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GOLDMAN-CECIL MEDICINE

VOLUME 1

LEE GOLDMAN
ANDREW I. SCHAFER

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GOLDMAN-CECIL MEDICINE

26TH EDITION

Volume 1

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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 Dorshow 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, Itzhak 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. Guerant, 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.

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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, Dashed, 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.

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Physical and Chemical Injuries of the Lung

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Neoplasms of the Small and Large Intestine

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Bioterrorism

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Diseases of the Visual System

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Measuring Health and Health Care

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Listeriosis

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Fibromyalgia, Chronic Fatigue Syndrome, and Myofascial Pain

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Approach to the Patient with Endocrine Disease

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Treatment of Irreversible Renal Failure

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Varicella-Zoster Virus (Chickenpox, Shingles)

Myron S. Cohen, MD

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Approach to the Patient with a Sexually Transmitted Infection; Prevention of Human Immunodeficiency Virus Infection

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Pain

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Preoperative Evaluation

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Hodgkin Lymphoma

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Approach to the Patient in a Critical Care Setting

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Thyroid

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The Adaptive Immune System

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Diabetes Mellitus

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Leishmaniasis

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The Innate Immune System; Approach to the Patient with Rheumatic Disease; Systemic Lupus Erythematosus

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Salmonella Infections (Including Enteric Fever)

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Amyotrophic Lateral Sclerosis and Other Motor Neuron Diseases

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Principles of Occupational and Environmental Medicine

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Primary Immunodeficiency Diseases

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Smallpox, Monkeypox, and Other Poxvirus Infections

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Diseases of the Mouth and Salivary Glands

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Envenomation, Bites, and Stings

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Breast Cancer and Benign Breast Disorders

Lisa M. DeAngelis, MD

Lillian Rajtman 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

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Interventional and Surgical Approaches to Lung Disease

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Prevention of Human Immunodeficiency Virus Infection

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Approach to the Patient with Neurologic Disease

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Systemic Antifungal Agents

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Rhabdomyolysis

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Principles of Drug Therapy

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Nematode Infections

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Headaches and Other Head Pain

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Approach to the Patient with Cancer

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Papillomavirus

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Asthma

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Approach to the Patient with Urinary Tract Infection

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Urticaria and Angioedema

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Cytomegalovirus

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Antibacterial Chemotherapy

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Vascular Disorders of the Kidney

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Zoonoses

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Approach to the Patient with Suspected Enteric Infection

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Urticaria, Drug Hypersensitivity Rashes, Nodules and Tumors, and Atrophic Diseases

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Parainfluenza Viral Disease

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Crystal Deposition Diseases

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Testicular Cancer

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Principles of Anti-Infective Therapy

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Diseases of the Myocardium and Endocardium

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Tuberculosis

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Bioethics in the Practice of Medicine

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Leprosy (Hansen Disease)

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Hepatic Failure and Liver Transplantation

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Disorders of Neuromuscular Transmission

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Pseudomonas and Related Gram-Negative Bacillary Infections

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Diseases of the Esophagus

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ST Elevation Acute Myocardial Infarction and Complications of Myocardial Infarction

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Intimate Partner Violence

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Interventional and Surgical Approaches to Lung Disease

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Streptococcus Pneumoniae Infections

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Mechanisms of Inflammation and Tissue Repair

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Principles of Electrophysiology

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Overview of Anesthesia

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Throat Disorders

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Diseases of the Gallbladder and Bile Ducts

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Pancreatitis

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Rickettsial Infections

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Infective Endocarditis

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Rotaviruses, Noroviruses, and Other Gastrointestinal Viruses

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Approach to the Patient before and after Travel

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Immune Reconstitution Inflammatory Syndrome in HIV/AIDS

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Approach to Women's Health

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Endemic Mycoses

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Hemolytic Anemias: Red Blood Cell Membrane and Metabolic Defects

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Electrocardiography

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Ventricular Arrhythmias

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Cirrhosis and Its Sequelae

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Diseases Caused by Chlamydiae

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Nicotine and Tobacco

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Regenerative Medicine, Cell, and Gene Therapies

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Coronaviruses

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Clostridial Infections

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Amyloidosis

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Whooping Cough and Other Bordetella Infections

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Venous Thrombosis and Embolism

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Applications of Molecular Technologies to Clinical Medicine

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Systemic Manifestations of HIV/AIDS

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Mumps; Herpes Simplex Virus Infections

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Neisseria Gonorrhoeae Infections

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Mycoplasma Infections

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Approach to Medicine, the Patient, and the Medical Profession: Medicine as a Learned and Humane Profession; Approach to the Patient with Possible Cardiovascular Disease

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Approach to Cerebrovascular Diseases; Ischemic Cerebrovascular Disease

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Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis

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Cholera and Other Vibrio Infections; Trematode Infections

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Cystic Fibrosis

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Principles of Anti-Infective Therapy

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Rotaviruses, Noroviruses, and Other Gastrointestinal Viruses

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Inflammatory Myopathies

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Coma, Vegetative State, and Brain Death

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Approach to the Patient with Neurologic Disease

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Hereditary Nephropathies and Developmental Abnormalities of the Urinary Tract

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Nutrition's Interface with Health and Disease

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Nutrition's Interface with Health and Disease

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Whooping Cough and Other Bordetella Infections

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Transfusion Medicine

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Pericardial Diseases

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The Nontuberculous Mycobacteria

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Approach to the Patient with Jaundice or Abnormal Liver Tests

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Iron Overload (Hemochromatosis)

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Approach to the Patient with Respiratory Disease

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Approach to Fever or Suspected Infection in the Normal Host

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Approach to Fever and Suspected Infection in the Immunocompromised Host

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Legionella Infections

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Approach to the Patient with Liver Disease

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Vitamins, Trace Minerals, and Other Micronutrients

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Microbial Complications in Patients Infected with Human Immunodeficiency Virus

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Infections Due to Other Members of the Enterobacteriaceae, Including Management of Multidrug-Resistant Strains

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Infections of Bursae, Joints, and Bones

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Heart Failure: Management and Prognosis

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Approach to the Patient with Gastrointestinal Disease

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Approach to the Anemias

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Approach to the Patient with Nose, Sinus, and Ear Disorders

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Overview of Pneumonia

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Approach to Cardiac Arrest and Life-Threatening Arrhythmias

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Approach to the Patient with Allergic or Immunologic Disease

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Arboviruses Causing Fever and Rash Syndromes

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Epidemiology of Aging: Implications of an Aging Society

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Approach to the Patient with Urinary Tract Infection

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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. *Innere 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 images⁷ are also poised to revolutionize the interpretation of these images such 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 patterns⁹ 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 diseases¹² 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 to 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		
Fever	264, 265	Figures 265-1, 265-2; Tables 264-1 to 264-8
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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Constipation	127, 128	Figures 127-3, 128-1; Table 127-2
Fecal incontinence	136	Figure 136-5
Anal pain	136	
Genitourinary		
Dysuria	268, 269	Tables 268-3, 268-5, 269-2
Frequency	268	Table 268-3
Incontinence	23	Tables 23-1 to 23-3
Renal colic	117	Figure 117-1
Vaginal discharge	269	
Menstrual irregularities	223	Figure 223-3; Tables 223-3, 223-4
Female infertility	223, 227	Table 223-5
Hot flushes	227	Table 227-1
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
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E-TABLE 1-1 GUIDE TO THE APPROACH TO COMMON SYMPTOMS, SIGNS, AND LABORATORY ABNORMALITIES—cont'd

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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;136:243-246.

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 suicide¹⁷ 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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