

Chapter 1

Summary and Options

CONTENTS

	<i>Page</i>
Introduction	3
Request for the Study	4
The Terminology of Unconventional Cancer Treatments	4
Historical Perspective	4
Legal Issues	5
International Perspective on the Availability of Unconventional Cancer Treatments in the United States	7
Current Mainstream Treatments for Cancer	8
Controversies in Mainstream Cancer Treatment	10
Treatments Discussed in this Report	11
Categories of Unconventional Cancer Treatment	13
Practitioners of Unconventional Cancer Treatments	16
The Information Network for Unconventional Cancer Treatments	17
Patients Who Use Unconventional Cancer Treatments ... *	18
Costs and Insurance Coverage of Unconventional Cancer Treatments	18
Evaluating Unconventional Cancer Treatments	19
Options	24
Options To Broaden the Base of Information on the Use of Unconventional Cancer Treatments in the United States	24
Gathering and Making Available Information on Unconventional Cancer Treatments and Practitioners	25
Improving Information on the Efficacy and Safety of Treatments Used by U.S. Citizens	25
Making Available Information on Legal Sanctions Against Practitioners and Health Fraud Related to Unconventional Cancer Treatments	26

INTRODUCTION

Each year, thousands of U.S. cancer patients use treatments that fall outside the generally understood bounds of mainstream medicine. While the majority of cancer patients do not use such treatments, those who do represent a visible minority (though the exact numbers are unknown). Additional thousands may be interested in such unconventional treatments and seek information about them.

Although any examination of unconventional cancer treatments will fall short of capturing all the reasons for cancer patients' interest in them, certain factors seem clear. Effective treatments are lacking for many cancers, especially in advanced stages; many mainstream treatments entail considerable toxicity; and long-term survival may be uncertain even after apparently successful treatment. These realities of mainstream treatment, coupled with explicit or implicit promises of effective, nontoxic cancer control by unconventional means, and the strong support of cancer patients for them, motivate new patients to seek treatments outside the mainstream.

Unconventional treatments vary greatly in content, and range from some that may be used easily along with mainstream treatment to those that, either because of the nature of the treatment, or because of the stance of the practitioner offering them, are used exclusive of mainstream medicine. They also range from those that are entirely within legal rules and ethical assumptions to practices that rely on drugs and biologics that are not approved and are not within the bounds of U.S. law.

Additionally, regardless of the nature of the approach taken, patients seek not only a hopeful prognosis, but also treatment perceived as humane and caring and psychological support from caregivers and fellow patients. These are elements that at least some patients believe are missing from mainstream medicine. Another important aspect is the sense of personal control that may be gained from deciding on a course of treatment and pursuing it, sometimes in defiance of physicians, family, and friends.

“Unconventional treatments”—the phrase chosen for this report to describe treatments outside of mainstream medical practice and research—are not limited to treatments for cancer. They are of considerable public interest in the United States, but their use has received little formal study. The range of treatments offered, the people who offer them, the number and types of patients who use them, and their costs are largely undocumented. The reliability of information on the effectiveness and safety of these treatments is questioned by most mainstream medical authorities, in part because most reports are anecdotal or represent unsupported claims of practitioners. Research and clinical studies of unconventional cancer treatments generally have not been well designed and have not met with the approval of academic researchers. Supporters of unconventional treatments tacitly approve these reports in the absence of anything better. Thus, one of the major rifts separating supporters of unconventional treatments from those in mainstream medical care and research is a distinct difference in what they accept as evidence of benefit.

Objective, informed examination of unconventional treatments is thus difficult, if not impossible, in the United States today. Acrimonious debate between the unconventional and mainstream communities reaches well beyond scientific argument into social, legal, and consumer issues. Sides are closely drawn and the rhetoric is often bitter and confrontational. Little or no constructive dialog has yet taken place. In the course of this study, OTA involved individuals with a wide spectrum of views about unconventional and mainstream treatments, and went to great lengths to open the process to allow all viewpoints to be aired. This spectrum was represented on the advisory panel as well as among the hundreds of outside providers of information and reviewers who took part in the study. It is fair to say, however, that, while OTA heard and reported the viewpoints, the process did not bridge the gulf between two highly polarized positions.

This report describes the unconventional cancer treatments that are most used by U.S. cancer patients; it describes the way in which people find out about them and how much they pay for them; reviews the claims made for them and the informa-

tion base in support of the claims; suggests possible ways of generating valid information about their safety and effectiveness; and presents the legal issues surrounding unconventional treatments that have brought civil and criminal litigation to bear on the subject.

We focus on unconventional cancer treatments, and not on the successes and failures of mainstream medicine, either in general or in treating cancer. To help describe the context in which unconventional treatments exist, however, a brief summary of the status of mainstream cancer treatment is included later in this chapter. But this report is neither a comparison of mainstream and unconventional treatments nor an equal critique of both. In many places, the discussions of unconventional treatments in the report are quite critical, e.g., of the quality of evidence offered to support the treatments, of the claims that are made, etc.

In addition, adverse effects are pointed out when there is information about them. These points are not intended to suggest that mainstream medicine is free of faults, that its promise is always realized, or that practitioners of mainstream medicine are aware of and use the best possible treatments for their patients. OTA and many other organizations and authors have produced critical analyses of various areas of mainstream research and medical practice, and these are available for the reader. The aim of this report, rather, is to produce an assessment of unconventional treatments, as far as is possible today.

REQUEST FOR THE STUDY

This report responds to a request by the U.S. House of Representatives Committee on Energy and Commerce (a committee with jurisdiction over a wide range of health issues), which asked OTA to examine the subject of unconventional cancer treatments. OTA also received letters signed by 42 individual Members of Congress, asking for an assessment of a particular treatment, Immuno-Augmentative Therapy (IAT). Their request was sparked by the closing of the IAT clinic by the Bahamian government in late 1986. Then-Congressman Guy Molinari of New York, among whose constituents were a number of clinic patients, asked his House and Senate colleagues to cosign letters of request to OTA concerning IAT. In response to the congressional interest, OTA under-

took, as part of this project, a case study to develop a protocol for a clinical trial to study the efficacy and safety of IAT. The results of this effort are reported in chapter 6.

THE TERMINOLOGY OF UNCONVENTIONAL CANCER TREATMENTS

“Unconventional” is just one of many terms, all imperfect descriptors, that were considered, for the purposes of this report, to refer to the wide variety of treatments that fall outside the bounds of mainstream medicine. Other terms used by proponents to describe all or some of these treatments include: alternative, complementary, nontoxic, holistic, natural, and noninvasive. Those used by the sharpest of critics include: unproven, questionable, dubious, quackery, and fraudulent. At the beginning of this study, the term “nontraditional” was used to describe the treatments, but was unacceptable since “traditional” is widely used to refer to various types of native healers and treatments, as in traditional Chinese medicine; nontraditional, therefore, could describe mainstream medicine. During much of the project, the adjective “unorthodox” was used, chosen as a term as free as possible from value judgments about the quality of the treatments being discussed. Eventually, protests from both sides of the debate prompted the change to the term “unconventional.” We intend no implicit message in the use of the word “unconventional;” it was chosen with the hope that debate engendered by this report could center not on that word, but on the issues themselves.

HISTORICAL PERSPECTIVE

Physicians and the organizations they have created have come to dominate health care and biomedical research in the United States during the 20th century. “Scientific medicine” owes much of its rise to major advances in public health: the success of vaccination in preventing infectious diseases; the advent of therapeutic radiation for a wide variety of diseases and for its diagnostic uses in the early part of the century; and the successful treatment of previously life-threatening infections with antibiotics in the period after World War II.

Evaluation methodology developed alongside potential clinical advances, as the need to distinguish the effective from the ineffective took on greater

significance. In addition, the rising toll of chronic diseases—with longer and more unpredictable courses—in the face of dramatically declining death rates from acute diseases heightened the need for reliable methods to gauge the effectiveness of treatments. A formal set of procedures, consistent with the ‘scientific method,’ now governs the clinical evaluation of new medical technology, particularly drugs and biologics. (In contrast, medical and surgical procedures—e.g., surgical operations and diagnostic techniques—are not always subject initially to such rigorous testing.¹) The formal approach has had particular emphasis in the evaluation of cancer treatments, and over the years has been incorporated into the processes and standards of evidence required by the Federal Government for the approval of new drugs and medical devices, and into the operations of the National Cancer Institute, which funds most cancer research in the United States. The greatest emphasis in cancer treatment, hence in the methods employed in cancer research, has been placed on finding treatments that directly kill cancer cells (cytotoxic agents).

The American Medical Association (AMA) has been the organizational leader of the U.S. medical community during this century. In addition to enhancing the authority of physicians and supporting the structured approach to clinical research, the AMA has attempted to eliminate alleged health fraud, and much of this activity has focused on cancer treatments. From the early 1900s onward, the task of combating activities designated as health fraud was the formal responsibility of one or another organizational unit within the AMA. In addition, **Morris Fishbein, editor of the *Journal of the American Medical Association (JAMA)* from 1924 to 1949, conducted several crusades against particular practitioners of unconventional cancer treatments and, in general, against what he considered quackery.**

In recent years, the AMA has reduced its formal activities against certain nonphysician providers and alleged health fraud. While the Division of Archival Services and Public Affairs now answers inquiries about unconventional medicine, the Committee on Quackery and the Department of Investigation were eliminated in 1975. One of the main functions of the Committee on Quackery, formed in 1962, was to

oppose recognition of chiropractors as legitimate health care providers. In the mid-1970s, Chester Wilk and three other chiropractors brought suit, charging that the AMA and several other professional societies had engaged in a conspiracy to boycott chiropractors (960). In 1987, after an 11-year lawsuit, the court ruled for the chiropractors and against the AMA (614). Both the Department of Investigation and the Committee on Quackery were eliminated in a 1975 restructuring of AMA.

The American Cancer Society (ACS) has also played a key role in defining the limits of orthodoxy in cancer treatment and in discouraging the use of treatments falling outside their definition. ACS has taken a leading role in efforts against practitioners of unconventional cancer treatments. Their ‘Unproven Methods List’ is frequently used by doctors in counseling their patients about unconventional treatments, and is used extensively by the insurance industry to determine whether patients should be reimbursed for the costs of treatment (577). It is often referred to as a ‘blacklist’ by the proponents of unconventional treatment.

A highly polarized situation exists today. As Lerner puts it:

In the “war over cancer therapies” that has been widely publicized in the American media for the past decade, both sides often describe the opposition as a malevolent monolith. Thus the cancer establishment has characterized the alternative and adjunctive cancer therapies as the work of quacks preying on desperate and credulous cancer victims, while the proponents of alternative therapies have depicted established therapies as the ‘cut, burn and poison’ therapies of a cynical and profit-driven conspiracy. These stereotypes are, from a sociological perspective, familiar to anyone who has studied the phenomenon of propaganda in conflict situations. Each side in the cancer therapies controversy accuses the other of being profit motivated, of preying on desperate cancer patients, of cynically suppressing or ignoring therapies that could be beneficial, and of representing an organized conspiracy to thwart progress in cancer. (528)

LEGAL ISSUES

The Federal Food, Drug, and Cosmetic Act (FDCA) and other laws regulate the manufacture, sale, and advertising of medical products. In enact-

¹The 1978 OTA report *Assessing the Efficacy and Safety of Medical Technologies* (863) cites Kerr White’s estimate that only 10 to 20 percent of all procedures used in mainstream medical practice have been shown to be efficacious by controlled trial.

ing these laws, Congress has operated on the premise that the Federal Government has a legitimate interest in protecting the health of its citizens, while at the same time respecting their freedoms. The system that has developed is one that requires reliable evidence of efficacy and safety accepted by the Food and Drug Administration (FDA) before medicines may be offered legally.² This status quo is supported by the “consumer protection” point of view. Opposition to this system, called the “freedom of choice” position by some advocates of unconventional cancer treatment, is based on a belief that Americans should be free to decide for themselves which treatments they want to take.

The “consumer protection” point of view is supported by the contention that the average consumer cannot be expected to make informed choices in a complex scientific field. In an early court case under the Food and Drugs Act of 1906, the judge, in his charge to the jury, said:

This law was not passed to protect experts especially, not to protect scientific men who know the meaning and value of drugs, but for the purpose of protecting ordinary citizens. (914,916)

In a case interpreting the 1938 FDCA, Justice Frankfurter stated:

The purposes of this legislation. . . touch phases of the lives and health of people which, in the circumstances of modern industrialism, are largely beyond self-protection. (913)

The argument for “freedom of choice” in medical care is based on the concept of an individual’s right of privacy. It is argued that this right prohibits the government from restraining individuals’ rights to obtain treatments of their choosing: “the patient should be permitted to opt for treatment consistent with his views of higher quality of life” (416). A parallel argument is made for the physician’s right and responsibility to provide medical care. It reasons that well-informed physicians, following their best judgment and having assessed the risks and benefits of a treatment, should be allowed to provide the care they deem best for their patients (950).

There are, in general, no legal restrictions on a U.S. patient’s right to choose a treatment for himself or herself, either in the United States or in foreign

countries (though parents choosing treatment for a child may be restricted by legal precedents). However, some treatments are excluded from choice in the United States because they involve the use of unapproved substances that could only be offered illegally here.

Variations on the freedom of choice position have been voiced in recent years. For instance, during the lengthy legal battles over the rights of cancer patients to use laetrile, the argument centered on the right of terminally ill patients to choose a treatment that did not meet the safety and efficacy requirements of the FDA. In the final decision of that case, which initially found for the plaintiffs at the Federal district and appeals court levels, the U.S. Supreme Court found that even terminally ill patients should be protected from potentially unsafe and ineffective medicines (918). The same case indirectly legitimized the autonomy of the FDA, which had been under siege by State legislatures who were independently permitting the use of a federally unapproved treatment within their States, when FDA regulation clearly prohibited State sanctioning.

Laws and regulations designed to protect patients from potentially harmful and ineffective treatments have been criticized by supporters of unconventional treatment for limiting patients’ access to treatments of their choice. When State laws have been passed permitting access to specific unconventional cancer treatments that would otherwise be illegal (e.g., laetrile, in the 1970s), they have been criticized by segments of the mainstream medical community for exposing patients to hazardous or ineffective treatments, or for dissuading patients from seeking potential curative treatment.

Relevant laws and regulations address the approval, labeling, advertising, and marketing of pharmaceuticals and medical devices; the certification of various types of medical practitioners; professional sanctions against certified practitioners for inappropriate care of patients; the general exclusion of noncertified individuals from medical practice; and the rules by which publicly funded programs pay for medical care. More generally, criminal and civil statutes, though developed to apply to a wide range of situations, sometimes have

²Technically, FDA approval must be obtained before drugs and biologics may be marketed in interstate commerce. This criterion excludes only an exceedingly small proportion of medicines.

applied to disputes involving unconventional cancer treatments.

U.S. laws provide for the regulation of the efficacy, safety, advertising, and sale of medical drugs and devices, under statutory authority of the FDA, the Federal Trade Commission, and the U.S. Postal Service. Professional standards apply to the practice of medicine and are designed to limit the bounds of medicine to practices with known or definable safety and effectiveness, or practices that are generally "accepted" by mainstream medicine, sometimes without formal evidence. Though the threat of professional sanctions exists, physicians appear to have considerable latitude in treating their patients; there are relatively few medical conditions for which the choices of physicians are entirely constrained.

In addition, the enforcement of laws and professional norms is incomplete, so that, in practice, even set bounds are readily exceeded without legal or professional consequences to the physician. The potential for legal action exists against those overstepping the bounds of law, but relatively few actions are actually taken by the Government or by disciplinary bodies. A member of the advisory panel for this study reported to OTA that, based on an informal survey he conducted, it appears that in the last three years an increasing number of disciplinary actions against unconventional practitioners may have taken place (219). In addition, at least some physicians with an interest in using unconventional treatments along with mainstream treatments have informed OTA that they are reluctant to do so because of the fear of legal action or professional sanctions (82,218).

This report describes the legal standing of unconventional treatments and their practitioners and the legal arguments on both sides of the issue. Laws and regulations affecting unconventional cancer treatments are discussed in chapter 10. Those that affect practitioners are discussed in chapter 11. It was not within the purview of the report to suggest an overhaul of the basic regulatory framework for drugs, and options that would accomplish that change are not included. However, the information in the report might be useful in considering a suggestion made in a joint letter to OTA by several members of the project advisory panel, should the Congress wish to consider changes. The panel members believe that it would be useful:

To find appropriate mechanisms in the Congress for thoughtful review of the fundamental issues raised by the "freedom of choice" versus "consumer protection" quandary, and to determine whether there are not better laws and regulations that would enhance both consumer protection and freedom of choice in the interests of Americans with cancer. (8)

INTERNATIONAL PERSPECTIVE ON THE AVAILABILITY OF UNCONVENTIONAL CANCER TREATMENTS IN THE UNITED STATES

*The FDCA codifies standards of safety and efficacy for new medical drugs and medical devices, but does not set standards for the practice of medicine; the medical profession sets its own standards for the conduct of physicians. A wide variety of unconventional cancer treatments are available in the United States despite the limits implied by these laws and professional standards. A book published in 1988, *Third Opinion* (289), lists 60 clinics and physicians in the United States offering alternatives to mainstream medicine.*

Advocates of unconventional cancer treatments often contrast the situation in the United States to the relative openness of a number of European countries—e.g., Switzerland, Germany, England, the Netherlands—to unconventional medicine. No thorough international comparison of the availability and legal status of unconventional cancer treatments has been done, and OTA did not undertake such a comparison. However, it is clear that many treatments not available legally in the United States are offered openly and legally in those countries. In those countries, it appears that, particularly for treatments that are supportive and adjunctive to mainstream treatment, they coexist more harmoniously with the mainstream community than is the case in the United States. For example, the Bristol Cancer Help Centre, in England, which offers a range of supportive psychological and nutritional approaches, has many cancer patients who were referred there by their physicians. Such programs exist in the United States, the Commonwealth Cancer Help Program, for instance; the issue of differential treatment internationally is not simply one of legality, but of acceptance.

Some unconventional treatments about which OTA has specific information are not in fact treated equally to mainstream medicine in other countries. In the case of IAT, for instance, though it is available at a clinic in West Germany, it is not licensed by that Government. According to an official of the German Government (422), the “effectiveness of the method described [in the patient brochure] is *not* proven by the statements advanced. Whether the treatment can lead to risks for patients is, from the submitted information, not clear, but cannot in any way be excluded” [emphasis in original]. The costs of treatment with IAT are not covered by social insurance carriers for German citizens. In other countries as well, unconventional treatments are not necessarily paid for by publicly funded health plans (e.g., the Netherlands (222)). In a joint letter to OTA, members of the advisory panel for this study commented on the “broad availability of insurance coverage in other countries, such as Germany, for many unconventional cancer therapies.”

Defenders of the U.S. drug approval system point to the many instances in other countries, Great Britain, for example, in which drugs never approved in the United States have been approved, later to be banned because of serious side effects not detected during pre-approval clinical studies (966). It is likely that more unsafe as well as ineffective products are approved in countries other than the United States. No comparative analysis of international drug laws as they relate to unconventional medicine exists so it is not possible to draw conclusions about the relative merits and deficiencies of each approach.

CURRENT MAINSTREAM TREATMENTS FOR CANCER

Surgery, radiation therapy, chemotherapy (drug therapy), hormonal therapy, and immunotherapy are the main tools of conventional cancer treatment. Surgery is the oldest and still most effective mainstream treatment for solid tumors, and is curative in many cases of localized cancer in which all or nearly all cancerous tissue can be removed. When used with chemotherapy, radiation, or both, surgery’s aim is to remove as much tumor as possible without disabling the patient, so that the other treatments have a greater chance of successfully eliminating the remaining tumor cells. In advanced stages of cancer, surgery is sometimes

used for palliative purposes, to alleviate the physical interference of a cancer with other organs.

Advances in oncologic surgery include a move toward less radical operations for some cancers, particularly early stage breast cancer. The shift is based on the results of large randomized clinical trials of various degrees of surgical removal (from removing the least amount of tissue, “lumpectomy,” to the most, radical mastectomy), which demonstrated that, combined with appropriate adjuvantive treatment, surgery that is less radical results in survival equivalent to that of more radical surgery. Another trend has been toward more aggressive surgical removal of metastatic tumors.

Chemotherapy and radiation therapy are used as primary treatments for some leukemias and lymphomas, and are used in addition to (“adjuvant” to) surgery for solid tumors that have advanced beyond their original location, including both regional and distant (metastatic) spread. Out of the thousands that have been tested, a relatively small number of drugs (about 30) are approved for use today. The regimens considered “state of the art” vary according to the site of the cancer, in some cases the type of cells that make up the tumor, the stage of the cancer, and, to some extent, characteristics of the patient.

General rules for mainstream cancer chemotherapy are that the highest tolerated doses be used, and that multiple drugs be used in combination. The use of high doses, the systemic administration, and the toxic properties of many anticancer drugs account for the often severe side effects of cancer treatment. The rules are based on the observation that some cancer cells are resistant to the effects of some drugs. One of the most widespread mechanisms of naturally occurring drug resistance is a molecular “pump” which works to transport chemotherapeutic drugs out of the cancer cell before any damage takes place. A number of other mechanisms are known, though all drug resistance is not explained with current knowledge (252). If clones of resistant cells proliferate, there is little hope for control with existing chemotherapy. The emergence of resistant clones and regrowth of drug-resistant cancers is a particular problem after treatment with lower than optimal doses of chemotherapy.

Efforts to improve the success of chemotherapy include developing means of more specifically targeting the drug to the tumor, and devising ways of increasing the doses. An example of the former is

linking cell-killing agents to monoclonal antibodies that are attracted to specific proteins on the surface of cancer cells. When the 'conjugated' molecule is administered, it will not find appropriate sites on most normal cells to which it can attach, but will link to cancer cells. Photodynamic therapy (PDT) is another approach still under development to provide localized cancer treatment, though its use is still quite limited. PDT capitalizes on the greater attraction of "hematoporphyrin" molecules (the "sensitizer" to tumor tissue than to normal tissue, though the basis of the attraction is not well understood. Some time after the sensitizer is administered, the area of the tumor is illuminated with light of a particular wavelength, either from the surface or from inserted fiber optics. The light provides energy for a chemical reaction that results in the release of oxygen, which kills cancer cells by damaging them physically.

Hormonal treatment has been successful for types of cancer that are "hormone dependent," notably breast and prostate cancers. The theory behind hormonal, or endocrine, therapy, is that hormones produced internally are "blocked" by drugs. These drugs bind to receptors on the surface of tumor cells where the hormones would normally bind, but they do not cause the cell to grow or replicate. These drugs are generally taken for long periods of time following surgery to prevent metastatic disease.

Radiation therapy is used most often as an adjunct to surgery, and maybe used before or after surgery in different situations. It is also used as a palliative measure, to reduce the pain of bone metastasis and to shrink tumors in other parts of the body. Radiation may be applied at or near the site of the tumor as an implant (by insertion of a radioactive isotope) or it may be delivered to the site of the tumor by a high-energy x-ray generator (teletherapy). (Whole-body irradiation is used to intentionally destroy the bone marrow of patients being prepared for bone marrow transplantation.) It is thought that the main effect of ionizing radiation on cells is to interfere with the capacity of the DNA molecule in the nucleus to reproduce, but cells may be harmed in other ways as well. In general, therefore, it is at the time the cells are dividing that they die. Since ionizing radiation also affects normal cells, the dose must be modulated to achieve the greatest antitumor effect while attempting to minimize effects on normal tissue, to optimize the "therapeutic index. "

The use of radiation therapy began early in the 20th century, preceding chemotherapy, and preceding the wide-scale use of randomized clinical trials to determine the effectiveness of medical treatments. It is only in recent years, therefore, that radiation therapy has been subjected to rigorous evaluation. It is likely that radiation has been used routinely beyond its effectiveness for many types of cancer; valid evidence for these practices still is being gathered. Advances in radiation therapy have centered on more precise delivery systems and on attempts to pair radiation with specific chemotherapeutic agents to enhance their effectiveness.

"Biologic therapy," the most recent approach in conventional cancer treatment, refers to "cancer treatment that produces antitumor effects primarily through the action of natural host defense mechanisms or by the administration of natural mammalian substances" (763). Though biologic treatments for cancer are relatively new, the field of biologic therapy, also called "biotherapy," developed from observations and experimentation in the late 19th century, which suggested that an immune response could effect tumor regressions (215). Biotherapy is based on the principle that tumor cells are immunologically "different" from normal cells, and that the immune system, which has developed to protect against "nonself," can be manipulated to destroy cancer cells.

Mainstream biologic therapy includes a number of approaches. One line of development has been to attempt to induce reaction in the patient's own immune system, either with nonspecific stimulators (e.g., *Bacillus Calmette-Guerin*; BCG) or, more currently, with stimulators related to the tumor itself. The latter includes efforts to develop "tumor vaccines" that would cause the body's immune system to activate against tumor cells. Another approach is to inject the patient directly with immune system products and cells (e.g. "lymphokine-activated killer cells' "). "Cytokines" (soluble proteins produced by certain immune system cells), particularly the interleukins, have been the focus of considerable attention in the last few years. Another group of cytokines, the interferon, was studied intensively throughout the 1970s and 1980s.

Many of the biological treatments that have been tried have produced some encouraging effects in cancer patients, but, as of yet, few are of lasting benefit to patients. Research in biological therapy is

geared toward increasing understanding of immune function and on developing effective ways to apply these tools in conjunction with other forms of cancer treatment.

The trend toward increased participation by patients in decisions about their medical treatment has affected mainstream medicine. Whereas in the past few people would have questioned the recommendation of a physician, questioning has become common, perhaps even the norm. In addition, public discussion about health and disease, including all aspects of cancer, has risen, and the level of detailed coverage of cancer by the press has grown continuously. Patients and their families openly discuss the disease. During the 1980s, patient support groups, many independent of organized medicine, have taken hold, and patients have much greater opportunities to exchange information about their treatments.

The participation of patients in decisionmaking about their treatment and their more active questioning of medical authority have also raised awareness of the importance of the quality of cancer patients' lives. A panel evaluating the measurement of progress against cancer (896) strongly emphasized the various dimensions embodied in "quality of life" as being aspects of the impact of cancer on which systematic data should be collected on a nationwide basis. Such dimensions include: physical side effects (of treatment) such as nausea, general health conditions, and pain; functional status including self-care (eating, dressing, and bathing), mobility, and physical activities such as walking and doing household chores; psychological morbidity including emotional distress, anxiety, and depression; and social interaction including everyday interpersonal contacts, social support, and the work role.

CONTROVERSIES IN MAINSTREAM CANCER TREATMENT

During the past few years, the rates of success of conventional cancer treatment have increasingly

been examined, debated, and subjected to criticism by both scientists and the general public. Attention has focused on the lack of substantial progress in successfully treating the most common and life-threatening types of cancer. While the last few decades have seen undisputed success in treating a number of cancers—particularly those affecting children and young adults—the gains in survival for most solid tumors (lung and colon cancer, in particular) are small or nil. The long-term survival advantage of some established treatments, particularly the treatment of early stage breast cancer, has been demonstrated definitively only recently (268). Long-term effects of some recent treatments, for example anew chemotherapy regimen for advanced colon cancer that has shown promise in early randomized clinical trials, are not yet known.

Individuals in the cancer research community and in government have begun to examine the results of the "War on Cancer," begun officially in 1971, and have noted a lack of significant progress in treating most cancers. The National Cancer Institute (NCI) has been criticized for misleading the public about what the results have actually been. One journal article, in particular, became a centerpiece of the debate. "Progress Against Cancer?" by John Bailar and Elaine Smith, which appeared in the *New England Journal of Medicine* in May 1986 (65), took abroad view of the emphases in cancer research and the changes in various measures of the disease since 1950, and noted that the age-adjusted mortality rate,³ which was chosen as a measure of overall progress, has risen since 1950. They concluded that treatment for most cancers hasn't gotten much better, and that the greatest promise for cancer control lies in research on prevention. Bailar commented further on his position in a later article (63), in which he stated: "Modern medicine already has much to offer to virtually every cancer patient, for palliation if not always for cure; the problem is the lack of any substantial recent *improvement* [emphasis in original] in treating the most common forms of cancer."

The article by Bailar and Smith stirred up interest and controversy, which was furthered by a report by the General Accounting Office (GAO, a congress-

³ mortality rate measures the proportion of the population dying during a given time period. An age-adjusted rate removes the effect of changes in population size and age distribution within the population, allowing direct comparison of the rate over time. In the United States, this allows for population growth, as well as growth in the percentage of people in older age groups.

⁴Bailar went on in that article to say: "There is no comfort here for the 'medical counterculture'; nonstandard (or 'unorthodox') treatments are likely to be dangerous as well as utterly ineffective."

sional agency) that looked at NCI'S reporting of cancer survival statistics. GAO examined changes in survival since 1950 for 12 different kinds of cancer and compared its independent findings with those reported by NCI. NCI reported gains for all 12 types. In each case, GAO found a more modest improvement than did NCI, or no gain at all. These results, released in early 1987, again raised controversy about the rate at which progress in treating cancer is being made, and further opened the debate about cancer treatment to public scrutiny. The article by Bailar and Smith and the GAO report have been used by supporters of unconventional treatments to challenge the dominance of the NCI, ACS, and mainstream medicine in general (see, e.g. 189).

The widespread use of chemotherapy among classes of patients unlikely to benefit, or for which benefits have not yet been demonstrated, also has drawn criticism from respected researchers (147). The cancer research community itself has been reexamining the value of long-accepted chemotherapy for certain types of cancer. An example is adjuvant treatment of cancers of the colon and rectum, the most common types of cancer in the United States. Debate was focused by a review of all the randomized clinical trials of radiotherapy and standard chemotherapy for these cancers, published in the *Journal of the American Medical Association* in 1988 (144). The review suggested that these treatments might offer little survival advantage, or at least less than had been assumed, beyond the benefits of surgery, which is the primary treatment. A debate in the medical literature ensued (see, e.g. 108,204) with opinions strongly held for and against the value of adjuvant treatment, based on differing interpretations of the same data. (This debate preceded the dissemination of the results of advanced colon cancer treatment with a new combination of agents, which has shown a survival advantage.)

Another debate concerns the use of adjuvant chemotherapy for women who have undergone surgery for early stage breast cancer. Early results from clinical trials prompted the NCI to issue a "Clinical Alert" (895), with the strong message that women with early (stage 2) breast cancer without evidence of cancer in the lymph nodes can benefit from adjuvant chemotherapy. The Clinical Alert elicited strong criticism from prominent members of the medical community, who objected mainly on grounds that the data available from the trials were only preliminary and that they were insufficient to

support recommending widespread treatment with toxic chemotherapy (391,572).

One result of the debate over progress in cancer was a request by the Senate Appropriations Committee to NCI in 1988 to establish a panel of technical experts and nonexpert public representatives from outside NCI to "recommend what measures or series of measures are most appropriate to assess progress in cancer" (874). The panel reviewed measures of progress currently in use and suggested additional approaches (896).

TREATMENTS DISCUSSED IN THIS REPORT

The phrase "unconventional cancer treatments" encompasses a tremendously heterogeneous group of practices. These treatments vary in content, probably in safety and effectiveness, and in the types of practitioners delivering them. They are defined in this report not by what they are, but by what they are not: they are not part of mainstream, conventional medicine in the United States. Because of this variety, the treatments described do not easily lend themselves to simple, general characterizations. Statements or judgments about one treatment cannot be assumed to apply to others; this applies equally to positive and negative aspects.

This report is about the common cancer treatments found by U.S. cancer patients outside of mainstream medicine; in using these treatments, patients may be rejecting conventional medicine, they may be seeking approaches to supplement conventional medicine, or they may believe that conventional medicine has given up on them. Though no census of patients receiving unconventional treatment exists, the literature and expert opinion strongly suggest that Americans are most likely to seek a wide variety of unconventional treatments in the United States, Mexico, or the Caribbean. A few seek particular unconventional treatments in Europe. A large number of unconventional treatments are available in the United States, some practiced in violation of the law and some within the bounds of the law.

Some treatments that might be considered unconventional are excluded from discussion in this report. One is the unconventional use of conventional cancer treatment, such as low-dose, high-frequency regimens of chemotherapy, or high-dose pulses of

chemotherapy. Although chemotherapeutic regimens are being used in unconventional ways, they are, nevertheless, approved drugs with known efficacy by some route of administration.⁵ Another type of treatment not included in this discussion is experimental treatment developed within conventional medical research channels, but applied to patients outside of the clinical trial system before they have been approved for use. The most prominent examples of this are the biological response modifiers (such as interleukin-2 and LAK cells) that were (until 1989) offered by Biotherapeutics, Inc. (Franklin, Tennessee) on a commercial basis to patients who were not eligible for or who chose not to participate in clinical trials involving these substances.

This report concentrates on unconventional treatments that are well known or that have been used by large numbers of patients. We do not attempt to cover the many individual treatments of various kinds that are offered on a small scale, perhaps to neighbors or friends. It is impossible even to approximate the number of such cases. More often than not, these types of treatment come to public attention only through the legal system, when patients or their survivors bring suit to try to recover money spent on allegedly ineffective treatments or to try to stop the practitioner from continuing to fraudulently treat patients (see, e.g., a recent case in Arizona) (398). The cases that do surface in this way may represent only the worst end of the spectrum, but there is no way to confirm this.

This report also does not attempt an account of unconventional treatments that once held the spotlight but have fallen out of favor. A 1949 report of the American Medical Association Council on Pharmacy and Chemistry, for instance, lists many unconventional cancer treatments largely unknown today—“collodaurum,” “HettCancer Serum,” “AF-2,” and the “orgone accumulator” (39). Some other treatments of the past—the Rife Ray Machine, Krebiozen—still have their supporters, but, by and large, they are no longer in widespread use and are not reviewed in this report.

Perhaps the most significant area not included consists of spiritual approaches, among the oldest human responses to illness. How patients express

their beliefs and what they do under such circumstances can take many different forms (419,529). Religious figures such as ministers, priests, and rabbis are often called on to counsel patients and their families. Some are also involved in various forms of religious healing, e.g., faith healing, laying on of hands, and prayer. People from all over the world have traveled to the famous religious shrine at Lourdes, France, to pray for miraculous cures. An estimated four million people visit Lourdes each year, 65,000 of whom are ill. The Lourdes medical board has examined thousands of cases claiming cures, and 64 of these have been designated by the Catholic Church as miraculous cures (264).

Several of the unconventional treatments discussed in other sections of this report also include a spiritual or religious component. In macrobiotics, for instance, the dietary guidelines are one aspect of a much larger philosophical and spiritual system. Similarly, Anthroposophic medicine, which includes the use of the herbal preparation Iscador for cancer patients, is based on a complex religious philosophy and “spiritual science” developed by Rudolph Steiner in the late 19th and early 20th centuries. Other unconventional treatments that were designed specifically for cancer patients include a spiritual component. Spiritual aspects of the original Kelley regimen, for example, reflected the developer’s strong religious beliefs. A physician who founded the first clinic in Tijuana offering laetrile to cancer patients, Ernesto Contreras, includes a strong spiritual orientation in his regimen and often leads services for patients at a chapel he built at his clinic.

Patients may also seek care from traditional healers (outside their own culture), e.g., Native American healers, curanderos, shamans, and others, who use a strong spiritual component in their approach to treatment. Although the extent of use of traditional healing methods by U.S. cancer patients is undocumented, the popular literature suggests that some approaches have become relatively common in recent years. The ‘New Age’ movement beginning in the 1960’s and 1970’s in the United States has popularized a number of mystical practices, such as crystal healing, channeling, and ‘neo-shamanism,’ as well as some traditional healing practices involving curanderos, herbalists, and others (421).

⁵This is distinguished from the use of a substance for cancer treatment that is approved only for indications not related to cancer, such as the use in unconventional cancer treatment of dimethyl sulfoxide, a drug currently approved only for the treatment of interstitial cystitis. Uses such as these are within the scope of this report.

While most spiritual approaches treat cancer as any other disease or misfortune, some techniques with spiritual or mystical components are often associated specifically with cancer. "Psychic surgery" refers to a procedure involving removal of spirits or physical manifestations of spiritual pathology from a patient. Some Americans travel to the Phillipines for "psychic surgery," where it is practiced in its original context of religious and traditional healing (419,530). Psychic surgeons from the Phillipines have also come to the United States, holding treatment sessions as they travel around the country. They have often been pursued by legal authorities and some have been convicted of practicing medicine without a license. Psychic surgery is considered by many in the unconventional community to be a "fringe" treatment.

Categories of Unconventional Cancer Treatment

The treatments described in this report are grouped, for convenience, into four general categories: *psychological and behavioral, nutritional, herbal, and pharmacologic and biologic*. These categories are not the only ones that could be devised, and the groupings do not connote commonality among their elements beyond the basic nature of the treatment. Since many of the treatments include a variety of components, however, assignment to certain categories was not straightforward and could have been done differently in a number of cases. In general, assignment to the categories was based on the nature of the central or unique element of each approach.

Chapter 2 of this report discusses behavioral and psychological approaches to cancer treatment. Many forms of psychological and behavioral intervention are used adjunctively to relieve pain and distress associated with cancer and its treatment, and generally, to improve a patient's psychologic outlook. Some individuals have claimed that psychological approaches can cause tumor regression and prolong survival. The potential contribution of psychosocial interventions to extending life has recently begun to be studied by mainstream researchers, with encouraging results. The efficacy of psychological and behavioral approaches in improving the course of cancer is still uncertain, however. The chapter describes three of the most popular psychological interventions for which claims of tumor regression or life extension have been made: *mental imagery,*

a method involving the creation and interpretation of mental images that was popularized by O. Carl Simonton, M.D., and Stephanie M. Simonton-Atchley; intensive meditation as practiced by the late Australian psychiatrist Ainslie Meares, M.D.; and a unique form of psychotherapy developed by Lawrence LeShan, Ph.D. While these methods are the ones cancer patients are likely to find out about, they have been widely adopted and modified by both mainstream and unconventional practitioners. Applications of psychological and behavioral approaches, particularly when used in addition to mainstream treatment, are considered by some as "middle ground" treatments.

Chapter 3 discusses treatments whose primary component is dietary. Three widely known regimens are included. Several other treatments described in this report, especially in the pharmacologic category, also include dietary components, but in these cases the dietary element is secondary to other components or is one of several other approaches used. The first discussed in chapter 3 is the Gerson regimen, consisting of a low-salt, high-potassium, vegetarian diet, various pharmacologic agents, and coffee enemas. It was developed in the 1940's and 1950's by the late Max Gerson, M.D., and is now offered at a clinic in Tijuana, Mexico. The second nutritional approach is the Kelley regimen, originally developed by William D. Kelley, D.D.S. The Kelley regimen as currently practiced by Nicholas Gonzalez, M.D., involves a complex nutritional program based on dietary guidelines, vitamin and enzyme supplements, and metabolic typing. Another treatment discussed is the macrobiotic diet, consisting largely of cooked vegetables and whole grains, which proponents recommend as part of an overall macrobiotic philosophy and belief system incorporating many aspects of daily living. The regimens presented here are examples of a wider group of approaches using nutritional components, many of which are poorly documented and are lesser known.

A dietary program, which is actually part of a multifaceted approach that includes conventional cancer treatment, stress reduction, exercise, and psychological support, developed by a practicing U.S. physician, Keith Block, M.D., is discussed as an example of a "middle ground" approach. In his practice, the dietary needs of cancer patients are assessed using a system that attempts to bring together findings from mainstream nutritional and

cancer research with a modified macrobiotic-type diet (without the ideologic underpinnings of macrobiotics). The results of this approach, however, have not yet been assessed in any formal way. Block may be representative of a type of physician who incorporates some dietary advice, often leaning toward a diet with little animal protein, with low fat and high fiber, and who may use psychological and behavior components as well in the treatment of cancer patients, though Block's program is probably more formal than most. There is no documentation of the number of physicians in this category or the content of their nutritional advice, since little has been written about it. However, according to some members of the advisory panel for this study:

It is our collective professional judgment that nutritional interventions are going to "follow" psychosocial interventions up the ladder into clinical respectability as adjunctive and complementary approaches to the treatment of cancer. (8)

Chapter 4 discusses five of the best known herbal substances used in unconventional cancer treatments. These include proprietary mixtures of herbal products, such as in the Hoxsey treatment, developed by the late Harry Hoxsey and currently offered in Tijuana; Iscador, made from a species of European mistletoe, used mainly in the context of Anthroposophic medicine in Europe; and Essiac, an herbal tea developed by the late Rene Caisse, R.N., and currently offered in Canada. Also discussed are single-agent treatments, such as chaparral tea, prepared from the leaflets and twigs of the creosote bush, a plant indigenous to the desert areas of the southwestern United States, and Pau d'Arco, a substance derived from the inner bark of trees native to Argentina and Brazil and sold in health food stores in the form of capsules, tea bags, or loose powder.

Many other herbal substances are sold in health food stores and are advocated for general health purposes in the unconventional literature, but few others for which information is available appear to be advocated specifically for cancer treatment (exceptions include, e.g., Jason Winters Herbal tea, which is specifically for cancer treatment).

Chapter 5 discusses a large and diverse group of unconventional cancer treatments that have as their central component a pharmacologic or biologic substance, such as biochemical agents, vaccines, blood products, and synthetic chemicals. One of the

treatments discussed is the regimen developed by the late Virginia Livingston, M.D., and offered at her clinic in San Diego. The main component of the regimen is a vaccine designed to treat and prevent infection with the microbe that Livingston believed to be a cause of cancer. The treatment regimen also includes a variety of components intended to bolster patients' immune responses in general and to counteract effects of microbial infection, including antibiotics, vitamin and mineral supplements, and a special diet.

Another treatment described is one offered by Stanislaw Burzynski, M.D., Ph.D., at his clinic in Houston. Burzynski uses what he calls "Antineoplastons," substances described as peptides or amino acid derivatives isolated from urine or synthesized in the laboratory. His current regimen for cancer patients includes oral and intravenous use of approximately 10 types of Antineoplaston, all of which are manufactured at the Burzynski Research Institute in Texas.

Another pharmacologic treatment is described by its developer, Emanuel Revici, M. D., as "biologically guided chemotherapy" and reported to consist of a variety of minerals, lipids, and lipid-based substances. Revici practices his regimen in New York.

"Eumetabolic" treatment offered by Hans Nieper, M.D., in Hannover, West Germany, is also described. Nieper prescribes a combination of conventional and unconventional agents (including pharmaceutical drugs, vitamins, minerals, and animal and plant extracts), and recommends that patients follow a special diet and avoid particular agents, foods, and physical locations ("geopathogenic zones") that he believes are damaging. Nieper reportedly treats a significant number of U.S. patients.

Chapter 5 also describes a number of other pharmacologic and biologic agents that are used as unconventional cancer treatments, some singly and some in combination. Examples include laetrile, a substance widely popular in the 1970's and currently offered in several clinics in Mexico; vitamin C, whose most prominent advocate for use in cancer treatment is the biochemist Linus Pauling, Ph.D.; dimethyl sulfoxide (DMSO), an industrial solvent often used in combination with laetrile and vitamin C; cellular treatment, processed tissue obtained from animal embryos or fetuses given orally or by injection; and various substances containing oxy-

gen, including hydrogen peroxide and ozone taken orally, rectally, or via blood infusion. Hydrazine sulfate, a substance that, from 1975 to 1982, was on the American Cancer Society's Unproven Methods List, was taken off when clinical trials under an investigational new drug exemption (IND) were started. The trials were controversial, however, and it is still considered in the context of unconventional cancer treatments. Its supporters persisted, however, and recent studies in major research institutions have suggested strongly that this substance may help to improve the nutritional status and prolong the lives of cancer patients by moderating the cachexia (the wasting of the body) that often accompanies late stage cancer. More definitive clinical trials are planned. Supporters of unconventional treatments often point to hydrazine sulfate as a treatment that was unfairly branded by the mainstream but which actually is effective.

Some of these pharmacologic and biologic treatments are offered only at single sites under the direction of their developer and chief proponent. Others are more widely available, are not necessarily associated with particular proponents, and may be used in combination with a variety of other unconventional treatments.

"Immuno-augmentative therapy" (IAT), offered by Lawrence Burton, Ph.D., at his clinics in the Grand Bahamas, West Germany, and Mexico, is the subject of chapter 6. IAT consists of daily injections of dilute serum fractions made from pooled blood samples. As a case study for this assessment, OTA attempted to develop a protocol for studying the efficacy and safety of IAT, in conjunction with Burton, and this attempt is described in the chapter, as is the treatment itself. The protocol attempt ended in a failure to arrive at a plan for study that both Burton and OTA believed would constitute a fair and valid test of IAT.

Information Included About Treatments

OTA drew from a variety of sources, including peer-reviewed literature, non-peer-reviewed or unpublished literature, patient brochures from individual practices or clinics, and personal communication with practitioners and their associates. The descriptions include, where possible, the approach taken in each treatment, how each is used to treat cancer, the proponents' claims for mode of action and intended outcome, potential adverse effects, and attempts at evaluating each treatment. The uneven coverage of

treatments results mainly from the paucity of information about some treatments.

In many cases, little or no specific information was available on adverse effects, though the absence of information cannot be taken by itself as an indication that the treatments are safe. According to one observer (21 8), one reason that little information has been generated about adverse effects of unconventional treatments is the implicit threat of personal legal actions for admitting an adverse effect. While mainstream physicians face little sanctioning for reporting adverse effects of mainstream treatments, an unconventional practitioner might find himself or herself the object of a disciplinary board investigation if he or she were to freely report adverse effects from giving an unconventional treatment. No efforts have been made by licensing boards or other responsible bodies to safeguard against such self-incrimination. For this and other reasons, in the case of each treatment covered in this report, instilient information exists to support an adequate evaluation of safety and efficacy, though, as mentioned earlier, common sense suggests that some treatments—e.g., psychological, behavioral, and some nutritional approaches—are likely to be inherently safe.

"Adverse effects" are defined broadly in this report to refer to at least five types of harm that may apply (to both unconventional and conventional treatments). These include hazards posed directly from the treatment itself (intrinsic harm); harm resulting from a patient's improper use of the treatment; harm caused by contaminated or otherwise substandard products resulting from poor manufacturing practices (quality control, design of equipment, etc.); harmful interactions or conflicts with other treatments (conventional or unconventional); and deterioration in a patient's condition caused by forgoing or seriously delaying other treatment that could have been effective. While all these types of adverse effects are possible, it is important to note that on the basis of current information, their significance and magnitude for any given unconventional treatment is unknown.

The standards we used for judging the quality of evidence for safety and efficacy are the same standards OTA has developed and applied in a wide range of studies. All past and current OTA studies, except this one, have dealt with mainstream medical practice and research. Many have been critical of the quality of studies and the inadequate basis they form

for making health policy decisions. These include studies of well-child care (871), glaucoma screening (873), computed tomography (CT) scanning (865), and alcoholism treatment (868), to name just a few. A number of earlier OTA studies have dealt specifically with the methods of technology assessment, including clinical research. The reader is referred to *Assessing the Efficacy and Safety of Medical Technologies* (863), *The Implications of Cost-Effectiveness Analysis of Medical Technology* (864), *Strategies for Medical Technology Assessment* (867), and *The Impact of Randomized Clinical Trials on Health Policy and Medical Practice* (869).

The standards that have developed are based on the experience of clinical trials over the last 30 years or so, largely during which time the methodology has been developed. What has emerged is an understanding of which type of study is likely to produce valid evidence and which is prone to produce answers that are later found, in better designed studies, not to be corroborated. The pros and cons of various study designs are discussed in chapter 12.

PRACTITIONERS OF UNCONVENTIONAL CANCER TREATMENTS

Practitioners of unconventional cancer treatments range from charismatic figures with no medical training to highly trained physicians or other health professionals who have departed entirely from mainstream practice. Another important group, though of unknown size and largely undocumented practice, are the “middle ground” physicians. Members of the advisory panel for this study offered the following opinion:

Most practitioners of unconventional cancer therapies . . . are interested in and attracted primarily to this “middle ground.” They seek to supplement judicious use of conventional therapies with spiritual, psychological, and nutritional approaches that they hope will improve quality of life and possibly contribute to life extension. (8)

These practitioners do not form a cohesive group and have been relatively silent in the public debate about unconventional cancer treatments.

There are also practitioners who are not licensed health professionals who promote specific unconventional cancer treatments, but it is impossible

even to estimate the number of such individuals in the United States. Some of these practitioners treat friends and neighbors, while some operate more widely, advertising in alternative publications and promoting themselves nationally. Since these individuals may be in contravention of the law by practicing medicine without a license, some are understandably quiet about their activities. After bad experiences, cancer patients or their families occasionally report these unlicensed practitioners, who then may be subject to civil and criminal charges.

A more readily identifiable group of unlicensed practitioners who often give advice about unconventional cancer treatments are some health food store employees. These individuals generally are not formally trained health professionals and are not permitted under law to dispense medical advice or prescribe treatments. A field study carried out for this assessment in three urban areas (420), as well as earlier work (839), suggest that many health food store personnel will, in fact, give medical referrals to unconventional practitioners, will in some cases discourage people from seeking conventional medical care, and will in other cases recommend specific products as treatment.

Historically, there have always been a number of well-known practitioners active at a given time. The practices of some, e.g., Max Gerson and Harry Hoxsey, are continued by associates or relatives after the developer dies. Those who become well known have generally been strong personalities, charismatic, who evoke great loyalty on the part of their patients.

Physicians in the United States are subject to civil and criminal laws related to the practice of medicine, as well as State licensing requirements and professional standards which, if violated, may lead to sanctions limiting the physicians’ ability to practice. Licensed physicians who practice unconventional medicine are subject to the same laws and standards, and have, occasionally, been charged with civil or criminal offenses, had their medical licenses revoked, or been subject to lesser professional sanctions. Some have also had privileges for reimbursement by the Federal Medicare program revoked.

THE INFORMATION NETWORK FOR UNCONVENTIONAL CANCER TREATMENTS

The mainstream medical literature contains very few substantive articles for physicians and patients who want to find out about unconventional cancer treatments. Very few scientific studies of these approaches have been done (529). Most reports that make their way into medical journals concern adverse effects of particular treatments or are generally negative.

The unconventional community publishes its own magazines and newsletters (e.g., *Health Freedom News*, *East West: The Journal of Natural Health and Living*, *Cancer Victors Journal*, *The Townsend Letter for Doctors*) with articles and advertisements for a wide range of unconventional medical treatments, including those for cancer. They commonly include articles critical of mainstream medicine and the government agencies involved in drug policy and health care, in particular the FDA.

“Alternative” papers and magazines, and sometimes the popular press, often report on unconventional treatments in an uncritical way, relying on individual case histories or the unsupported claims of proponents. Many of these publications also convey a strong anti-mainstream medicine viewpoint. Particular treatments occasionally are publicized through national magazines or television shows. *Penthouse*, for instance, has run a series of articles on alternative medicine over the past several years, and particular cancer treatments and practitioners have been featured (549,683,684). Some popular television shows, such as *60 Minutes* and *20/20* and talk shows such as *The Sally Jesse Raphael Show* and *The Morton Downey, Jr. Show* also have featured controversial figures in unconventional medicine, and these appearances have reportedly had enormous impact on the number of patients contacting their clinics (365).

Patients may decide to look into unconventional treatments after seeing a television show or reading an article on the subject, but most people are aware, even without a specific reminder, that such treatments exist. According to the few studies that have been done, most patients initially hear about particular treatments by word of mouth, from friends, relatives, or clergy. A large enough number of

people have used these treatments that an easily accessible body of descriptive and anecdotal information about them exists. Health food stores are often part of the discovery process, as well. Alternative newspapers and magazines, books and pamphlets, and the health food store personnel themselves are influential sources of information. Written material is available about specific treatments and about organizations that patients can contact for general information on unconventional cancer treatments.

From the cancer patient’s point of view, the decision to use an unconventional treatment maybe based on where treatments are offered and on the claims that are made for them. Most major clinics in the United States, Mexico, and the Caribbean produce brochures for prospective patients, and also give information by telephone. The brochures vary from those using scientific language and claiming various degrees of clinical success to those akin to resort brochures. A patient’s decision to take a particular treatment may be influenced by many factors, but in most cases is not made with the help of a physician.

Some patients become frustrated when they discover there is so little concrete information about the effectiveness and safety of specific unconventional treatments. Many will have been told, perhaps by a clinic itself, perhaps by other patients or advocates, that the treatment will improve their quality of life and will cause their cancer to regress and possibly disappear. They may have been told by prominent national groups (e.g., ACS, FDA) that, at best, the treatment is untested and therefore unproven, or worse, that it also has dangerous side effects. Based on the work done for this assessment, a common situation is that effectiveness is unknown and relevant information on adverse effects is nonexistent.

Patients often decide to go ahead with unconventional treatment because no reliable information confirms that the treatment *doesn’t* work or that it would likely be harmful. They may feel they have nothing to lose by trying it.

During the course of this project, OTA was contacted by dozens of patients or their friends or relatives who did want valid information for their decisions about unconventional treatments, and were frustrated to find so little.

PATIENTS WHO USE UNCONVENTIONAL CANCER TREATMENTS

An image persists, and is propagated by at least some mainstream medical literature, that patients taking unconventional treatments are gullible and unsuspecting, or desperate, alienated miracle seekers (see, e.g., (105,223)). Little systematic inquiry has been undertaken on which to base generalizations about these patients, but what has been done suggests that such stereotypes do not apply to many patients who use unconventional cancer treatments. Most of the systematic information that is available has come from patients who have gone to established unconventional treatment clinics, rather than from those treated by independent practitioners. Of the former group, many are highly motivated, college educated, and middle to upper class. Most have had little or no previous contact with unconventional treatments (177).

The slim evidence that exists suggests that most patients have had at least some conventional treatment before deciding to try an unconventional course, and many have had full courses of mainstream treatment. In some cases, however, people reject what could be curative conventional treatment in favor of the unconventional, either for themselves or for their children. Some cases have come to light when parents have made that decision for a minor child and legal proceedings against the parents have ensued. A highly publicized case in the late 1970's of this type involved a child with potentially curable leukemia, whose parents decided to forgo chemotherapy for laetrile (see ch. 10 for a discussion of this case). Some unconventional practitioners have been charged criminally with discouraging people, who later died of progressive cancer, from seeking possibly curative treatment, or for failing to encourage them to seek such treatment (see ch. 11).

Once begun on an unconventional course, many patients also continue to see mainstream medical practitioners, but many do not; one reason for this is that many mainstream physicians generally disapprove of unconventional treatments. In addition, some prominent unconventional practitioners discourage patients from returning to their doctors at home, and some insist that they not take any other treatment. In some cases, patients hide their unconventional treatment from mainstream physicians,

and hide mainstream treatment from unconventional practitioners. Followup on patients and, therefore, documentation of the course of their treatment and disease, are generally unreliable. In one of the few direct studies of patients who were using unconventional treatments, Cassileth and colleagues found that most, about 85 percent, had used both conventional and unconventional treatments during their illness. Fifteen percent had sought only unconventional treatment after diagnosis (177).

Whenever the characteristics of patients using unconventional treatments are discussed, the same few studies and surveys are mentioned: These usually include the study by Barrie Cassileth and colleagues (referred to above) of about 600 patients, half of whom were in treatment at a University-based cancer center and half of whom were patients at an established alternative clinic (177); and a 1986 Lou Harris survey for the FDA of a general population sample concerning their use of unconventional medical care of all kinds (566). Overall, too little information exists to characterize reliably the circumstances under which patients use unconventional cancer treatments. This is an area in which it is possible to gather information, however, and there are researchers interested in doing so. But according to some interested researchers, little money is available for this type of social science research (175).

COSTS AND INSURANCE COVERAGE OF UNCONVENTIONAL CANCER TREATMENTS

Since most health insurance policies-public and Private-do not cover charges for unconventional cancer treatments, patients generally pay for them directly. OTA gathered information on costs of unconventional cancer treatment at 44 clinics or other sites in the United States, Canada, Mexico, and the Bahamas, and on the practices of several major third-party payers regarding such treatments. It was found that the costs of treatment vary widely, from a few hundred to several hundred thousand dollars per patient; however, most major clinics currently charge between \$5,000 and \$40,000 for an "average" course of treatment. Some clinics charge a set fee for an entire course of treatment, while others charge by individual components, making it difficult

or impossible for patients to estimate in advance what treatment will cost.

Insurance coverage under the Federal Medicare program (for people 65 and over) is limited to care that is "reasonable and necessary," which for drugs generally refers to those that are FDA approved, and in some cases to drugs designated by NCI as "Group C" (Group C drugs have been found to have some therapeutic value in clinical trials, but have not yet been approved by FDA). Most Blue Cross/Blue Shield and private insurance plans have similar restrictions. Most health insurance contracts contain general language that excludes coverage of unconventional treatments, and some specify particular treatments by name. Examples in some plans are exclusions of coverage for laetrile, IAT, and cell therapy. Nevertheless, a number of clinics offering unconventional cancer treatments state or imply in their brochures that the treatments costs are covered under various insurance plans, perhaps creating an expectation that patients may be reimbursed. The IAT brochure, for example, states, "More and more insurance companies are readily accepting IAT claims for full or partial reimbursement" (429). Clinics may also advise or assist patients in filling out insurance claim forms; other clinics may be affiliated with a contractor who will submit reimbursement forms to insurers on a patient's behalf. In some cases, the claims are paid, but rarely if the claim explicitly states that it is for an unconventional treatment. A number of insurance fraud cases have involved unconventional cancer treatments.

Advocates of unconventional cancer treatments consider the lack of insurance coverage a major problem. In a joint letter to OTA, some members of the advisory panel for this study expressed their opinion on the need for a critical review of whether the U.S. health insurance system "is in fact acting in the public interest in seeking categorically to deny reimbursement for all forms of unconventional cancer therapies" (8). Refusal of reimbursement, they assert, extends to "psychosocial interventions for control of pain, nausea, and enhanced quality of life at leading teaching institutions." They also commented that " 'Fraudulent' claims are the social consequence of a reimbursement system that restricts itself to the narrowly construed cytotoxic and biomedical treatment of cancer. '

EVALUATING UNCONVENTIONAL CANCER TREATMENTS

In chapters 2 through 6 of this report, information is provided about a variety of unconventional cancer treatments. As mentioned above, and to the extent possible, the composition of treatments and the ways in which they are used are described, the rationales and theories provided by their supporters discussed, and the available evidence concerning their effects on cancer patients presented and critiqued. In these treatment "portraits," there are pieces of information, ideas, various fragments that some might find provocative, or suggestive of a worthwhile approach, and other pieces suggesting that a treatment is groundless.

No doubt this report will be used selectively by individuals wishing to portray various points of view, in support of or in opposition to particular treatments. The reason this is possible is that, almost uniformly, the treatments have not been evaluated using methods appropriate for actually determining whether they are effective. Regrettably, there is no guidance for new patients wanting to know whether these treatments are likely to help them. Digging through descriptive information, theoretical discussions, laboratory tests, or individual case histories of exceptional patients does not adequately answer the question of whether the treatment works—whether it prolongs or otherwise improves life, or effects a cure. The background information is useful, vital in some cases, to get to the point of evaluation. Regardless of the nature of the treatment, however, or of its intended effects, it is as true for unconventional as it is for mainstream treatments that in the final analysis, except for those extraordinarily rare treatments whose effects are dramatic, gathering empirical data from clinical trials in cancer patients using valid, rigorous methods is the only means currently available for determining whether a treatment is likely to be of value to cancer patients in general or to a class of patients. For none of the treatments reviewed in this report did the evidence support a finding of obvious, dramatic benefit that would obviate the need for formal evaluation to determine effectiveness, despite claims to that effect for a number of treatments.

Pursuit of evaluation by practitioners and supporters varies considerably among the wide range of treatments covered in this report. As portrayed by members of the project Advisory Panel, proponents of the “middle ground” (mainly psychological, behavioral, and dietary approaches used along with mainstream treatment) may be most interested in testing and refining their treatments, but they apparently find the current system for doing so unresponsive (8). An additional hurdle is posed by the different orientations toward evaluation in the social sciences, from which a number of psychological and behavioral approaches have come, as opposed to that in medicine. The former rely more heavily on inferences from uncontrolled, nonexperimental observation, whereas the evaluation of medical technologies relies heavily on experimental designs, particularly randomized clinical trials. At least some psychological practitioners and researchers (7) have expressed an explicit belief that such experimental methods are not necessary or appropriate to determine the effects of psychological and behavioral approaches.

From a methodological point of view, for treatments consisting of pharmacologic or biologic agents that are intended to extend survival time, with or without affecting the tumor directly, appropriate evaluation methods would be the same as those that have been developed and validated for mainstream pharmacologic and biologic treatments. Should new, validated methods become available--e.g., approaches currently being investigated under the rubric of “outcomes research” or “medical treatment effectiveness research” (880)--these, naturally, could apply to unconventional as well as conventional treatments. In the case of outcomes or effectiveness research, however, it will probably be some years before enough is learned about these techniques to gauge their long-term usefulness.

For many-faceted approaches e.g., combinations of dietary, psychological, and behavioral aspects--which have as major goals improved quality of life, some adaptation of methods maybe necessary, perhaps borrowing from social science research, where appropriate. But in the final analysis, the concepts basic to the unbiased evaluation of medical interventions and the reliance on randomized clinical trials will still apply. Practical problems, not methodologic ones, however, are likely to be the most significant obstacles to evaluating unconventional cancer treatments.

Chapter 12 of this report discusses past approaches to evaluating unconventional treatments, along with some ideas that might be adopted to further evaluation efforts. The term “evaluation” is used broadly here to describe the systematic gathering of evidence related to the effectiveness and safety of treatments, including information provided by supporters of unconventional treatments and individuals unaffiliated with specific treatments.

Review of Evidence for an Unconventional Treatment: An Example

For the most part, evidence put forward by individuals identified strongly with particular treatments has been of a type not acceptable to the mainstream medical community. A common format is a series of individual case histories, described in narrative. The endpoints are more often than not “longer than expected” survival times, sometimes with claims of tumor regression. In mainstream research, case reports of unexpected outcomes have been useful and do have a place, but they almost never can provide definite evidence of a treatment’s effectiveness.

An example, well known among supporters of unconventional treatments, of evidence put forth systematically by a proponent is a series of case reports of 50 patients treated by Kelley with his nutritional program, and described by Gonzalez, a physician, in his unpublished book about Kelley, *One Man Alone: An Investigation of Nutrition, Cancer, and William Donald Kelley* (353). (Gonzalez himself practices a variation of the Kelley program.) This series has been singled out by unconventional treatment proponents as one of the best of its kind, which has been ignored by mainstream medicine (529,596). OTA carried out a review of Gonzalez’ material by six members of the advisory panel for this project, three physicians generally supportive of unconventional treatments (though none associated directly with the Kelley program) and three mainstream oncologists. Each case was assigned randomly to one unconventional and one mainstream physician.

Fifteen cases were judged by the unconventional reviewer as definitely showing a positive effect of the Kelley program; the mainstream reviewer of each case found 13 of these unconvincing and 2 unusual. Nine cases were judged unusual or suggestive by the unconventional reviewer; the mainstream reviewer found these cases unconvincing. Fourteen

cases were judged by the unconventional reviewer to have been helped by a combination of mainstream plus Kelley treatment; the mainstream reviewer found 12 of these cases unconvincing and 2 unusual. Twelve cases were considered unconvincing to both the unconventional and mainstream reviewers.⁶

The mainstream reviewers had similar general comments about the cases. A general theme was that, based on the material presented, it was not possible to relate results to particular treatments. Nearly all patients had mainstream treatment, which, along with the natural variability of the disease, might have been sufficient to account for the observed outcome. One reviewer commented:

Those of us who have worked over the years with cancer patients have come to respect the vagaries of human biology wherein there are cancer patients who for unclear reasons fare better than we would have expected. (544)

Another common criticism was that comparing an individual patient's survival with average group statistics is misleading and an invalid use of data.

General comments of the unconventional reviewers were significantly different and, in general, positive about the Kelley treatment. One reviewer wrote:

... I would judge that the patients under my review appear probably, but not certainly, to have presented for the most part an unusual course, that the outcome exceeded normal management and that the effect of the Kelley treatment contributed significantly, although not necessarily exclusively, to the outcome. (218)

What this review demonstrates most clearly is that some of Gonzalez' cases may be convincing to physicians already supportive of unconventional treatment but that they were not convincing to the mainstream physicians who participated in the OTA review, and, because of the reasons given, probably would not be to most other mainstream physicians. Key issues appear to be lack of adequate documentation of the course of disease and reliance on unusually long survival rather than documented tumor regression in most cases.

Clinical Trials of Unconventional Cancer Treatments

Relatively recently, studies by independent researchers have contributed to the evaluation of unconventional treatments. Studies of particular note include two randomized trials, one of hydrazine sulfate by researchers at the University of California at Los Angeles (186), and the other of a psychological intervention, carried out by a psychiatrist-researcher at Stanford University (824). Both studies were methodologically sound, published in peer-reviewed journals, and, in both, the interventions were associated with increased longevity and with improvements in some more subjective measures. Further studies of these interventions have been planned as a result of these initial studies.

Formal attempts at evaluating unconventional cancer treatments have been made by the Federal Government in various ways. The best known are clinical trials of laetrile and vitamin C that were carried out by researchers at the Mayo Clinic under contract to NCI. In both instances, the Government was responding to the expanding popularity of these compounds with the public. In the case of laetrile, although it was not approved by FDA, by 1982 its use had been legalized by more than half the States and it could be used legally in the rest of the country as a result of a court order. The published laboratory studies of laetrile's activity did not suggest that it would be active against cancer, however, and no adequate study of cancer patients had been done. Interest in the use of vitamin C, a widely available product, grew as a result of studies of cancer patients reported by Ewan Cameron in the early 1970s, later in collaboration with Linus Pauling, and because of evidence from in vitro and animal studies suggesting beneficial effects of vitamin C. The laetrile experience is discussed here.

During its period of greatest popularity, laetrile was promoted mainly as an agent that acts directly against tumor cells, and it was treated as such when the Government decided to evaluate it. The first step taken was to look for evidence that laetrile caused tumors to regress. To do this, about 450,000 physicians and other health professionals were solicited for reports of patients with documented anti-tumor responses to laetrile. In the end, 67 cases had sufficient information to be evaluated independ-

⁶Termed "unconventional reviewers" and "mainstream reviewers" for purposes of this discussion.

ently. Out of these “best cases,” a blinded review resulted in establishing two complete and four partial remissions (274).

NCI decided to proceed with a prospective study of laetrile, carried out by researchers at the Mayo Clinic. They began with a typical “phase I” study to determine toxicity and dose (620). Those results were used in designing the phase II study of antitumor activity in 178 patients with a variety of cancer types (623). Among the 175 patients evaluable at the end of the study, one had a partial remission. No further clinical trials were deemed necessary, as the drug was considered ineffective.

A host of criticisms was heard from laetrile proponents. In the confrontational atmosphere that exists around unconventional cancer treatments, it appears impossible to resolve these questions conclusively, but this study appears to have been a fair test of the main claim for laetrile, that it was an antitumor agent.

Possibilities for Improved Evaluation of Unconventional Treatments

The basic principles of scientific evaluation are firm, but the process of reaching the point of formal evaluation and the practical problems of acquiring useful evidence about the efficacy and safety of unconventional treatments may be different in some ways from those encountered in mainstream treatments.

Multifaceted treatments, such as the Gerson treatment and macrobiotics, which would be difficult if not impossible to reproduce in a medical center for the purpose of evaluation, pose additional practical problems, and suggest the need for studies to occur in their own settings. It has been suggested that this might be possible with the participation of “dispassionate researchers, on site” (88), who would evaluate patients for objective evidence of effectiveness before and after treatment. It would not be possible to measure improved survival in this way (without an appropriate comparison group), but it might be possible to determine whether the treatment had antitumor effects. Descriptive information about quality of life could be gathered, but again, without an appropriate comparison, it would be difficult if not impossible to attribute benefits to the treatment.

Such studies would represent a new direction; OTA could identify no examples of methodologically sound clinical trials, assisted by dispassionate observers, of unconventional treatments carried out in their unconventional settings.

In principle, clinical trials are simple, but they can be extremely difficult to organize, even working entirely within the system. The added complications of working with an unconventional treatment render such trials a true challenge. OTA’s experience during this assessment in developing a clinical trial protocol for IAT illuminated some key points. One of the most significant is that, except in rare cases, evaluation should be initiated by and the responsibility of the practitioners using or otherwise positively interested in the treatment, though they need not be (and preferably are not) associated exclusively with the treatment. (The Federal Government has initiated evaluations only when treatments [e.g., laetrile and vitamin C] have become very popular and potentially affected large numbers of patients.) Whoever undertakes these studies, it is important to involve developers or other key practitioners of the treatment in developing a plan for the study, and in reporting and publishing its results. To ensure credibility and the availability of technical expertise, the trial should, if possible, be carried out in an accredited medical institution in the United States, with the consent of the appropriate Institutional Review Boards. Finally, it is of the greatest importance that in any study the safety of patients is ensured. This may be best accomplished by carrying out studies in accordance with FDA regulations governing new and unapproved drugs and devices (when applicable).

A “Best Case Series” Approach

New treatments for cancer coming from mainstream research typically progress through a sequence of preclinical and clinical studies before they are offered to cancer patients outside an experimental setting. Clinical trials generally continue even after anticancer agents are approved, building on the pre-approval research. Unconventional treatments currently in use have bypassed this system before being used to treat cancer patients. While OTA has not taken a position condoning or condemning the use of treatments unproven through generally accepted means, the fact that this is the case with unconventional treatments cannot be ignored.

In the course of this study, OTA explored the potential for using the experience of the self-selected patients who have undergone unconventional treatments to inform the evaluation process. It is possible that this experience, presented systematically, might be useful in generating interest in a treatment, and possibly in designing a clinical trial. However, no valid mechanism exists to use this retrospective patient experience to actually determine the efficacy and safety of these treatments. Except in rare circumstances, because of the heterogeneity of cancer patients' clinical courses, it is virtually impossible to predict what would have happened to a particular patient if he or she had had no treatment or a different treatment. Groups of patients who have chosen to take a particular treatment cannot be compared retrospectively with other groups of patients, even those with similar disease, to determine the effects of the treatment. The factors that set apart patients who take unconventional treatments from other cancer patients may be related to prognosis (these may be both physical and psychological factors), and the means do not exist currently to confidently 'adjust' for these factors in analyses. Examples of retrospective evaluations that have turned out to be wrong are well documented (see, e.g., (146)) as are problems with attempting to evaluate the efficacy of treatment from registries of cancer patients (145), though the problems are not necessarily widely appreciated.

Nonetheless, the clinical experience of practitioners with unconventional cancer treatments may be useful for: 1) providing preliminary evidence that can be used to support undertaking formal evaluation; and 2) helping design a formal evaluation, by identifying tumor types that might be responsive, by specifying dosages, and by suggesting potential adverse effects for which monitoring might be necessary. One way to summarize and communicate the clinical experience for these purposes is to conduct a formal retrospective review of "best cases," which would include full diagnostic, treatment, and outcome information for a group of patients treated previously and followed up. This is particularly well suited to treatments intended to cause tumor regression. The objective would be to provide clear evidence of tumor regression after the unconventional treatment which could not logically be ascribed to either other treatment or the natural

history of the disease itself. The responsibility for best case reviews would rest with the practitioners offering unconventional treatments, ideally with technical advice from appropriate experts. This approach, still untested, would place the burden of initiating the evaluation process on the practitioner. No matter how well done, however, a best case review cannot take the place of prospective clinical trials, and no firm statements about effectiveness could be made on the basis of a best case review. It is possible that, like the review of laetrile cases,⁷ relatively little will be learned from best case reviews, despite significant effort. This will depend, to some extent, on the availability of sufficiently detailed medical records, from both unconventional and mainstream treatment. The latter, particularly, may not be accessible to unconventional practitioners.

What might happen after a successful best case review is still an open question. In general, 'the aim would be to apply widely accepted research methods--preclinical, clinical, or both, depending on the intervention--to begin formal evaluation.

Improvements in survival, "disease-free survival" (surviving without signs of cancer), and quality of life are the desired outcomes of cancer treatment. As it turns out, treatments that thus far are known to improve survival have a direct effect on tumor cells, causing regression of tumor masses, so tumor size is also of interest as an indicator of antitumor activity. In some cases, tumor shrinkage, even if not complete, can relieve physical problems caused by the position and size of a tumor, increasing survival time and improving quality of life. However, because many chemotherapy regimens also have significant toxicity, the ability to shrink tumors does not necessarily correlate with improved survival (see, e.g., (91)).

Getting reliable evidence about antitumor effects, improvements in survival and disease-free survival, and quality of life requires formal clinical trials in almost all cases. Exceptions would be treatments that are dramatically effective, that produce long-term remissions in a sizable percentage of patients with advanced cancer. Unfortunately, such treatments are rare. The challenge is to find ways in which unconventional cancer treatments can be

⁷The laetrile review, however, was different from what is proposed here in that the Government conducted it.

evaluated adequately, and in which less dramatic but still worthwhile benefits could be detected.

If an unconventional treatment appears “promising” (e.g., on the basis of a best case review), there might be sufficient impetus for pursuing formal evaluation. There may, in addition, be other reasons for conducting an evaluation of an unconventional treatment. Such studies could be very important in terms of public health, though they might well not lead to advances in cancer treatment. A treatment’s popularity might influence the decision. It might be considered important, for public health reasons, to evaluate treatments used by large numbers of people, e.g., treatments offered by the long-established clinics or particular treatments that gain widespread acceptance without proper clinical trials (e.g., laetrile). This is not to suggest that negative evidence will always dissuade cancer patients or that mere popularity should be taken as a sign of effectiveness. Indeed, it is clear from past experience in both conventional and unconventional medicine that the two are not necessarily synonymous. Another factor that, in the real world, might stimulate consideration of an evaluation is political interest. This was the case in OTA’s undertaking protocol development for a clinical trial of IAT.

Technical and Financial Support for Evaluations

The Federal Government, through the NCI, is the country’s largest sponsor of cancer clinical trials. Others sources of funding do exist. The most obvious case is funding of research by pharmaceutical companies. Another recent model is the funding and running of clinical trials by AIDS activists. Their first, successful venture was a clinical trial of aerosolized pentamidine, a drug that inhibits the development of pneumocystis pneumonia in HIV-positive individuals. While this model is new, it is available to supporters of unconventional cancer treatments, and it bypasses the NCI peer review process. But funding by the Federal Government should be a real possibility, particularly for treatments that could, if they should prove effective, be made widely available to cancer patients.

While no formal barriers block requests from practitioners of unconventional cancer treatments for Government support of research, these practitioners, in general, will be unsuccessful in competing for research dollars without technical assistance. The informal barriers are formidable.

The most serious problem in attempting to assure that evaluations of unconventional treatments are scientifically credible is that many or most practitioners of unconventional cancer treatments are not familiar with mainstream clinical research methods, nor do they have easy access to experts who are. What is needed, and would be particularly helpful at the stage of preparing best case series or conducting small studies within unconventional settings, is technical assistance to make sure that the standards of evidence are understood, and for helping the practitioner prepare a work plan for the project. It is in the public interest for the Federal Government, NCI in this case, to be involved in providing some technical assistance, and easing access to NCI review of formal best case series. NCI can help assure the quality of any such best case reviews that are submitted, and, if the results are promising, assist in developing a plan for further evaluation.

Funding by the Federal Government carries with it conditions on research that some parts of the unconventional community may find problematic. These include a general prohibition against funding clinical trials outside the United States, the requirement that clinical trials be carried out in compliance with FDA regulations, the particular requirements for informed consent of patients participating in clinical trials, and the general concerns for complete disclosure and reporting.

OPTIONS

Options To Broaden the Base of Information on the Use of Unconventional Cancer Treatments in the United States

- 1a. **Studies on the Characteristics and Motivations of Cancer Patients Who Use Unconventional Treatments**—Relatively little is known about the types of patients who use unconventional treatments, and their motivations for doing so. The few studies that have been done do not support the stereotype of the desperate, ignorant miracle seeker. Research could be carried out to gather this information through broadly based surveys of patients in the United States. As with all research of this type, the anonymity of the patients surveyed should be guaranteed. It might be useful to consider studies specifically in “SEER” (Surveillance, Epidemiology, and End Results) areas, in which incidence data are routinely collected. Such information would be

useful for determining the types of information the public desires and developing the best means of targeting that information.

- 1b. Utilization Studies--Studies could be done to determine the types of unconventional cancer treatment used in the United States and the extent of use. This information, together with the information from studies of patients (option 1), could be used to determine the appropriate priority to be given evaluations of unconventional cancer treatments.**

Gathering and Making Available Information on Unconventional Cancer Treatments and Practitioners

- 2. Studies on Information Dissemination by Federal Agencies--The National Cancer Institute could have its Cancer Information Service (and Cancer Communications Office) evaluated for the adequacy and quality of information it supplies about widely used unconventional cancer treatments in relation to the information requirements of its users.**

Improving Information on the Efficacy and Safety of Treatments Used by U.S. Citizens

- 3. Mandated Responsibility of NCI To Pursue Information About and Facilitate Examination of Widely Used Unconventional Cancer Treatments for Therapeutic Potential--NCI does not now formally seek out information on a wide range of unconventional treatments. Most of their activities in the past have been in reaction to reported problems or as a result of congressional pressure. Activities might take place in various sections of NCI (e.g., the Natural Products Branch would be the logical place for herbal treatments to be examined). Particularly with a new set of in vitro screening tests coming into use by NCI, consideration could be given to screening appropriate components of unconventional treatments. (Many herbal compounds have been screened in the past, with a mixture of positive and negative test results.)**
- 4. Facilitating "Best Case Series" of Unconventionally Treated Patients**
- 4a. NCI could develop and circulate widely specifications for a simple process for assembling "best case" series in a form that might be**

acceptable for publication in the peer-reviewed literature. NCI might consider providing for a meeting with the preparer after the review has been completed, to discuss the review, for the purpose of minimizing avoidable ambiguities or misunderstandings.

- 4b. NCI could provide funding to recruit and support a small group of consultant experts in evaluation methodology to advise unconventional practitioners or their advocates who wish to plan and carry out evaluations. These could range from advising on plans for "best case" series to planning randomized trials, when appropriate. These consultants could also assist with filing IND applications, should evaluation reach that stage.**

One possible mechanism for carrying out this option would be to contract, on a competitive basis, with a university or other appropriate organization to assemble and direct the consultant group. Consultants would most likely be academics or researchers who would devote a limited amount of time per year to this activity, but to whom unconventional practitioners could have easy access. Initially, this group could be given the task of drawing up specifications for best case reviews.

- 5. Providing Funds for Meritorious Evaluations of Unconventional Cancer Treatments--In a time-limited demonstration project, the Federal Government, either through NCI or through another office, could provide funds for evaluating unconventional cancer treatments. A review committee could be established to review proposals for evaluations, which would have to meet appropriate methodologic standards. The committee should include both mainstream scientists/physicians and scientists/physicians identified with unconventional treatments. Four years might be an appropriate time period for the demonstration, divided into the two phases described below. If implemented, the program should be evaluated after three or four years to determine whether the mechanism has stimulated worthwhile evaluative efforts, and whether it should be continued. The amount of funds that would be used for such a demonstration depends on balancing two conflicting factors: funds would need to be large enough to provide for a fair test of the program, but the Government needs to limit the amount to reasonable levels until the value of such an effort**

is demonstrated. During the first phase, research proposals would be solicited and reviewed. The review committee would be funded in this phase, but no actual research funds would be allocated. Estimates of annual funding requirements for phase two would be based on the quantity and quality of proposals received during the first phase.

- 6. Reporting System for Remissions With Unconventional Treatments or Without Treatment—The Federal Government could maintain a registry for reports of documented tumor regressions that follow unconventional treatment in circumstances where the regression cannot plausibly be ascribed to the effects of previous or concurrent conventional treatments, and for regressions occurring in the absence of any treatment. Criteria for documentation of cases would be specified. This would be of value not only to gather information about potentially useful unconventional treatments, but also to further knowledge about spontaneous remissions.*
- 7. Reporting System for Adverse Effects of Unconventional Treatment—The Federal Government could maintain a registry for reports of*

documented adverse effects of unconventional cancer treatments (and of unconventional treatments in other major disease). Currently, physicians are required to report adverse reactions to prescription drugs, but no such requirement exists for unapproved substances. Criteria for acceptable cases would be specified.

Making Available Information on Legal Sanctions Against Practitioners and Health Fraud Related to Unconventional Cancer Treatments

- 8. Information About Prosecutions for Practicing Medicine Without a License--Little information is currently available to the public on practitioners of unconventional cancer treatments who have been convicted for practicing medicine without a license. This information might be useful to patients seeking background information on available treatments and on the practitioners. States' Attorneys General offices might assemble this information and make it more readily accessible to the public. A Federal effort could link information from the States.*