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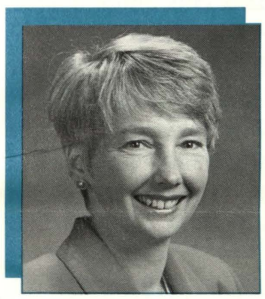
Ethics committee responds to professional and patient concerns

Looking for solutions to ethical problems in the clinic

Ethics



Rebecca Pentz is a clinical ethicist and associate professor of clinical ethics in the Office of the Vice President for Patient Care

Some terminally ill patients favor the right to die. Others demand heroic, extraordinary care to stave off death as they await a medical miracle. As medical technology creates support systems that can sustain life when there is no hope of recovery, physicians find themselves confronting choices that depend far more on moral values than on medical knowledge. Is it right to use a ventilator to prolong a painful death? Is it right to let a patient terminally ill with AIDS die of a curable pneumonia? To help physicians serve patients and protect their patients' rights, Rebecca Pentz, Ph.D., clinical ethicist at The University of Texas M. D. Anderson Cancer Center, trained a Clinical Ethics Committee to provide counsel in tough situations.

Clinical ethics, a relatively new field, is a discipline that examines the ethical implications of medical decisions in very practical situations. Physicians are trained to evaluate what is best for a patient from a medical standpoint—predicting the probable course of a disease and the chance for the patient's recovery. Although a concern for ethics has always governed the obligations of physicians, Pentz pointed out that clinical ethics can help physicians apply bioethical principles to modern dilemmas. These principles mandate the use of medical treatments that provide more benefit than burden to the patient, the right of the patient to decide for or against any medical treatment, the right for a legal substitute to determine treatment for a patient who lost or never had autonomy, and the duty of health care professionals to act with fairness in giving every individual judicious care.

Code of Ethics

In 1982, Charles LeMaistre, M.D., president of M. D. Anderson Cancer Center, appointed a committee, co-chaired by Jan van Eys, M.D., and James Bowen, Ph.D., to begin development of a code of ethics. Two years later, after input from employees, patients, and patients' families, M. D. Anderson became the first major cancer center to adopt a set of ethical principles as a standard against which professionals could evaluate medical and nonmedical decisions. The goal guiding these principles is the care of patients with cancer in an environment dedicated to the prevention and eradication of the disease.

Clinical Ethics Committee

M. D. Anderson was one of the first institutions in which policies for managing patients with end-stage disease evolved. According to Michael S. Ewer, M.D., associate professor of medicine in the Cardiology Section, Department of Medical Specialties, "Because of the desire not to burden patients or families in cases of medical futility, mechanisms for removing terminally ill patients from life support systems were evolved in the intensive care unit in the early 1980s." Ewer, as medical director of the intensive care unit, proposed in 1989 that a "decision triangle" be used to balance the desires of patients and families, the recommendations of a health care team, and the medical appropriateness of a life support system. When the argument for or against intervention with a life support system is clear, physician input increases, but in the absence of a medical community consensus, patient and family input increases. Lester J. Peters, M.D., professor and head of the Division of Radiotherapy, emphasized in an article in *Oncolog* in 1990 that "unless a physician involves the patient in the decision-making process, the physician may not be giving the patient the treatment he really wants." Ethical problems cannot be solved within the walls of the clinic only.

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"...the very structure of the Clinical Ethics Committee ensures that any specific question is examined from several viewpoints."

For this reason, in June 1993 M. D. Anderson formed an expanded ethics committee to deal with dilemmas in life-threatening situations, as well as to provide institution and community education and to revise ethically sensitive policies.

The standing ethics committee is an interdisciplinary group of 21 members: eight physicians, eight nurses, and five allied health professionals (one each from social work, patient advocacy, legal affairs, chaplaincy, and inpatient management services). Because of the multiple disciplines represented, the very structure of this committee ensures that any specific question is examined from several viewpoints. In addition to their professional training, each member of the committee completes mandatory training in bioethics. Pentz outlined the required training: "An in-depth knowledge of the history of bioethics, the philosophy of bioethics, and the current literature must be mastered." Working under the guiding principles introduced by the 1984 Code of Ethics, three members of the Clinical Ethics Committee are always on call and can—within 20 minutes—consult with the health care team round-the-clock concerning the ethical principles of a case.

The committee examines the sorts of treatments available, the complications and risks involved, and the anticipated results on a case-by-case basis. Although about three quarters of referrals to the committee are initiated by physicians, other health care workers or patients' families can refer a decision to the committee. Ordinarily, both the attending physician and the patient's nurse must be present at the consulting session. The patient's family must be present if a member of the family has requested the advice, but the attending physician may request that the patient's family attend any session.

Because health care providers encounter conflicts between value systems, the committee's goal is to provide the tools necessary to clarify medical and moral issues by proposing different ways of thinking about the choices available. Pentz explained that M. D. Anderson's Clinical Ethics Committee is trained to search for the best conduct in ethical dilemmas by approaching the choices with a standard procedure. Dr. Pentz described the process: "After gathering all the facts we can, we first review the ethical principles that might apply to the case. If there are analogous cases, we also review them. We state the options and weigh the benefits and the burdens of each option. Then we make a recommendation suggesting an option that is best for this particular patient in this particular circumstance."

Patient values guide committee's decisions

Religious, cultural, and family values are given priority in the decision-making process of the committee. Thus, decisions that were previously the sole responsibility of the physician are now shared with the family. Because patients treated at M. D. Anderson come from diverse geographic locations and ethnic groups, physicians encounter a wide variety of cultural responses to life-threatening situations. Pentz explained: "Some individuals want the physician to make the decisions in a life-threatening disease; others refuse to take advantage of modern technology, even when they know it significantly lowers their risk; and some families want both the hospital staff and the physician to lie to the patient."

Patients' families do not always recognize the physician's obligation to give complete information to very ill patients. These families prefer to protect their loved ones and so object to "truth-telling" in life-threatening circumstances. Pentz said that studies have shown that patients do better when they know the likely outcome of their disease, even when that outcome is a bad one. In one study on Huntington's disease, the group that did worst was the one composed of patients in whom genetic information was insufficient to determine whether or not the disease would develop—even worse than the group composed of those informed that they would be victims of the disease. Because of studies such as these, the Clinical Ethics Committee always errs on the side of truth. The exception would be when an individual, perhaps for cultural reasons, autonomously chooses not to know. "Even then we would have to be convinced that the choice not to know the truth was autonomous," stated Pentz.

Avoiding futile or inappropriate care

Despite technological advances, clinicians have no responsibility to offer or to provide treatments that are not medically indicated. Pentz stated that

although some patients and their families have become more knowledgeable about their rights to determine whether to accept a specific medical treatment, they often lack essential medical knowledge and demand medical procedures that are inappropriate for their disease. Although the physician sees the medical futility of a certain procedure, he or she is caught between the family's wishes and medical expertise. The result of this tug-of-war can be a patient who lies in a persistent vegetative state. Pentz described the case of a patient at another institution who remained alive through resuscitation, ventilation, and artificial hydration for 33 years. To avoid a similar situation, the bioethics committee can mediate between caregivers and families in decisions regarding medically futile treatments. As part of its policy responsibilities, the Clinical Ethics Committee is joining a consortium of Houston hospitals to draft a policy on medically futile and inappropriate care.

The difficulty of making life and death decisions is magnified when patients are unable to speak for themselves and surrogates must be consulted. To represent the wishes of patients as accurately as possible, M. D. Anderson's Clinical Ethics Committee assists in identifying the person most likely to know the patient's intentions in a tragic circumstance. The legal surrogate, when not predesignated by a durable power of attorney for health care by the patient, is specified in order of priority by Texas statute: first, a patient's spouse; next, an adult child of the patient who has the waiver and consent of all other adult children to make the decisions; a majority of the patient's reasonably available children; the patient's parents; the individual the patient clearly identified to act on his or her behalf before the patient became incapacitated; the nearest living relative; or, finally, a member of the clergy. The legal surrogate, however, is not always the person the attending physician feels speaks best for a patient. In one tragic case, Pentz related, the physician felt that the legal surrogate did not have the patient's best interest in mind, so an ethics consultation was called. The consultation team recommended that the health care team work on an interim basis with the person who did best represent the patient, an ethical surrogate, while the transfer of legal surrogacy was pursued.

Another frequent area of conflict is the area of the living will. Living wills—although occasionally designed to be specific—are usually very limited documents that restrict extraordinary treatment measures in a patient who is judged terminally ill by two physicians when the disease is not reversible. "A family member," Pentz said, in describing a hypothetical situation, "has suffered with a terminally ill patient, and when the patient contracts pneumonia, the family member thinks enough is enough and wants to withhold treatment. The physician's medical expertise, however, judges that pneumonia is a reversible disease that he is obliged to cure." The ethics committee has frequently been called to balance conflicting values in cases such as these.

Other ethical concerns

The Clinical Ethics Committee also addresses conflicts other than those involving patients. An ethical question that arises frequently at M. D. Anderson concerns the rights of minors selected as bone marrow donors. Although bone marrow aspiration from the hip is considered to be a relatively risk-free procedure, there is no direct benefit to the donor. Because of the possibility of side effects in donors, investigation into the value of an institutional policy that would require an automatic consultation by the Clinical Ethics Committee when the donor is a minor is under way.

At times physicians refer cases to the committee for advice when they are just unable to determine the best ethical procedure. Pentz confirmed that differences of opinion exist between professionals concerning appropriate care. An example is whether a surgeon should perform a resection if the results are cosmetically unacceptable and the chance for the patient's survival is only 10%.

Another area of ethical problems arises from the funding or reimbursement policies of health management organizations and government agencies that finance medical care. Limited resources produce questions of determining how much care is available, who gets treated, and who decides which procedures are necessary.

—Linda N. Eppich

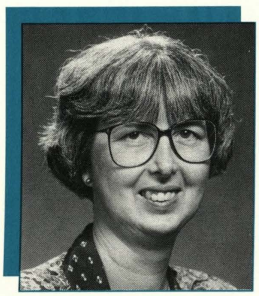
Prior articles published in *Oncolog* that describe ethical issues are "Is Malpractice Litigation Undermining Informed Consent?" (Jan.–Mar. 1990, Vol. 35, No. 1) and "Decision Making in Critical Illness: Who Knows Best?" (Jan.–Mar. 1991, Vol. 36, No.1).

Physicians who desire a copy of M. D. Anderson's Code of Ethics or additional information may write Dr. Pentz, Department of Clinical Ethics, Box 111, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, TX 77030, or call (713) 794-5727. ■

Prevention the ultimate goal

Colon cancer registry coordinates treatment, education, and research

Cancer Registries



Linda Howard is a senior research nurse in the Department of Gastrointestinal Oncology and Digestive Diseases

Webster's Dictionary defines a registry as an official record book. But a family medical registry is more. "Our registry isn't a box of data—it's air-traffic control," said Linda Howard, R.N., B.S.N., coordinator of the Hereditary Colon Cancer Registry of The University of Texas M. D. Anderson Cancer Center. "We try to identify those patients at high risk for developing colon cancer so that we can see that they receive the proper treatment, counseling, and education. It's more holistic than you would think." The M. D. Anderson registry was formed in 1988 by its medical director, Patrick M. Lynch, M.D., J.D., of the Department of Gastrointestinal Oncology and Digestive Diseases, and comprises patients with two forms of hereditary colon cancer (HCC): familial adenomatous polyposis (FAP) and hereditary nonpolyposis colon cancer (HNPCC).

Because these diseases are inherited in an autosomal dominant fashion, children who have one parent with either disease have a 50% chance of having the disease themselves. Early detection can mean the difference between life and death for people who inherit the disease. "For the most part, if you find colon cancer early, it's curable. If you find it later, there is not much you can do. And any patient who has one of the *HCC* genes and develops colon cancer is at high risk of developing other forms of cancer," said Howard. The current method of diagnosis is colonoscopy, a process too costly to use to screen the general population but well worth the price for people with HCC. "In FAP patients, we cannot remove all the polyps we see by colonoscopy, but we can watch them carefully and delay removal of the colon, which is the definitive treatment of the disease," said Howard. "In HNPCC patients, we can remove the occasional polyps we see by colonoscopy, and we can offer early medical and surgical intervention for the cancers we find."

The problem is identifying the people who have HCC, which is one of the goals of the registry. Colon cancer is the second most common cancer in the U.S., but it is usually a disease of old age, developed by people in their 60s or older. But like most hereditary forms of common diseases, HCC develops much earlier. The approximately 6% of colon cancer patients with HCC can begin to develop polyps as early as puberty.

Because physicians are not used to seeing young patients with colon cancer, these patients often go undiagnosed. "Many of these people have had symptoms for a long time, but their doctors never think to do colonoscopy, because the patients are 'not old enough' to have colon cancer," said Howard. "A big job that we have, both within M. D. Anderson and externally, is to educate physicians and all kinds of health care workers about the specifics of high-risk patients." Lynch and Howard spread the word about the M. D. Anderson registry and about recent advances in colon cancer treatment and research through the *HCC Newsletter,* a quarterly bulletin published by M. D. Anderson. The newsletter reaches about 2500 physicians, researchers, and patients worldwide.

A recent issue of *HCC Newsletter* described the cloning of the genes for FAP and HNPCC, which Howard said has made identifying people with HCC both easier and more confusing. "Since there has been a lot in the papers about the colon cancer genes, there's a lot of misunderstanding about who can be tested and what the tests can reveal," she said. There are no 100% accurate genetic tests for FAP or HNPCC. If both a parent and child with colon cancer have the same change in their colon cancer genes, the genetic change probably caused the cancer. Some genetic changes do not cause disease, however, and whether this is true for colon cancer has not been confirmed. (For more information on genetic testing and other registries, see "Familial cancer syndromes a focus of cancer genetics research," *M. D. Anderson Oncolog,* July-September 1994.) Currently about half of the index cases (first patients identified in each family) in the M. D. Anderson registry have undergone genetic testing for HCC.

How patients and others use the information they receive from genetic tests can cause problems. "One patient was denied the opportunity to upgrade a life insurance policy. It was one that he had upgraded every year or two, but this time his insurance company refused because he had HNPCC." Because of the possibility of such repercussions, the fact that a patient has been diagnosed

as having HCC by genetic tests is not put on patient records at M. D. Anderson. "We say that their families are being evaluated," said Howard, "and the information will not be given to a physician without the consent of the patient."

Referrals to the M. D. Anderson registry come from all sorts of people and places. M. D. Anderson surgeons and pediatricians refer their young patients with colon cancer, as do physicians outside M. D. Anderson who think that their patients may have a hereditary form of colon cancer. And some patients simply call the main switchboard themselves and are referred to Howard or Lynch. The registry currently contains about 125 families with confirmed hereditary colon cancer and another 50 that are being assessed. The largest has 164 members. "I know people in that family who don't know each other," said Howard with a laugh. "I've watched one set of kids grow up."

Howard's first step in assessing whether a family has HCC is to gather information on who in the family has colon cancer and to construct a pedigree, or family tree. She estimates that gathering this initial information for the average family of one colon cancer patient and five relatives takes an average of 30 hours. It is time well spent, however, because even without genetic tests Howard and Lynch can often determine from the pedigree alone who in the family has an elevated risk of developing colon cancer. Studies have shown that if a person has one first-degree relative (parent, child, sister, or brother) with colon cancer, the person's probability of developing colon cancer is 3% greater than that of people without a first-degree relative with colon cancer. If an individual has two first-degree relatives with colon cancer, the probability is 17% greater, and yearly colonoscopy is recommended.

To meet the broad range of needs of families with HCC, Lynch and Howard can call on many clinical and research professionals at M. D. Anderson, including John M. Skibber, M.D., of Surgical Oncology and Ayten Cangir, M.D., of Pediatrics for testing and treatment; Bernard Levin, M.D., vice president for cancer prevention, for suggestions on how to prevent colon cancer; Walter Baile, M.D., of Psychiatry and Ellen Gritz, Ph.D., of Behavioral Science for counseling; Susan Peterson, M.P.H., of Patient Education for educational assistance; and Marsha Frazier, Ph.D., of Gastrointestinal Oncology and Digestive Diseases for genetic testing. In turn, the patients can volunteer to participate in HCC research. The M. D. Anderson registry serves as a source of cases for clinical trials of colon cancer treatment being conducted at M. D. Anderson. One trial is testing the usefulness of sulindac, a nonsteroidal anti-inflammatory drug originally used to treat arthritis. Its efficacy against colon cancer was discovered by chance: when FAP patients took sulindac for arthritis, their polyps regressed too, delaying the need for surgery.

The knowledge that Howard and Lynch have about HCC and what resources are available for HCC patients extends outside M. D. Anderson. For instance, Howard recently assisted a family from Missouri. "It was a nightmare," she said. "They had just moved to Missouri and had no money and no insurance, and they weren't eligible for Medicaid. The woman's husband had died of colon cancer caused by FAP. He had had no family history of colon cancer but apparently had the gene for it." (Because the gene is highly mutable, said Howard, this is not unusual.) "The woman had her 15-year-old son tested with colonoscopy, and he had it, and his doctors immediately suggested surgery. But the only procedure being performed in their town was complete colonectomy with an ileostomy, which is pretty traumatic for anyone of any age, much less a 15-year-old. So his mother called M. D. Anderson to see if any other procedures were available anywhere. I canvassed the people in our department and the Division of Surgery and identified physicians in Kansas City. The woman ended up taking her son there, where he had less radical surgery performed."

Howard stressed that this is the value of the registry—matching resources with the people that need them, taking into account their individual wants. "Family dynamics can be a problem, because every family is unique. The way you contact people, the way you handle people has to be a little different in each case. That's the one thing a family registry can do for a family doctor—offer expertise and support. We'd like to become more involved in the grass roots of primary care. Part of the mission of M. D. Anderson is to educate and to support prevention. And this is the ultimate form of prevention."

—Maureen E. Goode

Physicians who desire additional information may write Ms. Howard or Dr. Lynch, Department of Gastrointestinal Oncology and Digestive Diseases, Box 78, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, or call Ms. Howard at (713) 794-5451 or Dr. Lynch at (713) 792-2828. To receive the *HCC Newsletter*, call the M. D. Anderson Department of Scientific Publications at (713) 792-3305. ■

"Interferon is just one piece of the whole tumor suppression puzzle."

Interferon

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clinically significant entity. Gutterman compares these cancers with cardiovascular disease: both have early signs that, if detected and corrected, may prevent serious disease later on. "Although the biology of the two appear unrelated, they have subtle similarities; furthermore, both begin with a clinically undetectable genetic defect that causes progressive damage and leads over 20 or 30 years to a serious, even fatal, medical condition. Like cardiovascular disease, cancer is exacerbated by environmental factors, which accelerate the rate of conversion of the altered or damaged cells to malignancy." Furthermore, the similarities between the two are the key to early detection of cancer: Gutterman foresees a method of measuring early signs of cancer, that is, the abnormal genes, as blood pressure measurement now detects the early signs of cardiovascular disease.

The abnormal genes that cause cancer comprise at least three types: oncogenes, which, when altered, encourage the abnormal growth and division that characterize cancer; tumor suppressor genes, which, when altered, fail to control this abnormal growth and division; and the newly discovered DNA repair genes, which, when altered, fail to repair mutations that can lead to cancer. Researchers believe that there are about 30 to 40 tumor suppressor genes in the body, each of which produces a protein, and they are starting to believe that these proteins are controlled by "master" tumor suppressor proteins such as Rb (for retinoblastoma, with which it was first associated) and p53 (associated with many different tumors). Evidence from the laboratory suggests that returning just one of these tumor suppressor genes to its normal function can appreciably reduce the aggressiveness of the malignancy if not stop the growth.

Gutterman became intrigued by interferon when it was discovered to inhibit cell growth; it was also known to have certain positive effects on the immune system. He now considers it analogous to a tumor suppressor protein: it inhibits the growth of cells, particularly malignant cells, it blocks the effects of many oncogenes and growth factors, and unlike other biological agents, it inhibits cell motility (cell motility is critical to the process of metastasis). Gutterman suspects that this inhibition of cell motility is at least as important as the inhibition of cell growth in stopping the growth of cancer.

Cells are embedded in the extracellular matrix, which comprises fluids, proteins, micromolecules, and other substances around the cells and allows the cells to communicate with each other. Controlling this communication are cytokines, which are secreted by cells into the plasma and extracellular matrix. They work rather like a neighborhood cop (in Gutterman's words) to keep the cells and their extracellular environment in a balanced, homeostatic state.

Intercellular communication is dependent on the proper functioning of all the structural components of the tissue through which the messages are conveyed: the matrix, the cell membrane, the cytoskeleton, and the cell itself. In cancer, the communication network between cells is disrupted. If the cytoskeleton is disrupted, the messages don't get through to the nucleus and the nucleus begins to function abnormally. Since the nucleus is the site where the oncogenes or tumor suppressor genes get switched on or off, this abnormal functioning can lead to malignancy. When this happens, the cells start growing irregularly and do not differentiate. They may start to move and disrupt other cells. Gutterman believes that interferon, probably in concert with other extracellular and cellular substances, restores the balance, the homeostasis, making sure the messages get through properly. It stops growth, stops motility, and enhances the ability of the cell, through adhesion molecules, to respond to its environment. It corrects defects, injuries, in the cytoskeleton. Interferon has also been found to block angiogenesis, the initial step in the formation of new blood vessels that is essential to the growth of malignancies. Moreover, it blocks fibrosis, a response to injury that stimulates many different kinds of cells and promotes cell growth.

Traditional chemotherapy has taken the approach of interrupting the functioning of cells, especially division, with little attention to the surrounding structures. The success of this strategy in most cancers may have been limited, suggested

Gutterman, because it does not address this disruption of the extracellular environment.

Tumor suppressor proteins Rb and p53 work within the cell to regulate the cell cycle. Interferon, working outside the cell, is believed to induce and regulate Rb (its relationship with p53 is not well understood). Gutterman believes that interferon may, in concert with the tumor suppressor proteins inside the cell, mediate the tumor suppressor function, and that the protein inside the cell cannot be totally effective without adequate interferon outside the cell. He speculates that attempts to stop cancer by replacing defective tumor suppressor genes with functioning genes that will produce the effective tumor suppressor protein in the cells might be successful only if extracellular levels of proteins such as interferon are adequate.

Although aging and certain environmental insults such as cigarette smoking may deplete interferon levels, inadequate levels of interferon cannot be remedied by simply administering the protein to the body. For one thing, interferon is toxic in pharmacologic doses. Fortunately, technology can provide solutions: interferon can be administered in tiny physiologic doses that are effective but not toxic; interferon analogues can be synthesized that suppress tumor growth without toxic effects; or endogenous production of interferon can be induced or increased by gene therapy. For this reason, Gutterman sees cytokine biology as an important emerging field. He is quick to say that he does not see interferon as a cure-all for cancer, but that the way researchers are looking at the protein is changing: "We are asking totally different questions than we did 15 years ago."

Chemoprevention of cancer may be one application of interferon if the problems with toxicity and route of administration can be solved. Only oral agents are feasible for large population-based chemoprevention trials, and right now interferon is administered only by injection. One form of interferon, interferon-alpha, has been used in a few studies in conjunction with retinoids, naturally occurring and synthetic analogues of vitamin A that are known to have inhibitory effects on cancer development. The results were encouraging in that interferon did appear to have a potentiating effect on the retinoids.

Interferon is in a period of transition. Gutterman believes that cancer researchers are going to have to start looking at new ways of treating cancers and assessing what constitutes an effective drug. His work has indicated that interferon is not effective in advanced cancers. If he'd been discouraged and stopped there, he never would have learned that the protein can be very effective in very early stage disease. He says that we will have to change the way we think about biological agents: biologicals and chemotherapy are very different approaches and should not be evaluated in the same ways. They may be effective in stopping or stabilizing cancers, not in shrinking large tumors.

Gutterman is especially excited about two areas of research now active at M. D. Anderson. One is the search for inhibitors of angiogenesis; one of the most promising is a fungus called fumagillin, which has the potential to act synergistically with interferon, limiting the proliferation of tumor cells. The combination is being tried in patients with prostate cancer, but the studies are still at very early stages. The other area, the combination of interferon with replacement of abnormal tumor suppressor genes, is still in the laboratory, although the researchers hope to have a clinical protocol under development soon. This reflects the new way of thinking of interferon as an extracellular tumor suppressor protein. It is probable that interferon will not work to suppress tumors on its own, but will be used with the replaced tumor suppressor protein in place to inhibit tumor growth. "Interferon is just one piece of the whole tumor suppression puzzle," affirmed Gutterman.

Gutterman believes that the interrelationship of carcinogenesis, angiogenesis, and fibrosis in cancer development suggests that cancer is the result of an injury to tissues or cells. In the way the body responds to them, tumors are in some ways very like wounds, and interferon heals them: it stops the cells from moving around, it stops the fibrosis, it stops the blood vessels, it stops the growth. Gutterman feels certain that, given time, we will be able to harness these qualities and use them to stop the growth of cancer.

—KATHRYN L. HALE

Physicians who desire more information may write to Dr. Gutterman, Department of Clinical Immunology and Biological Therapy, Box 41, The University of Texas M. D. Anderson Cancer Center, 1515 Holcombe Blvd., Houston, Texas 77030, or call (713) 792-2676. ■

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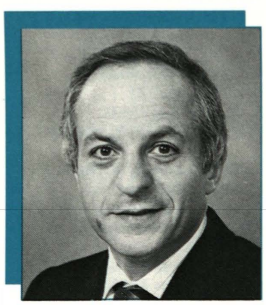
Treatment Update



Jordan Gutterman is chairman of the Department of Clinical Immunology and Biological Therapy

When interferon was discovered in 1957, it was hailed as a significant antiviral agent. In the late 1970s, interferon made a big splash as a symbol of recombinant gene technology and the medical breakthroughs it would bring. Fifteen years later, interferon is a symbol of something quite different—the complexity of the biological processes of cancer and the value of endurance and persistence in tackling this complexity.

Jordan Gutterman, M.D., chairman of the Department of Clinical Immunology and Biological Therapy, The University of Texas M. D. Anderson Cancer Center, was one of the foremost experts on the then little-known interferon when it became an "overnight sensation" in 1980 as one of the first proteins to be produced by recombinant gene technology. Having witnessed the evolution of interferon's status, Gutterman has seen firsthand how progress in the understanding of cancer biology comes not through big breakthroughs but through the steady accumulation of discoveries. Recalled Gutterman, "In 1980, the public perception of interferon was as a big breakthrough, but it wasn't a sudden thing. It was merely one event in the long process of learning everything we can about the protein's role in cancer so that we can determine its clinical applications. It is this steady progress toward elucidation that is exciting and leads to innovation. Discovery is only the first step—development is a much more deliberate, long-term endeavor.

"Interferon wasn't approved by the U.S. Food and Drug Administration for clinical use until 1986, nearly 30 years after its discovery. Because of the expense and duration of the drug development process, fewer anticancer agents will be developed for the clinic in the future. To help us choose the drugs with the greatest potential, we need to improve our understanding of the underlying physiological events leading to cancer."

Gutterman believes that information gained from the study of interferon in the last 15 years has opened the door to a new way of thinking about cancer—as a chronic disease. With a few exceptions, cancers, including the epithelium-derived adult carcinomas, take many years to evolve into a

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