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BETHESDA CONFERENCE REPORT

29th Bethesda Conference: Ethics in Cardiovascular Medicine (1997)*

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This Conference, sponsored by the American College of Cardiology, was held at Heart House, Bethesda, Maryland, October 23–24, 1997.

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*The recommendations set forth in this report are those of the Conference participants and do not necessarily reflect the official position of the American College of Cardiology.

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JACC Vol. 31, No. 5
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JACC Vol. 31, No. 5
April 1998:917–49

29th BETHESDA CONFERENCE

Introduction

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The revolution in managed care has not only drastically altered the practice of medicine but has raised a whole new set of ethical dilemmas for physicians. In the past, many ethical issues seemed to cross all boundaries of medicine. With the advent of managed care, however, the ethical issues facing the primary care physician may be much different than those facing the specialist. For example, in the past cardiologists were accused of financial conflict of interest when they "self-referred" patients for a series of tests they performed, such as stress testing, echocardiography, catheterization, and angioplasty. The dynamics of the emerging health care system, especially capitation, however, has shifted the financial conflict of interest back to the primary care physician, who may profit or at least please his employer by restricting tests performed by specialists. It is in the setting of dramatic changes in health care such as these that the American College of Cardiology (ACC) has organized this Bethesda Conference to review the ethical dilemmas facing today's cardiovascular specialists. This conference is divided into three task forces. Task Force 1 discusses current external influences on the practice of cardiology. Task Force 2 discusses ethical dilemmas surrounding end of life decisions. Finally, Task Force 3 discusses clinical trial monitoring and ethical issues associated with the explosion of scientific knowledge in molecular biology and genetics. Like its predecessor, this conference on ethics cannot hope to address all of the current ethical issues facing cardiovascular specialists. The focus on selected topics, however, will provide valuable information to the reader in important areas.

This is the second Bethesda Conference on Ethics conducted by the American College of Cardiology. The first was held on October 5 to 6, 1989 and was subsequently published in the *Journal of the American College of Cardiology* (1). It is interesting to compare these two as a marker of changing times. First of all, it is important to recognize that the major goal of both conferences is to stimulate an increased interest and focus on ethical issues in cardiovascular practice. In and of itself, we hope that this heightened awareness will sensitize the "ethical" physician to act appropriately. We assume that physicians in general want to uphold the ideals of our profession. By understanding the issues, we are in a better position to act.

The first ethics conference focused on three major issues: 1) the relation of cardiovascular specialists to patients, other physicians and physician-owned organizations; 2) perspectives on the allocation of limited resources in cardiovascular medicine; and 3) scientific responsibility and integrity in medical research. Despite the differing topics of the two conferences, five general perspectives on ethical issues in cardiovascular medicine have not changed (1):

1. Cardiovascular physicians must recognize the central importance of morals in health care delivery.
2. Cardiovascular physicians must recognize that value conflicts occur in the daily practice of clinical cardiology and cardiovascular research and must be prepared to deal with these conflicts in a fair, honest and consistent manner.
3. The cardiovascular physician must recognize the importance of the autonomy of the patient in health care decision making, and that this may at times be in conflict with the goal of achieving the best medical interests of the patient.
4. Cardiovascular physicians must be knowledgeable about such ethical issues in health care as informed consent, respect for persons, confidentiality and conflicts of interest.
5. The just allocation of health care resources requires the cooperation of physician, patients, and society.

The first Bethesda Conference on Ethics concluded with a series of case studies, which could form the basis for discussion among a group of practitioners, cardiology fellows and faculty, or other similar groups. Subsequent review at the annual training program director's meeting suggested that these cases usefully formed the basis of many conferences for fellows in cardiology training programs. Based on this previous experience, therefore, we have included a series of case studies at the end of each task force report. It is hoped that these will likewise be helpful as a basis for discussion of ethical dilemmas at appropriate teaching conferences.

Ethical Issues in Managed Care

Managed care raises new ethical dilemmas for physicians and requires reconsideration of existing dilemmas. Cardiologists in particular may face unprecedented ethical issues because procedures such as echocardiography, catheterization, or angioplasty are commonly subjected to utilization review and practice guidelines. Authorization may be denied for procedures that the cardiologist recommends. Also, beneficial interventions such as tissue-type plasminogen activator for acute myocardial infarction may not be considered as cost-

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effective as its less expensive alternative. Furthermore, although managed care plans try to control unwarranted referrals to specialists, recent studies suggest that the increased access to the expertise of cardiologists is associated with improved patient outcomes for patients with myocardial infarction and other problems (2–6). Finally, the public has become concerned that financial incentives in managed care may create conflicts of interest for physicians, leading doctors to deny beneficial services that would be in the patient's best interests. Such public concerns have led to recent legislation to prohibit gag rules, ensure reimbursement for emergency care, and require disclosure of financial incentives and practice guidelines that might lead physicians to restrict indicated services.

Rationale for Managed Care

Managed care has grown because of the need to control health care expenditures. National health expenditures were $949.4 in 1994, or 13.7% of gross domestic product (GDP). In 1960 health expenditures consumed 5.1% of GDP; annual percentage growth between 1960 and 1988 was 0.2 to 0.3%. Between 1988 and 1992 annual percentage growth in health expenditures as a portion of GDP exceeded 0.5%; in 1993 growth slowed to 0.3% and in 1994 0.1%, the result of an accelerating economy and a slowing of growth in health care expenditures (7). The United States spends more of its GDP on health care than other countries that have comparable or better health outcomes. Both private employers and public programs such as Medicare and Medicaid insist on controlling premiums to keep health insurance affordable. To achieve the goal of restraining costs, managed care organizations may use financial incentives, administrative measures such as utilization review, practice guidelines, and authorization of referrals to specialists by primary physicians; and organizational arrangements such as restricted provider panels. Although these measures can be justified because containing health care expenditures is an important social goal, they may also raise serious ethical concerns.

Reinterpretation of Ethical Guidelines

Under managed care, traditional ethical guidelines of respect for patient autonomy, beneficence, and justice need to be reconsidered and may require expansion or revision.

Autonomy. Respect for patient autonomy is the basis for the legal doctrine of informed consent. Physicians must disclose information that is pertinent to the patient's condition, so that the patient can make informed choices about care. Disclosure traditionally encompasses information about the patient's condition, the options for care, and the benefits, risks, and consequences of each option. In the managed care era, disclosure may need to be expanded to include other information about potentially beneficial interventions that are not covered by the plan. Recently enacted bans on "gag rules" remove barriers to such disclosure by physicians. Similarly, patients may need information about financial incentives and about practice guidelines that may influence the physician's recommendations in order to make informed choices about their care.

Beneficence. The guideline of beneficence enjoins physicians to act in the best interests of their patients. As professionals, doctors are regarded as having a fiduciary obligation to act in the best interests of their patients, not in their own self-interest, the interests of the plan, or the interests of other enrollees in the plan. This fiduciary obligation of physicians is rooted in the vulnerability of patients when they are sick, the discrepancy in expertise between physicians and patients, and the difficulties patients may have in judging physicians' recommendations. This fiduciary duty to act in the patient's interests distinguishes the profession of medicine from a mere business.

With pressures for cost containment, the physician's obligation to act in the best interests of the patient may be more important than ever. The physician may need to act as the patient's advocate in order to help the patient gain coverage for interventions that are likely to prove beneficial in clinically significant ways. The patient's case may be a legitimate exception to practice guidelines. Or the patient may have a clear indication for a nonformulary drug. In other cases, denial of coverage may result from administrative delay or misunderstanding. In such situations, the physician should be expected to spend a reasonable amount of effort and time advocating on behalf of patients.

Managed care, by making caregivers responsible for a population of patients, creates opportunities to correct underutilization of interventions as well as overutilization. Many effective interventions, such as angiotensin-converting enzyme inhibitors, beta-adrenergic blocking agents and cholesterol reduction after myocardial infarction, are utilized less often by generalist physicians than by cardiology specialists (5). Cardiologists can help develop innovative practices to disseminate beneficial interventions more broadly, for example, by using computerized medical records to identify patients who have not received these beneficial interventions and by increasing collaborative management of patients through mandated consultations, informal consultations or case review by specialists. As leaders of managed care organizations, physicians can also promote such innovative practices by assuring that specialists are compensated fairly for their efforts in identifying and addressing underutilization of services.

Managed care, however, raises two concerns about beneficence as an ethical guideline. First, do certain financial incentives compromise the physician's duty of beneficence? Financial incentives assume that physician behaviors are guided by self-interest, at least when benefits to the patient are marginal. Critics of managed care contend that some financial incentives are inappropriate because they create an unacceptable likelihood that physicians will withhold medically appropriate care. For example, some incentives may place too much of the physician's income at risk, are tied too closely to individual patient care decisions or fail to adjust for severity of illness. Recent regulations by the Health Care Financing Administration (HCFA) regarding Medicare and Medicaid managed care

JACC Vol. 31, No. 5
April 1998:917–49

plans identify bonus or withholding levels of 25% of potential income as being sufficiently problematic to trigger requirements of satisfaction surveys of enrollees and stop-loss insurance (8).

A second and more fundamental question is whether the physician's loyalty to the individual patient needs to be reconsidered. In managed care, capitated premiums establish a pool of funds to provide health care services for all enrollees in the plan. If funds from the capitation pool are spent on one patient, they will not be available later for that patient or other patients in the plan. Physicians have expertise regarding the benefits and risks of medical interventions and make recommendations to patients. If physicians take no responsibility for restraining costs, the socially important goal of cost containment will fail or will be carried out in ways that fail to take into account individual patient circumstances. Without physician judgment in particular cases, restrictions on care will be meted out by administrators with no clinical expertise. In this view, given the importance of controlling the costs of health care, physicians need to use their clinical judgment to implement cost-containment measures. For these reasons, some argue that the physician has an ethical duty to act as a steward, "a person morally responsible for the careful use of money, time . . . or other resources, especially with regard to the principles or needs of a community or group" (9). The physician would no longer act as the patient's advocate if evidence-based guidelines regarded the potential benefit to the patient as clinically insignificant or extremely unlikely, or if the patient had agreed on enrollment that interventions judged not cost-effective would not be provided.

Critics object to the role of stewardship for physicians in managed care. First, prudent patients and physicians have no assurance that any savings in health care expenditures will benefit patients, their families or others in the community. Instead, savings may be dispensed as salaries for executives or dividends to shareholders of for-profit plans. Second, the size of the common resource pool can be increased. Some health care plans spend 27% of premiums on administrative costs or profits, whereas others spend only 5% on these items. Critics contend that restrictions on care would not be required, or would be less stringent, if administrative costs and profits were reduced.

Justice. As an ethical guideline, distributive justice has received relatively little attention in traditional clinical and professional ethics. In the managed care era, considerations of justice can no longer be ignored. Justice enjoins physicians to allocate scarce medical resources in an equitable manner. As already discussed, physicians need to use their expertise to help fulfill the socially important goal of controlling the costs of care. In allocating resources, justice or fairness requires that patients who are similar in clinically and ethically relevant ways should be treated similarly. Disturbingly, decisions by managed care plans may be inconsistent. In disputed cases, insurance plans may be more likely to authorize coverage when patients are more persistent and knowledgeable in their demands. In one noncardiac study, insurers varied considerably in their willingness to cover autologous bone marrow transplantation for patients with metastatic breast cancer (10). A single insurance plan would make different coverage decisions for clinically similar patients. Insurers were significantly more likely to cover transplantation for patients who have a lawyer. Such data suggest that although allocation decisions are inevitable, they need to be made on a more equitable basis.

Reassessment of Professionalism

In response to changes brought about by managed care, individual physicians and professional organizations can play an important role in resolving new ethical dilemmas.

Physicians should serve as patient advocates when a managed care organization does not authorize interventions that are likely to provide significant clinical or functional benefits for a patient. Under these circumstances, physicians need to reaffirm their ethical duty to act in the best interests of the patient, regardless of any financial or other incentives. General practice guidelines cannot take into account individual circumstances that make a particular case a legitimate exception. Because of their clinical expertise and judgment, physicians are in a unique position to determine whether a particular case is an exception to practice guidelines. Physicians should inform patients of such beneficial interventions, whether or not the insurance plan would cover them. Without such information, patients cannot decide to appeal the coverage decision or pay for an intervention out of pocket. If an exception is justified, physicians should be forceful advocates for patients and try to convince the insurance plan to cover the intervention (11). On the other hand, physicians should not advocate for patients when interventions are only marginally beneficial and an exception to the guidelines is not justified, but should explain to the patient why the intervention is not recommended at this time.

Physicians can help ensure that managed care institutions are ethically responsible. It makes little sense to hold physicians to ethical responsibilities without giving attention to the responsibilities of managed care organizations that constrain and influence the actions of individual doctors. If the organizational context is not ethically sound, physicians may be placed in the bind of having ethical and professional responsibilities that are extremely difficult to carry out.

Physicians and professional societies can help managed care organizations establish practice guidelines and standards for utilization review. Physicians can help evaluate published studies critically and provide expert judgments. Professional organizations like the ACC can play an important role in recommending practice guidelines, particularly as new knowledge about cardiology procedures is published. When developing such guidelines, physicians need to recognize their own self-interest in obtaining greater insurance coverage and compensation for their services. Because of such conflicts of interest, physicians need to adopt procedures to enhance

impartiality of deliberations and ensure that guidelines are based on rigorous evidence.

Physicians have responsibility for financial incentives and utilization review within independent practice association (IPA)-model health maintenance organizations (HMOs), in which multispecialty physician groups assume financial risk and organize the delivery of care. Some financial incentives may be too powerful, and some utilization review procedures may be too restrictive, creating an unacceptable risk that appropriate care will be denied. Some organizations may schedule patients so tightly that physicians have no real opportunity to discuss options for care with patients or to serve as patient advocates when coverage for beneficial care is denied. Multispecialty physician groups often adopt the same types of financial incentives and utilization review procedures as managed care plans themselves (12). Thus, physicians who complain that some incentives and utilization review undermine their professional integrity need to accept the challenge of helping to devise better ways of achieving the goals of cost-effective, coordinated care.

In summary, managed care raises important new ethical issues for all physicians, particularly cardiologists. Physicians can play an important role in resolving these dilemmas as clinicians and leaders in health care organizations and as members of professional societies.

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JACC Vol. 31, No. 5
April 1998:917–49

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The core values of the medical profession are being decided not by physicians and surgeons acting through medical societies, but by lawyers and judges taking action in courtrooms and by managed care administrators overriding the decisions of trained medical professionals in response to the imperatives of commodified medicine. American medicine is in crisis (1).

Introduction

Central to the relationship of the cardiologist to society is a covenant—the unique interaction between the doctor and the patient. The covenant derives from the patient's reliance not only on the physician's scientific competence, but also on the physician's commitment to act in the patient's best interest regardless of financial concerns or other pressures. To this relationship physicians must bring the virtues of trustworthiness, integrity, humility, patient advocacy, compassion, wisdom, prudence and effacement of self-interest. The importance of the covenant was stated by the late Cardinal Bernadin (2) before the American Medical Association House of Delegates in December 1995, shortly before his death:

> The "covenant" is grounded in the moral obligations that arise from the nature of the doctor-patient relationship. They are moral obligations—as opposed to legal or contractual obligations—because they are based on fundamental human concepts of right and wrong. While it is not currently fashionable to think of medicine in terms of morality, morality is, in fact, the core of the doctor-patient relationship and the foundation of the medical profession. Why do I insist on a moral model as opposed to the economic and contractual models now in vogue? Allow me to describe four key aspects of medicine that give it a moral status and establish a covenantal relationship:
>
> First, the reliance of the patient on the doctor. Illness compels a patient to place his or her fate in the hands of a doctor. A patient relies not only on the technical competence of a doctor, but also on his or her moral compass, on the doctor's commitment to put the interests of the patient first.
>
> Second, the holistic character of medical decisions. A physician is a scientist and a clinician but as a doctor, is and must be, more. A doctor is and must be a caretaker of the patient's person, integrating medical realities into the whole of the patient's life. A patient looks to his or her doctor as a professional adviser, a guide through some of life's most difficult journeys.
>
> Third, the social investment in medicine. The power of modern medicine—of each and every doctor—is the result of centuries of science, clinical trials, and public and private investments. Above all, medical science has succeeded because of the faith of people in medicine and in doctors. This faith creates a social debt and is the basis of medicine's call—its vocation—to serve the common good.
>
> Fourth, the personal commitments of doctors. The relationship with a patient creates an immediate, personal, nontransferable fiduciary responsibility to protect that patient's best interests. Regardless of markets, government programs, or network managers, patients depend on doctors for a personal commitment and for advocacy through an increasingly complex and impersonal system. This moral center of the doctor-patient relationship is the very essence of being a doctor. It also defines the outlines of the covenant that exists between physicians and their patients, their profession, and their society. The covenant is a promise that the profession makes, a solemn promise—that it is and will remain true to its moral center. In individual terms, the covenant is the basis on which patients trust their doctors. In social terms, the covenant is the grounds for the public's continued respect and reliance on the profession of medicine.

The 29th Bethesda Conference recognized that the emergence of managed care* has created a new set of ethical dilemmas which must be addressed thoughtfully. Central to these new ethical dilemmas is a new principle. Society looks to physicians to conserve financial resources, while simulta-

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*The phrase *managed care* means different things to different people. In this document we have used "managed care" in its broadest sense, to refer to a system of health care delivery. Managed care organizations (MCOs) include not-for-profit and for-profit corporations as well as health insurance companies. The ethical issues discussed in this document are not universally found in all MCOs, nor are other alternative health care systems free of ethical issues.

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neously serving as an advocate for individual patients. The challenge that managed care creates for the ethical physician reflects the vast difference that exists in the ethics of the marketplace, and that of the bedside. For example, the physician dealing with a patient on a "one on one" basis finds that some aspects of managed care, and some purveyors of this form of health care delivery, confound the fundamental precepts of patient autonomy, justice, beneficence, nonmaleficence, truth-telling, and fidelity (3). This Task Force report explores concerns about these external influences that threaten the ethical principles on which society's trust in physicians is based. Failure of physicians to act according to "a code of ethics that recognizes the primacy of the patient's interests risks the loss of public trust, which may cost professional autonomy. The danger then is that ethical dilemmas will be settled by rules rather than by judgments" (4).

The 29th Bethesda Conference discussed how the ethics of medical practice can be reconciled with those of the business world, particularly those of managed care. The central conclusion of the Bethesda Conference is that there must be a national debate on how society wishes to allocate medical care in order to preserve financial resources. The debate creates the need for a clearly defined code of ethics for all health care providers in the era of managed care.

The Relationship of Medical and Business Ethics

Business ethics dates to early commerce (5–7). Capitalism, founded upon the theories of Adam Smith in the 18th century (7,8), has historically been motivated by the preeminence of profit generation within a free market system (5,6,9). This principle holds that the primary purpose of a corporation is to maximize financial performance and that business organizations must honor this primary fiduciary duty. The dominance of profit over other business goals is now being widely challenged as an insufficient mission for a business organization (9). Ethical codes have been developed by corporations (7), and the definition of business ethics has been expanded. Business ethics has become "the study of business action—individual or corporate—with special attention to its moral adequacy" (7).

In the business world, health care is unique because the consumer—the patient—is highly vulnerable and is easily exploited as a result of loss of health, lack of knowledge, and financial jeopardy. It is therefore crucial that business ethics in health care incorporate those ethical principles that preserve patients' rights: beneficence, nonmaleficence of patient autonomy, and justice (10). These are the same ethical principles to which physicians must adhere. The mutual acceptance of the principle that there must be no difference between the ethics of health care business and medicine would have a profound influence on the actions and behavior of all those involved in the business of health care in any capacity. But within the business of health care, the acceptance of these principles has not yet occurred or at best is in its infancy (11). This was a matter of critical concern to the Bethesda Conference.

Table 1. Benefits Achieved by Pressures to Reduce Health Care Costs

Attention to cost and reduction of waste and redundancy
Better coordinated care
Focus on health promotion and disease prevention
Development of methods to measure quality of care
Lower hospitalization rates
Increased use of outpatient procedures
Heavy investment in information systems

The Advantages and Limitations of Managed Health Care Systems

Although managed care may theoretically enhance the value of health care through the close integration of the financing and delivery of health care (12,13), it has significantly complicated, and in some cases initiated, the patient-physician relationship (13–16). As a business solution to a social issue, for-profit managed care is driven by the capitalistic forces of the marketplace (17). In consequence, some systems of managed care cause division of physician loyalties between the patient and the business organization controlling the financial and professional relationships (11). For instance, financial incentives, disincentives, and other hidden relationships, are successful in modifying physician behavior in ways that may not be in the patient's interest (11,18).

In this new era of medicine, physicians in both fee-for-service and managed care systems have instituted changes in practice to reduce the overall cost of hospital care. The changes in health care have both benefits and limitations. Some remarkable benefits have been achieved as a result of the pressures from managed care (Table 1).

Physicians also have taken the initiative in the development of practice guidelines. The American College of Cardiology (ACC), for instance, has published over 18 Practice Guidelines and Expert Consensus Statements dealing with cardiologic practice since 1990. These treatment pathways specify optimal care, and in the best of circumstances, reduce the length of hospital stay by both improving the quality and reducing the variability of care.

Ethical Dilemmas Created by Managed Care

Of greatest concern to the Bethesda Conference Task Force 1 is the threat of managed care to the ethical foundations of the medical profession. The ethical conflicts created by the mandate to reduce the cost of patient care fall into four broad categories (Table 2): denial of care; financial incentives and disincentives to limit care; withholding of information from patients; and coercive practices designed to limit care. One way to understand and resolve these conflicts is through development of a code of ethics. Although no such code exists

JACC Vol. 31, No. 5
April 1998:917–49

Table 2. Practices That May Create Ethical Conflicts in Patient Care

Denial of care
Requirement that physicians must have their decisions approved by an individual or entity not involved in the patient's care
Refusal to provide care because it is extremely costly
Financial incentives and disincentives
Reduced payment for care until the end of the year
Year-end bonuses for limiting the total cost of care
A fund allocated for specific services; the pool decreases each time it is used
Withholding information
Failure to disclose enrollee (coverage) or patient treatment options
Failure to disclose financial arrangements adverse to patient's interest
Failure to disclose options available to patients receiving inadequate care
"Gag clauses" that prohibit open discussion between physician and patient
Coercive practices designed to limit care
Monitoring referrals, then inducing physicians to provide care for which they are not qualified
Limitation of primary care physician's capacity to refer patients to qualified specialists
Nonrenewal of a physician contract based on financial rather than medical performance

for managed care, the courts have provided a potential societal view on the ethical issues through judicial rulings in which the ethical dilemma was a central issue. In this section, we will describe ethical conflicts, using case examples that resulted in rulings that clarify the appropriate action expected of physicians.

Denial of Appropriate Care

In certain managed care models physicians are required to seek prior authorization for expensive medical and surgical interventions. The managed care organization (MCO) may deny authorization in accordance with unilaterally established criteria to which the physician has no access. Thus, a medical decision is made by an individual not directly involved in the patient's care. This financially motivated denial of care is a threat to the ethical principles of beneficence and nonmaleficence, and to patient and physician autonomy. This type of decision ignores the moral covenant described by Cardinal Bernadin. The ethical dilemma is created when a physician is asked to accept a medical decision, potentially adverse to the patient's interest, which may be based, at least in part, on the financial interest of the insurer.

A landmark case illustrating the potential ethical dilemma of denial of care involved a forty-year old woman who was approved for a 10-day hospitalization for placement of an abdominal vascular prosthesis (19). In the postoperative period, the graft occluded, necessitating additional surgery and prolongation of her hospitalization. Based on the postoperative complication, the patient's surgeons filed a request for an eight-day extension. Her third-party payer, however, approved only four days of additional hospitalization. Consequently, her physicians discharged her early. Out of the hospital, the patient's graft again failed, leading to an above-knee amputation. This case illustrates multiple and complex ethical issues, including the physician's obligation of beneficence and nonmaleficence, and the patient's right of autonomy. In a subsequent lawsuit the court gave its view of this ethical dilemma in unequivocal terms:

> The physician who complies without protest with the limitations imposed by a third party payor, when his medical judgment dictates otherwise, cannot avoid the ultimate responsibility for his patient's care. He cannot point to the health care payer as the liability scapegoat when the consequences of his own determinative medical decisions go sour (19).

This decision is consistent with a long history of American common law. This 29th Bethesda Conference concurs that the principle of beneficence unequivocally establishes that physicians must be their patient's advocate, consistent with their medical judgment, and that this principle must retain highest priority.

Financial Incentives to Withhold Access to Appropriate Care

Since World War II medical progress, exemplified by a 40% to 50% reduction in age-adjusted cardiovascular mortality (20), has come largely from the specialties. Specialists now comprise 70% of American doctors. Limiting access to specialists and restraining their use of expensive technology is an important strategy for reducing MCO costs (21,22). Frequently, the mechanism of limitation of specialty care comes through use of a "gatekeeper" primary care physician who receives a financial incentive to limit specialty referrals.

A fundamental ethical tenet of medical practice articulated in antiquity by Hippocrates and Maimonides, and most recently expressed by the American Medical Association (AMA) Council on Ethics and Judicial Affairs, is that physicians have a fiduciary responsibility that prohibits them from placing their own financial interest above the welfare of their patients (23). The potential for violation of this tenet clearly exists in both fee-for-service medicine and managed care, but the nature of the problem is quite different. In fee-for-service medicine there is the possibility of providing excessive care which can cause harm as well as waste valuable resources. There is no doubt that some doctors have been guilty of such practices. However, these practices are clearly in violation of the AMA ethical code of organized medicine and the oath which the physician has taken.

An equally serious problem is financial incentives designed to limit the use of appropriate expensive diagnostic and therapeutic modalities. Used by many MCOs, financial incentives are designed to reduce cost through reduction of medical diagnostic and therapeutic services. Without question, this practice has resulted in adverse patient outcomes. In addition, disincentives may include reduced reimbursement or contract termination for what the MCO deems to be excessive numbers

of hospitalizations, excessive lengths of stay, or excessive referrals to specialists. Doctors subjected to such pressures over a protracted period of time may unwittingly modify their medical decisions without even realizing that they are no longer acting in the interest of their patients but in their own self-interest (17).

The most widely publicized case involving the ethics of an incentive to withhold care occurred in Southern California, when a thirty-five year old woman visited her primary care physician with a chief complaint of severe abdominal and rectal pain (24). Based on the clinical presentation and his physical examination, the physician diagnosed peptic ulcer. The patient did not improve on appropriate ulcer therapy. She returned several times, complaining of worsening symptoms. For approximately three months, despite her continuing severe pain, the physician refused to do additional tests or refer her to a specialist. After repeated requests from the woman and her husband, the physician referred the woman to a specialist. Within a few days, she was found to have widely metastatic colon carcinoma. In the jury trial that followed her death, the family argued that the physician's MCO contract encouraged the doctor and his group to limit both referrals and diagnostic tests. Further, the family alleged that the physician had failed to disclose these incentives. In his testimony the physician conceded that reduction in referrals to medical specialists increased the income to his medical group. The jury found for the plaintiff. As with other ethical issues in medicine, there is no consensus on the meaning of this important case. From a number of similar cases, however, it seems apparent that some juries have a clear perception of the physician's ethical fiduciary responsibility. Such decisions suggest that juries are unlikely to accept incentives designed to restrict a patient's access to appropriate care when that decision violates patient autonomy and results in an adverse patient outcome.

Physicians also face powerful disincentives. Although "gag clauses" which prohibit doctors from discussing forms of treatment not available or not covered by a given contract have been outlawed, both by federal legislation and many state legislatures, nonetheless subtle disincentives still exist. These negative incentives include termination without a defined cause or due process. Personal financial incentives and disincentives threaten multiple ethical principles, and create conflicts of interest and moral dilemmas.

It should be pointed out that not all financial incentives are adverse to patient care. For instance, incentives can be structured so that the revenues they create are reinvested in other aspects of care, e.g., better medical equipment or medical libraries. When employed, therefore, financial incentives should be oriented toward reducing costs and improving quality of care.

This Bethesda Conference concludes that financial incentives have the potential to violate both the ethical principle of patient autonomy and the moral values inherent in physician integrity. Therefore, financial incentives must be disclosed.

The Legal Shield for Unethical Medical Business Practices: ERISA

To be effective, an ethical code must be enforceable when violation occurs. One federal law, unrelated to medical care at the time it was written, has had major impact on attempts to resolve the ethical issues created by the emergence of managed care. The Employee Retirement Income Security Act (ERISA) passed by Congress in 1974 governs employee benefit plans. Initially the plan was designed to protect pensions. As written, however, the law is applicable to self-insured health plans offered by employers to their employees. When an MCO refuses to precertify payment for necessary medical services, courts have held that the action is covered under the federal law preempting any state laws governing employee health plans. Whereas restriction of access to a specialist by a primary care physician resulted in the malpractice judgment in the preceding case example, similar restriction of referrals by MCOs generally does not result in parallel liability. One example is the case of a middle-aged man who sustained a large myocardial infarction in a midwestern city (25). In the recovery period based on inducible ventricular tachycardia which placed the patient "at high risk for sudden death," his cardiologist determined that the patient required electrophysiologically guided left ventricular aneurysmectomy. Because the local hospitals did not perform this procedure, the cardiologist concluded that his patient's best chance for survival lay in referral to Barnes Hospital in St. Louis. The surgeons were contacted and arrangements were made for his surgery. Because St. Louis lay outside its service area, however, Lincoln National Health Plan refused to pre-certify payment. After a substantial delay, a second plan-retained cardiologist evaluated the patient. This consultant agreed that the patient should be transferred to Barnes, 4 months after the original recommendation. In that period, however, his cardiac function had further deteriorated, precluding the possibility of surgical repair. He was put on a cardiac transplantation list, but died three months later while awaiting a suitable heart. The patient's family sued. The court held that when the proposed surgery was canceled in response to the Lincoln National refusal to certify payment, it was not providing the patient with medical advice and could not be liable for medical malpractice.

The decision in this case was based upon the ERISA exemption. Thus, the courts have typically found that denial of care is an insurance benefit decision. The remarkable outcome of this reasoning is that the liability of the MCO is limited to payment of the cost of denied insurance benefit, whereas the physician remains liable for both improper treatment and for additional punitive damages for willful disregard of the patient's interest. ERISA, therefore, creates a unique dichotomy in which the physician may assume the liability for a plan's decision with which he or she does not agree, while the plan's nonphysician decision maker is protected from liability. The Bethesda Conference concluded that the ERISA preemption negatively impacts the attempt to develop an ethical code and must be modified to meet the emergence of managed care.

JACC Vol. 31, No. 5
April 1998:917–49

The Impact of Managed Care Practices on Physician and Patient Attitudes

Many managed health care plans put substantial pressure on physicians to limit the time spent with an individual patient, making it difficult to provide considerate, thoughtful and ethical care. The patient is therefore often not informed about the rationale for various tests and procedures, and their outcome. Working under these stressful conditions has resulted in unprecedented physician dissatisfaction with their professional life and even with their choice of profession. The dissatisfaction relates to both ethical and financial issues. A mail poll of 1,141 California physicians under the age of 40 (26) revealed that one third of these young physicians would not choose to enter medicine again. A vast majority were dissatisfied with their relationships with MCOs and 72% indicated that their patient care decisions were influenced by reimbursement or capitation issues (59% sometimes, 20% frequently). They also reported that 53% of their patients believe that treatment decisions are influenced too heavily by reimbursement considerations.

Similar levels of dissatisfaction with managed care have recently been reported in surveys of patients. In the most comprehensive evaluation yet undertaken in California, researchers at the University of California at Berkeley (UC Berkeley) and the Field Research Corporation surveyed 1,200 patients (27). Only 3% of Californians with private medical coverage have traditional fee-for-service plans, so the results deal almost exclusively with managed care. Forty-two percent of the individuals surveyed reported problems with managed care, involving denial or delays in getting medical treatment, inappropriate care, or difficulty in getting referrals to physician specialists. Projecting from the 21% of the patients who reported that their medical condition had worsened as a result of these problems, the survey estimated that approximately 1.4 million people in California were adversely affected by these managed care practices. The California survey was the second recent survey to find significant patient dissatisfaction with managed care. A study by Harvard University researchers and the Kaiser Family Foundation found that 51% of Americans believed that managed care had lowered the quality of medical care, compared to 32% who said it had improved the quality (27).

The UC Berkeley-Field study was commissioned by California Governor Pete Wilson as part of the preparation for comprehensive recommendations on health care reform. An additional key finding of the survey was that consumers reported varying levels of satisfaction depending on the type of managed care plan to which they belonged. Patients enrolled in group/staff model not-for-profit health maintenance organizations (HMOs) (the Kaiser Foundation accounts for nearly all such members in California) were the most satisfied. In contrast, only 29% in network or independent practice association (IPA) model HMOs (the great majority of California HMOs) were "very satisfied." The relative satisfaction that physicians experience with their professional lives is of great importance, for it is difficult to envision a disgruntled physician providing thoughtful, high quality and optimistic medical care.

Table 3. Questions for Employers and Patients to Ask Before They Join a Health Maintenance Organization

1. Do primary care doctors get more money if they deny referrals to specialists or hospitals?
2. Does the HMO contract allow termination if it believes the doctor is overutilizing services?
3. Does the plan have an "experimental/investigative" or "not medically necessary" exclusion?
4. What are the most frequently denied procedures by the HMO using this criterion?

HMO = health maintenance organization.

Methods for Dealing With the New Ethical Problems

The simplest approach to the ethical dilemmas posed by managed care is public education. Many have argued that with the emergence of managed care, the purchaser of health care, be it an individual or a corporation, has the same responsibility for due diligence that exists in any other business transaction. For instance, the ethical dilemmas have been made explicit in a spectrum of "buyer beware" warnings from consumer advocates and health care attorneys. One such compendium entitled "Questions for Employers and Patients to Ask Before They Join an HMO," circulated by California health care attorney Mark Hiepler is shown in modified form in Table 3 (28).

It seems clear that these questions are predominantly the counterpart of the ethical conflicts identified in Table 2. Nonetheless, the appropriate answer may not be clear, even to a reasonably well informed purchaser. A more serious problem in the "buyer beware" strategy is that the patient is extraordinarily vulnerable, both by lack of knowledge, urgency of circumstances and the emotional stress of illness. This is a particular concern for the aging Medicare patient who is offered medical coverage by MCOs at low cost, often with free prescription drugs. Although such plans may appear very attractive at the time, they may not provide the coverage which meets the medical needs of the patient. Leaving these decisions up to the individual patient may be a disservice to many older and/or poorly educated individuals. The Bethesda Conference concluded that this approach is inadequate as a stand-alone strategy.

An alternative approach is legislation. In November 1997 President Clinton's Advisory Commission on Protection and Quality in the Health Care Industry published its recommendations for consumer rights and responsibilities in the health care industry. These recommendations have been made available on the Internet (http://www.hcqualitycommission.gov/cborr/consbil.htm). The eight major categories of rights and responsibilities are summarized in Table 4.

From the section titles of the Consumer Bill of Rights and Responsibilities, it is apparent that the Advisory Commission has set out to legislate an ethical code for the health care industry, applicable to both fee-for-service and managed care medicine. The Bethesda Conference strongly supports the

Table 4. Consumer Rights and Responsibilities

Information disclosure
Choice of providers and plans
Access to emergency services
Participation in treatment decisions
Respect and nondiscrimination
Confidentiality of health information
Complaints and appeals
Consumer responsibilities

principles expressed in this document. Nonetheless, the Conference also concludes that legislation alone will not eliminate the need for a code of ethics.

Development of a Code of Medical Business Ethics in the Managed Care Era

Professions are founded on ethical values (29). In the medical profession, these values develop trust, based on the primacy of the patient's interest. When asked or forced to do something he/she feels is not in the patient's interest, the physician is asked to deny his/her professional and personal integrity. In the view of some, professionalism is under attack. The Chief Medical Officer of United Health Care has stated "patients and health care purchasers are challenging the effectiveness of professionalism." He contends that it is up to managed care to test and measure competency and whether the patient's best interest is being served. In this view, "professionalism" cannot be relied upon to accomplish this goal (30). The problem created by the transfer of medical decisions from the attending physician to a remote corporate location is the absence of a code of ethics governing the new decision-maker. The specific problem has recently led to a call for development of a uniform code of medical ethics in Great Britain (31). The Bethesda Conference concluded there is a need for a national dialog directed at development of consensus on a managed care code of ethics.

The American Association of Health Plans has recognized that the managed care industry does not have a defined standard of ethics that deals with the new ethical problems created by managed care practices. Medical ethicist Bradford H. Gray states that even among nonprofit plans of high repute, there is no defined standard of ethics (32). As a consequence, physicians working under managed care may not have the capacity or the motivation to act as advocates for patients (33). Further, there is no ready system for monitoring the quality of medical care, in particular underutilization caused by MCOs.

In the face of widespread concern about the ethics of managed care, ICOs and consumer groups have begun a dialog (34). Some organizations such as the National Committee for Quality Assurance have begun to develop methods to measure clinical effectiveness in both MCOs and fee-for-service systems. Use of beta-blockers after myocardial infarction, annual eye examinations in diabetes, and treatment for patients with hyperlipidemia are among the surrogates used to measure quality of care. Methods of evaluating the quality of medical care provided to patients with complex conditions such as congestive heart failure, however, have not yet been developed. In the absence of effective measures of quality, most organizations have to rely on simple measurements such as length of hospital stay and hospital mortality. The development of reliable and reproducible measures of outcome is essential to evaluate the quality of care provided to our patients. There are now several recent studies that document that care provided by cardiologists for the management of acute myocardial infarction is superior to that provided by general physicians (20,35,36). There must also be less complex conditions that can be equally well cared for by general physicians at potentially lower cost. In considering the long-term outlook for managed care, Health Care International warns that practices which save costs in the short term may prove untenable in the long term (32). This admonition may be interpreted to mean that the long-term consequences of cost saving through delaying and denying sophisticated and expensive medical services may have unfavorable implications which are, as yet, not apparent.

The Bethesda Conference concluded that unilateral attempts by MCOs or by legislatures are unlikely to develop a useful code of medical ethics. There needs to be a preceding dialog on whether, and how much, the nation now wishes to restrain the cost of medical care, recognizing there are potential adverse consequences for some patients. Only with the establishment of a code of managed care ethics can physicians in such systems be stewards of society's resources and patient advocates.

Conclusion

The Bethesda Conference consensus is that a substantial decline in ethical medical practice has accompanied the development of methods to reduce health care cost. To maintain the integrity of the medical profession it is essential to reverse this trend. The ethical principles and the moral values traditionally held by physicians, however, are not physician specific. All those involved in health care in any capacity must act with the highest personal and professional integrity. Since all members of health care organizations are responsible for the professional status of health care, any action, policy or contract formulation or patient contact should conform to these ethical principles (18).

Physicians in particular are at risk of subjugating their basic ethical ideals, compromising the patient-physician relationship for financial and other business reasons, and losing the professional status granted by society (11). The challenge for physicians is to return to the ideals of the medical profession; care of the sick and relief of their suffering within the structure of the moral physician-patient covenant (37). Beyond the physicians' awareness of their unique role in society, physicians must also recognize the uniqueness of the business of health care (11) and be proactively involved in defining the mission, strategies, goals and cultures of health care organizations.

Finally, they must advocate a national dialog on the often conflicting mandates to reduce the cost of health and to provide the best care for their patients. The central question that must be debated is whether the historic moral covenant will be changed to an economic/contractual arrangement whereby physicians are reduced to mere managers of commercial and societal resources (38). In this dialog, physicians must maintain their role of patient advocate.

In summary, the challenge to physicians is to clearly articulate the ethical code of medicine. The challenge to MCOs is to actively direct the organization toward greater enlightened social responsibility. It is only through the acceptance of these ethical principles that the highest quality of patient care will be attained and made universally available to all members of society.

Bethesda Conference Recommendations

Each of the recommendations were voted on by the Bethesda Conference attendees. All received a majority vote of >75%.

1. Establishing a national dialog on ethical standards throughout the health care system. Health care providers need to develop a consensus on medical ethics. Only when principles are agreed upon, can physicians take responsibility for being both the patient advocate and the steward of society's resources.
2. Stipulating that the code of ethics applies to physicians, hospital administrators, managed care executives, medical directors and all those involved directly or indirectly with patient care.
3. Redirecting financial incentives from withholding care to improving care.
4. Requiring full disclosure of the mechanism, distribution and actual dollar amounts of financial incentives and disincentives offered to physicians.
5. Requiring an independent expedited appeals process to resolve patient disputes.
6. Protecting physicians against sanctions when they appeal medical decisions on their patients' behalf.
7. Requiring full disclosure of medical services that are covered and those that are excluded.
8. Confirming the patient's right to direct access to reasonable specialty care.

Appendix

Case Studies for Task Force 1

Case 1. An asymptomatic 46-year old man in a "gatekeeper" HMO has severe mitral valve prolapse involving both valve leaflets. His annual transthoracic echocardiogram shows an increase in end-diastolic left ventricular (LV) diameter from 4.8 cm to 5.8 cm and after discussion with his family physician he is referred by his cardiologist for consideration of surgery to prevent irreversible deterioration of LV function. The surgeon requests a transesophageal echocardiogram (to assess the likelihood of valve repair vs. replacement so that these possibilities can be discussed with the patient), as well as a cardiac catheterization and coronary angiography. The cardiologist and the surgeon are informed by the family physician that permission for these studies has been denied because they are not necessary; an operation is appropriate even if valve replacement proves necessary, and catheterization is unlikely to alter the patient's management.

Will this scenario become more common in an era of managed care and/or limited resources? How should the cardiologist and surgeon react to these alterations in their routine for preoperative evaluation? What should they tell the patient? What should they tell the family physician? Do they have a responsibility to conserve resources ("stewardship"), that must be weighed against their responsibility to do the utmost good for the patient ("beneficence")? For example, should they consider it sufficient if the patient has a negative thallium stress test?

Case 2. A physician in a multihospital MCO develops methodology that improves outcome in patients with AIDS. The corporate marketing division reports that release of this information is likely to substantially increase the number of AIDS patients that enroll in the MCO, and thereby significantly reduce profit margin.

Do medical ethics require that the MCO institute the improved methodology throughout the health care system, even though profits will suffer, and must the information be made available to the public?

Case 3. A physician vigorously disagrees with the hospital pharmacy and therapeutics committee's decision regarding a very costly new therapy. The decision will deny therapy to her patient. The decision of the committee is clearly influenced, at least in part, by financial consideration.

Is the physician ethically obliged to challenge the decision? If the physician carries her concern to the local newspaper, should she be punished by the organization?

Case 4. A 55-year old businessman is admitted for relatively asymptomatic recurrent atrial fibrillation. He is found at echocardiography to have segmental ventricular dysfunction. Cardiac catheterization revealed severe triple-vessel obstructive coronary disease requiring bypass surgery. This unexpected development, as might be anticipated, caused the patient great emotional distress. However, he agreed to have bypass surgery the following day. The managed care organization who provided his coverage, upon learning of the scheduled surgery, insisted that the patient be transferred to another hospital with which it had a contract for cardiac surgery. This would have required the patient, already under great duress, to be transferred to another hospital with cardiologists and cardiac surgeons unknown to him. The patient objected vehemently to being transferred. The MCO refused to discuss the matter with the attending cardiologist, but insisted on the transfer.

Should the patient's cardiologist transfer the patient as directed by the MCO? Should the cardiologist, feeling that the stress imposed by transfer would be potentially dangerous to his patient, insist that the surgery be done as scheduled? Does the MCO have a moral and ethical responsibility to consider the extenuating circumstances and bend its policy in this instance for the good of the patient? Is an exclusive contract by an MCO with a specific hospital in a given city with other institutions of comparable quality in itself ethical?

Case 5. A cardiologist is treating a patient with advanced coronary disease with a lipid-lowering agent, a beta-blocker and an angiotensin-converting enzyme inhibitor. The patient is controlled effectively and tolerates the medications well. The cardiologist receives a communi-

cation from a pharmaceutical distribution company under contract to or owned by the MCO to which the patient belongs. The cardiologist is requested to change the medications to similar but somewhat different products.

Is it ethical for the MCO through its pharmaceutical distribution company to make such a request? Should the cardiologist accede to the request knowing that there are nuances of difference between the medications involved; perhaps difference is in the patient's tolerance and perhaps some psychological reluctance on the part of the patient to make the change?

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Task Force 2: Application of Medical and Surgical Interventions Near the End of Life

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Introduction

Improved technology and an aging population cause physicians and particularly cardiovascular specialists to be increasingly confronted with decisions about the application of complex, sophisticated, and often expensive technology in end-of-life situations. "End-of-life" is defined for purposes of this discussion as applying to critically ill persons whose survival is in doubt, whose anticipated survival is severely limited, and to the chronically ill whose prognosis is similarly limited.

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The level of health care spending is a function of national wealth and societies' willingness to allocate resources to the health care sector. As society seeks to constrain costs of medical care, the expenditure of resources in end-of-life situations becomes a particularly inviting target for cost savings, and intensifies the ethical issues surrounding this vulnerable subset of patients. "Advance care directives," "do not resuscitate orders," "comfort care," "futile care," and "physician-assisted suicide" are terms which suggest the need for a particular ethical sensitivity lest these become a coercion for patients, families, and physicians to capitulate to the economic forces driving contemporary medical practice.

The ethic of distributive justice is referred to in the 21st Bethesda Conference "Ethics in Cardiovascular Medicine." "In the context of limited resources and continually expanding technology, physicians and institutions face increasingly difficult decisions as they attempt to use available medical resources in a technically and ethically justifiable way to ensure appropriate care for patients" (1).

Distributive justice—the justifiable ways in which benefits and burdens are distributed in a society under prevailing conditions of economic scarcity—is perhaps the central health policy issue of our time, the dominant theme of this second Bethesda Conference on ethics, and one which has a special poignancy for those near the end of life.

It is beyond the scope of this report to analyze the health care expenditures in patients near the end of life, much less to suggest in what circumstances potentially beneficial care should be given and when it should be withheld. It is commonly held that older patients are often treated aggressively with costly but futile technology at the end of life, thus driving up total U.S. health care costs. Others regard this as a misconception and point out facts to the contrary. In a recently published study entitled "Seven Deadly Myths—Uncovering the Facts about the High Cost of the Last Year of Life," it was found that age was not a reliable predictor in determining who would benefit from aggressive treatment; advance directives frequently have little impact on treatment decisions; and aggressive care for those over 65 accounted for only six-tenths of 1% of the nation's total health care bill (2).

In this section we examine the ethical issues raised in caring for patients near the end of life and the particular tension which exists for the cardiovascular specialist in the enlightened, appropriate, and compassionate application of medical and surgical technology to the individual patient, mindful of the societal responsibilities with which he or she is entrusted.

Application of Complex Medical and Surgical Interventions in the Elderly

Cast me not off in the time of old age; forsake me not when my strength faileth.

—Psalms 71:9

Age-based stereotyping by which the elderly were once dismissed as candidates for many forms of surgery and aggressive therapies has been in decline but has not disappeared (3). To the contrary, it is clear that age per se is a poor predictor of medical outcomes. This is not to say that age is not an important factor in clinical decision making. For example, age is an independent risk factor for hospital mortality in patients undergoing coronary artery bypass grafting. Univariate analysis of 230,730 patients in the Society of Thoracic Surgeons National Database harvest, 1995–1996, shows a mortality rate of 1.77% for patients less than 65 years compared to 4.19% for those 65 and older (4). Moreover, medical risk and cost increase continuously with age. Operative mortality, perioperative stroke rate, and mean postoperative length of stay for isolated coronary artery bypass grafting as a function of age are depicted in Figures 1 to 3 (5).

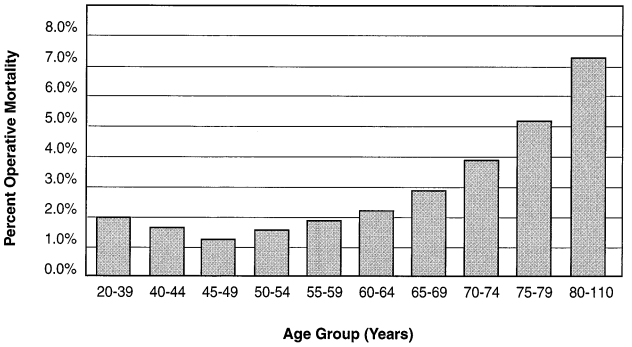
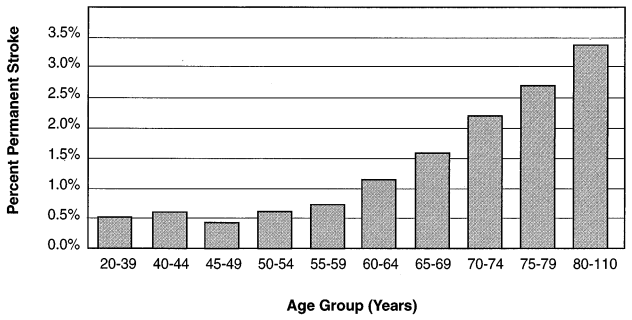


Figure 1. 1995 to 1996 Society of Thoracic Surgeons Cardiac Surgery National Database: percent operative mortality by age group for isolated coronary artery bypass graft surgery.

Outcomes data in other complex medical and surgical interventions show similar increased risk with increasing age (6,7). Despite the increased risk of adverse outcomes as a function of age, the vast majority of elderly patients derive significant benefit from such interventions (8–10).

Covert rationing based on *ageism*, i.e., a tendency to regard older persons as debilitated or unworthy of attention, is manifested as withholding appropriate care for "medical" reasons. The elderly may be particularly vulnerable to misleading representations regarding the hazards and futility of com-

Figure 2. 1995 to 1996 Society of Thoracic Surgeons Cardiac Surgery National Database: percent permanent stroke by age group for isolated coronary artery bypass graft surgery.



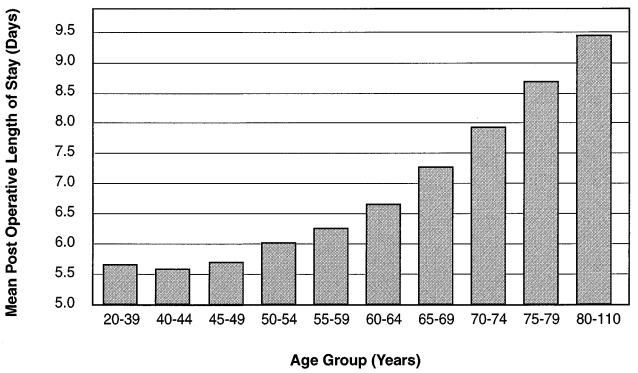


Figure 3. 1995 to 1996 Society of Thoracic Surgeons Cardiac Surgery National Database: mean postoperative length of stay by age group for isolated coronary artery bypass graft surgery.

plex medical interventions in older patients, because of their unwillingness to be a burden to their families or to society.

There are quite legitimate instances of rationing health care based on age. Denial of organ transplantation to the elderly because of the scarcity of donor organs is one example, which is consistent with the ethic of distributive justice and has become accepted medical and social policy.

Other clinical situations are less clear. The greater the risk, the higher the cost, the more uncertainty as to the potential benefit (especially when improved survival is one of the chief benefits), the older the patient, the greater is the disposition to withhold care.

Futile care will be discussed in a subsequent section, but needs to be mentioned briefly here. Truly futile care in which medical and surgical technology has no reasonable chance of benefiting the patient is inappropriate and, worse, may prolong suffering and waste scarce resources and is to be condemned for any age patient no matter what the wishes of the patient or family.

The cardiovascular specialist caring for elderly patients has an intensified ethical responsibility in clinical decision-making. The always difficult distinction between *critical* and *terminal* illness is more difficult as patients near the end of their natural lives. Patients who have outlived friends and are isolated from family may not wish to undergo complex interventions, and may not be able to articulate their preference to be left alone and allowed to die. Family members, motivated by guilt rather than compassion, may insist on aggressive care with little chance of success. A risky intervention may be deferred because of age only to be applied later in an emergency situation in which the indications for treatment are clear, but a favorable outcome much less likely.

Many believe that explicit rationing of expensive health care for the elderly is inevitable, and will result from a public discussion of societal priorities (3). Others believe that such a public discussion would be so disruptive that it will not, and should not occur, and that hidden rationing will be tacitly accepted (11).

It is our position that ageism has no place in contemporary clinical decision making, that complex medical and surgical interventions have an important place in the care of the elderly with due consideration for appropriateness based on clinical experience and scientific knowledge, and consistent with the patient's wishes and best interests.

Palliative Care

It is not death, but dying which is terrible.
—Henry Fielding, *Amelia* (1751)

Palliative care near the end of life should be the least controversial aspect of end of life decisions. Most medical care is, in fact, palliative in contradistinction to preventive or curative care. In the context of this section, palliative care refers to the care of patients in the terminal stages of illness in whom the goal of medical management is to provide comfort. Such care has been, to an increasing extent, formalized into "comfort care" clinical pathways.

In the 150th anniversary edition of the Code of Medical Ethics of the American Medical Association (AMA), the first principle enumerated is "A physician should be dedicated to providing competent medical service with compassion and respect for human dignity" (12). The 21st Bethesda Conference: "Ethics in Cardiovascular Medicine" states as its principle in guiding physician behavior, "A commitment to relieve pain and suffering and when possible to heal both body and mind" (1). These admonitions are not new but come from Hippocrates and especially from Thomas Percival, the English physician and philosopher, who published his code of ethics in 1803 and on which the AMA code was originally based. Indeed, from antiquity to the present no one disagrees that a patient's suffering should be relieved. Why then is this an issue for ethical consideration?

There are two areas that need to be discussed. First, palliative care at the present time: how well is it being done, how well are we educating new physicians about care at the end of life, and what are the unique problems in caring for cardiac patients at the end of life that differ from care for patients with a more predictable time to death? Second, how does the emergence of managed care influence the availability and provision of adequate palliation?

How Well Are We Providing Palliative Care?

Since all agree that it should be done, how well are we relieving pain and suffering near the end of life? Most residents and many physicians, young and not so young, have had limited experience dealing with patients and families when end of life decisions must be made. It has been found that only 5 of 126 medical schools provide a separate course on the care of the dying. In addition, of 7,048 residency programs, only 26 offer a course on care at the end of life (13). Kathleen Foley of Sloan Kettering Cancer Center in New York writing in the *New England Journal of Medicine* states (14), "Several studies concluded that poor communications between physicians and

patients, physician lack of knowledge about national guidelines for such care and their lack of knowledge about control of symptoms are barriers to the provision of good care at the end of life" (15–17). The SUPPORT study (Study to Understand Prognosis and Preferences for Outcomes and Risk of Treatments) examined patients and families from five teaching hospitals. In order to better understand the experience of dying from the perspective of the surrogate decision makers who were usually family members, a medical record review of 9,105 seriously ill patients was carried out (18). In this study approximately half of the patients died and, when interviewing the family members, it was found that 55% of the patients were conscious during the last 3 days of life. Forty percent had severe pain, 80% severe fatigue, and 63% had difficulty tolerating physical or emotional symptoms. Another paper from the same patient cohort examined patient opinions (19). In this study patients were interviewed and, when they could not be interviewed due to illness, a surrogate was interviewed. Nearly 50% reported pain. After adjustment for confounding variables, the older and sicker patients reported less pain, but patients with greater co-morbidity, depression and anxiety reported more pain. Pain was much more common in cancer patients, especially in patients with cancer of the colon. Based on the experience from the SUPPORT study and others, it would seem that the provision of care for patients near the end of life needs significant improvement, including control of pain and other symptoms.

Although cardiovascular disease remains the number one cause of death, the mode of death and therefore the care required will vary according to the disease condition. Although sudden death accounts for a large percentage of cardiovascular deaths, the second leading condition appropriate for hospice care behind cancer is heart failure. Whereas pain relief may be the major requirement in patients with cancer, relief of symptoms such as dyspnea and profound weakness are the sine qua non for palliative care of patients with heart failure. Depression and its many expressions is also a prominent feature in patients dying of heart failure. Recognition and management of depression should be vigorously pursued in patients expected to die as in those expected to recover. Once it is apparent that the patient will not survive, it is crucial that palliative care involve all appropriate measures including continuing efforts to correct physiologic abnormalities which are producing discomfort such as pulmonary congestion. Much of the suffering experienced by heart failure patients is caused by cardiorespiratory and other support devices. Many patients receiving mechanical ventilation are conscious and aware, even though incapable of communicating, and need to be relieved of the support-device-related discomfort as much as possible.

Palliative Care in the Managed Care Environment

As managed care plays an increasing role as the engine of cost containment, ethical issues regarding palliative care near end of life specific to the managed care environment arise. Under a fee-for-service system, physicians and hospitals are rewarded for continuing efforts to sustain life and provide comfort. Under capitated plans, financial incentives are structured to provide less care rather than more. Whereas conflicts of interest are present in both fee-for-service and capitated reimbursement systems, the latter creates a financial disincentive to provide palliative care, especially over prolonged periods. The danger, posed by managed care, now well recognized, is the possibility that economics can diminish palliative care in favor of a hastened or assisted death (20). The *AMA Code of Medical Ethics* states that quality of life is defined by the patient's interests and values. "This is not to be superseded by avoidance of a burden for family or society." "The duty of patient advocacy is fundamental to physician-patient relationships that should not be altered by the system of health care delivery." The goal of palliative care is to relieve pain and suffering and to improve the quality of life, not necessarily the duration of life. However, provision of competent palliative care may result in an alteration in the duration of life as well, but this should not be proscriptive if the primary goal of palliation (relief of suffering) is being achieved.

The patient's wishes may also be influenced by the physician and the physician's attitude toward palliative care. Emanuel and Emanuel (21) found that patients with cancer and depression favored physicians who acknowledged willingness to assist in death; patients with cancer suffering from pain viewed such physicians with suspicion. Several studies have found that the desire for death has been closely related to depression; pain and lack of support are contributing factors. Depression remains a major component of suffering which competent palliative care may alleviate (21,22). In a managed care system, the provision of competent palliative care should not be compromised. Measures such as educating health care workers and the public of the needs of the terminally ill and expanding the use of hospice care, are important considerations for any health care system.

Excellence in palliative care will not be cheap. Programmable drug delivery skin patches, implantable pumps, and other automated delivery systems may be expensive. Most important, however, is the training and experience of physicians and other care givers, and the commitment of resources. Neither, futile care nor physician-assisted suicide should be allowed to substitute for competent palliative care at the end of life.

Futile Care

Futile care is that which provides little or no benefit to the patient or which has proven to be useless in achieving its desired effect. In struggling for a more precise definition ethicists and physicians have sought to define futile care in both quantitative and qualitative terms. Both approaches fall short of their intended purpose of reaching a clear and unambiguous definition of futility, the former because of the inherent variability and subjectivity of physician experience, and the latter because of the lack of consensus among patients about what level of functional outcome would be considered satisfactory or acceptable.

Quantitative Definitions

Schneiderman and colleagues (23) define that a treatment should be considered futile if it has failed to produce the desired effect in 100 consecutive cases. Failure is defined as death, permanent unconsciousness, or permanent dependence on intensive medical care. This definition is subjective since one physician's last 100 cases may be very different from those of another, and the reliance on selective recollection and experiential prejudices make this definition even more inconsistent (24,25). Furthermore, although the major underlying disease process may be the same, individual critical care cases vary dramatically. Hence, defining what determines a cohort group consisting of the last 100 like patients can be difficult if not impossible. Furthermore, the literature defining quantitative futility is sparce compared to the vast literature defining successful interventions. For example, Faber-Langendoen published a review that sought to demonstrate that cardiopulmonary resuscitation for patients with metastatic cancer was futile (no survivors to hospital discharge in 11 cases) (26); conversely, the Sloan-Kettering group published a similar cohort showing a 10% survival rate (27). These conflicting reports simply underscore the need for further research.

Other attempts at defining quantitative futility have been more lenient implying that the chances of success as very low or rare (28,29). A recent survey revealed that most physicians considered a treatment futile if there was less than a 10% chance of achieving the intended goal (30). Surprisingly, 20% of those physicians surveyed chose the threshold of 20% or even higher as compatible with the definition of futility. This wide difference in opinion by physicians as to the definition of quantitative futility is in many ways a reflection of the varying opinions in the medical and ethics literature on the subject. Generally, quantitative futility for an individual patient with a specific illness will depend on a combination of the results in the medical literature pertaining to the case as well as to the treating physician's personal experience. Hence, this particular estimate of futility will always be subject to inconsistency.

In speaking with families it is important to use words carefully. A clear distinction must be made between *treatment* and *care*. A specific treatment may be futile; care (especially palliative care) is never futile.

The concept of futile care is not simply related to cost and the ethic of distributive justice. Our professional integrity demands choices based on factors beyond financial considerations in recommending treatments to our patients. We reject the notion that as physicians we will do anything so long as it is paid for.

Qualitative Definitions

Qualitative definitions of futility are equally problematic. This is because qualitative definitions rely on making value judgments about quality of life (31) and when such quality is so diminished as to render "allowing to die" the preferred option. "Futile care is any clinical circumstance in which the doctor and his consultants, consistent with the available medical literature, conclude that further treatment (except for comfort care) cannot within reasonable possibility, cure, ameliorate, improve, or restore a quality of life that would be satisfactory to the patient" (32).

The issue of what is an acceptable quality of life is clearly a personal one. Ethicists and physicians agree that patient autonomy should be paramount, and hence, the patient's values become the determining standard (23). But, often, the patient's views cannot be expressed at the time of need because of unconsciousness or incompetence (33,34). When this is the case, the physician in concert with others involved in the patient's care and with various family members should tackle these issues with great sensitivity. Family members often have difficulty being objective when making informed choices about futile care of a loved one (35,36). Decisions are often influenced by love, feelings of guilt, fear of loss or loneliness, or by self gain. Often, the physician and health care team members are expected to play a pivotal role in the determination of qualitative futility. In this case, extreme caution should be exercised and the patient's best interests should be the overriding standard.

More recently, Schneiderman et al. (23) also included the quality of life in their definition of futility: "If the treatment fails to release the patient from being preoccupied with the illness and incapable of achieving any other life goal, that treatment should also be regarded as futile." The majority of citizens regard a life totally dependent on intrusive organ-replacing medical care, when high brain functions are seriously or permanently lost, to be a fate worse than death (37,38).

Although the attempts to define futile care more precisely have been useful, we are left with the notion that the distinction between potentially beneficial and futile care is a complex calculus which must take into account the individual patient's medical status, education, ethnicity, family support structure, as well as the physician's experience with and understanding of the proposed intervention.

Decisions to Forego Treatment and Advance Care Planning

During the past 20 years, a standard of practice has emerged that recognizes the right of patients to forego life-sustaining treatment, even if this results in their death. This includes the right to withhold (not start) or withdraw (stop) cardiopulmonary resuscitation, mechanical ventilation, dialysis, antibiotics, and artificial nutrition and hydration. This right is grounded in the ethical principle of respect for patient autonomy and protected by the legal doctrine of informed consent.

A valid consent has three elements: disclosure, capacity, and voluntariness. The key elements of *disclosure* include the risks and benefits of the proposed test or treatment as well as any alternative tests or treatment. Although standards for disclosure may vary from one jurisdiction to another, the physician should disclose all the information that a reasonable

person in the patient's situation would want or need to know before making a decision, including any information about risks that are likely or serious. Moreover, it is prudent for the physician to explain any benefits, risks or alternative tests or treatments that may have special significance for the particular patient. Effective communication skills are essential to the process of obtaining informed consent. The physician should spend sufficient time to ensure that the patient has the opportunity to understand the information provided by the physician and to have his/her questions answered.

Capacity can be defined as the ability to understand relevant information and appreciate the consequences of a particular decision or lack of decision. Unfortunately, there are no widely available clinical measures to assess patient capacity in practice. If there is doubt about the assessment, consultation from a psychiatrist, hospital attorney, or ethicist may be helpful; the ultimate judge of a patient's capacity is a court. If the patient is deemed incapable, he/she should be told that he/she has been deemed incapable, and that someone else will be making decisions on his/her behalf. This should be done in a sensitive manner appropriate to the clinical circumstances, and the patient may wish to challenge the finding of incapacity.

Voluntariness means that patients should be able to make treatment choices without undue external coercion.

In sum, capable, informed patients acting voluntarily have the right to not start or stop life-sustaining treatment.

In theory incompetent patients have the same right as competent individuals, but in practice they cannot exercise it. To address this paradox, policy makers, judges and legislators have developed a system known as "substitute decision making" to permit others to exercise the incapable person's right to consent on his/her behalf.

Substitute decision making poses two main questions: "who should make the decision for the incompetent person and how should the decision be made?" The appropriate answer to these questions varies from one jurisdiction to another and physicians are encouraged to gain familiarity with the legal standards in their place of practice. However, the overall goal of substitute decision making is to approximate the decision the patient would make if he/she were still capable to do so.

With regard to who should make decisions, the most appropriate person is someone appointed by the patient him/herself, while competent, through a proxy advance directive (AD) (39). Other substitute decision makers, in their usual order or priority, include a court-appointed guardian, spouse, child, parent, brother or sister, any other relative or concerned friend. In some jurisdictions a public official will serve as substitute decision maker for a patient who has no substitute decision maker available.

The standards for how the decisions should be made, in decreasing order of priority, are wishes, values and beliefs, and best interests. *Wishes* are prior expressions by the patient, while capable, that seem to apply to the actual decision that needs to be made; sometimes patients will have recorded their wishes in an AD. *Values and beliefs* are less specific than wishes but they allow the substitute decision maker to impute what the patient would have decided based on other choices the patient made in his/her life and the patient's approach to life in general; they are often the answer to the question, "What would Fred have wanted?" *Best interests* are "objective" estimates of the benefits and burdens of treatment of the patient.

A true emergency is an exception to the usual requirement to obtain informed consent. The justification for the exception is that a reasonable person would want treatment, and the time delay to obtain consent would result in serious harm to the patient. The limit on this exception is when a patient had refused the treatment previously, in which case an emergency situation does not justify providing it.

Advance care planning (ACP) is a process of communication among patients, their health care providers, their families, and important others regarding the kind of care that will be considered appropriate when the patient cannot make decisions (40).

ACP may contain written ADs. Completed by a person when he/she is capable an AD is used at a time when the person has become incapable. ADs indicate whom a person would want to make treatment decisions on his or her behalf, and/or what treatments a person would or would not want in various situations.

The laws vary with respect to the scope of ADs, who can be proxies, witnessing requirements, and procedures for activating the AD. Physicians should familiarize themselves with the legislation in their jurisdiction.

Initial excitement toward ADs and ACP has been dampened by the disappointing results of the SUPPORT study, which showed no effect of ACP on various cost and utilization outcomes (41). However, the SUPPORT study may not have captured the most important outcome related to ACP—helping people face death in the context of their families.

The primary role of the physician in ACP is that of educator. The physician who raises the issue of ACP with a patient is performing a valuable public education service. If a patient requests assistance from a physician regarding ACP, the physician should refer the patient to information sources on ADs and ACP. Once a patient has learned about ADs and ACP generally, the physician can perform an important service by helping the patient tailor the instruction directive of the AD to the patient's own health situation. The physician can also ensure that the patient has correctly interpreted the information contained in preprinted ADs, and that the patient is capable of completing an AD. Physicians should suggest that their patients review their ADs and ACP when the patient's health status changes. When the patient becomes incapable, and the AD takes effect, the physician will become involved. At this point, the physician will seek consent for the proposed treatment plan from the proxy(ies) appointed in the AD, as discussed above on substitute decision making.

Culture and gender affect decisions to forego treatment and advance care planning in unique and unchartered ways. Physicians should be vigilant for their effects and address these issues with sensitivity and respect.

Do Not Resuscitate Orders

Do not resuscitate (DNR) orders are initiated in institutional settings (hospital, nursing home, hospice) to prevent personnel working in these institutions from responding to a cardiopulmonary arrest with resuscitation and life support in patients who are near the end of life and who are not candidates for aggressive therapies. DNR orders are usually initiated by the patient's physician in consultation with the patient, if competent, and the patient's family, or surrogates. A competent patient may request DNR status; his/her desire not to be resuscitated may be part of an AD.

It would be impossible to list all specific clinical circumstances in which DNR orders might be appropriate. Obvious examples are patients in prolonged coma, advanced metastatic cancer, advanced dementia requiring total care, and Class IV heart failure (transplant not indicated).

DNR orders are often the initial step in a cascade of events that follow the recognition and acknowledgment of a patient's terminal status, are a prerequisite to entering a formalized "comfort pathway," and may be followed by other steps consistent with the patient's wishes, such as withdrawal of life sustaining treatment.

Physician-Assisted Suicide

The issue of doctor-assisted suicide is derived from the confluence of expanded medical technology and patient autonomy, both relatively new developments for patients and physicians.

Technology has allowed many patients to live years beyond what would have been possible just a few decades ago with a genuine quality of life. On the other hand, technology can imprison persons within bodies which offer a very poor quality of life and prolong the dying process. The overuse of technology has led patients to fear dying more than death itself. Medical technology has changed the way we die and the way we think about death. As Daniel Callahan remarks, "what was once a tame way to die has been replaced by a wild death with endless tubes and treatments such as radiation, chemotherapy, and the respirator with side-effects which frighten the patient" (42).

The substitution of patient autonomy for physician paternalism creates a new problem in the moral use of freedom. Since the 1970s when paternalism became a bad word and was replaced by the principle of autonomy, various means have been used to guarantee that the desires of patients would be respected. The principle of autonomy recognizes the patient's right to refuse treatment. An extension of this principle is the right to control one's death.

The proponents of physician-assisted suicide argue that to take one's life is to exercise to its fullest the principle of autonomy and that an "act or practice of painlessly putting to death persons suffering from incurable and distressing disease is an act of mercy" (43). If one accepts the role of the physician to include the obligation to relieve suffering and countenances the ending of life by foregoing or withdrawing treatment, it can be argued that one has already accepted in principle and in practice doctor-assisted suicide.

Opponents of doctor-assisted suicide point out that autonomy is a limited principle, the duty to relieve suffering is a limited duty, that there will always be some suffering in human experience, and that the consequences of allowing assisted suicide, especially by the healing profession, suggest a slippery-slope with immoral results which we neither desire nor should have in our civilized society.

Support for the slippery-slope argument can be found in the Dutch experience where physician-assisted suicide and euthanasia have been legalized. In response to three articles published in the *New England Journal of Medicine* (44–46) describing Dutch studies of assisted suicide and euthanasia in The Netherlands, Hendin et al. conclude in an editorial in the same journal (47), "The 1990 and 1995 studies document that 59% of Dutch physicians do not report their cases of assisted suicide and euthanasia, more than 50% feel free to suggest euthanasia to their patients, and about 25% admit to ending patient's lives without their consent."

On June 26, 1997, the U.S. Supreme Court voted unanimously to uphold state laws that make it a crime for physicians to give life-ending medication to mentally competent, terminally ill patients who want to die. In two separate decisions, *Washington v. Glucksberg* (48), and *Vacco v. Quill* (49), the Court rejected constitutional challenges to laws in Washington and New York that criminalize physician-assisted suicide. In doing so the Court broadly rejected the argument that either the Due Process clause or the Equal Protection clause of the U.S. Constitution guarantees terminally ill patients a right to physician-assisted suicide. The Justices left the door open for future challenges, however, suggesting in concurring opinions that perhaps there might be particular situations quite different from those in the Washington or New York cases in which an interest in hastening death is legitimate and entitled to constitutional protections (50).

As Chief Justice Rehnquist recognized in *Vacco* (51), a moral distinction can be shown to exist between doctor-assisted suicide and letting die. In letting die a fatal pathology is the *cause* of death; in doctor-assisted suicide the physician who administers the injection is the direct cause of death. In letting die the *method* of death is determined by the disease; in doctor-assisted suicide the physician or the patient chooses the method. In letting die the *intention* is to recognize that further treatment is futile; in doctor-assisted suicide the intention is to hasten or complete that which medical science is unable to stop (42).

We need to do a better job of pain management and providing psychological support to those who suffer near the end of life and we must recognize that our technology, misapplied, may contribute to a sense of desperation that leads to the consideration of euthanasia.

Are we willing to reject a tradition which goes back to the age of Hippocrates and now ask the healer to actively, and with

JACC Vol. 31, No. 5
April 1998:917–49

intention, become the agent of death for a competent, suffering patient with a terminal disease?

Conclusions

- Cardiovascular physicians have an ethical obligation to provide high quality end of life care.
- As society seeks to constrain costs of medical care, the expenditure of resources in end of life situations becomes a particularly inviting target for cost savings and intensifies the ethical issues surrounding the care of this vulnerable subset of patients.
- Although mortality, morbidity, and cost do increase with age in the application of complex medical technology, age, per se, is a poor predictor of medical outcomes. Such applications properly selected, in elderly patients, are associated with favorable, beneficial outcomes, often in circumstances in which alternative management strategies are not available or are not effective.
- Palliative care should provide relief of suffering and preserve the dignity of patients who have end-stage heart disease.
- Palliative care is valuable to patients and should be a priority for resource allocation in health care systems.
- The knowledge and skills to provide good palliative care should be included in undergraduate, graduate, and postgraduate medical education.
- We encourage research in methods of provision of care at the end of life.
- The physician should provide competent palliative care regardless of financial considerations.
- Treatment that is expected to provide little sustained benefit or has proven useless in achieving its desired effect, should be discontinued in favor of palliative care, despite pressures to pursue such futile treatment.
- Patients have the right to forgo life-sustaining treatment—a right grounded in the ethical principle of respect for patient autonomy and protected by the legal doctrine of informed consent.
- The cardiovascular physician should play an important role as educator and facilitator in ACP by patients and families.
- We advocate palliative care and support patient decisions to forgo treatment (we do not advocate or support physician-assisted suicide).

Appendix

Case Studies for Task Force 2

Case 1. A family practitioner calls you about an 82-year old woman in a nursing home with severe dementia who was found today to be in pulmonary edema. The patient's legal guardian is unavailable. The patient had an echocardiogram 5 years ago for an episode of fluid retention and has been on lasix and digoxin since.

What course should you follow?

Case 2. An 88-year old woman with end-stage congestive heart failure is living with a niece, is bed bound and has very little appetite. You see her at home and she asks for assurance that she won't be hospitalized again.

What should you tell her?

Case 3. A 73-year old man presents with a cold, cyanotic right lower extremity, absent peripheral pulses and no motor function. The patient had coronary artery bypass graft surgery (CABG) 10 years ago, is known to have peripheral vascular disease (multiple peripheral angioplasties; bilateral carotid bruits), moderately impaired left ventricular function (ejection fraction 0.4), chronic atrial fibrillation, diabetes mellitus, hypertension, hyperlipidemia, and hemiparesis caused by a prior stroke.

An embolectomy was done restoring blood flow to the lower extremity. On the third postoperative day he sustained an anterior wall myocardial infarction (MI) complicated by heart failure and cardiogenic shock.

How should this patient be managed after the acute AMI? Should further interventions be considered "futile" ? What additional information (medical, functional, social, financial) is necessary to make appropriate recommendations for subsequent care?

Case 4. A 75-year old man presents to the emergency room with a leaking (blood in left pleural space) atherosclerotic aneurysm of the descending thoracic aorta. He was known to have the aneurysm for about five years, but elective aneurysmectomy was not recommended because of several coexisting medical conditions, including emphysema, a history of two MIs and a rest creatinine level of 3.0.

The patient is mentally alert, has solicitous family, and is eager to know what his internist recommends. His internist calls in a cardiologist who treated the patient in the past and a cardiovascular surgeon who saw the patient in consultation some years earlier and recommended against elective aneurysmectomy at that time.

What should the consultants do?

Case 5. A prominent 75-year old retired physician sustained a witnessed cardiac arrest, was successfully resuscitated, although he sustained an aspiration pneumonia and remained unconscious. He was intubated, placed on mechanical ventilation, given intravenous antibiotics and nasogastric tube feedings.

His family insisted he would recover and demanded frequent progress reports. After 15 days he remained unresponsive and the consensus of the physicians and nursing staff was that the outlook for meaningful survival was hopeless. The family did not agree to the recommendation to withdraw support.

How does the physician deal with such an impasse?

Case 6. A 73-year old man is transferred to your hospital with a long history of hypertension and two remote MIs. The patient has unstable angina with anterior ischemia on the electrocardiogram, a creatinine of 3 mg%, and moderate chronic obstructive pulmonary disease. Echocardiography reveals depressed left ventricular function; coronary arteriography shows diffuse coronary occlusive disease with a new 90% proximal left anterior descending coronary artery narrowing, compared to a study done two years previously. The patient refuses surgical revascularization and consents to angioplasty. During the course of angioplasty, a left main dissection occurs and evidence of an acute myocardial infarction and hypertension are noted in the catheterization laboratory.

Should the patient undergo emergency CABG at this time?

Case 7. A 19-year old woman underwent a second cardiac transplant six months ago. The first transplant was done at age 12 for end-stage heart failure after multiple cardiac surgeries for congenital

disease (transposition of the great arteries, ventricular septal defect, subpulmonary stenosis). The second cardiac transplant was done after the diagnosis of accelerated, graft coronary atherosclerosis and was complicated by an episode of severe rejection in the early postoperative period which was also treated successfully. The patient has been receiving psychological support throughout. She now comes to you telling you that she has decided that she no longer wants to live and has stopped taking all immunosuppressive medications.

What do you do? What are your obligations to your patient?

Case 8. You have been following a 75-year old man with crippling angina and such severe comorbidities that he cannot have surgery. He has had several angioplasties, all of which were ineffective. He asks you for barbiturates in large doses and says "it's enough." You are seeing him at his assisted living center.

What should you do?

Case 9. A 75-year old retired electrical engineer had several heart attacks at age 70. Heart failure resulted and required aggressive treatment with antiotensin-converting enzyme inhibition, a diuretic and digoxin. At age 71 he began having recurrent sustained symptomatic ventricular tachycardia which could not be completely prevented with either sotalol or amiodarone. An implantable cardioverter-defibrillator (ICD) was placed. The ICD fired three times over the next four years. Recently heart failure symptoms worsened and patient required admission to hospital for intravenous inotropic therapy. Heart failure symptoms abated slightly but ventricular tachycardia (VT) associated with severe hypotension occurred. The patient was shocked multiple times while still awake. The patient demanded that the ICD be turned off and that he be allowed to die. This was done and the patient had another episode of VT which degenerated into ventricular fibrillation and the patient died.

Can this action by the physician be considered as physician-assisted suicide?

Case 10. A 65-year old man with dilated cardiomyopathy is considered for transplantation with class IV heart failure. He was noted to have severe fluid overload, was dependent on two intravenous inotropes and was in renal failure.

He was alert, oriented × 3, with a creatinine of 7.5 and a blood urea nitrogen of 90. His ejection fraction was 10%; he had severe tricuspid regurgitation with a pulmonary capillary wedge pressure of 42 mm Hg, cardiac index of 1.61/min per m^2 and Pao_2 saturation of 38%. To reach transplantation he required chronic hemodialysis and a left ventricular assist device.

What type of care is appropriate?

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Task Force 3: Clinical Research in a Molecular Era and the Need to Expand Its Ethical Imperatives

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Ethical Consideration and the Conduct of Clinical Trials: Introduction

In the 21st Bethesda Conference, the first to address Ethics in Cardiovascular Medicine, it was clearly stated that "the goals of scientific research define the major responsibilities of the researcher: to acquire and interpret knowledge about natural phenomenon and to communicate this information accurately to others" (1). In addition it acknowledged that many biomedical researchers have a threefold obligation that arises simultaneously from their responsibilities to patient care, clinical research and teaching that often engender conflict. Task Force IV of that Bethesda Conference discussed a Scientific Responsibility and Integrity in Medical Research with care and thoroughness such that the general topic requires only our strong reaffirmation here with no major abridgement necessary a decade later.

However, accompanying the increasing involvement of commerce into medical care, we are also witnessing a shift of funding of biomedical research away from the public and into the private sector. Accordingly, it seems prudent to expand on two statements made in the Bethesda 21 document relating to the social contract of the scientist which states that research should be undertaken with the intent of sharing findings with the scientific community, sponsors and the public. The two statements are: 1) "The investigator must accept that publicly supported research is intended to yield public benefit; personal gain, financial and otherwise, should only be incidental and not at the expense of the public benefit"; and 2) "Research that is entirely privately supported maybe to yield private benefit, but the responsibilities of the investigator are, with few exceptions, the same as for the investigator with public funding." It follows from this that industry or privately funded research should follow the same accepted laboratory and research practices, including all the elements of proper design, conduct and reporting, as publicly funded research (2,3).

Trial Design

The immediate and long-term objectives of the research should be clearly formulated and presented in a research protocol that must receive approval by an Institutional Review Board (IRB) operating in conformance with the regulations of the Department of Health and Human Services. All investigators and IRB members are obliged to disclose any conflicts of interest, financial and otherwise, that exist. This is the only way to guarantee the protection of the rights and welfare of human subjects (4), assure the humane use of laboratory animals (5) and protect the safety of self, co-workers and the environment (6,7).

The study design must effectively address the scientific question and minimize the likelihood of incorrect or misleading results. Estimates of therapeutic benefit on clearly specified endpoints must be realistic and based on other similar investigations, pilot data, appropriate meta-analyses or properly analyzed observational studies to the extent they exist. This well known tenant of trial design has relevance to both industry sponsored and publicly funded research because it is on

"estimates of benefit" that sample size is based which in turn determines the budget that must be allocated to the study.

Data and Safety Monitoring Boards (DSMBs)

Influenced by the example and favorable impact of DSMBs on the conduct of clinical trials funded by the National Institutes of Health, it has now become axiomatic that conventional clinical trials that involve patient risk require a properly assembled DSMB (or a similar independent body charged with the responsibility of periodic review). These Boards serve as a safety net both for society at large and the investigational subjects in particular where their primary goal is to serve as the conscience of the study in ensuring patient safety and the quality of the clinical study itself. The Board should include members with expertise in medical ethics, biostatistics, as well as the medical issues relevant to the subject and clinical trial expertise.

The National Heart, Lung, and Blood Institute (NHLBI) recently developed new guidelines for the operation of DSMBs (8) that specify the Board will regularly monitor the data from the study, review the quality of performance of its operations and, as appropriate, make recommendations to the principal investigator and sponsor with respect to:

- Performance of the individual centers (including possible recommendations to be taken regarding any center that performs unsatisfactorily)
- Interim results of the study for evidence of efficacy or adverse effects
- Possible early termination of the study because of early attainment of study objectives, safety concerns or inadequate performance
- Desirability of proceeding to a full-scale trial upon completion of the initial or pilot phase, when appropriate, and
- Possible modification of the study protocol

This Task Force believes these guidelines, which specifically apply to government-funded clinical research, are applicable to privately funded research when processes are not already subject to regulatory controls. In addition, DSMBs should also assume the responsibility of determining the relevance of emerging data from other trials.

The responsibilities for review, interpretation and recommendations based on highly confidential data gives rise to great sensitivity within the cardiology and clinical trials research community to the critical importance of avoiding conflict of interest or the appearance thereof. Much has been written about conflict of interest in science and medicine (1) and there are those who debate it as an issue largely in need of financial disclosure. In the matter of DSMBs we would subscribe to the conflict of interest statement generated by the NHLBI and acknowledge that it extends to matters relating not only to industrial relationships but to professional and scientific conflicts as well (9). David Blumenthal (personal communication, March 1998) has pointed out that 54% of research is now supported by industry in the United States and that the collaboration of life science faculty from the academic medical center with the businessperson from venture capital often beget valuable products of research (10). These include lucrative patents, valuable trade secrets and potential great wealth for investigators, all of which may serve to increase the likelihood of bias and lower the barriers for fraud. The moral imperative for handling fraud, however, has always been clear.

Less clear are the answers to some of the continuing questions arising from clinical research regardless of funding source, such as:

- How many more patients do we need to put at risk?
- How do you apply stopping rules when one variable is both a marker of safety and an endpoint variable?
- In those pharmacologic or procedural studies where bleeding is an acknowledged risk, how many transfusions should be considered excessive? What number is acceptable?
- What is the equitable way of arriving at stopping rules for futility?

The answer to these questions in an individual study can only be determined by an assessment of the potential risks and benefits by a knowledgeable independent body, free of bias and conflicts of interest.

Reporting of Research

Investigators are responsible for reporting research clearly, accurately, completely and honestly. As much care must be devoted to identifying and reporting data that reject the hypothesis being tested as is given to identifying and reporting data that support it. Research results should be reported in a timely fashion and in the formal literature of science as well as at its scientific meetings.

As biomedical scientists and trialists are increasingly entering the world of for-profit commerce, publishing the results of negative trials or results that may be interpreted as unfavorable for the sponsor are giving rise to deep concern. There are increasing experiences of investigators confronting opposition and even suppression of the publication of trial results that are deemed unfavorable "in the marketplace" (11). Here the investigator should obtain a clear expression of what the publication policy *will be in writing before undertaking sponsored research*. Such an understanding should clearly indicate full access to all pertinent data, without restriction by the investigators.

Patient Data Confidentiality

The security and confidentiality of clinical information on patients has been the focus of numerous legislative initiatives at the federal and state levels (12). There has been an increasing tendency to restrict access to identified patient data for any reason. Clearly, there are good reasons to protect patients who may see their lives severely disrupted by the

malicious or accidental release of such highly confidential information. There have been cases where insurance companies and employers have used medical record information to deny insurance coverage or employment. Thus, the fear of being identified may cause patients to avoid seeking care.

The Task Force recognizes the debate centering upon the need to track patients over spans of time and at the same time assuring patient confidentiality. In order to do this, the investigator must take appropriate measures to protect the privacy of individuals, to ensure confidentiality and to prevent harm to participants in research studies.

These issues present important ethical and legal considerations that are likely to be discussed in the forthcoming report of the National Committee on Vital and Health Statistics (NCVHS).

Background to Genetics

Medical bioethics is usually revisited when major changes occur such as development of a new disease or a new therapy. The recent application of the techniques of molecular biology in medicine, and in particular in molecular genetics, is expected to revolutionize both the diagnosis and treatment of many diseases including cardiovascular disorders. The impact of procedures such as genetic screening for risk factors will probably exceed that of any previous major change in health care (including health maintenance organizations). It is threatening to affect major safety umbrellas of society, such as life and health insurance and employee rights, or may even influence selection of one's marriage partner. Some have referred to it as the civil rights issue of the 21st century. Molecular biology had its founding in 1953 by Watson and Crick (13), but the birth of modern molecular biology is usually attributed to the 1970s (14). It was then that the techniques evolved to generate recombinant DNA molecules and to clone multiple copies of a specific DNA fragment. The era of genetic engineering was born and has essentially undergone exponential growth since that time. Molecular genetics was specifically boosted in 1978 (15), with the development of more convenient chromosomal markers and greatly accelerated in 1989 with the development of short tandem repeat markers that spanned the human genome and could be detected in hours by polymerase chain reaction (PCR) rather than days, as was necessary with previous markers using Southern blotting. These advances together with improved computerized techniques made it possible to map the chromosomal location (locus) of a gene responsible for disease even in a small family (7 to 10 living affected) without the necessity of knowing the specific etiology or responsible protein. PCR provides a means of within 3 to 4 hours of obtaining 1 million copies or in 24 hours of 1 billion copies of a DNA fragment, which significantly upstages cloning with a maximum capacity of 1 million copies and requires days to weeks. The expected rapidity and the impact are well subtended by the statement of Leroy Hood during his plenary address of the 1991 Annual Scientific Session of the American College of Cardiology: "appropriate application of the techniques of molecular biology and genetics will advance cardiology more over the next 20 years than has occurred in the preceding 2000." This was appropriately balanced by Francis Collins, Director of the Human Genome Project, in his statement "Genetic testing has the potential to revolutionize medicine. But revolutions can have casualties."

Human Molecular Genetics and Its Progress

In the late 1980s the National Institutes of Health (NIH) and the Department of Energy (DOE) conceived a mammoth project to be referred to as the Human Genome Project (HGP) (16). The goal of the HGP initiated in 1990 was to sequence the whole of the human genome by 2005. The genome refers to the DNA inside the nucleus of a cell which contains all of the genes required to make a human being. The number of genes responsible for a human being is estimated to be between 50,000 and 100,000. The human genome consist of multiple copies of four bases—adenine, thymidine, cytosine, and guanine—each of which is attached to a sugar deoxyribose and a phosphate group which in turn are strung together in a linear sequence. The sequence whereby these four bases are joined together determines the information to be passed on to the next generation. The number of bases in a gene probably averages 20,000 but varies from a few thousand to millions. The DNA of the human genome is contained in 23 chromosomes; 22 are paired with a duplicate homologous chromosome and the remaining unpaired are the X and Y, giving a total of 46. Each chromosome is a single DNA molecule. Although ones speaks of one human genome, there is of course many human genomes since there is enough variation in the sequence of the DNA from one individual to the other to make each genome unique. It is this unique sequence of each genome that is exploited in forensic medicine and in many other situations. Nevertheless, the sequence difference from one individual to another is extremely minute, with less than one unique base in every 1000, the reciprocal being 99.9% of the DNA sequence is identical. Given there are 3 billion base pairs in the human genome, the sequence difference accounting for the difference among all humankind is at maximal a total of only 3 million base pairs. It is likely that many of these changes (mutations) are of minimal significance or occur infrequently, thus, frequent significant mutations may number only a few hundred thousand. Once these are known (which is only a few years away), detection should be feasible and rapid. The HGP has several interim subsidiary goals such as developing a genetic map with landmarks every million base pairs. This was completed ahead of schedule in 1994 with over 5,000 markers spanning the chromosomes separated by only 700,000 base pairs. A second goal was development of a physical map in which unique sequences of 100 to 300 base pairs would be identified every 100,000 base pairs referred to as sequence tagged sites (STS) to be completed in 1998. Since only about 5% to 10% of the available DNA exits the nucleus to code for protein (expressed), another goal was to tag every 100,000

bases of the expressed DNA by identifying 100 to 200 unique sequences referred to as expressed tagged sequences (ESTs) as opposed to the STS which may or may not be expressed. Over 50,000 such expressed genes have been in part cloned, tagged with ESTs, and stored in various bacterial libraries. A worldwide computerized gene bank has been established for information accessibility. The overall project is considered ahead of schedule by at least two years (2003 vs 2005). It is highly likely that if the exponential growth continues, the project will be completed even earlier. The date of completion is almost irrelevant to the ethical issues since thousands of genes will be identified by the year 2000 and for most, the function will be unknown.

It will represent a new paradigm in medicine, namely instead of searching for the etiology of a disease, there will be thousands of etiologies (genes) searching for a disease. There is an intense thrust behind the HGP since it is assumed that a host of benefits (diagnosis, therapies and products) will automatically follow in the wake of sequencing the human genome. The biotechnology industry is already a multibillion dollar concern; the use of DNA in the courts is now permissible and routine. The success of the HGP, namely, the development of a genetic map, a physical map, a worldwide gene bank, was equally matched by the success of independent investigators who rapidly and wisely took advantage of the new information. This has accelerated not only the identification of genes responsible for disease but also the development of promising forms of therapy. The European age of discovery of our earth by notable explorers such as Vasco da Gama and Columbus was continued with man's search to understand the earth's atomic and subatomic structure. The HGP is an equivalent search to understand life and oneself by discovering the fundamental blocks that design the body structure and implement the many functions that must be integrated to respond appropriately to the environment. In an attempt to dramatize the HGP, it has been compared to that of the Manhattan Project (the atomic bomb), or the Apollo Project (man on the moon). While all of these projects gave rise to a new body of information and spurred a new set of societal, legal and ethical concerns, the effects of the HGP on each individual will be much greater, the nature of which will be unlike any previous revolution. There is little doubt that decoding all of human genes will represent a giant step toward unraveling the mysteries of life.

The alphabet of DNA is simple, consisting of only four letters, referred to as A, C, G, and T, which correspond to adenine, cytosine, guanine, and thymidine. Proteins have a slightly more complex alphabet of 20 letters which refer to the building blocks of proteins, namely the 20 amino acids. Nature devised a universal translation code to go from DNA to protein whereby messenger RNA (single-stranded) copied from the DNA leaves the nucleus with the sequence of bases that in turn codes for the amino acids and the sequence whereby they are joined together in the protein. Each amino acid is encoded in a condon of three bases together with start and stop condons. It should be evident that any mutations that cause disease must affect the amino acid sequence of the protein to have an effect on function. The genes remain aloof from plebeian activities but by being responsible for the regulation and synthesis of proteins are also responsible for all of the body's activities.

Patterns of Inheritance Relevant to Genetic Testing

Unfortunately, inherited diseases do not follow a single pattern and do not affect both sexes to the same extent. The complexity of even simple Mendelian inheritance makes genetic testing less straightforward than desired. Diseases due to a single gene referred to as monogenic disorders follow Mendelian inheritance while those due to multiple genes, referred to polygenic disorders, do not follow Mendelian inheritance. Single gene disorders are classified as autosomal dominant, autosomal recessive, or X-linked. Everyone has two copies of each gene; however, in autosomal dominant despite only one gene being mutated, it is enough to induce the disease, hence the name dominant. Diseases inherited as autosomal dominant (AD) have vertical transmission affecting each generation with 50% of the offspring having the gene and affects males and females equally. In contrast, recessive disorders require both genes to be mutated to get the disease, which introduces the term "carrier," meaning that someone who has an abnormal and a normal gene will not get the disease, but if they mate with a spouse that is a carrier and produce an offspring, 25% will have the disease, 50% will be a carrier, and the remaining 25% will be normal. The transmission is not vertical and thus a generation may occur without anyone having the disease. In X-linked disease, the female seldom develops the disease (has two X chromosomes) while the male having only one copy of the X chromosome almost always develops the disease. Inherited diseases of the mitochondria are unique in that the mitochondria has its own DNA which makes 37 genes in the human. However, the mitochondrial DNA can only be obtained from the female since mitochondria are absence from the sperm. Thus, familial disease of mitochondrial DNA must have a maternal origin, but once inherited, affects both males and females and may be recessive or dominant. The monogenic disorders are further complicated by the terms referred to as penetrance and expressivity. Penetrance is defined as the percentage of individuals with the mutant gene who develop the disease. The penetrance of genes can vary anywhere from 30% to 100%. Expressivity refers to the marked variation in clinical features manifested by the same gene or even the same mutation.

The relevance of this information with respect to monogenic disorders for genetic screening is illustrated by an autosomal dominant disease such as hypertrophic cardiomyopathy (HCM). In this disease, despite having the mutant gene, most individuals have no feature of the disease until after puberty and other individuals may not develop any feature of the disease throughout their lifetime. Secondly, even with the

JACC Vol. 31, No. 5
April 1998:917–49

same mutation within the same family, there is marked variability with respect to the severity of the disease, the incidence of sudden death, the number of clinical features manifested, as well as the length of their lifespan. It is the rule in autosomal dominant disease that clinical features are not manifested until the second, third or fourth decade of life. In conjunction with all of these considerations, it is now necessary to take into account that even for monogenic disorders, other genes referred to as modifier genes can play a pivotal role in whether they develop the disease and the extent and severity. In the case of HCM, if one happens to also inherit the DD allele for the angiotensin-converting enzyme gene as opposed to the II alleles, the extent of cardiac hypertrophy is much greater with the former and the incidence of sudden death is significantly increased. Similar modification is observed with the alleles of endothelin gene and as we identify the thousands of genes that are routinely used to maintain the heart as an organ, we can anticipate many modifier genes for most monogenic disorders. Gene to gene interaction is in part responsible for the variation in penetrance and expressivity of a particular mutation within the same family. Lastly, we must consider the influence of the environment. Interaction of the primary causative gene and its modifier genes with the environment plays a major role in the developed phenotype (clinical features). This is dramatically demonstrated in the case of familial HCM (FHCM) due to beta-MHC (17). beta-MHC is abnormal throughout the heart (right and left ventricles) and in over half of the skeletal muscles, yet the disease is virtually confined to the left ventricle. The development of the high pressure in the left ventricle exploits the propensity of the mutant beta-MHC gene to develop left ventricular hypertrophy, whereas the work load in the right ventricle or skeletal muscles is unable to do so. In determining genetic risk, it is necessary to consider not only the primary mutant gene, but gene modifiers, environmental risk factors, and the natural history of the disease associate with a particular mutation.

While simple monogenic disorders exhibit several caveats to be considered for genetic screening and diagnosis, the complexity of the polygenic disorders cannot yet be anticipated due to our lack of knowledge in this form of inherited disease. These are disorders which we think make up 60% of all human disease. They require multiple genes coordinated together to induce the disease. One example is atherosclerosis, where we know that many components enter into the ultimate phenotype of myocardial infarction and death. It is known that smooth muscle proliferation is a component, as are accumulation of macrophages and their inflammatory cytokines, the development of thrombosis and altered vasomotor tone. Thus, multiple genes are involved with multiple distinct functions that must come together within an individual and frequently will only manifest the disease if interacting with the appropriate triggering environmental factors (smoking, high cholesterol). Genetic testing for polygenic disorders is in its infancy at this time but will inevitably be resolved to play a major role in risk stratification in the near future.

The Need for Widespread Education in Genetics

Education of the cardiovascular physician and allied health personnel in the fundamentals of molecular genetics together with the implications for genetic diagnosis, testing and counseling is recommended as essential. It is recommended that the American College of Cardiology (ACC) take a leadership role in providing such educational programs. Recent surveys show that most professionals do not have the knowledge or necessary background to integrate genetics into clinical practice. It is estimated that less than one third of physicians ordering genetic tests are capable of interpreting their results. Since genetics is extremely new to cardiology, it is more likely to be only 5% to 10% who have any understanding of genetic testing. As genetic tests and therapies become available, there will be too few genetic counselors and medical geneticists to meet the demands for present-day testing and services let alone what it will be in the year 2000 (18).

The Ethical, Legal and Social Implications of the HGP

It was recognized from the very beginning by Jim Watson and his colleagues that the HGP would require a parallel formal initiative to anticipate the ethical, legal and societal implications (ELSI) of this dramatic paradigm. The NIH allocated 5% of the HGP budget for ELSI and the DOE 3% of the HGP budget. The ethical, legal and social concerns have previously been addressed on a case by case basis. The accelerated pace of new discoveries from HGP beckons a more global approach. This led to the creation of ELSI which is a grant-making and policy-making body within the NIH. A detailed review of the HGP and ELSI has been prepared by the U.S. Department of Energy and the Human Genome Project and made available on the Internet *(http://www.ornl.gov/hgmis/tko/)*. The HGP will inevitably lead to widespread genetic testing that will be faster, cheaper, more accurate and applicable to a multitude of human diseases. The problems related to research in the field of molecular biology and genetics such as gene therapy were anticipated very early. In 1975 the National Academy of Sciences formed the NIH Recombinant DNA Advisory Committee (RAC) which was created to oversee and approve the safety of experimentation in molecular biology and genetics. In a commission led by Congressman Albert Gore, Jr., the distinction was made between gene therapy for somatic cells and that of germline cells. This brought to the forefront that gene therapy was not morally different from other forms of experimental therapies as long as it did not involve germline cells. This was interpreted to mean that gene therapy should not involve eugenics. The recent bill in 1997 by President Clinton upstaged this by establishing that any attempt to clone a human being would be illegal. The recommendations by RAC pertained to research which together with those outlined for research in general (1991 Bethesda Conference and the preceding discussion)

continue to provide necessary guidelines for research in this arena. The working group for ELSI developed an agenda which has as its main goals as follows: 1) stimulate research on issues through grant making; 2) refine the research agenda through workshops, commissioned papers and invited lectures; 3) solicit public input; 4) provide massive education through multiple media including the Internet; and lastly, 5) encourage international collaboration. A major objective would be to develop policies regarding professional, institutional, governmental, and societal levels to ensure that genetic information would be used to maximize benefit to individuals and society. Three issues were identified as particularly important: privacy of genetic information, safety and efficacy of new testing options and fairness in the use of genetic information. Nevertheless, as indicated by the group at the time, ELSI has no authority to effect policy and no privileged route to communicate the information it would gather to the national policy arena.

Protecting the Privacy of Genetic Information

A central and major problem to be solved is maintaining confidentiality on genetic information acquired by the physician or otherwise (19). While confidentiality of information exchanged between physician and patient have been relatively protected, there have been no formal legal measures to protect this information from getting into the hands of third parties such as insurance companies. The "perils" of the loss of insurability and employability together with the stigmatization that may follow if genetic information is available to third parties such as life insurance companies, medical insurance companies, and employment agencies could be frightening. There is certainly no question that genetic screening for risk factors whether it be the long QT syndrome, Alzheimers disease or hypertrophic cardiomyopathy, raises many important and difficult issues. The problems are real. They are here now. Attempts in several states have been made to prohibit genetic discrimination.

State and Federal Legislation/Regulation

In 1975, North Carolina passed legislation prohibiting employers from discriminating against individuals with the trait or the disease of sickle cell anemia (20), and four other states have passed similar laws. In 1989, Oregon made it unlawful for an employer to subject an employee to different types of tests such as a breath analyzer (21). While genetic screening was not mentioned, it is conceivable that it might be interpreted to include such a test in 1997. In 1991, Wisconsin prohibited workplace discrimination by prohibiting the employer access to genetic test results (22). Wisconsin's criminal code also specifically makes it unlawful to disclose genetic information without written and informed consent of the individual (23). New Jersey went a step further and prohibits retaliation by employers if an employee refuses to take a genetic test (24). In the state of New York an employer may require a specified genetic test as a condition of employment where such a test is shown to be directly related to the employer's job or occupational environment. Recently, several federal initiatives have been developed by the Equal Opportunity Employment (EOE) Commission to prevent genetic discrimination. One bill typifying the contents of these initiatives was that introduced by Domenici entitled *To protect the genetic privacy of individuals and for other purposes* (S. 1895, June 24, 1996). All bills concerning genetic privacy and discrimination were defeated in 1996. Five separate pieces of legislature dealing with genetic information confidentiality and privacy have been introduced in 1997 and are now being considered by Congress. A major concern of the Domenici bill in 1996 was the proclamation that the DNA sample remain the property of the individual and could be withdrawn or eliminated at the will of the individual. This would significantly curtail genetic research. The 1997 bill by Domenici (bill 422) is much improved and no longer states the DNA sample should be the property of the donor. Anonymous use of the sample prospectively or retrospectively is not restricted.

NAPBC and ELSI Group Recommendations

A major concern of the various attempts by federal agencies to protect the individual's privacy is they may also deny the individual and society the benefits of genetic testing. Thus, the hereditary susceptibility working group of the National Action Plan on Breast Cancer (NAPBC) coordinated by the PHS Office on Women's Health, recently joined with the NIH/DOE ELSI group to address the issue of genetic information in the workplace. It is hoped that in the future, legislative and regulatory strategies to address discrimination and privacy in the workplace will be considered along the NAPBC and ELSI Working Group recommendations recently published in *Science* (25). These recommendations are indicated below:

1. Employment organizations should be prohibited from using genetic information to affect the hiring of an individual or to affect the terms, conditions, privileges, benefits, or termination of employment unless the employment organization can provide that this information is job related and consistent with business necessity.
2. Employment organizations should be prohibited from requesting or requiring collection or disclosure of genetic information prior to a conditional offer of employment, and under all other circumstances, employment organization should be prohibited from requesting or requiring collection or disclosure of genetic information unless the employment organization can provide this information is job related and consistent with business necessity, or otherwise mandated by law. Written and informed consent should be required for each request, collection or disclosure.
3. Employment organizations should be restricted from access to genetic information contained in medical records re-

JACC Vol. 31, No. 5
April 1998:917–49

leased by individuals as a condition of employment, in claims filed for reimbursement of health care costs, and other sources.
4. Employment organizations should be prohibited from releasing genetic information without prior written authorization of the individual. Written authorization should be required for each disclosure and include to whom the disclosure will be made.
5. Violators of these provisions should be subject to strong enforcement mechanisms, including a private right of action.
6. The Task Force recommends genetic testing be made available to individuals in the context of clinical investigation and research, however, the information obtained must remain available only to the patient, physician, and investigator. Information must not be made available to any other party or individual.

It is hoped that these recommendations will stimulate a comprehensive approach to address genetic privacy and discrimination not only in the workplace but also in research genetic testing and for group and individual insurances. It must be appreciated that just as the science of genetic screening and gene therapy are rapidly evolving, so will the legislature and ethics evolve to protect both societal and individual rights. The sensitivity and potential devastating effects of genetic risk stratification must, by its very nature, be analyzed by many legislative groups before a final decision can be expected.

Genetic Diagnosis and Screening

There is consensus on certain rules that must be followed in performing genetic testing as follows: 1) informed written consent must be obtained prior to obtaining the sample; 2) genetic testing must not be performed unless accompanied with genetic counseling; and 3) every effort should be made to provide the necessary education in terms understandable to the concerned individual. There is not, as yet, any consensus on who should undergo genetic testing, how to protect the privacy of the results, and how this information will be applied in the routine practice of medicine. Presently, most genetic testing in cardiology is performed as research and as such is regulated by RAC and the local Institutional Review Board. In discussing who should undergo genetic testing, one other question that must be asked, will it affect the natural course or overall management of the disease? Prevention and treatment often follow more widespread application of diagnostic testing, but genetic testing because of its potential stigmatization and other deleterious effects, cannot perhaps be performed so freely.

Task Force Recommendations

The following guidelines are offered for the evolving debate on the clinical, educational, ethical, social and legal issues regarding genetic testing: 1) The use of genetic testing and diagnosis as a research tool should continue along the guidelines outlined for research. 2) Genetic testing (usually prenatal) for devastating fetal disease or early onset disease, such as Down syndrome, is performed routinely and should be continued. It has been shown if the results are positive whether the parents seek an abortion or not the information provided is considered beneficial. 3) Use of genetic testing in someone with a phenotype to confirm or exclude a genetic cause, should be permitted. An example would be FHCM with concomitant hypertension. 4) In families with a known history of a familial disease, genetic testing when sought by a family member should be performed. Testing of other members of the family should be performed only at their request. 5) Testing at birth or during childhood for asymptomatic disorders that develop later in life remain investigational until more data are available. Should one test for hyperlipidemia which is associated with morbidity and mortality in the third, fourth or fifth decade? While there is no specific therapy to cure the defect, the use of appropriate diet and lipid-lowering agents particularly when implemented in early adolescence or even as a child, are likely to markedly decrease morbidity, prolong life and possibly bridge the gap until a more appropriate cure arises. Such disease would benefit from genetic testing prior to adolescence as well as providing the opportunity for genetic counseling with respect to marriage or having children. Should someone screen at birth for a recessive disorder in the parent? If one parent is positive, the other parent must be checked and if both are positive, such as for Tay-Sachs' disease, then the choice is whether they should have a child or if they wait until one child is born then genetic testing would provide advice as to whether they should have other children or consider the use of a surrogate mother or father. Others would argue that with results of genetic testing parents can be advised about future pregnancies and the genetic risk of recurrence. Nevertheless, testing for late-onset diseases at birth, although increasingly possible, is often not recommended unless preventive treatments exist. It has been customary not to perform genetic screening in high school students unless there is an immediate medical benefit. However, recent studies from Montreal and Hong Kong show that genetic screening during high school has successfully decreased the incidence of Tay-Sachs disease and beta-thalassemia. A major issue facing the cardiovascular disorder of FHCM, the most common cause of sudden death in the young, particularly in the athlete, is whether athletes at the high school and college level with a family history or suspected HCM phenotype should be screened prior to participating in competitive sports.

Medical Insurance

Medical insurance cannot be determined on the presence or absence of disease risk. It does indeed beckon the need for a universal health insurance program. If genetic risk is assessed as priority for medical insurance, it would be devastating and inhuman. This must be interpreted in the context of having available all of the genes for humankind, which would leave

legitimately or illegitimately a significant proportion of the population uninsured and stigmatized.

An Overall Recommendation

The beneficial effects of the application of the techniques of molecular biology cannot be overestimated at this time. We must, therefore, follow the advice of Thomas Jefferson, one of the founding fathers of America when he said: "We must continue to pursue truth but with reason." Others might say it is more judgment we need than reason.

Appendix

Case Studies for Task Force 3

Case 1. A 13-year old world-class gymnast has experienced several episodes of syncope while performing. She has a long QT interval. You recommend that the patient refrain from competitive sports and receive appropriate therapy. The parents and child decline to follow your advice.

What is the physician's obligation?

Case 2. Clinical trial of a cardiovascular drug. A preliminary trial demonstrates significant benefit. Two years into the main four-year trial, the DSMB ascertains that there is significant harm in the treatment group and recommends that the trial be stopped. The principal investigator refuses, arguing that this is a "statistical quirk."

What are the ethical issues? What processes should be followed?

Case 3. A large multicenter study of an established cholesterol-lowering agent shows equivocal to negative results. The sponsor elects not to publish the results.

What is the appropriate response of the principal investigator?

What is the role of the DSMB?

Case 4. The DSMB of a large study evaluating a promising agent that prevents restenoses following interventional procedures notes halfway into the trial that there is an excess of bleeding complications in the group receiving the active agent. One month earlier, a European study of a related agent was published, showing a significant reduction of the restenoses rate, with an increased but acceptable rate of bleeding complications.

How should the DSMB evaluate and respond to this situation?

Case 5. A young man 17 years old comes to the family physician accompanied by his father, who has been informed by the school physician that his son may have an enlarged heart and should be seen by a cardiologist. Examination of this young man and Doppler echocardiography show that he has familial hypertrophic cardiomyopathy (HCM). In addition, the mutation is shown to be Arg^{403} Gln, which is associated with a high incidence of premature sudden death. Electrophysiologic testing shows that unifocal ventricular tachycardia is inducible with a single stimulus. An indwelling defibrillator is recommended together with genetic counseling that includes examination of the rest of the family. However, the family physician feels that it is a "bit too much to insert a pacemaker for someone at this young age." Approximately 10 days later the young man is found dead in bed by his father, who within hours contacts the genetic counselor who then informs the family physician of this event. We know that there is another 15-year old at home who is playing football.

Is the family physician liable for negligence? Is it the responsibility of the cardiologist to insist that the rest of the family at home be evaluated for HCM and/or undergo genetic testing? Is the cardiologist liable for allowing the person to go home without the ICD? (P.S. One of the siblings did have familial HCM and did have a defibrillator inserted two days after his brother's funeral.)

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