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Preface

The Editors are pleased to present the 20th edition of *Harrison's Principles of Internal Medicine.* This 20th edition is a true landmark in medicine, spanning 68 years and multiple generations of trainees and practicing clinicians. While medicine and medical education have evolved, readers will appreciate how this classic textbook has retained enduring features that have distinguished it among medical texts—a sharp focus on the clinical presentation of disease, expert in-depth summaries of pathophysiology and treatment, and highlights of emerging frontiers of science and medicine. Indeed, *Harrison's* retains its conviction that, in the profession of medicine, we are all perpetual students and lifelong learning is our common goal.

Harrison's is intended for learners throughout their careers. For *students*, Part 1, Chapter 1 begins with an overview of "The Practice of Medicine." In this introductory chapter, the editors continue the tradition of orienting clinicians to the *science* and the *art* of medicine, emphasizing the values of our profession while incorporating new advances in technology, science, and clinical care. Part 2, "Cardinal Manifestations and Presentation of Diseases" is a signature feature of *Harrison's*. These chapters eloquently describe how patients present with common clinical conditions, such as headache, fever, cough, palpitations, or anemia, and provide an overview of typical symptoms, physical findings, and differential diagnosis. Mastery of these topics prepares students for subsequent chapters on specific diseases they will encounter in courses on pathophysiology and in clinical clerkships. For *residents* and *fellows* caring for patients and preparing for board exams, *Harrison's* remains a definitive source of trusted content written by internationally renowned experts. Trainees will be reassured by the depth of content, comprehensive tables, and illuminating figures and clinical algorithms. Many exam questions are based on key testing points derived from *Harrison's* chapters. A useful companion book, *Harrison's Self-Assessment and Board Review*, includes over 1000 questions, offers comprehensive explanations of the correct answer, and provides links to the relevant chapter in the textbook. *Practicing clinicians* must keep up with an ever-changing knowledge base and clinical guidelines as part of lifelong learning. Clinicians can trust that chapters are updated extensively with each edition of *Harrison's*. The text is an excellent point-of-care reference for clinical questions, differential diagnosis, and patient management. In addition to the expanded and detailed Treatment sections, *Harrison's* continues its tradition of including "Approach to the Patient" sections, which provide an expert's overview of the practical management of common but often complex clinical conditions.

This edition has been modified extensively in its format as well as its content. We have reincorporated chapters that in previous editions were available only online. The 20th edition marks the return of *Harrison's* "Further Reading" citations at the end of each chapter, providing references carefully selected by our contributors. The authors and editors have rigorously curated and synthesized the vast amount of information that comprises general internal medicine—and each of the major specialties—into a highly readable and informative two-volume book. Readers will appreciate the concise writing style and consistency of format that have always characterized *Harrison's*. This book has a sharp focus on essential information with a goal of providing clear and definitive answers to clinical questions.

In addition to the printed book, *Harrison's* is available on multiple digital platforms, including eBook and app versions, and via an online subscription available through McGraw-Hill's popular Access Medicine (*www.accessmedicine.com*) collection. The digital editions feature an array of supplementary videos, databases, and photographic atlases as well as new literature updates, tutorials, animations, and audio discussions covering key topics in medicine. *Harrison's Manual of Medicine* is a condensed pocket version of clinical essentials derived from the more comprehensive *Harrison's Principles of Internal Medicine*. The *Manual* is also available as an eBook and an app and via Access Medicine. Together, these platforms form a potent *Harrison's* collection of reference, test prep, and point-of-care online content.

In the 20th edition, examples of new chapters include "Promoting Good Health," focusing on prevention and practical lifestyle changes to enhance longevity and well-being; "Health Care Systems in Developed Countries," providing a comparison of health delivery models from around the world; "Pharmacogenomics," applying new approaches for selecting precision medicines and appropriate doses; "Bacterial Resistance to Antimicrobial Agents," highlighting the widespread and often inappropriate use of antibiotics in clinical care and agriculture; "LGBT Health," outlining strategies to enhance access and care models for populations with distinctive health care needs; "Neuromyelitis Optica," summarizing disorders with similarities to multiple sclerosis but requiring different treatments; "Worldwide Changes in Patterns of Infectious Disease," reviewing the dynamic evolution of new infectious diseases and the containment of older disorders, some of which have plagued humankind for centuries; and "Approach to the Medical Consultation," providing practical advice to ensure that the consultant addresses the needs of the referring clinician. In addition to these and other new topics, the 20th edition presents a fascinating new series of chapters entitled "Frontiers," which foreshadows cutting-edge science that will change medical practice in the near term. Examples of new Frontier chapters include "Telomere Disease," "The Role of Epigenetics in Disease and Treatment," "The Role of Circadian Biology in Health and Disease," and "Behavioral Economics and Health."

In addition to these new topics, major advances in each subspecialty of internal medicine have been incorporated into this edition. Of particular note in this 20th edition are critical updates in the classic chapter on HIV/AIDS, which offers a clinically pragmatic focus as well as a comprehensive and analytical approach to pathogenesis. The updates cover the latest treatment protocols and address the issue of combination prevention modalities, making the chapter the most up-to-date treatise on HIV disease available.

Readers will find expanded coverage of neurodegenerative diseases, highlighting important advances in their classification and management and delineating new mechanisms responsible for the deposition and spread of pathogenic protein aggregates in these disorders. Practical guidance for the use of highly effective therapies for multiple sclerosis is another highlight of the new edition. The chapter on chronic hepatitis discusses in detail the dramatic new discoveries in the use of direct-acting antiviral agents for the treatment and cure of chronic hepatitis C virus disease; these agents are responsible for some of the most exciting therapeutic advances in medicine today.

The promise of the Human Genome Project continues to be realized in clinical medicine. This is reflected throughout the book but particularly highlighted by advances in our understanding of genetic heterogeneity of cancers, including molecular nosology that distinguishes distinct entities that share histologic similarities. The tools of genetics also inform the use of therapies targeting specific genetic lesions and immune system activation. Genetic counseling for patients with genetic predisposition to cancer (e.g., BRCA 1/2) is informing prevention strategies and reducing cancer risk. Our understanding of the microbiome, its relevance to normal physiology and disease pathogenesis, and its implications for treatment of a variety of diseases is expanding rapidly, and these advances are captured in a completely rewritten chapter "The Human Microbiome" and a thoroughly updated chapter "Microbial Genomics and Infectious Disease." The classification and management of diabetes has been thoroughly updated on the basis of new studies, clinical guidelines, and treatments. Updated guidelines for testosterone management and replacement are based on the results of new clinical trials.

We have many people to thank for their efforts in producing this book. First, the authors have done a superb job of producing authoritative chapters that synthesize vast amounts of scientific and clinical data to create informative and practical approaches to managing patients. In today's information-rich, rapidly evolving environment, they have ensured that this information is current. We are most

grateful to our colleagues who work closely with each editor to facilitate communication with the authors and help us keep *Harrison's* content current. In particular, we wish to acknowledge the expert support of Patricia Conrad, Patricia L. Duffey, Gregory K. Folkers, Julie B. McCoy, Elizabeth Robbins, Anita Rodriguez, and Stephanie Tribuna. Scott Grillo and James Shanahan, our long-standing partners at McGraw-Hill Education's Professional Publishing group, have inspired the creative and dynamic evolution of *Harrison's*, guiding the development of the book and its related products in new formats. Kim Davis, as Managing Editor, has adeptly ensured that the complex production of this multi-authored textbook proceeded smoothly and efficiently. Priscilla Beer and Armen Ovsepyen oversaw the production of our videos and animations. Jeffrey Herzich, along with other members of the McGraw-Hill Education staff, shepherded the production of this new edition.

We are privileged to have compiled this 20th edition and are enthusiastic about all that it offers our readers. We learned much in the process of editing *Harrison's* and hope that you will find this edition uniquely valuable as a clinical and educational resource.

The Editors

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1 The Practice of Medicine

The Editors

ENDURING VALUES OF THE MEDICAL PROFESSION

No greater opportunity, responsibility, or obligation can fall to the lot of a human being than to become a physician. In the care of the suffering, [the physician] needs technical skill, scientific knowledge, and human understanding.... Tact, sympathy, and understanding are expected of the physician, for the patient is no mere collection of symptoms, signs, disordered functions, damaged organs, and disturbed emotions. [The patient] is human, fearful, and hopeful, seeking relief, help, and reassurance.

—*Harrison's Principles of Internal Medicine,* 1950

The practice of medicine has changed in significant ways since the first edition of this book appeared in 1950. The advent of molecular genetics, sophisticated new imaging techniques, robotics, and advances in bioinformatics and information technology have contributed to an explosion of scientific information that has changed fundamentally the way physicians define, diagnose, treat, and attempt to prevent disease. This growth of scientific knowledge is ongoing and accelerating.

The widespread use of electronic medical records and the Internet have altered the way physicians access and exchange information as a routine part of medical practice **(Fig. 1-1)**. As today's physicians strive to integrate copious amounts of scientific knowledge into everyday practice, it is critically important to remember two things: first, the ultimate goal of medicine is to prevent disease and, when it occurs, to diagnose it early and provide effective treatment; and second, despite nearly 70 years of scientific advances since the first edition of this text, a trusting relationship between physician and patient still lies at the heart of successful patient care.

THE SCIENCE AND ART OF MEDICINE

Deductive reasoning and applied technology form the foundation for the solution to many clinical problems. Spectacular advances in biochemistry, cell biology, and genomics, coupled with newly developed imaging techniques, allow access to the innermost parts of the cell and provide a window into the most remote recesses of the body. Revelations about the nature of genes and single cells have opened a portal for formulating a new molecular basis for the physiology of systems. Increasingly, physicians are learning how subtle changes in many different genes can affect the function of cells and organisms. Researchers are deciphering the complex mechanisms by which genes are regulated. Clinicians have developed a new appreciation of the role of stem cells in normal tissue function, in the development of cancer and other disorders, and in the treatment of certain diseases. Entirely new areas of research, including studies of chronobiology, the human microbiome, and epigenetics, have become important for understanding both health and disease. Information technology enables the interrogation of medical records from millions of individuals, yielding new insights into the etiology, characteristics, and stratification of many diseases. The knowledge gleaned from the ***science of medicine*** continues to enhance the understanding by physicians of complex pathologic processes and to provide new approaches to disease prevention, diagnosis, and treatment. Yet skill in the most sophisticated applications of laboratory technology and in the use of the latest therapeutic modality alone does not make a good physician.

When a patient poses challenging clinical problems, an effective physician must be able to identify the crucial elements in a complex history and physical examination; order the appropriate laboratory, imaging, and diagnostic tests; and extract the key results from densely populated computer screens to determine whether to treat or to "watch." As the number of tests increases, so does the likelihood that some incidental finding, completely unrelated to the clinical problem at hand, will be uncovered. Deciding whether a clinical clue is worth pursuing or should be dismissed as a "red herring" and weighing whether a proposed test, preventive measure, or treatment entails a greater risk than the disease itself are essential judgments that a skilled clinician must make many times each day. This combination of medical knowledge, intuition, experience, and judgment defines the ***art of medicine***, which is as necessary to the practice of medicine as is a sound scientific base.

CLINICAL SKILLS

History-Taking The recorded history of an illness should include all the facts of medical significance in the life of the patient. Recent events should be given the most attention. Patients should, at some early point, have the opportunity to tell their own story of the illness without frequent interruption and, when appropriate, should receive expressions of interest, encouragement, and empathy from the physician. Any event related by a patient, however trivial or seemingly irrelevant, may provide the key to solving the medical problem. A methodical review of systems is important to elicit features of an underlying disease that might not be mentioned in the patient's narrative. In general, patients who feel comfortable with the physician will offer more complete information; thus, putting the patient at ease contributes substantially to obtaining an adequate history.

An informative history is more than an orderly listing of symptoms. By listening to patients and noting the way in which they describe their symptoms, physicians can gain valuable insight. Inflections of voice, facial expression, gestures, and attitude (i.e., "body language") may offer important clues to patients' perception of their symptoms. Because patients vary considerably in their medical sophistication and ability to recall facts, the reported medical history should be corroborated whenever possible. The social history also can provide important insights into the types of diseases that should be considered and can identify practical considerations for subsequent management. The family history not only identifies rare Mendelian disorders but often reveals risk factors for common disorders, such as coronary heart disease, hypertension, autoimmunity, and asthma. A thorough family history may require input from multiple relatives to ensure completeness and accuracy. An experienced clinician can usually formulate a relevant differential diagnosis from the history alone, using the physical examination and diagnostic tests to narrow the list or reveal unexpected findings that lead to more focused inquiry.

The very act of eliciting the history provides the physician with an opportunity to establish or enhance a unique bond that forms the basis for a good patient–physician relationship. This process helps the physician develop an appreciation of the patient's view of the illness, the patient's expectations of the physician and the health care system, and the financial and social implications of the illness for the patient. Although current health care settings may impose time constraints on patient visits, it is important not to rush the encounter. A hurried approach may lead patients to believe that what they are relating is not of importance to the physician, and thus they may withhold relevant information. The confidentiality of the patient–physician relationship cannot be overemphasized.

Physical Examination The purpose of the physical examination is to identify physical signs of disease. The significance of these objective indications of disease is enhanced when they confirm a functional or structural change already suggested by the patient's history. At times, however, physical signs may be the only evidence of disease and may not have been suggested by the history.

The physical examination should be methodical and thorough, with consideration given to the patient's comfort and modesty. Although

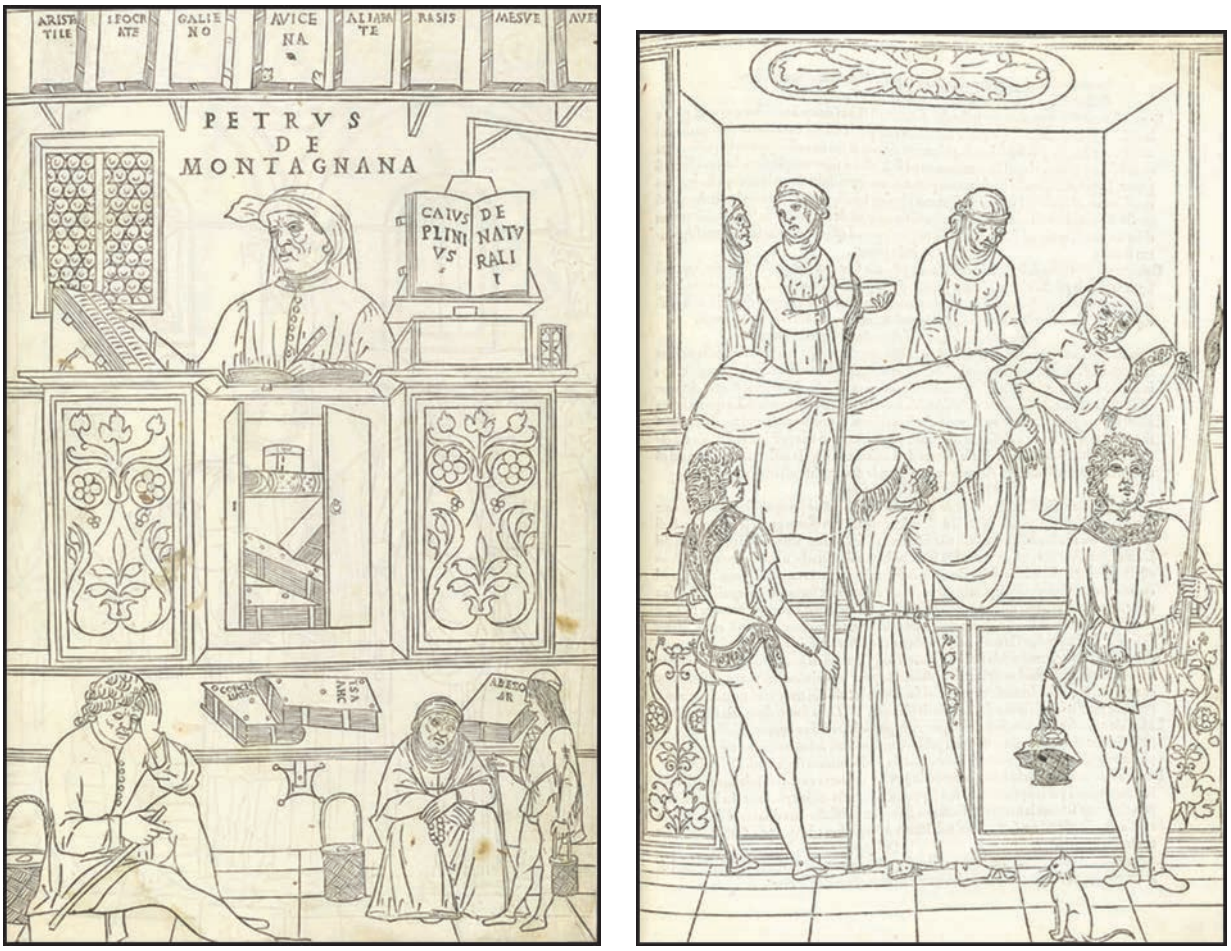

FIGURE 1-1 Woodcuts from Johannes de Ketham's *Fasciculus Medicinae*, the first illustrated medical text ever printed, show methods of information access and exchange in medical practice during the early Renaissance. Initially published in 1491 for use by medical students and practitioners, *Fasciculus Medicinae* appeared in six editions over the next 25 years. *Left:* Petrus de Montagnana, a well-known physician and teacher at the University of Padua and author of an anthology of instructive case studies, consults medical texts dating from antiquity up to the early Renaissance. *Right:* A patient with plague is attended by a physician and his attendants. *(Courtesy, U.S. National Library of Medicine.)*

attention is often directed by the history to the diseased organ or part of the body, the examination of a new patient must extend from head to toe in an objective search for abnormalities. The results of the examination, like the details of the history, should be recorded at the time they are elicited—not hours later, when they are subject to the distortions of memory. Physical examination skills should be learned under direct observation of experienced clinicians. Even highly experienced clinicians can benefit from ongoing coaching and feedback. Simulation laboratories and standardized patients play an increasingly important role in the development of clinical skills. Although the skills of physical diagnosis are acquired with experience, it is not merely technique that determines success in identifying signs of disease. The detection of a few scattered petechiae, a faint diastolic murmur, or a small mass in the abdomen is not a question of keener eyes and ears or more sensitive fingers, but of a mind alert to those findings. Because physical findings can change with time, the physical examination should be repeated as frequently as the clinical situation warrants.

Given the many highly sensitive diagnostic tests now available (particularly imaging techniques), it may be tempting to place less emphasis on the physical examination. Indeed, many patients are seen by consultants after a series of diagnostic tests have been performed and the results are known. This fact should not deter the physician from performing a thorough physical examination since important clinical findings may have escaped detection. The act of examining (touching) the patient also offers an opportunity for communication and may have reassuring effects that foster the patient–physician relationship.

Diagnostic Studies Physicians rely increasingly on a wide array of laboratory and imaging tests to make diagnoses and ultimately to solve clinical problems. However, accumulated results do not relieve the physician from the responsibility of carefully observing and examining the patient. It is also essential to appreciate the limitations of diagnostic tests. By virtue of their apparent precision, these tests often gain an aura of certainty regardless of the fallibility of the tests themselves, the instruments used in the tests, and the individuals performing or interpreting the tests. Physicians must weigh the expense involved in laboratory procedures against the value of the information these procedures are likely to provide.

Single laboratory tests are rarely ordered. Instead, physicians generally request "batteries" of multiple tests, which often prove useful and can be performed with a single specimen at relatively low cost. For example, abnormalities of hepatic function may provide the clue to nonspecific symptoms such as generalized weakness and increased fatigability, suggesting a diagnosis of chronic liver disease. Sometimes a single abnormality, such as an elevated serum calcium level, points to a particular disease, such as hyperparathyroidism or an underlying malignancy.

The thoughtful use of screening tests (e.g., measurement of low-density lipoprotein cholesterol) may allow early intervention to prevent disease **(Chap. 4)**. Screening tests are most informative when they are directed toward common diseases and when their results indicate whether other useful—but often costly—tests or interventions are needed. On the one hand, biochemical measurements, together with simple laboratory determinations such as routine serum chemistries, blood counts, and urinalysis, often provide a major clue to the presence of a pathologic process. On the other hand, the physician must learn to evaluate occasional screening-test abnormalities that do not necessarily connote significant disease. An in-depth workup after the report

of an isolated laboratory abnormality in a person who is otherwise well is often wasteful and unproductive. Because so many tests are performed routinely for screening purposes, it is not unusual for one or two values to be slightly abnormal. Nevertheless, even if there is no reason to suspect an underlying illness, tests yielding abnormal results ordinarily are repeated to rule out laboratory error. If an abnormality is confirmed, it is important to consider its potential significance in the context of the patient's condition and other test results.

There is almost continual development of technically improved imaging studies with greater sensitivity and specificity. These tests provide remarkably detailed anatomic information that can be pivotal in informing medical decision-making. Ultrasonography, CT, MRI, a variety of isotopic scans, and positron emission tomography (PET) have supplanted older, more invasive approaches and opened new diagnostic vistas. In light of their capabilities and the rapidity with which they can lead to a diagnosis, it is tempting to order a battery of imaging studies. All physicians have had experiences in which imaging studies revealed findings that led to an unexpected diagnosis. Nonetheless, patients must endure each of these tests, and the added cost of unnecessary testing is substantial. Furthermore, investigation of an unexpected abnormal finding may be associated with risk and/or expense and may lead to the diagnosis of an irrelevant or incidental problem. A skilled physician must learn to use these powerful diagnostic tools judiciously, always considering whether the results will alter management and benefit the patient.

MANAGEMENT OF PATIENT CARE

Team-Based Care Medical practice has long involved teams, particularly physicians working with nurses. Advances in medicine have increased our ability to manage very complex clinical situations (e.g., intensive care units [ICUs], bone marrow transplantation) and have shifted the burden of disease toward chronic illnesses. Because an individual patient may have multiple chronic diseases, he or she may be cared for by different specialists as well as a primary care physician. In the inpatient setting, care may involve multiple consultants along with the primary admitting physician. Communication through the medical record is necessary but not sufficient, particularly when patients have complex medical problems or when difficult decisions need to be made about the optimal management plan. Physicians should willingly meet face-to-face or by phone to ensure clear communication and thoughtful planning. It is important to note that patients often receive or perceive different messages from various care providers; attempts should be made to provide consistency among these messages to the patient. Management plans and treatment options should be outlined succinctly and clearly for the patient.

Another dimension of team-based care involves allied health professions. It is not unusual for a hospitalized patient to encounter physical therapists, pharmacists, respiratory therapists, radiology technicians, social workers, dieticians, and transport personnel (among others) in addition to physicians and nurses. Each of these individuals contributes to clinical care as well as to the patient's experience with the health care system. In the outpatient setting, disease screening and chronic disease management are often carried out by nurses, physician assistants, or other allied health professionals.

The growth of team-based care has important implications for medical culture, student and resident training, and the organization of health care systems. Despite diversity in training, skills, and responsibilities among health care professionals, common values need to be espoused and reinforced. Many medical schools have incorporated interprofessional teamwork into their curricula. Effective communication is inevitably the most challenging aspect of implementing team-based care. While communication can be aided by electronic devices, including medical records, apps, or text messages, it is vitally important to balance efficiency with taking the necessary time to speak directly with colleagues.

The Dichotomy of Inpatient and Outpatient Internal Medicine The hospital environment has experienced sweeping changes over the last few decades. Emergency departments and critical care units have evolved to manage critically ill patients, allowing them to survive formerly fatal conditions. In parallel, there is increasing pressure to reduce the length of stay in the hospital and to manage complex disorders in the outpatient setting. This transition has been driven not only by efforts to reduce costs but also by the availability of new outpatient technologies, such as imaging and percutaneous infusion catheters for long-term antibiotics or nutrition, minimally invasive surgical procedures, and evidence that outcomes often are improved by reducing inpatient hospitalization.

In addition to traditional medical beds, hospitals now encompass multiple distinct levels of care, such as the emergency department, procedure rooms, overnight observation units, critical care units, and palliative care units. A consequence of this differentiation has been the emergence of new specialties (e.g., emergency medicine and end-of-life care) and the provision of in-hospital care by hospitalists and intensivists. Most *hospitalists* are board-certified internists who bear primary responsibility for the care of hospitalized patients and whose work is limited entirely to the hospital setting. The shortened length of hospital stay means that most patients receive only acute care while hospitalized; the increased complexities of inpatient medicine make the presence of an internist with specific training, skills, and experience in the hospital environment extremely beneficial. *Intensivists* are board-certified physicians who are further certified in critical care medicine and who direct and provide care for very ill patients in critical care units. Clearly, an important challenge in internal medicine today is to ensure the continuity of communication and information flow between a patient's primary care physician and those who are in charge of the patient's hospital care. Maintaining these channels of communication is frequently complicated by patient "handoffs"—i.e., transitions from the outpatient to the inpatient environment, from the critical care unit to a general medicine floor, from a medical to a surgical service and vice versa, and from the hospital to the outpatient environment.

The involvement of many care providers in conjunction with these transitions can threaten the traditional one-to-one relationship between patient and primary care physician. Of course, patients can benefit greatly from effective collaboration among a number of health care professionals; however, *it is the duty of the patient's principal or primary physician to provide cohesive guidance through an illness*. To meet this challenge, primary care physicians must be familiar with the techniques, skills, and objectives of specialist physicians and allied health professionals who care for their patients in the hospital. In addition, primary care physicians must ensure that their patients benefit from scientific advances and the expertise of specialists, both in and out of the hospital. Primary care physicians should explain the role of these specialists to reassure patients that they are in the hands of physicians best trained to manage an acute illness. However, the primary care physician should assure patients and their families that decisions are being made in consultation with these specialists. The evolving concept of the "medical home" incorporates team-based primary care with subspecialty care in a cohesive environment that ensures smooth transitions of care.

Mitigating the Stress of Acute Illness Few people are prepared for a new diagnosis of cancer or anticipate the occurrence of a myocardial infarction, stroke, or major accident. The care of a frightened or distraught patient is confounded by these understandable responses to life-threatening events. The physician and other health providers can reduce the shock of life-changing events by providing information in a clear, calm, consistent, and reassuring manner. Often, information and reassurance need to be repeated. Caregivers should also recognize that, for outsiders, hospital emergency rooms, operating rooms, ICUs, and general medical floors represent an intimidating environment. Hospitalized patients find themselves surrounded by air jets, buttons, and glaring lights; invaded by tubes and wires; and beset by the numerous members of the health care team—hospitalists, specialists, nurses, nurses' aides, physicians' assistants, social workers, technologists, physical therapists, medical students, house officers, attending and consulting physicians, and many others. They may be

transported to special laboratories and imaging facilities replete with blinking lights, strange sounds, and unfamiliar personnel; they may be left unattended at times; and they may be obligated to share a room with other patients who have their own health problems. It is little wonder that patients may be stressed by this environment. Physicians who appreciate the hospital experience from the patient's perspective and who make an effort to guide the patient through this experience may make a stressful situation more tolerable and enhance the patient's chances for an optimal recovery.

Medical Decision-Making Medical decision-making is a fundamental responsibility of the physician and occurs at each stage of the diagnostic and therapeutic process. The decision-making process involves the ordering of additional tests, requests for consultations, decisions about treatment, and predictions concerning prognosis. This process requires an in-depth understanding of the pathophysiology and natural history of disease. Formulating a differential diagnosis requires not only a broad knowledge base but also the ability to assess the relative probabilities of various diseases for a given patient. Application of the scientific method, including hypothesis formulation and data collection, is essential to the process of accepting or rejecting a particular diagnosis. Analysis of the differential diagnosis is an iterative process. As new information or test results are acquired, the group of disease processes being considered can be contracted or expanded appropriately. Whenever possible, decisions should be evidence-based, taking advantage of rigorously designed clinical trials or objective comparisons of different diagnostic tests. *Evidence-based medicine* is in sharp contrast to anecdotal experience, which is often biased. Unless attuned to the importance of using larger, objective studies for making decisions, even the most experienced physicians can be influenced to an undue extent by recent encounters with selected patients. Evidence-based medicine has become an increasingly important part of routine medical practice and has led to the publication of many useful practice guidelines.

Despite the importance of evidence-based medicine, much medical decision-making still relies on good clinical judgment, an attribute that is difficult to quantify or even to assess qualitatively. Physicians must use their knowledge and experience as a basis for weighing known factors, along with the inevitable uncertainties, and then making a sound judgment; this synthesis of information is particularly important when a relevant evidence base is not available. Several quantitative tools may be invaluable in synthesizing the available information, including diagnostic tests, Bayes' theorem, and multivariate statistical models. Diagnostic tests serve to reduce uncertainty about an individual's diagnosis or prognosis and help the physician decide how best to manage that individual's condition. The battery of diagnostic tests complements the history and the physical examination. The accuracy of a particular test is ascertained by determining its sensitivity (true-positive rate) and specificity (true-negative rate) as well as the predictive value of a positive and a negative result. **See Chap. 3 for a more thorough discussion of decision-making in clinical medicine.**

Practice Guidelines Many professional organizations and government agencies have developed formal clinical-practice guidelines to aid physicians and other caregivers in making diagnostic and therapeutic decisions that are evidence-based, cost-effective, and most appropriate to a particular patient and clinical situation. As the evidence base of medicine increases, guidelines can provide a useful framework for managing patients with particular diagnoses or symptoms. Clinical guidelines can protect patients—particularly those with inadequate health care benefits—from receiving substandard care. These guidelines also can protect conscientious caregivers from inappropriate charges of malpractice and society from the excessive costs associated with the overuse of medical resources. There are, however, caveats associated with clinical-practice guidelines since they tend to oversimplify the complexities of medicine. Furthermore, groups with different perspectives may develop divergent recommendations regarding issues as basic as the need for screening of women by mammography or of men by serum prostate-specific antigen (PSA). Finally, guidelines, as the term implies, do not—and cannot be expected to—account for the uniqueness of each individual and his or her illness. The physician's challenge is to integrate into clinical practice the useful recommendations offered by experts without accepting them blindly or being inappropriately constrained by them.

Precision Medicine The concept of *precision* or *personalized medicine* reflects the growing recognition that diseases once lumped together can be further stratified on the basis of genetic, biomarker, phenotypic, and/or psychosocial characteristics that distinguish a given patient from other patients with similar clinical presentations. Inherent in this concept is the goal of targeting therapies in a more specific way to improve clinical outcomes for the individual patient and minimize unnecessary side effects for those less likely to respond to a particular treatment. In some respects, precision medicine represents the evolution of clinical practice guidelines, which are usually developed for populations of patients or a particular diagnosis (e.g., hypertension, thyroid nodule). As the pathophysiology, prognosis, and treatment responses of subgroups within these diagnoses become better understood, the relevant clinical guidelines incorporate progressively more refined recommendations for individuals within these subgroups. The role of precision medicine is particularly important for cancers in which genetic testing is able to predict responses (or the lack thereof) to targeted therapies **(Chap. 69)**. One can anticipate similar applications of precision medicine in pharmacogenomics, immunologic disorders, and diseases in which biomarkers better predict treatment responses.

Evaluation of Outcomes Clinicians generally use *objective* and readily measurable parameters to judge the outcome of a therapeutic intervention. These measures may oversimplify the complexity of a clinical condition as patients often present with a major clinical problem in the context of multiple complicating background illnesses. For example, a patient may present with chest pain and cardiac ischemia, but with a background of chronic obstructive pulmonary disease and renal insufficiency. For this reason, outcome measures such as mortality, length of hospital stay, or readmission rates are typically risk-adjusted. An important point to remember is that patients usually seek medical attention for *subjective* reasons; they wish to obtain relief from pain, to preserve or regain function, and to enjoy life. The components of a patient's health status or quality of life can include bodily comfort, capacity for physical activity, personal and professional function, sexual function, cognitive function, and overall perception of health. Each of these important domains can be assessed through structured interviews or specially designed questionnaires. Such assessments provide useful parameters by which a physician can judge patients' subjective views of their disabilities and responses to treatment, particularly in chronic illness. The practice of medicine requires consideration and integration of both objective and subjective outcomes.

Many health systems use survey and patient feedback data to assess qualitative features such as patient satisfaction, access to care, and communication with nurses and physicians. In the United States, HCAHPS (Hospital Consumer Assessment of Healthcare Providers and Systems) surveys are used by many systems and are publically reported. Social media is also being used to assess feedback in real time as well as to share patient experiences with health care systems.

Errors in the Delivery of Health Care A series of reports from the Institute of Medicine (now the National Academy of Medicine [NAM]) called for an ambitious agenda to reduce medical error rates and improve patient safety by designing and implementing fundamental changes in health care systems. It is the responsibility of hospitals and health care organizations to develop systems to reduce risk and ensure patient safety. Medication errors can be reduced through the use of ordering systems that rely on electronic processes or, when electronic options are not available, that eliminate misreading of handwriting. Whatever the clinical situation, it is the physician's responsibility to use powerful therapeutic measures wisely, with due regard for their beneficial actions, potential dangers, and cost. Implementation of infection

control systems, enforcement of hand-washing protocols, and careful oversight of antibiotic use can minimize the complications of nosocomial infections. Central-line infection rates have been dramatically reduced at many centers by careful adherence of trained personnel to standardized protocols for introducing and maintaining central lines. Rates of surgical infection and wrong-site surgery can likewise be reduced by the use of standardized protocols and checklists. Falls by patients can be minimized by judicious use of sedatives and appropriate assistance with bed-to-chair and bed-to-bathroom transitions. Taken together, these and other measures are saving thousands of lives each year.

Electronic Medical Records Both the growing reliance on computers and the strength of information technology now play central roles in medicine, including efforts to reduce medical errors. Laboratory data are accessed almost universally through computers. Many medical centers now have electronic medical records (EMRs), computerized order entry, and bar-coded tracking of medications. Some of these systems are interactive, sending reminders or warning of potential medical errors.

EMRs offer rapid access to information that is invaluable in enhancing health care quality and patient safety, including relevant data, historical and clinical information, imaging studies, laboratory results, and medication records. These data can be used to monitor and reduce unnecessary variations in care and to provide real-time information about processes of care and clinical outcomes. Ideally, patient records are easily transferred across the health care system. However, technological limitations and concerns about privacy and cost continue to limit broad-based use of EMRs in many clinical settings.

For all of the advantages of EMRs, they can create distance between the physician and patient if care is not taken to preserve face-to-face contact. EMRs also require training and time for data entry. Many providers spend significant time entering information to generate structured data and to meet billing requirements. They may feel pressured to take short cuts, such as "cutting and pasting" parts of earlier notes into the daily record, thereby increasing the risk of errors. EMRs also structure information in a manner that disrupts the traditional narrative flow across time and among providers. These features, which may be frustrating for some providers, must be weighed against the advantages of ready access to past medical history, imaging, laboratory data, and consultant notes.

It is important to emphasize that information technology is merely a tool and can never replace the clinical decisions that are best made by the physician. Clinical knowledge and an understanding of a patient's needs, supplemented by quantitative tools, still represent the best approach to decision-making in the practice of medicine.

THE PATIENT–PHYSICIAN RELATIONSHIP

The significance of the intimate personal relationship between physician and patient cannot be too strongly emphasized, for in an extraordinarily large number of cases both the diagnosis and treatment are directly dependent on it. One of the essential qualities of the clinician is interest in humanity, ***for the secret of the care of the patient is in caring for the patient****.*

—Francis W. Peabody, October 21, 1925,
Lecture at Harvard Medical School

Physicians must never forget that patients are individuals with problems that all too often transcend their physical complaints. They are not "cases" or "admissions" or "diseases." Patients do not fail treatments; treatments fail to benefit patients. This point is particularly important in this era of high technology in clinical medicine. Most patients are anxious and fearful. Physicians should instill confidence and offer reassurance, but they must never come across as arrogant or patronizing. A professional attitude, coupled with warmth and openness, can do much to alleviate anxiety and to encourage patients to share all aspects of their medical history. Empathy and compassion are the essential features of a caring physician. The physician needs to consider the setting in which an illness occurs—in terms not only of patients themselves but also of their familial, social, and cultural backgrounds. The ideal patient–physician relationship is based on thorough knowledge of the patient, mutual trust, and the ability to communicate.

Informed Consent The fundamental principles of medical ethics require physicians to act in the patient's best interest and to respect the patient's autonomy. These requirements are particularly relevant to the issue of informed consent. Patients are required to sign consent forms for most diagnostic or therapeutic procedures. Many patients possess limited medical knowledge and must rely on their physicians for advice. Communicating in a clear and understandable manner, physicians must fully discuss the alternatives for care and explain the risks, benefits, and likely consequences of each alternative. The physician is responsible for ensuring that the patient thoroughly understands these risks and benefits; encouraging questions is an important part of this process. It may be necessary to go over certain issues with the patient more than once. This is the very definition of *informed consent*. Complete, clear explanation and discussion of the proposed procedures and treatment can greatly mitigate the fear of the unknown that commonly accompanies hospitalization. Often the patient's understanding is enhanced by repeatedly discussing the issues in an unthreatening and supportive way, answering new questions that occur to the patient as they arise. Clear communication can also help alleviate misunderstandings in situations where complications of intervention occur.

Special care should be taken to ensure that a physician seeking a patient's informed consent has no real or apparent conflict of interest.

Approach to Grave Prognoses and Death No circumstance is more distressing than the diagnosis of an incurable disease, particularly when premature death is inevitable. What should the patient and family be told? What measures should be taken to maintain life? What can be done to optimize quality of life?

Transparency of information, delivered in an appropriate manner, is essential in the face of a terminal illness. Even patients who seem unaware of their medical circumstances, or whose family members have protected them from diagnoses or prognoses, often have keen insights into their condition. They may also have misunderstandings that can lead to additional anxiety. The patient must be given an opportunity to talk with the physician and ask questions. A wise and insightful physician uses such open communication as the basis for assessing what the patient wants to know and when he or she wants to know it. On the basis of the patient's responses, the physician can assess the right tempo for sharing information. Ultimately, the patient must understand the expected course of the disease so that appropriate plans and preparations can be made. The patient should participate in decision-making with an understanding of the goal of treatment (palliation) and its likely effects. The patient's religious beliefs should be taken into consideration. Some patients may find it easier to share their feelings about death with their physician, nurses, or members of the clergy than with family members or friends.

The physician should provide or arrange for emotional, physical, and spiritual support and must be compassionate, unhurried, and open. In many instances, there is much to be gained by the laying on of hands. Pain should be controlled adequately, human dignity maintained, and isolation from family and close friends avoided. These aspects of care tend to be overlooked in hospitals, where the intrusion of life-sustaining equipment can detract from attention to the whole person and encourage concentration instead on the life-threatening disease, against which the battle ultimately will be lost in any case. In the face of terminal illness, the goal of medicine must shift from *cure* to *care* in the broadest sense of the term. *Primum succurrere*, first hasten to help, is a guiding principle. In offering care to a dying patient, a physician should be prepared to provide information to family members and deal with their grief and sometimes their feelings of guilt or even anger. It is important for the physician to assure the family that everything reasonable is being done. A substantial challenge in these discussions is that the physician often does not know how to gauge the prognosis. In addition, various members of the health care team may offer different opinions. Good communication among providers is

essential so that consistent information is provided to patients. This is especially important when the best path forward is uncertain. Advice from experts in palliative and terminal care should be sought whenever appropriate to ensure that clinicians are not providing patients with unrealistic expectations. **For a more complete discussion of end-of-life care, see Chap. 9.**

Maintaining Humanism and Professionalism Many trends in the delivery of health care tend to make medical care impersonal. These trends, some of which have been mentioned already, include (1) vigorous efforts to reduce the escalating costs of health care; (2) the growing number of managed-care programs, which are intended to reduce costs but in which the patient may have little choice in selecting a physician; (3) increasing reliance on technological advances and computerization; and (4) the need for numerous physicians and other health professionals to be involved in the care of most patients who are seriously ill.

In light of these changes in the medical care system, it is a major challenge for physicians to maintain the *humane* aspects of medical care. The American Board of Internal Medicine, working together with the American College of Physicians–American Society of Internal Medicine and the European Federation of Internal Medicine, has published a *Charter on Medical Professionalism* that underscores three main principles in physicians' contract with society: (1) the primacy of patient welfare, (2) patient autonomy, and (3) social justice. While medical schools appropriately place substantial emphasis on professionalism, a physician's personal attributes, including integrity, respect, and compassion, also are extremely important. In the United States, the Gold Humanism Society recognizes individuals who are exemplars of humanistic patient care and serve as role models for medical education and training.

Availability to the patient, expression of sincere concern, willingness to take the time to explain all aspects of the illness, and a nonjudgmental attitude when dealing with patients whose cultures, lifestyles, attitudes, and values differ from those of the physician are just a few of the characteristics of a humane physician. Every physician will, at times, be challenged by patients who evoke strongly negative or positive emotional responses. Physicians should be alert to their own reactions to such situations and should consciously monitor and control their behavior so that the patient's best interest remains the principal motivation for their actions at all times.

Another important aspect of patient care involves an appreciation of the patient's "quality of life," a subjective assessment of what each patient values most. This assessment requires detailed, sometimes intimate knowledge of the patient, which usually can be obtained only through deliberate, unhurried, and often repeated conversations. Time pressures will always threaten these interactions, but they should not diminish the importance of understanding and seeking to fulfill the priorities of the patient.

EXPANDING FRONTIERS IN MEDICAL PRACTICE

The Era of "Omics" In the spring of 2003, announcement of the complete sequencing of the human genome officially ushered in the genomic era. However, even before that landmark accomplishment, the practice of medicine had been evolving as a result of insights into both the human genome and the genomes of a wide variety of microbes. The clinical implications of these insights are illustrated by the complete genome sequencing of H1N1 influenza virus in 2009 and the rapid identification of H1N1 influenza as a potentially fatal pandemic illness, leading to the swift development and dissemination of an effective protective vaccine. Today, gene expression profiles are being used to guide therapy and inform prognosis for a number of diseases, and genotyping is providing a new means to assess the risk of certain diseases as well as variations in response to a number of drugs. Despite these advances, the use of complex genomics in the diagnosis, prevention, and treatment of disease is still in its early stages. The task of physicians is complicated by the fact that phenotypes generally are determined not by genes alone but by the interplay of genetic and environmental factors.

Rapid progress is also being made in other areas of molecular medicine. *Epigenetics* is the study of alterations in chromatin and histone proteins and methylation of DNA sequences that influence gene expression **(Chap. 471)**. Every cell of the body has identical DNA sequences; the diverse phenotypes a person's cells manifest are the result of epigenetic regulation of gene expression. Epigenetic alterations are associated with a number of cancers and other diseases. *Proteomics*, the study of the entire library of proteins made in a cell or organ and the complex relationship of these proteins to disease, is enhancing the repertoire of the 23,000 genes in the human genome through alternate splicing, posttranslational processing, and posttranslational modifications that often have unique functional consequences. The presence or absence of particular proteins in the circulation or in cells is being explored for diagnostic and disease-screening applications. *Microbiomics* is the study of the resident microbes in humans and other mammals, which together compose the microbiome. The human haploid genome has ~23,000 genes, whereas the microbes residing on and in the human body encompass more than 3–4 million genes; these resident microbes are likely to be of great significance with regard to health status. Ongoing research is demonstrating that the microbes inhabiting human mucosal and skin surfaces play a critical role in maturation of the immune system, in metabolic balance, and in disease susceptibility. A variety of environmental factors, including the use and overuse of antibiotics, have been tied experimentally to substantial increases in disorders such as obesity, metabolic syndrome, atherosclerosis, and immune-mediated diseases in both adults and children. *Metagenomics*, of which microbiomics is a part, is the genomic study of environmental species that have the potential to influence human biology directly or indirectly. An example is the study of exposures to microorganisms in farm environments that may be responsible for the lower incidence of asthma among children raised on farms. *Metabolomics* is the study of the range of metabolites in cells or organs and the ways they are altered in disease states. The aging process itself may leave telltale metabolic footprints that allow the prediction (and possibly the prevention) of organ dysfunction and disease. It seems likely that disease-associated patterns will be found in lipids, carbohydrates, membranes, mitochondria, and other vital components of cells and tissues. *Exposomics* is the study of the exposome—i.e., the environmental exposures such as smoking, sunlight, diet, exercise, education, and violence that together have an enormous impact on health. All of this new information represents a challenge to the traditional reductionist approach to medical thinking. The variability of results in different patients, together with the large number of variables that can be assessed, creates challenges in identifying preclinical disease and defining disease states unequivocally. Accordingly, the tools of *systems biology* and *network medicine* are being applied to the enormous body of information now obtainable for every patient and may eventually provide new approaches to classifying disease. **For a more complete discussion of a complex systems approach to human disease, see Chap. 476.**

The rapidity of these advances may seem overwhelming to practicing physicians. However, physicians have an important role to play in ensuring that these powerful technologies and sources of new information are applied judiciously to patient care. Since "omics" are evolving so rapidly, physicians and other health care professionals must engage in continuous learning so that they can apply this new knowledge to the benefit of their patients' health and well-being. Genetic testing requires wise counsel based on an understanding of the value and limitations of the tests as well as the implications of their results for specific individuals. **For a more complete discussion of genetic testing, see Chap. 457.**

The Globalization of Medicine Physicians should be cognizant of diseases and health care services beyond local boundaries. Global travel has implications for disease spread, and it is not uncommon for diseases endemic to certain regions to be seen in other regions after a patient has traveled to and returned from those regions. The outbreak of Zika virus infections in the Americas is a cogent example of this phenomenon. In addition, factors such as wars, the migration of refugees, and climate change are contributing to changing disease

profiles worldwide. Patients have broader access to unique expertise or clinical trials at distant medical centers, and the cost of travel may be offset by the quality of care at those distant locations. As much as any other factor influencing global aspects of medicine, the Internet has transformed the transfer of medical information throughout the world. This change has been accompanied by the transfer of technological skills through telemedicine and international consultation—for example, interpretation of radiologic images and pathologic specimens. **For a complete discussion of global issues, see Chap. 460.**

Medicine on the Internet On the whole, the Internet has had a positive effect on the practice of medicine; through personal computers, a wide range of information is available to physicians and patients almost instantaneously at any time and from anywhere in the world. This medium holds enormous potential for the delivery of current information, practice guidelines, state-of-the-art conferences, journal content, textbooks (including this text), and direct communications with other physicians and specialists, expanding the depth and breadth of information available to the physician regarding the diagnosis and care of patients. Medical journals are now accessible online, providing rapid sources of new information. By bringing them into direct and timely contact with the latest developments in medical care, this medium also serves to lessen the information gap that has hampered physicians and health care providers in remote areas.

Patients, too, are turning to the Internet in increasing numbers to acquire information about their illnesses and therapies and to join Internet-based support groups. Patients often arrive at a clinic visit with sophisticated information about their illnesses. In this regard, physicians are challenged in a positive way to keep abreast of the latest relevant information while serving as an "editor" as patients navigate this seemingly endless source of information, the accuracy and validity of which are not uniform.

A critically important caveat is that virtually anything can be published on the Internet, with easy circumvention of the peer-review process that is an essential feature of academic publications. Both physicians and patients who search the Internet for medical information must be aware of this danger. Notwithstanding this limitation, appropriate use of the Internet is revolutionizing information access for physicians and patients and in this regard represents a remarkable resource that was not available to practitioners a generation ago.

Public Expectations and Accountability The general public's level of knowledge and sophistication regarding health issues has grown rapidly over the last few decades. As a result, expectations of the health care system in general and of physicians in particular have risen. Physicians are expected to master rapidly advancing fields (the *science* of medicine) while considering their patients' unique needs (the *art* of medicine). Thus, physicians are held accountable not only for the technical aspects of the care they provide but also for their patients' satisfaction with the delivery and costs of care.

In many parts of the world, physicians increasingly are expected to account for the way in which they practice medicine by meeting certain standards prescribed by federal and local governments. The hospitalization of patients whose health care costs are reimbursed by the government and other third parties is subjected to utilization review. Thus, a physician must defend the cause for and duration of a patient's hospitalization if it falls outside certain "average" standards. Authorization for reimbursement increasingly is based on documentation of the nature and complexity of an illness, as reflected by recorded elements of the history and physical examination. A growing "pay-for-performance" movement seeks to link reimbursement to quality of care. The goal of this movement is to improve standards of health care and contain spiraling health care costs. In many parts of the United States, managed (capitated) care contracts with insurers have replaced traditional fee-for-service care, placing the onus of managing the cost of all care directly on the providers and increasing the emphasis on preventive strategies. In addition, physicians are expected to give evidence of their current competence through mandatory continuing education, patient record audits, maintenance of certification, and relicensing.

Medical Ethics and New Technologies The rapid pace of technological advances has profound implications for medical applications that go far beyond the traditional goals of disease prevention, treatment, and cure. Cloning, genetic engineering, gene therapy, human–computer interfaces, nanotechnology, and use of targeted therapies have the potential to modify inherited predispositions to disease, select desired characteristics in embryos, augment "normal" human performance, replace failing tissues, and substantially prolong life span. Given their unique training, physicians have a responsibility to help shape the debate on the appropriate uses of and limits placed on these new techniques and to consider carefully the ethical issues associated with the implementation of such interventions. As medicine becomes more complex, shared decision-making is increasingly important, particularly in areas such as genetic counseling and end-of-life care, but also in most instances of considering diagnostic and treatment options.

Learning Medicine More than a century has passed since the publication of the Flexner Report, a seminal study that transformed medical education and emphasized the scientific foundations of medicine as well as the acquisition of clinical skills. In an era of burgeoning information and access to medical simulation and informatics, many schools are implementing new curricula that emphasize lifelong learning and the acquisition of competencies in teamwork, communication skills, system-based practice, and professionalism. The tools of medicine also change continuously, necessitating formal training in the use of EMRs, large datasets, ultrasound, robotics, and new imaging techniques. These and other features of the medical school curriculum provide the foundation for many of the themes highlighted in this chapter and are expected to allow physicians to progress, with experience and learning over time, from competency to proficiency to mastery.

At a time when the amount of information that must be mastered to practice medicine continues to expand, increasing pressures both within and outside of medicine have led to the implementation of restrictions on the amount of time a physician-in-training can spend in the hospital and in clinics. Because the benefits associated with continuity of medical care and observation of a patient's progress over time were thought to be outstripped by the stresses imposed on trainees by long hours and by fatigue-related errors, strict limits were set on the number of patients that trainees could be responsible for at one time, the number of new patients they could evaluate in a day on call, and the number of hours they could spend in the hospital. In 1980, residents in medicine worked in the hospital more than 90 hours per week on average. In 1989, their hours were restricted to no more than 80 per week. Resident physicians' hours further decreased by ~10% between 1996 and 2008, and in 2010 the Accreditation Council for Graduate Medical Education further restricted (i.e., to 16 hours per shift) consecutive in-hospital duty hours for first-year residents. The impact of these changes is still being assessed, but the evidence that medical errors have decreased as a consequence is sparse. An unavoidable by-product of fewer hours at the bedside is an increase in the number of "handoffs" of patient responsibility from one physician to another. These transfers often involve a transition from a physician who knows the patient well, having evaluated that individual on admission, to a physician who knows the patient less well. It is imperative that these transitions of responsibility be handled with care and thoroughness, with all relevant information exchanged and acknowledged.

The Physician as Perpetual Student From the time physicians graduate from medical school, it becomes all too apparent that this milestone is symbolic and that they must embrace the role of a "perpetual student." This realization is at the same time exhilarating and anxiety-provoking. It is exhilarating because physicians can apply constantly expanding knowledge to the treatment of their patients; it is anxiety-provoking because physicians realize that they will never know as much as they want or need to know. Ideally, physicians will translate the latter feeling into energy through which they can continue to improve and reach their potential. It is the physician's responsibility to pursue new knowledge continually by reading, attending

conferences and courses, and consulting colleagues and the Internet. This is often a difficult task for a busy practitioner; however, a commitment to continued learning is an integral part of being a physician and must be given the highest priority.

The Physician as Citizen Being a physician is a privilege. The capacity to apply one's skills for the benefit of fellow human beings is a noble calling. The physician–patient relationship is inherently unbalanced in the distribution of power. In light of their influence, physicians must always be aware of the potential impact of what they do and say and must always strive to strip away individual biases and preferences to find what is best for their patients. To the extent possible, physicians should also act within their communities to promote health and alleviate suffering. Meeting these goals begins by setting a healthy example and continues in taking action to deliver needed care even when personal financial compensation may not be available.

Research, Teaching, and the Practice of Medicine The word *doctor* is derived from the Latin *docere*, "to teach." As teachers, physicians should share information and medical knowledge with colleagues, students of medicine and related professions, and their patients. The practice of medicine is dependent on the sum total of medical knowledge, which in turn is based on an unending chain of scientific discovery, clinical observation, analysis, and interpretation. Advances in medicine depend on the acquisition of new information through research, and improved medical care requires the transmission of that information. As part of their broader societal responsibilities, physicians should encourage patients to participate in ethical and properly approved clinical investigations if these studies do not impose undue hazard, discomfort, or inconvenience. Physicians engaged in clinical research must be alert to potential conflicts of interest between their research goals and their obligations to individual patients. The best interests of the patient must always take priority.

To wrest from nature the secrets which have perplexed philosophers in all ages, to track to their sources the causes of disease, to correlate the vast stores of knowledge, that they may be quickly available for the prevention and cure of disease—these are our ambitions.

—William Osler, 1849–1919

FURTHER READING

Cheston CC et al: Social media use in medical education: A systematic review. Acad Med 88:893, 2013.

Cooke M et al: American medical education 100 years after the Flexner report. N Engl J Med 355:1339, 2006.

Institute of Medicine: Dying in America: Improving quality and honoring individual preferences near the end of life. Washington, DC, National Academies Press, 2015.

Institute of Medicine: Improving diagnosis in health care. Washington, DC, National Academies of Sciences, Engineering, and Medicine, 2015.

Jameson JL, Longo DL: Precision medicine—personalized, problematic, and promising. N Engl J Med 372:2229, 2015.

Reeves S et al: Interprofessional education: Effects on professional practice and healthcare outcomes (update). Cochrane Database Syst Rev 28:CD02213, 2013.

Stern DT, Papadakis M: The developing physician—becoming a professional. N Engl J Med 355:1794, 2006.

Vickrey BG et al: How neurologists think: A cognitive psychology perspective on missed diagnoses. Ann Neurol 67:425, 2010.

West P et al: Intervention to promote physician well-being, job satisfaction, and professionalism. A randomized clinical trial. JAMA Intern Med 174:527, 2014.

2 Promoting Good Health

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GOALS AND APPROACHES TO PREVENTION

Prevention of acute and chronic diseases before their onset has been recognized as one of the hallmarks of excellent medical practice for centuries, and is now used as a metric for highly functioning healthcare systems. The ultimate goal of preventive strategies is to avoid premature death. However, as longevity has increased dramatically worldwide over the last century (largely as a result of public health practices), increasing emphasis is placed on prevention for the purpose of preserving quality of life and extending the healthspan, not just the lifespan. Given that all patients will eventually die, the goal of prevention ultimately becomes compression of morbidity toward the end of the lifespan; that is, reduction of the amount of burden and time spent with disease prior to dying. As shown in Fig. 2-1, normative aging tends to involve a steady decline in the stock of health, with accelerating decline over time. Successful prevention offers the opportunity both to extend life and to extend healthy life, thus "squaring the curve" of health loss during aging.

Prevention strategies have been characterized as tertiary, secondary, primary, and primordial. *Tertiary prevention* requires rapid action to prevent imminent death in the setting of acute illness, such as through percutaneous coronary intervention in the setting of ST-segment elevation myocardial infarction. *Secondary prevention* strategies focus on avoiding the recurrence of disease and death in an individual who is already affected. For example, tamoxifen is recommended for women with surgically treated early-stage, estrogen-receptor-positive breast cancer, because it reduces the risk of recurrent breast cancer (including in the contralateral breast) and death. *Primary prevention* attempts to reduce the risk of incident disease among individuals with a risk factor. Treatment of elevated blood pressure in individuals who have not yet experienced cardiovascular disease represents one example of primary prevention that has proven effective in reducing the incidence of stroke, heart failure, and coronary heart disease.

Primordial prevention is a more recent concept (first introduced in 1979) which focuses on prevention of the development of *risk factors* for disease, not just prevention of disease. Primordial prevention strategies emphasize upstream determinants of risk for chronic diseases, such as eating patterns, physical activity, and environmental and social determinants of health. It therefore encompasses medical treatment strategies for individuals as well as a strong reliance on public health and social policy. It is increasingly clear that primordial prevention represents the ultimate means for reducing the burden of chronic diseases of aging. Once risk factors develop, it is difficult

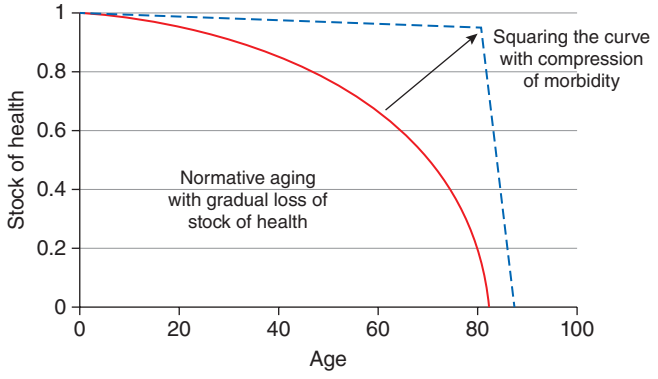

FIGURE 2-1 Loss of health with aging. Representation of normative aging with loss of the full stock of health with which individuals are born (indicating gain of morbidity), contrasted with a squared curve with greater longevity and fuller stock of health (less morbidity) until shortly before death. The "squared curve" represents the likely ideal situation for most patients.

to restore risk to the low level of someone who never developed the risk factor. The time spent with adverse levels of the risk factor often causes irreversible damage that precludes complete restoration of low risk. For example, individuals with hypertension who are treated back to optimal levels (<120/<80 mmHg) do have a lower risk compared with untreated patients with hypertension, but they still have twice the risk of cardiovascular events as those who maintained optimal blood pressure without medications. Patients with elevated blood pressure that is subsequently treated have greater left ventricular mass index, worse renal function, and more evidence of atherosclerosis and other target organ damage as a result of the time spent with elevated blood pressure; such damage cannot be fully reversed despite efficacious therapy with antihypertensive medications. Conversely, as described below in greater detail, individuals who maintain optimal levels of all major cardiovascular risk factors into middle age through primordial prevention essentially abolish their lifetime risk of developing cardiovascular disease while also living substantially longer and having a lower burden of other comorbid illnesses (compression of morbidity).

Prevention strategies should be distinguished from disease screening strategies. Screening attempts to detect evidence of disease at its earliest stages, when treatment is likely to be more efficacious than for advanced disease **(Chap. 4)**. Screening can be performed in service of prevention, especially if it aids in identifying pre-clinical markers associated with elevated disease risk.

HEALTH PROMOTION

In recent decades, medical practice has increasingly focused on public health approaches to promote health, and not just prevent disease. Prevention of disease is a worthy individual and societal goal in and of itself, but it does not necessarily guarantee health. Health is a broader construct encompassing more than just absence of disease. It includes biological, physiological, and psychological domains (among others) in a continuum, rather than occurring as a dichotomous trait. Health is therefore somewhat subjective, but attempts have been made to use more objective criteria to define health in order to raise awareness, prevent disease, and promote healthy longevity.

For example, in 2010 the American Heart Association (AHA) defined a new construct of "cardiovascular health" based on evidence of associations with longevity, disease avoidance, healthy longevity, and quality of life. The definition of cardiovascular health is based on seven health behaviors and health factors (eating pattern, physical activity, body mass, smoking status, and levels of blood pressure, blood cholesterol, and blood glucose) and includes a spectrum from poor to ideal. Individuals with optimal levels of all seven metrics simultaneously are considered to have ideal cardiovascular health. The state of cardiovascular health for an individual or a population can be assessed with simple scoring by counting the number of ideal metrics (out of 7) or applying 0 points for each poor metric, 1 point for each intermediate metric, and 2 points for each ideal metric, thus creating a composite cardiovascular health score ranging from 0 to 14 points. Higher cardiovascular health scores in younger and middle ages have been associated with greater longevity, lower incidence of cardiovascular disease, lower incidence of other chronic diseases of aging (including dementia, cancer, and more), compression of morbidity, greater quality of life, and lower healthcare costs, achieving both individual and societal goals for healthy aging, and further establishing the critical importance of primordial prevention and cardiovascular health promotion.

Focusing on health promotion, rather than just disease prevention, may also provide greater motivation for patients to pursue lifestyle changes or adhere to clinician recommendations. Extensive literature suggests that providing patients solely with information regarding disease risk, or risk reduction with treatment, is unlikely to motivate desired behavior change. Empowering patients with strategies to achieve positive health goals after discussing risks can provide more effective adherence and better long-term outcomes. In the case of smoking cessation, enumerating only the risks of smoking can lead to patient inertia and therapeutic nihilism, and has proven an ineffective approach, whereas strategies that incorporate positive health messaging, support and feedback, with appropriate use of evidence-based therapies, have proven far more effective.

PRIORITIZING PREVENTION STRATEGIES

In secondary prevention, the patient already has manifest clinical disease, and is therefore at high risk for progression. The approach should be to work with the patient to implement all evidence-based strategies that will help to prevent recurrence or progression. This will typically include drug therapy as well as therapeutic lifestyle changes to control ongoing risk factors which may have caused disease in the first place. Juggling priorities can be difficult, and barriers to implementation are many, including costs, time, patient health literacy, and patient and caregiver capacity to organize the regimen. Addressing these potential barriers with the patient can help to forge a therapeutic bond and may improve adherence; ignoring them will likely lead to therapeutic failure. Numerous studies demonstrate that, even in high-functioning health systems, only ~50% of patients are taking recommended, evidence-based secondary prevention medications, such as statins, by 1 year after a myocardial infarction.

In patients who are eligible for primary prevention strategies, it is important to frame the discussion around the overall evidence base as well as an individual patient's likelihood of benefit from a given preventive intervention. A first step is to understand the patient's estimated absolute risk for disease in the foreseeable future, or during their remaining lifespan. However, absolute risk estimation and presentation of those risks is generally insufficient to motivate behavior change. It is critical to assess the patient's understanding and tolerance of the risk, their readiness to implement lifestyle changes or adhere to drug therapy, and their overall preferences regarding use of drug therapy to prevent an event (e.g., cancer, myocardial infarction, stroke). The clinician can help the patient by informing them of the risks for disease and potential for absolute benefits (and harms) from the available evidence-based choices. This may take more than one conversation, but given that diseases, such as cancer and cardiovascular disease, are the leading causes of premature death and disability, the time is well spent.

Partnering with the patient through motivational interviewing may assist in the process of selecting initial approaches to prevention. Selecting an area that the patient feels they are ready to change can lead to better adherence and greater achievement of success in the short and longer term. If the patient is uncertain what course to choose, prudence would dictate focusing on control of risk factors that may lead to the most rapid reduction in risk for acute events. For example, blood pressure is both a chronic risk factor and an acute trigger for cardiovascular events. Thus, if a patient has both significant elevations in blood pressure and dyslipidemia, it would be appropriate to focus initial efforts on blood pressure control. Likewise, focus on smoking cessation can lead to more rapid reductions in risk for acute events than some other lifestyle interventions.

PREVENTION AND HEALTH PROMOTION ACROSS THE LIFE COURSE

Periodic Health Evaluations The "routine annual physical" has in many ways become an expected part of the patient-physician relationship in primary care practice. However, evidence for the efficacy of the periodic health evaluation in asymptomatic adults unselected for risk factors or disease is mixed, and depends on the outcome. Systematic reviews and meta-analyses of published trials have consistently observed lack of benefit (and also lack of harm) in terms of total mortality in association with periodic health evaluations. Data are more heterogeneous but overall suggest no benefit for cancer- or cardiovascular-specific mortality, with the potential for either benefit or harm depending on number of evaluations and patient-level factors. Well-designed studies on non-fatal clinical events and morbidity have been sparsely reported but there appear to be no large effects.

Periodic health evaluations do appear to lead to greater diagnosis of certain conditions such as hypertension and dyslipidemia, as expected. Likewise, periodic health examinations also improve the delivery of recommended preventive services, such as gynecologic examinations