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GOLDMAN'S

CECIL MEDICINE

西氏内科学

第24版

内科学总论

LEE GOLDMAN
ANDREW I. SCHAFER

北京大学医学出版社

Cecil

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24TH EDITION

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LEE GOLDMAN, MD
Dean of the Faculties of Health Sciences and Medicine
Executive Vice President for Health and Biomedical Sciences
Harold and Margaret Hatch Professor of the University
Professor of Medicine and of Epidemiology
Columbia University
New York, New York

ANDREW I. SCHAFER, MD
Chairman, Department of Medicine
The E. Hugh Luckey Distinguished Professor of Medicine
Weill Cornell Medical College
Physician-in-Chief
New York-Presbyterian Hospital/Weill Cornell Medical Center
New York, New York

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Department of Medicine
University of Virginia Health System
Charlottesville, Virginia

PREFACE

The 24TH Edition of *Goldman's Cecil Medicine* symbolizes a time of extraordinary advances in medicine and in technological innovations for the dissemination of information. This textbook and its associated electronic products incorporate the latest medical knowledge in formats that are designed to appeal to learners who prefer to access information in a variety of ways.

The contents of *Cecil* have remained true to the tradition of a comprehensive textbook of medicine that carefully explains the *why* (the underlying normal physiology and pathophysiology of disease, now at the cellular and molecular as well as the organ level) and the *how* (now frequently based on Grade A evidence from randomized controlled trials). Descriptions of physiology and pathophysiology include the latest genetic advances in a practical format that strives to be useful to the nonexpert. 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 counteract this tendency 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 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 abnormalities 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 Medicine* 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 new associate editors—Wendy Levinson, Donald W. Landry, Anil Rustgi, and W. Michael Scheld—we also express our appreciation to Nicholas LaRusso and other associate editors from the previous editions on whose foundation we have built. Our returning associate editors—William P. Arend, James O. Armitage, David Clemmons, Jeffrey M. Drazen, and Robert C. Griggs—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 Medicine* is that all chapters are written by distinguished experts in each field. We are also most grateful for the editorial assistance in New York of Theresa Considine and Silva Sergenian. 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. We also thank Faten Aberra, Reza Akari, Robert C. Brunham, Ivan Ciric, Seema Daulat, Gregory F. Erikson, Kevin Ghassemi, Jason H. Huang, Caron Jacobson, Lisa Kachnic, Bryan T. Kelly, Karen Krok, Heather Lehman, Keiron Leslie, Luis Marcos, Michael Overman, Eric Padron, Bianca Maria Piraccini, Don W. Powell, Katy Ralston, James M. Swain, Tania Thomas, Kirsten Tillisch, Ali Turabi, Mark Whiteford, and Y. Joseph Woo, who contributed to various chapters. At Elsevier, we are most indebted to Dolores Meloni and Linda McKinley, and also thank Cathy Carroll, Taylor Ball, Virginia Wilson, Linda Van Pelt, Suzanne Fannin, and Steve Stave, who have been critical to the planning and production process under the direction of Mary Gatsch. Many of the clinical photographs were supplied by Charles D. Forbes and William F. Jackson, authors of *Color Atlas and Text of Clinical Medicine*, Third Edition, published in 2003 by Elsevier Science Ltd. We thank them for graciously permitting us to include their pictures in our book. 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—Robert H. Gifford, Lloyd H. Smith, Jr., Frank Gardner, and William Castle. Finally, we would like to thank the Goldman family—Jill, Jeff, Abigail, Mira, Daniel, and Robyn Goldman—and the Schafer family—Pauline, Eric, Pam, John, Evan, and Kate—for their understanding of the time and focus required to edit a book that attempts to sustain the tradition of our predecessors and to meet the needs of today's physician.

LEE GOLDMAN, MD
ANDREW I. SCHAFER, MD

CONTENTS

SOCIAL AND ETHICAL ISSUES IN MEDICINE

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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 28). Others (Chapter 38) 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 this time, of the normal physiology of the circulatory system, almost all of modern medicine is based on discoveries made within the past 150 years. Until the late 19th century, the paucity of medical knowledge was perhaps 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 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's Cecil Textbook of Medicine* focuses on the discipline of *internal medicine,* from which neurology and dermatology, which are also covered in substantial detail in this text, are relatively recent evolutionary branches. The term *internal medicine,* which is often misunderstood by the lay public, was developed in 19th-century Germany. *Inneren medizin* was to be distinguished from clinical medicine because it emphasized the physiology and chemistry of disease, not just the patterns or progression of clinical manifestations. *Goldman's Cecil Textbook of 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 264) is now guided by a detailed understanding of the human immune system and its response to foreign antigens (Chapters 44 to 48).

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 (Chapter 40), medical science increasingly understands the complex interactions that underlie multigenic traits (Chapter 41). In the not-so-distant future, the decoding of the human genome holds the promise that personalized health care 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 and their adjusted dosing schedules. Currently, knowledge of the structure and physical forms of proteins helps explain abnormalities as diverse as sickle cell anemia (Chapter 166) and prion-related diseases (Chapter 424). Proteomics, which is the normal and abnormal protein expression of genes, also holds extraordinary promise for developing drug targets for more specific and effective therapies.

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 9). 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 10). 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 73), 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 needed. An understanding of human genetics will 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.

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 and assure that care is coordinated among the patient's various health care providers.

APPROACH TO THE PATIENT

Patients commonly have complaints (symptoms). These symptoms may or may not be accompanied by abnormalities on examination (signs) or on laboratory testing. 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's Cecil Textbook of 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 73), chronic obstructive lung disease (Chapter 88), obstructive uropathy (Chapter 125), inflammatory bowel disease (Chapter 143), gallstones (Chapter 158), rheumatoid arthritis (Chapter 272), hypothyroidism (Chapter 233), tuberculosis (Chapter 332), and virtually any known medical condition in adults.

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 50), diarrhea (Chapter 142), neck or back pain (Chapter 407), or a variety of more than 100 common symptoms, signs, or laboratory abnormalities, *Goldman's Cecil Textbook of 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's Cecil Textbook of 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. 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 38) 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.

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 220) and appropriate exercise (Chapter 15), is the cornerstone to reducing the epidemics of obesity (Chapter 227), coronary disease (Chapter 70), and diabetes (Chapter 237). Public health interventions to provide immunizations (Chapter 17) and to reduce injuries and the use of tobacco (Chapter 31), illicit drugs (Chapter 33), and excess alcohol (Chapter 32) can collectively produce more health benefits than nearly any other imaginable health intervention.

APPROACH TO THE MEDICAL PROFESSION

In a profession, practitioners put the welfare of clients or patients above their own welfare. Professionals have a duty that may be thought of as a contract with society. The American Board of Internal Medicine and the European Federation of Internal Medicine have jointly proposed that medical professionalism should emphasize three fundamental principles: the primacy of patient welfare, patient autonomy, and social justice. 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 5).

TABLE 1-1

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

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

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 and to eliminate disparities in health and health care.

To promote these fundamental principles, a series of professional responsibilities has been suggested (Table 1-1). These specific responsibilities represent 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.

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.

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 11), outcomes ranging from rates of screening mammography (Chapter 204) to mortality rates with coronary artery bypass graft surgery (Chapter 74) 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, it is likely that the historic relationship between the patient and the truly professional physician will be fundamentally compromised.

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, and genetic counseling (Chapter 39) 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's Cecil Textbook of Medicine* seeks to be a comprehensive approach to modern internal medicine.

SUGGESTED READINGS

Ioannidis JP. Expectations, validity, and reality in omics. *J Clin Epidemiol.* 2010;63:945-949. *Perspectives on how modern biologic measurements and assays may individualize health care if appropriately validated.*

Mostaghimi A, Crotty BH. Professionalism in the digital age. *Ann Intern Med.* 2011;154:560-562. *Practical commentary.*

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Rogers W, Ballantyne A. Towards a practical definition of professional behavior. *J Med Ethics.* 2010;36:250-254. *Emphasizes the importance of responsibility; relationships with and respect for patients; probity and honesty; self awareness, and capacity for reflection.*

2

BIOETHICS IN THE PRACTICE OF MEDICINE

EZEKIEL J. EMANUEL

It commonly is argued that modern advances in medical technology, antibiotics, dialysis, transplantation, and intensive care units have created the bioethical dilemmas that confront physicians in the 21st century. In reality, however, concerns about ethical issues are as old as the practice of medicine itself. The Hippocratic Oath, composed sometime around 400 BC, attests to the need of ancient Greek physicians for advice on how to address the many bioethical dilemmas that they confronted. The Oath addresses issues of confidentiality, abortion, euthanasia, sexual relations between physician and patient, divided loyalties, and, at least implicitly, charity care and executions. Other Hippocratic works address issues such as termination of treatments to dying patients and telling the truth. Whether we agree with the advice dispensed or not, the important point is that many bioethical issues are not created by technology but are inherent in medical practice. Technology may make these issues more common and may change the context in which they arise, but there are underlying bioethical issues that seem timeless, inherent in the practice of medicine.

Many physicians have been educated that four main principles can be invoked to address bioethical dilemmas: autonomy, nonmaleficence, beneficence, and justice. Autonomy is the idea that people should have the right and freedom to choose, pursue, and revise their own life plans. Nonmaleficence is the idea that people should not be harmed or injured knowingly; this principle is encapsulated in the frequently repeated phrase that a physician has an obligation to "first do no harm"—*primum non nocere.* This phrase is not found either in the Hippocratic Oath or in other Hippocratic writing; the only related, but not identical, Hippocratic phrase is "at least, do not harm." Whereas nonmaleficence is about avoiding harm, beneficence is about the positive actions that the physician should undertake to promote the well-being of his or her patients. In clinical practice, this obligation usually arises from the implicit and explicit commitments and promises surrounding the physician-patient relationship. Finally, there is the principle of justice as the fair distribution of benefits and burdens.

Although helpful in providing an initial framework, these principles have limited value because they are broad and open to diverse and conflicting interpretations. In addition, as is clear with the principle of justice, they frequently are underdeveloped. In any difficult case, the principles are likely to conflict. Conflicting ethical principles are precisely why there are bioethical dilemmas. The principles themselves do not offer guidance on how they should be balanced or specified to resolve the dilemma. These principles, which are focused on the individual physician-patient context, are not particularly helpful when the bioethical issues are institutional and systemic, such as allocating scarce vaccines or organs for transplantation or balancing the risks and benefits of mammograms for women younger than 50 years. Finally, these four principles are not comprehensive. Other fundamental ethical principles and values, such as communal solidarity, duties to future generations, trust, and professional integrity, are important in bioethics but not encapsulated except by deformation in these four principles.

There is no formula or small set of ethical principles that mechanically or magically gives answers to bioethical dilemmas. Instead, medical practitioners should follow an orderly analytic process. First, practitioners need to obtain the facts relevant to the situation. Second, they must delineate the basic bioethical issue. Third, it is important to identify all the crucial principles and values that relate to the case and how they might conflict. Fourth, because many ethical dilemmas have been analyzed previously and subjected frequently to empirical study, practitioners should examine the relevant literature, whether it is commentaries or studies in medical journals, legal cases, or books. With these analyses, the particular dilemma should be reexamined; this process might lead to reformulation of the issue and identification of new values or new understandings of existing values. Fifth, with this information, it is important to distinguish clearly unethical practices from a range of ethically permissible actions. Finally, it is important not only to come to some resolution of the case but also to state clearly the reasons behind the decisions, that is, the interpretation of the principles used and how values were balanced. Although unanimity and consensus may be desirable ideals, reasonable people frequently disagree about how to resolve ethical dilemmas without being unethical or malevolent.

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

PHYSICIAN-PATIENT RELATIONSHIP: INFORMED CONSENT

History

It commonly is thought that the requirement for informed consent is a relatively recent phenomenon. Suggestions about the need for a patient's informed consent can be found as far back as Plato, however. The first recorded legal case involving informed consent is the 1767 English case of *Slater v. Baker and Stapleton,* in which two surgeons refractured a patient's leg after it had healed improperly. The patient claimed they had not obtained consent. The court ruled:

> *[I]t appears from the evidence of the surgeon that it was improper to disunite the callous without consent; this is the usage and law of surgeons: then it was ignorance and unskillfulness in that very particular, to do contrary to the rule of the profession, what no surgeon ought to have done.*

Although there may be some skepticism about the extent of the information disclosed or the precise nature of the consent obtained, the notable fact is that an 18th-century court declared that obtaining prior consent of the patient is not only the usual practice but also the ethical and legal obligation of surgeons. Failure to obtain consent is incompetent and inexcusable. In contemporary times, the 1957 case of *Salgo v. Leland Stanford Junior University Board of Trustees* constitutes a landmark by stating that physicians have a

positive legal obligation to disclose information about risks, benefits, and alternatives to patients; this decision popularized the term *informed consent.*

Definition and Justification

Informed consent is a person's autonomous authorization of a physician to undertake diagnostic or therapeutic interventions for himself or herself. In this view, the patient understands that he or she is taking responsibility for the decision while empowering someone else, the physician, to implement it. Not any agreement to a course of medical treatment qualifies as informed consent, however.

There are four fundamental requirements for valid informed consent: mental capacity, disclosure, understanding, and voluntariness. Informed consent assumes that people have the mental capacity to make decisions; disease, development, or medications can compromise patients' mental capacity to provide informed consent. Adults are presumed to have the legal competence to make medical decisions, and whether an adult is incompetent to make medical decisions is a legal determination. Practically, physicians usually decide whether patients are competent on the basis of whether patients can understand the information disclosed, appreciate its significance for their own situation, and use logical and consistent thought processes in decision making. Incompetence in medical decision making does not mean a person is incompetent in all types of decision making and vice versa. Crucial information relevant to the decision must be disclosed, usually by the physician, to the patient. The patient should understand the information and its implications for his or her interests and life goals. Finally, the patient must make a voluntary decision (i.e., one without coercion or manipulation by the physician). It is a mistake to view informed consent as an event, such as the signing of a form. Informed consent is viewed more accurately as a process that evolves during the course of diagnosis and treatment.

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

Empirical Data

Fairly extensive research has been done on informed consent. In general, studies show that in clinical situations, physicians frequently do not communicate all relevant information for informed decision making. In a study of audiotapes from 1057 outpatient encounters, physicians mentioned alternatives in only 11.3% of cases, provided pros and cons of interventions in only 7.8% of situations, and assessed the patient's understanding of the information in only 1.5% of decisions. The more complex the medical decisions, the more likely it was that the elements of informed consent would be fulfilled. Importantly, data suggest that disclosure is better in research settings, both in the informed consent documents and in the discussions. For instance, in recorded interactions between researchers and prospective participants, the major elements of research, such as that the treatment was investigational and the risks and benefits, were disclosed in more than 80% of interactions. Greater disclosure in the research setting may be the consequence of requiring a written informed consent document. Some have suggested that for common medical interventions, such as elective surgery, standardized informed consent documents should include the risks and benefits as quantified in randomized controlled trials, as well as acceptable alternatives.

Patients frequently fail to recall crucial information disclosed, although they usually think they have sufficient information for decision making. Whether patients fail to recall key information because they are overwhelmed by the information or because they do not find much of it salient to their decision is unclear. The issue is what patients understand at the point of decision making, not what they recall later.

Studies aimed at improving informed consent in the clinical setting suggest that interactive media, such as videos, can improve understanding by patients. Conversely, data from the research setting suggest that interactive media do not improve participants' understanding, whereas more personal interaction, whether as an additional telephone call by a research nurse or as an additional face-to-face meeting, does enhance understanding.

One of the most important results of empirical research on informed consent is the gap between information and decision making. Many studies show that most patients want information, but far fewer prefer decision-making authority. One study showed that most patients wanted information, but only about one third desired decision-making authority, and patients' decision-making preferences were not correlated with their information-seeking preferences. Several investigators found that patients' preference for decision-making authority increases with higher educational levels and declines with advancing age. Most important, the more serious the illness, the more likely patients are to prefer that physicians make the decisions. Several studies suggest that patients who have less of a desire to make their own decisions generally are more satisfied with how the decisions were made.

TABLE 2-1 FUNDAMENTAL ELEMENTS FOR DISCLOSURE TO PATIENTS

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

Practical Considerations

Implementing informed consent raises concerns about the extent of information to be disclosed and exceptions to the general requirement. A major area of ethical and legal disagreement has been what information to disclose and how to disclose it. As a practical matter, physicians should disclose at least six fundamental elements of information to patients: (1) diagnosis and prognosis; (2) nature of the proposed intervention; (3) alternative interventions, including no treatment; (4) risks associated with each alternative; (5) benefits of each alternative; and (6) likely outcomes of these alternatives (Table 2-1). Because risk is usually the key worry of physicians, it generally is recommended that physicians disclose (1) the nature of the risks, (2) their magnitude, (3) the probability that each risk will occur, and (4) when the consequence might occur. Some argue that minor risks need not be disclosed. In general, all serious risks, such as death, paralysis, stroke, or chronic pain, even if rare, should be disclosed, as should common risks.

The central problem is that the physician should provide this detailed information within reasonable time constraints and yet not overwhelm patients with complex information in technical language. The result has been various legal standards defining how much information should be disclosed. The *physician* or *customary* standard, adapted from malpractice law, states that the physician should disclose information "which a reasonable medical practitioner would make under the same or similar circumstances." Conversely, the *reasonable person* or *lay-oriented* standard states that physicians should disclose all information that a "reasonable person in the patient's circumstances would find material to" the medical decision. The physician standard is factual and can be determined empirically, but the patient-oriented standard, which is meant to engage physicians with patients, is hypothetical. Currently, each standard is used by about half the states.

There are exceptions to the requirements of informed consent. In emergency situations, consent can be assumed because patients' interests concentrate on survival and retaining maximal mental and physical functioning; as a result, reasonable persons would want treatment. In some circumstances, physicians may believe the process of informed consent could pose a serious psychological threat. In rare cases, the "therapeutic privilege" promoting a patient's well-being trumps autonomy, but physicians should be wary of invoking this exception too readily.

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

The *substituted judgment* standard states that the proxy should choose what the patient would choose if he or she were competent. The *best interests* standard states that the proxy should choose what is best for the patient. Frequently, it is not clear how the patient would have decided because the situation was not discussed with the patient and he or she left no living will. Similarly, what is best for a patient is controversial because there are usually tradeoffs between quality of life and survival. These problems are exacerbated because a proxy's predictions about a patient's quality of life are poor; proxies tend to underestimate patients' functional status and satisfaction. Similarly, proxy predictions are inaccurate regarding life-sustaining preferences when the patient is mentally incapacitated; families tend to agree with patients less than 70% of the time in deciding whether to provide life-sustaining treatments if the patient became demented, when chance alone would generate

agreement in 50% of the cases. Such confusion about how to decide for incapacitated patients can create conflicts among family members or between the family and medical providers. In such circumstances, an ethics consultation may be helpful.

TERMINATION OF MEDICAL INTERVENTIONS

History

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

Definition and Justification

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

Empirical Data

Data show that termination of medical treatments is now the norm. More than 85% of Americans die without cardiopulmonary resuscitation, and more than 90% of decedents in intensive care units do not receive cardiopulmonary resuscitation. Of decedents in intensive care units, 90% die after the withholding or withdrawal of medical treatments, with an average of 2.6 interventions being withheld or withdrawn per decedent. Since the 1990s, the trend has been to stop medical interventions more frequently.

Despite extensive public support for use of advance care directives and the passage of the Patient Self-Determination Act mandating that health care institutions inform patients of their right to complete such documents, only about 47% of Americans have completed one. Data suggest that over 40% of patients required active decision-making about terminating medical treatments in their final days, yet 70% lack decision-making capacity, thereby emphasizing the importance of advance directives. Efforts to improve completion of advance care directives have generated mixed results. Unfortunately, even successful pilot efforts have not been adopted or easily scaled. A persistent problem has been that even when patients complete advance care directives, the documents frequently are not available, physicians do not know they exist, or they tend to be too general or vague to guide decisions. The widespread use of electronic health records should create the possibility that advance directives will be available whenever the patient presents to a health care provider.

Just as proxies are poor at predicting patients' wishes, data show that physicians are probably even worse at determining patients' preferences for life-sustaining treatments. In many cases, life-sustaining treatments are continued even when patients or their proxies desire them to be stopped; conversely, many physicians discontinue or never begin interventions unilaterally without the knowledge or consent of patients or their surrogate decision makers. These discrepancies emphasize the importance of engaging patients early in their care about treatment preferences.

Practical Considerations

There are many practical considerations in enacting this right (Table 2-2). First, patients have a right to refuse any and all medical interventions, from blood transfusions and antibiotics to respirators, artificial hydration, and nutrition. Although initiation of cardiopulmonary resuscitation was the focus of the early court cases, this issue is viewed best as addressing just one of the many medical interventions that can be stopped or withheld. The attempt to distinguish ordinary from extraordinary or heroic treatments has been unhelpful in determining which treatments may be stopped.

TABLE 2-2

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

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

Third, competent patients have the exclusive right to decide about terminating their own care. If there is a conflict between a competent patient and his or her family, the patient's wishes are to be followed. It is the patient's right to refuse treatment, not the family's right. For incompetent patients, the situation is more complex; if the patients left clear indications of their wishes, whether as explicit oral statements or as written advance care directives, these wishes should be followed. Physicians should not be overly concerned about the precise form patients use to express their wishes; because patients have a constitutional right to refuse treatment, the real concern is whether the wishes are clear and relevant to the situation. If an incompetent patient did not leave explicit indications of his or her wishes or designate a proxy decision maker, the physician should identify a surrogate decision maker and rely on the decision maker's wishes while being cognizant of the potential problems noted.

Fourth, the right to refuse medical treatment does not translate into a right to demand any treatment, especially treatments that have no pathophysiologic rationale, have already failed, or are known to be harmful. Futility has become a justification to permit physicians unilaterally to withhold or withdraw treatments despite the family's requests for treatment. Some states, such as Texas, have enacted futility laws, which prescribe procedures by which

TABLE 2-3

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

physicians can invoke futility either to transfer a patient or to terminate interventions. However, the principle of futility is not easy to implement in medical practice. Initially, some commentators advocated that an intervention was futile when the probability of success was 1% or lower. Although this threshold seems to be based on empirical data, it is a covert value judgment. Because the declaration of futility is meant to justify unilateral determinations by physicians, it generally has been viewed as an inappropriate assertion that undermines physician-patient communication and violates the principle of shared decision making. Similar to the distinction between ordinary and extraordinary, futility is viewed increasingly as more obfuscating than clarifying, and it is being invoked much less often.

ASSISTED SUICIDE AND EUTHANASIA

History

Since Hippocrates, euthanasia and physician-assisted suicide have been controversial issues. In 1905, a bill was introduced into the Ohio legislature to legalize euthanasia; it was defeated. In the mid-1930s, similar bills were introduced and defeated in the British Parliament and the Nebraska legislature. As of 2010, physician-assisted suicide is legal in Oregon and Washington State, based on state-wide public referenda, and euthanasia and physician-assisted suicide are legal in the Netherlands, Belgium, Luxembourg, and Switzerland. Recently, the Montana Supreme Court did not recognize a constitutional right to physician-assisted suicide, but it ruled that the law permitting the termination of life-sustaining treatment protected physicians from prosecution if they helped hasten the death of a consenting, rational, terminally ill patient.

Definition and Justification

The terms *euthanasia* and *physician-assisted suicide* require careful definition (Table 2-3). So-called passive and indirect euthanasia are misnomers and are not instances of euthanasia, and both are deemed ethical and legal.

There are four arguments against permitting euthanasia and physician-assisted suicide. First, Kant and Mill thought that autonomy did not permit the voluntary ending of the conditions necessary for autonomy, and as a result, both philosophers were against voluntary enslavement and suicide. Consequently, the exercise of autonomy cannot include the ending of life because that would mean ending the possibility of exercising autonomy. Second, many dying patients may have pain and suffering because they are not receiving appropriate care, and it is possible that adequate care would relieve much pain and suffering (Chapter 3). Although a few patients still may experience uncontrolled pain and suffering despite optimal end-of-life care, it is unwise to use the condition of these few patients as a justification to permit euthanasia or physician-assisted suicide for any dying patient. Third, there is a clear distinction between intentional ending of a life and termination of life-sustaining treatments. The actual acts are different—injecting a life-ending medication, such as a muscle relaxant, or providing a prescription for one is not the same as removing or refraining from introducing an invasive medical intervention. Finally, adverse consequences of permitting euthanasia and physician-assisted suicide must be considered. There are disturbing reports of involuntary euthanasia in the Netherlands, and many worry about coercion of expensive or burdensome patients to accept euthanasia or physician-assisted suicide. Permitting euthanasia and physician-assisted suicide is likely to lead to further intrusions of lawyers, courts, and legislatures into the physician-patient relationship.

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

In its 1997 decisions, the U.S. Supreme Court stated that there is no constitutional right to euthanasia and physician-assisted suicide but that there also is no constitutional prohibition against states legalizing these interventions. Consequently, the legalization of physician-assisted suicide in Oregon and Washington State was constitutional.

Empirical Data

Attitudes and practices related to euthanasia and physician-assisted suicide have been studied extensively. First, surveys indicate that about 60 to 70% of the American and British public support legalizing euthanasia and physician-assisted suicide for terminally ill patients who are suffering intractable pain. However, public support declines significantly for euthanasia and physician-assisted suicide in other circumstances. American and British physicians, however, are much less likely to support euthanasia and physician-assisted suicide, with oncologists, palliative care physicians, and geriatricians among the least supportive. Second, approximately 18 to 25% of American physicians have received requests for euthanasia or physician-assisted suicide; 43 to 63% of oncologists have received requests. Third, multiple studies indicate that less than 5% of American physicians have performed euthanasia or physician-assisted suicide. Among oncologists, 4% have performed euthanasia and 11% have performed physician-assisted suicide during their careers. Fourth, in many cases, the safeguards are violated. One study found that in 54% of euthanasia cases, it was the family who made the request; in 39% of euthanasia and 19% of physician-assisted suicide cases, the patient was depressed; in only half of the cases was the request repeated.

In the Netherlands and Belgium, where euthanasia and physician-assisted suicide are legal, less than 2% of all deaths are by these measures, with 0.4 to 1.8% of all deaths as the result of euthanasia without the patient's consent. In Oregon, about 0.2% of all deaths are by physician-assisted suicide.

Counterintuitively, data indicate that it is not pain that primarily motivates requests for euthanasia or physician-assisted suicide but rather psychological distress, especially depression and hopelessness. Interviews with physicians and with patients with amyotrophic lateral sclerosis, cancer, or infection with human immunodeficiency virus show that pain is not associated with interest in euthanasia or physician-assisted suicide; instead, depression and hopelessness are the strongest predictors of interest. Studies of patients in Australia

and the Netherlands confirm the importance of depression in motivating requests for euthanasia. The desire to avoid dependence and loss of dignity are key motivations.

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

Practical Considerations

There is widespread agreement that if euthanasia and physician-assisted suicide are used, they should be considered only after all attempts at physical and psychological palliation have failed. A series of safeguards have been developed and embodied in the Oregon and the Dutch procedures, as follows: (1) the patient must be competent and must request euthanasia or physician-assisted suicide repeatedly and voluntarily; (2) the patient must have pain or other suffering that cannot be relieved by optimal palliative interventions; (3) there should be a waiting period to ensure that the patient's desire for euthanasia or physician-assisted suicide is stable and sincere; and (4) the physician should obtain a second opinion from an independent physician. Oregon and Washington State require patients to be terminally ill, whereas the Netherlands, Belgium, and Switzerland have no such requirement. Although there have been some prosecutions in the United States, there have been no convictions—except for Dr. Kevorkian—when physicians and others have participated in euthanasia and physician-assisted suicide.

FINANCIAL CONFLICTS OF INTEREST

History

Worrying about how payment and fees affect medical decisions is not new. In 1899, a physician reported that more than 60% of surgeons in Chicago were willing to provide a 50% commission to physicians for referring cases. He subsequently argued that in some cases, this fee splitting led to unnecessary surgical procedures. A 1912 study by the American Medical Association confirmed that fee splitting was a common practice. Selling patent medicines and patenting surgical instruments were other forms of financial conflicts of interest thought to discredit physicians a century ago. In the 1990s, the ethics of capitation for physician services and pharmaceutical prescriptions and payments by pharmaceutical and biotechnology companies to clinical researchers raised the issue of financial conflicts of interest.

Definition and Justification

It commonly is argued that physicians have certain primary interests: (1) to promote the well-being of their patients, (2) to advance biomedical research, (3) to educate future physicians, and, more controversially, (4) to promote public health (Table 2-4). Physicians also have other, secondary interests, such as earning income, raising a family, and pursuing avocational interests. These secondary interests are not evil; typically, they are legitimate, even admirable. A conflict of interest occurs when one of these secondary interests compromises pursuit of a primary interest, especially the patient's well-being.

Conflicts of interest are problematic because they can or appear to compromise the integrity of physicians' judgment, compromising the patient's well-being or research integrity. Conflict of interest can induce a physician to do something—perform a procedure, fail to order a test, or distort data—that would not be in a patient's best interest. These conflicts can undermine the trust of patients and the public, not only in an individual physician but also in the entire medical profession. The appearance of conflicts of interest can be damaging because it is difficult for patients and the public "to determine what motives have influenced a professional decision." The focus is on financial conflicts of interest, not because they are worse than other types of conflicts but because they are more pervasive and more easily identified and regulated compared with other conflicts. Since ancient times, the ethical norm on conflicts has been clear: the physician's primary obligation is to patients' well-being, and a physician's personal financial well-being should not compromise this duty.

TABLE 2-4

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

Empirical Data

Financial conflicts are not rare. In Florida, it was estimated that nearly 40% of physicians were involved as owners of freestanding facilities to which they referred patients. Studies in the early 1990s consistently showed that self-referring physicians ordered more services, frequently charged more per service, and referred patients with less established indications. In one study, 4 to 4.5 times more imaging examinations were ordered by self-referring physicians than by physicians who referred patients to radiologists. Similarly, patients referred to joint-venture physical therapy facilities have an average of 16 visits compared with 11 at non–joint-venture facilities. Of great concern, licensed physical therapists at joint-venture facilities spent about 28 minutes per patient per visit compared with 48 minutes at non–joint-venture facilities. There are no comparable data on the influence of capitation on physicians' judgment.

Similarly, multiple studies have shown that interaction with pharmaceutical representatives can lead to prescribing of new drugs, nonrational prescribing, and decreased use of generic drugs by physicians. Industry funding for continuing medical education payment for travel to educational symposia increases prescribing of the sponsor's drug.

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

Practical Considerations

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

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

Fourth, rules—whether laws, regulations, or professional standards—to regulate conflicts of interest are based on two considerations: (1) the likelihood that payment or other secondary interests would create a conflict and (2) the magnitude of the potential harm if there is compromised judgment. Rules tend to be of three types: (1) disclosure of conflicts, (2) management of conflicts, and (3) outright prohibition. Federal law bans certain types of self-referral of physicians in the Medicare program. The American Medical Association and the Pharmaceutical Research and Manufacturers of America have established joint rules that permit physicians to accept gifts of minimal value but "refuse substantial gifts from drug companies, such as the costs of travel, lodging, or other personal expenses . . . for attending conferences or meetings."

Fifth, although there is much emphasis on disclosure of conflicts, which may be useful in publications, it is unclear whether this is a suitable safeguard in the clinical setting. Disclosure just may make patients worry more. Patients may have no context in which to place the disclosure or to evaluate the physician's clinical recommendation, and patients may have few

other options in selecting a physician or getting care, especially in an acute situation. Furthermore, self-disclosure often is incomplete, even when required.

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

FUTURE DIRECTIONS

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

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

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3

CARE OF DYING PATIENTS AND THEIR FAMILIES

ROBERT ARNOLD

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

The burden associated with these illnesses is high. Patients report multiple physical and psychological symptoms that lower their quality of life. The economic pressures associated with medical care may adversely affect patients' socioeconomic status and cause family stress. In addition, these chronic illnesses are incurable and often will ultimately contribute to or result in death.

The discipline of palliative care was developed to decrease the burden associated with chronic illness. The recent National Consensus Project defines palliative care as follows:

The goal of palliative care is to prevent and relieve suffering and to support the best possible quality of life for patients and their families. Palliative care is operationalized through effective management of pain and other distressing symptoms, while incorporating psychosocial and spiritual care with consideration of family and patient needs, preferences, values, beliefs, and culture .... Palliative care affirms life by supporting the patient and family's goals for the future, including their hopes for cure or life-prolongation, as well as their hopes for peace and dignity throughout the course of illness, the dying process, and death.

Four points deserve special emphasis. First, palliative care can be delivered at any time during the course of an illness and is often provided concomitantly with disease-focused, life-prolonging therapy. Waiting until a patient is dying to provide palliative care is a serious error. Prognostication is an inexact science. In addition, although most elderly patients with chronic incurable illnesses are in the last 10 years of their lives, they do not consider themselves to be dying. If palliative care is to have an impact on patients' lives, it should be provided earlier in a patient's illness, in tandem with other treatments.

Second, palliative care primarily focuses on the illness's burden rather than treating the illness itself. Because these burdens can be physical, psychological, spiritual, or social, good palliative care requires a multidisciplinary approach.

Third, palliative care takes the family unit as the central focus of care. Treatment plans must be developed for both the patient and the family.

Finally, palliative care recognizes that medical treatments are not uniformly successful and that patients die. At some point in a patient's illness, the treatments may cause more burden than benefit. Palliative care recognizes this reality and starts with a discussion of the patient's goals and the development of an individualized treatment plan.

Many people confuse palliative care with hospice—an understandable confusion because hospices epitomize the palliative care philosophy. The two, however, are different. In the United States, hospice provides palliative care, primarily at home, for patients who have a life expectancy of 6 months or less and who are willing to forgo life-prolonging treatments. However, the requirement that patients must have a life expectancy of less than 6 months limits hospice's availability because this degree of prognostication is difficult to achieve for many diseases. Moreover, doctors and patients often are unwilling to cease potentially life-prolonging treatments until very late in the disease course, and thus, most patients are not enrolled in hospice until a month before death.

Palliative care, both as a philosophy of care and as a subspecialty, now includes training of medical students and residents. Although every physician should have basic knowledge about palliative care, the creation of the new subspecialty of palliative medicine allows for a growing number of physicians capable of helping with difficult patient issues, educating other physicians, and expanding the knowledge base of palliative care.

PALLIATIVE CARE DOMAINS

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

Is the Patient Physically Comfortable?

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

The first step to improve symptom management is a thorough assessment. Standardized instruments such as the Brief Pain Inventory (Fig. 3-1) measure both patients' symptoms and their effect on their lives. Use of standardized instruments assures that physicians will identify overlooked or underreported symptoms and, as a result, will enhance the satisfaction of both the patient and family.

The evidence for the treatment of end-stage symptoms continues to improve. Physicians now can use proven therapies to manage pain (Chapter 29), dyspnea (Chapters 50 and 83), and depression (Chapter 404). The use of nonsteroidal anti-inflammatory agents and opioids can result in effective pain management in more than 75% of patients with cancer.[1] Advances such as intrathecal pumps and neurolytic blocks are helpful in the remaining 25%. Opioids are effective in patients with unrelieved dyspnea, and oxygen is helpful for short-term relief of hypoxemia.[1] Depression can be treated effectively with medications and psychotherapy.[1]

Is the Patient Psychologically Suffering?

Patients may be physically comfortable but still suffering. Psychological symptoms and syndromes such as depression, delirium, and anxiety are common in patients with life-limiting or chronic illnesses. It may be difficult

TABLE 3-1

SYMPTOM	ASSESSMENT	TREATMENT
Pain	How severe is the symptom (as assessed with the use of validated instruments) and how does it interfere with the patient's life? What is the etiology of the pain? Is the pain assumed to be neuropathic or somatic? What has the patient used in the past (calculate previous days' equal analgesic dose)?	Prescribe medications to be administered on a standing or regular basis if pain is frequent. For mild pain: use acetaminophen or a nonsteroidal anti-inflammatory agent (see Table 29-3 in Chapter 29). For moderate pain: titrate short-acting opioids (see Table 29-4 in Chapter 29). For severe pain: rapidly titrate short-acting opioids until pain is relieved or intolerable side effects develop; start long-acting opiates once pain is controlled. Rescue doses: prescribe immediate-release opioids—10% of the 24-hour total opiate every hour (orally) or every 30 minutes (parenterally) as needed. Concomitant analgesics (e.g., corticosteroids, anticonvulsants, tricyclic antidepressants, and bisphosphonates) should be used when applicable (particularly for neuropathic pain). Consider alternative medicine and interventional treatments for pain.
Constipation	Is the patient taking opioids? Does the patient have a fecal impaction?	Prescribe laxatives for all patients on opiates. If ineffective, add drugs from multiple classes (e.g., stimulant, osmotic laxatives, and enemas). Prescribe methylnaltrexone if still constipated.
Shortness of breath	Ask the patient to assess the severity of the shortness of breath. Does the symptom have reversible causes?	Prescribe oxygen to treat hypoxia-induced dyspnea, *but* not if the patient is not hypoxic. Opioids relieve breathlessness without measurable reductions in respiratory rate or oxygen saturation; effective doses are often lower than those used to treat pain. Aerosolized opiates do not work. Fans or cool air may work through a branch of the trigeminal nerve. Consider anxiolytics (e.g., low-dose benzodiazepines) and use reassurance, relaxation, distraction, and massage therapy.
Fatigue	Is the patient too tired to do activities of daily living? Is the fatigue secondary to depression? Is a disease process causing the symptom or is it secondary to reversible causes?	Provide cognitive education about conserving energy use. Treat underlying conditions appropriately.
Nausea	Which mechanism is causing the symptom (e.g., stimulation of the chemoreceptor trigger zone, gastric stimulation, delayed gastric emptying or "squashed stomach" syndrome, bowel obstruction, intracranial processes, or vestibular vertigo)? Is the patient constipated?	Prescribe an agent directed at the underlying cause (Chapter 134). If persistent, give antiemetic around the clock. Multiple agents directed at various receptors or mechanisms may be required.
Anorexia and cachexia	Is a disease process causing the symptom, or is it secondary to other symptoms (e.g., nausea and constipation) that can be treated? Is the patient troubled by the symptom or is the family worried about what not eating means?	A nutritionist may help find foods that are more appetizing (Chapter 220). Provide counseling about the prognostic implications of anorexia (Chapter 226).
Delirium	Is the confusion acute, over hours to days? Does consciousness wax and wane? Are there behavioral disturbances, marked by a reduced clarity in the patient's awareness of his environment, e.g., a problem of attention? Does the patient have disorganized thinking? Does the patient have an altered level of consciousness—either agitated or drowsy? Is there a reversible reason for the delirium? **D:** Drugs (opioids, anticholinergics, sedatives, benzodiazepines, steroids, chemotherapies and immunotherapies, some antibiotics) **E:** Eyes and ears (poor vision and hearing, isolation) **L:** Low-flow states (hypoxia, MI, CHF, COPD, shock) **I:** Infections **R:** Retention (urine/stool), Restraints **I:** Intracranial (CNS metastases, seizures, subdural, CVA, hypertensive encephalopathy) **U:** Underhydration, Undernutrition, Undersleep **M:** Metabolic disorders (sodium, glucose, thyroid, hepatic, deficiencies of vitamin B_{12}, folate, niacin, and thiamine) and toxic (lead, manganese, mercury, alcohol)	Identify underlying causes and manage symptoms (Chapter 27). Recommend behavioral therapies, including avoidance of excess stimulation, frequent reorientation, and reassurance. Ensure presence of family caregivers and explain delirium to them. Prescribe haloperidol, risperidone, or olanzapine.
Depression	Are you feeling down, depressed, or hopeless most of the time over the last 2 weeks? Do you find that little brings you pleasure or joy over the last 2 weeks? (Somatic symptoms are not reliable indicators of depression in this population.)	Recommend supportive psychotherapy, cognitive approaches, behavioral techniques, pharmacologic therapies (see Table 404-5 in Chapter 404), or a combination of these interventions; prescribe psychostimulants for rapid treatment of symptoms (within days) or selective serotonin reuptake inhibitors, which may require 3 to 4 weeks to take effect; tricyclic antidepressants are relatively contraindicated because of their side effects.
Anxiety (applicable also for family members)	Does the patient exhibit restlessness, agitation, insomnia, hyperventilation, tachycardia, or excessive worry? Is the patient depressed? Is there a spiritual or existential concern underlying the anxiety?	Recommend supportive counseling and consider prescribing benzodiazepines.
Spiritual distress	Are you at peace?	Inquire about spiritual support.

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