMINATION

DAVID L. SIMEL

OVERVIEW

Physicians may have multiple objectives with varying degrees of importance in their encounters with patients. These goals include, but are not limited to, the translation of symptoms and signs into diagnoses, the assessment of stability or change in known conditions, the provision of information and counseling for future prevention, and the reaffirmation or alteration of therapeutic interventions. For a healthy adult with no symptoms or signs of a problem, a comprehensive annual physical examination has low diagnostic value.

The interaction between the patient and physician represents not only a scientific encounter, but also a social ritual centered on locus of control and meeting each other's expectations. Patients expect a competent assessment of their health care needs and concerns. Physicians need to feel that they have not missed something important, an occasional need to put limits on the time available for each interaction, and a need to maintain objectivity. The expertly performed rational clinical examination enhances the social ritual and the likelihood of acquiring relevant data. It also optimizes the physician's ability to understand the patient's symptoms and concerns, as well as to facilitate the healing process.[1]

MEDICAL HISTORY

The history begins by asking patients to describe, in their own words, the reason for seeking medical care (Table 6-1). Although patients may have many reasons for initiating a visit to the physician, they should be encouraged to select the one or two most important concerns they have. Physicians should reassure patients with multiple worries that other concerns will not be ignored, but emphasize that it is important to understand what worries them most.

History of the Present Illness

Open-ended questions facilitate descriptions of problems in the patient's own words. Subsequently, specific questions fill in gaps and help clarify important points. However, wise clinicians realize that when they are talking, they are not listening. Nonetheless, when the patient is acutely ill, the physician should limit the amount of time spent in open-ended discussion and move promptly to the most important features that allow quick evaluation and management. In general, the history of the problem under consideration includes the following:

- Description of onset and chronology
- Location of symptoms
- Character (quality) of symptoms
- Intensity
- Precipitating, aggravating, and relieving factors
- Inquiry into whether the problem or similar problems occurred before and, if so, whether a diagnosis was established

It is often helpful to ask patients to express what they believe is the cause of the problem or what concerns them the most. This approach often uncovers other pertinent factors and helps establish that the physician is trying to meet the patient's needs.

Past Medical and Surgical History

An astute clinician recognizes that patients may not report all their prior problems because they may forget, may assume that previous events are unrelated to their current problem, or simply may not want to discuss past events. Open-ended statements such as "Tell me about other medical illnesses that we did not discuss" and "Tell me about any operations you had" prompt the patient to consider other items. The physician should ask the patient about unexplained surgical or traumatic scars.

A list of current medications includes prescriptions, over-the-counter medications, vitamins, and herbal preparations. Patients who do not recall the names of medications should bring all medication bottles to the next visit. Patients may not consider topical medications (e.g., skin preparations or eyedrops) as important, so they may need prompting.

Information about allergies (Chapter 239) is particularly important, but challenging, to collect. Patients may attribute adverse reactions or intolerances to allergies, but many supposed allergic reactions are not truly drug allergies. For example, less than 20% of patients who claim a penicillin allergy are allergic on skin testing. Eliciting the patient's actual response to medications facilitates a determination of whether the response was a true allergic reaction.

Social and Occupational History and Risk Factors

The social history not only reveals important information but also improves understanding of the patient's unique values, support systems, and social situation. It can be helpful to ask the patient to describe what they would do during a typical day.

Data that may influence risk factors for disease should be gathered, including a nonjudgmental assessment of substance abuse (Chapter 31). The tobacco history should include the use of snuff, chewing tobacco, cigar and cigarette smoking, and electronic nicotine delivery systems (Chapter 29). Alcohol use should be determined quantitatively and by the effect that it has had on the patient's life (Chapter 30). Past or present use of prescription pain medications, sedatives, or illicit substances should be assessed (Chapter 31). The sexual history should address sexual orientation and gender identity, as well as current and past sexual activity. The best way to address sexual orientation and gender identity may be to ask the patient whether they think of themselves as "lesbian, gay, or homosexual; as straight or homosexual; as bisexual; as something else; or whether they 'don't know.' " The employment history should include the current and past employment history, as well as any significant hobbies. All adult patients should be asked if they served in the military. Military veterans should be asked about their combat history, years of service, and areas of deployment.[2] In patients in whom exposure to trauma has been established, screening for post-traumatic stress disorder (PTSD; Chapter 369) can be done with several simple questions (Table 6-2).[3]

The physician should obtain information on socioeconomic status, insurance, the ability to afford or obtain medications, and past or current barriers to health care (Chapter 4). Marital status and the living situation (i.e., whom the patient lives with, significant stressors for that patient) are important as risk factors for disease and to determine how best to care for the patient. A patient's culture (Chapter 4) and values should be known, including any prior advance directives or desire to overrule them (Chapter 3).

Family History

The family history allows risk stratification, which affects the pretest probability for an increasing number of disorders (e.g., heart disease, breast cancer, or Alzheimer disease). For common diseases such as heart disease, additional inquiry into the age of onset in first-degree relatives and death attributed to the disease should be obtained (Chapter 46). Patients may lack appropriate information about the absence of disease. The expansion of knowledge about genetic diseases (Chapter 36) requires that clinicians improve their skills in eliciting the family history.

Review of Systems

The review of systems elicits symptoms or signs not covered or overlooked in the history of the present illness (Table 6-3). In contrast to the open-ended nature of collecting the medical history, which allows the patient to "claim" or "deny" a variety of symptoms, the direct questioning technique of the review of systems leads the patient to "accept" or "reject" symptoms. The review of systems is more efficient if at least some questions are restricted to a specific period (e.g., "a recent change in your vision" or "shortness of breath, wheezing, or coughing this past week") or by having the patient fill out a previsit questionnaire.

PHYSICAL EXAMINATION

Chaperones

When a guest or friend accompanies the patient, the clinician should either ask the patient if they would like their companion to stay during the examination or ask the guest to wait outside the room. Patients can be offered the option of a chaperone, especially when the clinician and patient are of different genders and a comprehensive examination is planned. For example, many adult women (29%) and adolescent girls (46%) express a preference for a chaperone during a breast, pelvic, or rectal examination by a male physician (especially during their first examination). Many examiners prefer a chaperone to allay their own anxieties attributable to gender differences or to achieve a