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The Future of Complementary and Alternative Medicine for Cancer

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This article explores why cancer patients use complementary and alternative medicine (CAM), why CAM use should be of interest to physicians who treat cancer patients, and how physicians may appropriately support their patients' quest for comfort, quality of life, and healing. We use the term ''CAM'' to refer to substances and practices that have been available primarily outside of the American medical mainstream, that have sources other than medical doctors and allied health care providers, and that are not commonly recommended by medical doctors as treatments for a given condition. *Alternative* treatments are those used instead of conventional medicine; *complementary* treatments are those used in addition to conventional medicine.

Keywords Alternative medicine; Complementary medicine; Cancer; Integrative medicine

WHY CANCER PATIENTS USE CAM

Nearly 40 percent of the general population of the United States[1,2] reports having used some form of CAM for an extended period of time.[3] People without life-threatening illnesses use CAM for health promotion/disease prevention, to treat minor ailments or conditions that conventional medicine cannot or will not address, or to enhance the quality of their lives. Although the vast majority of patients with biopsy-proven cancers who use CAM also receive conventional treatment,[4,5] cancer patients have, aside from cancer-related reasons, the same reasons as other people for using CAM.

In the last half of the twentieth century, cancer survivorship in the United States increased dramatically; mean 5-year survival for cancer of all sites rose from 35 percent in 1950–1954 to 63.1 percent in 1989–1997.[6] As of 1999, 8.9 million people in the United States (3 percent of the population) were cancer survivors, including 2 million women with breast cancer and 1.3 million who were >20-year survivors (http://dccps.nih.gov/ocs/prevalence/index.html). These figures reflect the aging of the large baby boomer cohort, the association of cancer with age, and improvements in screening and treatment. But the extended life expectancy of cancer patients is not an unmitigated blessing. Most cancer survivors have more health problems than individuals of the same age and sex who have not been diagnosed with cancer. Many of those whose disease is in remission live with the awareness that it may recur.[7] A recent survey of 913 cancer patients found that 94 percent experienced disease-related symptoms not addressed by, and/or side effects attributable to, their conventional treatment. Although respondents were relatively satisfied with the conventional treatment they received for their cancer, they were less satisfied with the attention paid to their symptoms and side effects.[8]

Cancer patients today have access to more information about their disease and treatment options than ever before. Many choose to participate in treatment decisions and to explore more options in treatment and self-care than are presented to them by their conventional physicians. Patients who reported experiencing fatigue, for example, visited their doctor 24 percent more often than those who did not, and were nearly twice as likely to use CAM.[8]

A recent survey of 356 cancer patients showed that 70 percent used some type of CAM and 17 percent used a CAM provider. This use was associated with higher educational

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attainment (but not income), undergoing multiple cancer treatments, and being female. Women were 5 times more likely than men to see a CAM provider ($p<0.05$). Motives for choosing CAM for cancer varied across CAM therapies and included enhancing general health and well being (83–97 percent) as well as for cancer treatment (8–56 percent).[9]

In a survey we conducted recently, CAM use was only slightly more prevalent among newly diagnosed cancer patients than among their relatives and friends.[10] As cancer patients go through treatment and deal with the long-term effects of their disease and/or with recurrent disease, they may become more likely to use CAM.[11] The major CAM modalities and the concerns they raise among some physicians are shown in Table 1 below.

Table 1 does not list benefits not because CAM has no benefits, but because reported benefits are largely anecdotal, nonspecific, and not a reason for concern. Potential adverse health effects of CAM also are largely undocumented, but are a cause for concern, particularly until additional research can clarify the risks. In addition, CAM use may affect health care costs, at least for the patient, and alter the doctor-patient relationship for better or worse.

Table 2 shows the relationship of CAM use to patient status. In general, patients use CAM to meet needs that

TABLE 1
CAM modalities used by cancer patients

Modality	Examples	Physicians' concerns
Nutritional supplements	Multivitamins Antioxidants (vitamins C and E, selenium, etc.)	Adverse interaction of antioxidants with radiation therapy and chemotherapy[12]
Herbs and botanicals	PC-SPES Soy Essiac	Contamination (http://nccam.nih.gov/research/news/pcspes.html); (see text box), estrogenicity,[13] adverse interactions with conventional treatments[14]
Other biologicals	Shark cartilage Melatonin	Contamination,[15] adverse interactions with other treatments[16]
Mind-body healing approaches	Support groups Meditation Music therapy Prayer	Potential effect on doctor-patient relationship; false hope[17]
Traditional systems of medicine	Traditional Chinese medicine (herbal medicines, acupuncture, body work) Ayurvedic medicine (dietary modification, herbal medicines, colon cleansing, etc.)	Contamination of ingested agents,[18] adverse effects from invasive procedures[19]
Manual treatments	Massage Reflexology	Tissue damage; cancer spread[20]
Energy therapies	Reiki Magnets Qi gong	False hope[21]
Special treatments and cancer clinics	Burzynski clinic Gonzales treatment Revici treatment	Safety; false hope[22,23]
Special diets	Low fat Macrobiotic Vegan	Malnutrition[24]

TABLE 2
Type of CAM use by patient status

Patient status	Primary purpose of CAM use		
	Cancer-directed	Wellness	Relief of symptoms or treatment side effects (includes palliative care)
Early stage, receiving primary biomedical treatment	—	Promotion of overall health, immune function, etc. Nutritional supplements Lower fat/more vegetarian diet Manual therapies Mind/body practices Herbal agents	Herbal agents Energy therapies Manual therapies Mind/body practices Nutritional supplements
Treatment completed, no evidence of disease	—	(same as above)	(same as above)
Advanced or recurrent disease	Specialized cancer diets Cancer clinics Cancer-specific biologicals Herbal agents Mind/body practices	(same as above)	(same as above)

conventional medicine does not address, but those needs depend, in part, on whether the patient is receiving treatment, has completed treatment, or has advanced disease. Patients with early-stage disease, who are receiving mainstream treatment or are in remission, are less likely than those with advanced disease to use CAM specifically directed against the cancer, although many believe or hope that adopting a more healthy lifestyle can minimize side effects and reduce the likelihood of recurrence. Patients with advanced disease have been found to be more likely to use more extreme therapies (those involving substantial expense and effort) than other patients.[11,22]

WHY CAM USE SHOULD BE OF INTEREST TO PHYSICIANS WHO TREAT CANCER PATIENTS

Potential Benefits

A positive reason to find out about patients' use of CAM is that some therapies actually may relieve symptoms or side effects or improve quality of life. What patients find beneficial, even in the short term, may be important information—and it is certainly important to patients that their doctor show interest in their comfort and quality of life. Also, it may result that one or more of the very large number of CAM treatments used by cancer patients may actually prove to have a cancer-directed benefit.[25]

Evidence of the benefits of CAM therapies that are not cancer-directed is mounting; for example, hypnosis appears to reduce pain, and acupuncture appears to reduce nausea due to chemotherapy.[26] If patients using a particular CAM therapy appear to fare better than expected with respect to those conditions or the cancer itself, well-maintained records may facilitate the conduct of a best-case series, often the first step in clinical research on the efficacy of CAM.

Failure to Mention CAM Use

Most surveys have found that one-third to one-half of CAM use is not reported to the patient's doctor.[2,8,27,28] Part of the reason may be that many patients do not think some of what they do use is medically relevant in the strict sense. People may adopt dietary changes touted as desirable by numerous health columns in the mass media, but not even think of telling their doctor.[24] Similarly, prayer is not generally considered to be the province of scientific medicine (or even necessarily that of CAM), and the role of the physician in the patient's religious life is a topic on which opinions differ.[17] Not every aspect of life requires medical approval, but lifestyle can affect health. Patients often do not appreciate whether or how some aspects of lifestyle may affect health in general or responses to cancer treatments, in particular. Without sufficient discussion, patients may not understand what information their doctor needs to help them maintain an optimal lifestyle for coping with cancer and maintaining well-being.[29]

Less well-understood and accepted forms of CAM, such as detoxification treatments and the use of certain herbal or

animal products as medicines, may be of concern or even alarming to physicians, especially if the modalities are used concurrently with chemotherapy or radiation therapy, since little is known about potential interactions. Some patients do not report their CAM treatments because they do not expect the doctor to know much about these approaches, because they wish to avoid incurring the doctor's disapproval, or because they do not feel that they should be accountable to the doctor for everything they do.[17] But, as popular media attention to CAM increases, patients seem to be becoming more assertive about their CAM use.

Potential Adverse Effects, Including Adverse Interactions with Conventional Treatment

Confronted by both popular press reports of dramatic cures or adverse effects, and a dearth of solid scientific data, physicians are appropriately concerned about the impact that CAM may have on their patients. Several CAM treatments have been associated with complications such as liver and kidney toxicity[14] and anaphylaxis.[30] But immediate toxicity may not be the only concern. For example, many patients take antioxidant supplements during chemotherapy with the hope of minimizing toxic side effects, although the efficacy of such supplements for that purpose has not been determined. Some medical and radiation oncologists are concerned that antioxidant supplementation during treatment may reduce its benefits. It has been argued that antioxidants may suppress the oxygen free radicals that radiation and chemotherapeutic drugs generate and, therefore, reduce the efficacy of these treatments.[31] However, research to date has not shown that taking antioxidants reduces the efficacy of conventional treatment, and some evidence suggests that a free radical scavenger can control treatment side effects.[32,33] Amifostine, a conventional drug prescribed to control chemotherapy side effects, is characterized as a powerful free-radical scavenger, and has been studied extensively and found not to affect long-term outcomes adversely.[34,35] Antioxidants of the dietary supplement type may, similarly, confer benefit without detriment.

Another aspect of CAM use, one that should concern medical investigators conducting research on new conventional cancer treatments, is the undisclosed use of CAM among patients participating in clinical trials. A recent survey of 100 cancer patients participating in intramural clinical trials of new drug therapies at the National Institutes of Health found that 63 percent were using CAM.[36] Even when trial participants are asked not to use other agents, some did so anyway.[37]

Integration of CAM with Conventional Treatment

In the past few years, a number of medical centers and cancer centers have opened programs that provide a variety of complementary services to cancer patients and others.[38,39] These programs may be intended to provide: 1) opportunities for conventional and CAM practitioners to interact both on and offsite and learn from one another; 2) settings in which knowledgeable physicians can integrate CAM with conventional medicine, supervise the provision of CAM, or conduct studies of the efficacy and safety of CAM; or 3) profit centers/loss leaders.

Unfortunately, the mere presence of CAM providers in a medical center does not guarantee effective interaction with conventional physicians or optimal management of patients, nor is an onsite complementary care program necessarily the best means to the end of integration of care. One obstacle to effective incorporation of CAM therapies with a conventional medicine treatment program is lack of information for physicians on how to evaluate the credentials and training of CAM practitioners. This issue is less of a problem for practitioner categories that are subject to state licensure (e.g., acupuncture, chiropractic, massage), but for many popular CAM modalities (e.g., herbal medicine, some practitioners of ethnic medical systems), the United States has no national or state licensing or credentialing, or even a broadly recognized association capable of reviewing practitioner skills. Although some groups of practitioners are working to professionalize themselves, many CAM experts fear that, before this is accomplished, licensing criteria may be imposed by a group that does not have a real knowledge of the modality or its practitioners, or that they will be managed by a bureaucracy that does not serve the best interest of patients. Further, the high overhead that comes with operating in a large medical center may place practitioners of such services as nutrition consultation, yoga, massage, and Traditional Chinese Medicine (TCM), at a competitive disadvantage compared with independent community practitioners.

Another concern is that bringing CAM modalities into a conventional medical or research setting may alter the way they are practiced. Some CAM advocates oppose reducing a unified philosophical approach to a set of techniques and procedures and replacing herbal compounds with purified extracts that can easily be incorporated into the biomedical model. However, cutting CAM modalities off from their roots can be successful. For example, in TCM, acupuncture is customized to the patient and provided in the context of a TCM diagnosis and treatment plan. However, even when separated from its TCM origins and provided to a standardized set of points on the body, acupuncture has been found to be effective as a treatment for nausea.[38] In settings where a standardized CAM treatment has not proved efficacious, it has sometimes been interpreted as discrediting the entire modality, or even CAM in general. For example, a Chinese herb, dong quai, delivered as a single herbal remedy was found not to be efficacious as treatment for menopausal hot flashes; however, in TCM, dong quai is not used as a single agent as it was used in this trial. The results of this study, despite attempts at clarification by the authors were widely interpreted as showing the inefficacy of dong quai for this indication.[39]

In another model of attempted integration of services, a number of freestanding multimodality CAM centers, have opened. Some provide CAM services under medical or nursing supervision. It is not clear whether substantial numbers of patients will pay the higher cost for CAM under medical supervision unless their health insurance covers it; nor is it known whether covering CAM, in or out of medical centers, will improve patient outcomes or be cost-effective for insurers.[40,41] Cancer patients, like other health care consumers, are likely to continue using CAM in a variety of settings.

HOW PHYSICIANS MAY APPROPRIATELY SUPPORT THEIR PATIENTS' QUEST FOR COMFORT, QUALITY OF LIFE, AND HEALING

By Asking Patients About Their CAM Use and Systematically Recording Their Answers

Given insufficient clinical research data about safety and efficacy of CAM therapies, and CAM interactions, whether favorable or adverse, with conventional treatment, some physicians may feel that the safest course is to discourage all CAM use. But doing so is likely either to drive patients away or to keep them from reporting their CAM use. Obviously, patients should be discouraged from using treatments that have been shown to be harmful. However, in the absence of data, a more useful approach is to ask about CAM use in a nonjudgmental way at each visit. Physicians should systematically record this information so that they can attempt to document observed effects, or lack thereof. They can also follow trends in the types of CAM being used by their patients and keep an eye out for new published reports about CAM that are increasingly available in the medical literature. When a patient experiences an adverse event potentially attributable to an identifiable CAM agent, taken orally or topically, the patient should bring the bottle/container to the practitioner so it can be properly identified, and the adverse event should be reported to the Food and Drug Administration (FDA). Suspected adverse events from any medication can be reported to the FDA's MedWatch system via the Internet (www.fda.gov/medwatch), telephone (800-FDA-1088), or fax (800-FDA-0178). However, a comprehensive national system for reporting adverse events specifically attributed to CAM therapies is sorely needed. Experts in several other countries have been tackling the same problem, and the United States can learn from their experiences as we develop our own system.

By Developing Working Relationships with CAM Practitioners

A few oncologists have begun incorporating CAM into their clinical practice, either by themselves developing expertise in one or more CAM modalities, or by collaborating with local CAM practitioners such as acupuncturists and herbalists. One way to begin to learn about CAM is to ask patients about their CAM use, to identify the CAM practitioners who are treating these patients, and to ask patients for permission to contact these practitioners. Initiating such a dialogue can benefit both that patient and others. If a Traditional Chinese Medicine practitioner, for example, appears to have helped a patient manage side effects during chemotherapy, the oncologist should consider the practitioner worthy of at least a telephone call. Making this contact may require patience and willingness to learn a terminology that may be unfamiliar to the physician as medical jargon may be to the CAM patient. But dialogue is possible, and CAM practitioners, for their part, are often eager to access medical test results that help them to see how their therapies may be working. When a subsequent patient expresses interest in this modality, the experience of the previous patient may be worth mentioning.[42] The legal liability associated with such counseling and referral is a valid concern but is manageable.[43] Apart from that issue, assessing the quality of practitioners of an unfamiliar and unlicensed modality is not simple, but patients face the same problem. Typically, they proceed by inquiring of friends, other CAM providers, and the Internet. Physicians are at least as well equipped as patients to process the results of such inquiries and to assess credentials and recommendations.

Patients with advanced disease are more likely than other patients to explore the more extreme and expensive CAM therapies. In an ideal world, providers of such therapies would collaborate with clinical investigators who, by collecting observational data via best-case series and other designs, could begin to evaluate claims of efficacy. Meanwhile, in the absence of evidence of adverse effects, intentional misrepresentation, or greater benefit from a conventional treatment, oncologists should continue to follow their CAM-using patients and, if possible, initiate and maintain communication with their patients' CAM practitioners.

Some cancer patients turn to CAM at the end of life. Certain CAM modalities used in this setting, such as acupuncture, psychosocial support, and imagery, may be as effective as, less expensive than, synergistic with, or less likely to cause side effects than conventional palliative care.[44] Discussing and understanding patients' choices should benefit all concerned.

The National Institutes of Health National Center for Complementary and Alternative Medicine (NCCAM) and National Cancer Institute's (NCI) Division of Complementary and Alternative Medicine, as well as other organizations, are increasingly funding research that will in time validate or refute claims of benefit for some cancer-directed CAM therapies (NCCAM web site).[45] In addition, in other countries treatments in use or under study show promise of improving patient outcomes. Given the large number of CAM therapies in use, and the limitations of even the expanded funding, it will be a long time before the evidence that patients and physicians need is available. Meanwhile, oncologists can

try to learn from patients and CAM practitioners, why and how they use CAM and whether and how it can contribute to the goal of extending and enhancing the quality of cancer patients' lives.

THE TALE OF PC-SPES

Dr. Sophie Chen, who developed PC-SPES, received her Ph.D. in physical chemistry from Columbia University and conducted research on enzyme structures and function as a postdoctoral fellow at Cornell University. Following her work at Cornell, Dr. Chen worked as a group leader and codirector at Merck Sharp & Dome and Bayer, USA. In 1988, Dr. Chen began studying the effects of herbs used in Traditional Chinese Medicine on cancer. In the mid-1990s, while working at New York Medical College, she starting modifying a TCM herbal formula, and developed a mixture of eight herbal extracts that she named PC-SPES—PC for prostate cancer, and SPES, the Latin word for *hope* (http://www.nymc.edu/pubs/Chironian/Fall2001/pc101.htm).

In October 2001, at the American Medical Association's 20th Annual Science Reporters Conference in San Francisco, she reported that the formula lowered PSA levels among patients with advanced prostate cancer (http://www.ama-assn.org/ama/pub/article/4197-5455.html). Her company, BotanicLabs, manufactured PC-SPES and distributed it directly to patients, although the company was insistent that patients should discuss their use of PC-SPES with their doctors and be followed carefully for benefit and side-effects known to be similar to those of estrogen therapy. Numerous studies found an association of PC-SPES with clinical benefit, declines in PSA levels, and prostate cancer cell death.[46] The formula showed signs of becoming a success story for the herbal treatment of cancer.

In February 2002, the FDA reported that PC-SPES was contaminated with warfarin, diethylstilbestrol, and indomethacin. BotanicLabs voluntarily recalled the product and, in June 2002, closed down.

In August 2002, NCCAM announced that although it had stopped the four clinical studies it had funded of PC-SPES as a result of the reports of contamination, it was allowing the laboratory-based studies to resume. It also announced interest in working with potential new manufacturers of a contaminant-free research-grade PC-SPES so that clinical studies could resume.

Several groups of investigators are trying to produce a research-grade PC-SPES so that the clinical research can continue (Fulton L. Saier, M.D., personal communication). In addition, a number of commercial companies are now marketing look-alike products that have not been tested in clinical research. Patients with advanced prostate cancer, who had to give up PC-SPES when BotanicLabs closed, are using them and reporting their experiences to prostate cancer chat rooms (www.napc.info).

Investigators have reported that the mechanism of action of PC-SPES is different from that of DES.[47] Another team has found that only certain lots of PC-SPES contained DES.[48] The source of the contamination of BotanicLab's PC-SPES remains unknown.

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