Acupuncture: Role in Comprehensive Cancer Care—A Primer for the Oncologist and Review of the Literature

Andrea J. Cohen, MD, Alexander Menter, MD, and Lyndsey Hale

In recent studies, patients have reported an increased use of complementary and alternative medicine (CAM). Acupuncture is a popular complementary therapy for patients with cancer. This article will provide current cancer treatment providers with information on acupuncture as well as the research conducted on cancer symptoms and side effects of cancer treatments. Antiemetic studies are the most prevalent and contain the most promising results. Several studies have found that acupuncture significantly reduces the number of emesis (vomiting) episodes for patients receiving chemotherapy. While studies on pain control vary due to the heterogeneity of pain, there are few studies investigating pain caused from cancer and the removal of cancerous tumors. These studies, while promising, provide basic results that need further investigation for more definitive results. Although relatively few studies have been done on anxiety and depression, several researchers have found acupuncture to be just as effective as or more effective than antidepressants for patients without cancer. Studies on breathlessness, while small, have shown acupuncture to have a significant positive effect on chronic obstructive pulmonary disease, breathlessness associated with end-stage cancer, and asthma. Researchers studying xerostomic individuals who have received salivary gland irradiation found significant positive results in salivary flow rates compared to baseline. Patients with hot flashes due to hormonal imbalance may benefit from the use of acupuncture. A recent pilot study showed improvement of chronic postchemotherapy fatigue following acupuncture treatments. Many individuals with cancer have turned to acupuncture because their symptoms persisted with conventional treatments or as an alternative or complement to their ongoing treatments. Despite the immense popularity in the community, few large randomized trials have been conducted to determine the effects acupuncture has on cancer symptoms and side effects of treatments. A majority of the current studies have shown beneficial effects that warrant further investigation with large trial sizes.

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In recent years, there has been tremendous public interest in and use of complementary and alternative medicine (CAM). Eisenberg et al's landmark 1993 study[1] regarding the use of unconventional medical therapies revealed that 34% of respondents had used alternative therapy in the past year; 25% of these patients reported a history of cancer. A recent longitudinal study of 480 women with early-stage breast cancer showed nearly 40% of women in the study used some form of alternative medicine.[2] Other studies of cancer patients have found even higher rates of use, as much as 91%.[3] More recently, a study looking at patients participating in cancer clinical trials found that 63% of the respondents used at least 1 CAM therapy.[4] In addition, Richardson and colleagues[5] distributed questionnaires to 453 cancer patients; 83.3% reported use of at least 1 CAM therapy. Patients use complementary therapies to treat cancer pain and discomfort as well as chemotherapy and radiation side effects, to improve the quality of life, to treat cancer, and to stimulate the immune system.

While CAM therapies have become popular among patients, their acceptance has lagged within the medical community. Richardson and colleagues[5] found fewer than 25% of CAM users received information regarding CAM therapy from their physician. Another study distributed questionnaires to 417 men with prostate cancer.[6] Of the men reporting current CAM usage, roughly 50% had not spoken to their treating physician about their CAM usage. These studies show

AJC, AM, and LH are at the Division of Pulmonary Sciences and Critical Care Medicine, Division of Medical Oncology, University of Colorado Health Sciences Center, and the Complementary and Alternative Medicine Research Program, University of Colorado Cancer Center, Denver.

Correspondence: Andrea J. Cohen, MD, Division of Pulmonary Sciences and Critical Care Medicine, University of Colorado Health Sciences Center, Complementary and Alternative Medicine Research Program, University of Colorado Cancer Center, 4200 East Ninth Avenue, Box C272, Denver, CO 80262. E-mail: andrea.cohen@uchsc.edu.

that patients and their physicians often do not discuss CAM usage.

The Chinese and Japanese have used acupuncture to treat a variety of physical and emotional ailments. After President Nixon's visit to China in 1975, physicians in the West became interested in acupuncture's mechanism of action and therapeutic applications. Since then, many scientific studies have examined the efficacy of acupuncture in treating disease conditions. While many of these earlier studies contained serious methodological errors, evidence now shows that acupuncture has therapeutic effects that go beyond placebo effect and that acupuncture is efficacious for a number of specific ailments. The National Institutes of Health (NIH) has published a consensus statement that acknowledges the therapeutic efficacy of acupuncture in a number of conditions while also encouraging future research in the area.[7] The NIH consensus study recommended that acupuncture could be used for treating the nausea and vomiting that accompany chemotherapy as well as postoperative dental pain and tennis elbow. In addition, the NIH concluded that acupuncture could be used as an adjunct or alternative in comprehensive care programs for other ailments such as asthma, migraines, tennis elbow, osteoarthritis, back pain, myofascial pain, and other conditions. Early Western scientific explorations into acupuncture aimed to elucidate whether acupuncture was a placebo effect. There is a large body of data that confirms that acupuncture positively modulates biologic effects. The current question, however, is no longer whether acupuncture works but which conditions improve with acupuncture and what the benefits are of acupuncture in comparison to or in conjunction with Western treatments.

This article will (1) explore the historical and philosophical basis for acupuncture and illuminate current controversies regarding methods of acupuncture, (2) introduce the scientific rationale for acupuncture, (3) review the current literature as it relates to patients with malignancies, (4) briefly address current issues of cost and insurance coverage, (5) explore the current practices of acupuncturists, and (6) identify future areas of research.

Acupuncture Background

The Chinese have used traditional Chinese acupuncture for more than 5000 years in China; the earliest written descriptions of its use appeared in *The Yellow Emperor's Book of Internal Medicine*, or *Nei Jing*,[8] which dates from the second or third century BCE. The theoretical basis for traditional Chinese medicine is complex but boils down to a few basic concepts: (1) the body exists as a balance of basic elements and energies, (2) disease results from imbalance of these elements and energies, and (3) once the specific imbalance is diagnosed by history and a physical examination, then herbal remedies, moxibustion (burning cones of the herb mugwort, *Artemisia vulgaris*), and acupuncture can be used to correct the imbalance.

The energy of the body in Chinese medicine is known as qi (pronounced "chee") and is thought to circulate through the body within nonanatomical pipelike conduits known as meridians. Most of the meridians correspond to an organ system of the body. The 2 meridians that run up the back midline (Du/GV) and front midline (Ren/CV) do not correspond to an organ system. Although Chinese and Western organ systems share similar names, they differ conceptually. Acupuncture points are named according to the meridian or organ system to which they belong, such as "pericardium 6" or "gall bladder 30." In states of disease or imbalance, the flow of qi becomes disturbed at various points along the meridians. Acupuncture or moxibustion is employed to stimulate normal circulation of qi, thus returning the patient to a normal state of health.

Acupuncture as a term is poorly defined in the West, as the term tends to be applied to a broad range of interventions. Typically, acupuncture is thought of as the practice of inserting needles into the skin at points determined by the precepts of ancient Chinese medical philosophy. This is an example of Chinese-style acupuncture such as Five-Element acupuncture or traditional Chinese medicine (TCM) acupuncture. While these practices remain popular, there now exist several different styles of acupuncture with different rationales and varying practice. In addition to TCM acupuncture, other modalities include medical acupuncture, Japanese acupuncture, French auricular acupuncture, trigger-point acupuncture, acupressure, electroacupuncture, and transcutaneous electrical nerve stimulation (TENS) of acupuncture points. Five-Element acupuncture is an ancient type of acupuncture that emphasizes the assessment and treatment of psychological, spiritual, and emotional issues in addition to physical problems.[9] In the West, the therapist may use any number of these methodologies to treat a particular patient, depending on his or her training and clinical assessment. There are more than 3000 physicians in the United States who practice acupuncture and more than 14 000 licensed acupuncturists. In general, an acupuncturist must complete a 3- to 4-year master's program in Chinese medicine, pass national and/or state board exams, and be licensed by his or her state.[10] Many physician acupuncturists are associated with the American Academy of Medical Acupuncture. The purpose of the American Academy

of Medical Acupuncture is to "promote the integration of concepts from traditional and modern forms of acupuncture with Western medical training and thereby synthesize a more comprehensive approach to health care."[11]

Thus, acupuncture individualized assessment style in the community does not always reflect that which is studied in the literature. Nevertheless, it is generally safe to assume that patients will receive a detailed, multisystem history and physical, including pulse diagnosis. Pulse diagnosis is used to identify the abnormalities in qi and can localize the abnormality to a meridian. Typically, the radial pulse is palpated in 3 places on each wrist. The pulse is assessed while palpating both deeply and superficially. The pulse variance indicates an excess or deficiency of yin and/or yang (female and male energy), which is used to make diagnoses.[12] Based on the location and quality of the pulse, the practitioner can diagnose an abnormality or block in a specific meridian or organ system. Many TCM practitioners also use tongue diagnosis, and some acupuncturists use the patient's specific smell as part of the diagnosis. The tongue is thought to have branches from the Kidney, Heart, Liver, Spleen, Lung, and Stomach meridians, each with its own zone on the tongue. By examining the tongue's color, body, coating, and location of surface irregularities, the practitioner can make a diagnosis of abnormalities in the meridian and/or organ system and determine abnormalities in the patient's condition.[12] Once the diagnosis is established based on the history and the physical, the practitioner will frequently proceed by placing approximately 4 to 20 acupuncture needles into the patient depending on the patient's Chinese medical diagnosis. These needles are inserted and may also be manually manipulated until the practitioner feels a needle grab, or the patient feels an achy or numb sensation. The needles may then be left in place from 10 to 30 minutes with no, or intermittent, stimulation, or they may be attached to a low-voltage electrical generator for pain treatments. The practitioner may also use moxibustion, especially prior to needling. Moxibustion is burning the herb mugwort at the acupoints. This is believed to warm the qi at the acupoint and help move stagnant qi. In Five-Element acupuncture, needles are typically inserted briefly and then removed immediately. A Five-Element visit typically lasts an hour, and the practitioner usually remains in the room for the entire visit. Frequently, patients find the experience to be relaxing and sedating, but the treatment can be designed to be energizing when required. Depending on the condition being treated, and whether it is chronic, patients will be asked to return for a few or multiple follow-up treatments or maintenance. The costs range from $50 to $85 per treatment but can cost more than $100 in spas and some hospital clinics. Patients on a budget can visit an acupuncture school and receive treatment from a supervised acupuncturist in training for approximately $10 to $45. During chemotherapy, twice-weekly visits are felt by some to be optimum, but weekly visits are typical because of time and budget restraints.

Historical Problems With Acupuncture Research

Researchers have performed many excellent acupuncture research studies, but there are several problems with the acupuncture literature. Many earlier published studies suffer from small sample size, poor controls, lack of rigorous data analysis, inadequate presentation of numerical data, and/or lack of confirmatory studies. In addition, many studies have been published in foreign languages, which limits accessibility and acceptance among some Western physicians. This has greatly improved in the past few years, as more funding has become available from the NIH.

Much of the controversy regarding acupuncture research results from disputes as to which method of acupuncture is the authentic method. For example, a study performed by conventional medical acupuncturists looking at treating back pain with standardized acupuncture points may be criticized by classical Chinese acupuncturists as invalid because it does not allow for modification of acupoints based on the history, pulse diagnosis, physical examination, and Chinese medical diagnosis observed on that day. A study using classical diagnosis and seemingly arbitrary acupuncture points for different patients would be criticized as being improperly controlled and difficult to replicate. These controversies make study design arduous and also make it difficult for clinicians to know what to recommend to their patients. The methods used in research journals may not be the care provided in the community for a similar condition. While there are no easy answers to this controversy, the situation can be handled by comparing the relative efficacies of the various treatments and by knowing the acupuncturists in one's community and what style of acupuncture they tend to use.

Physiologic Background

Once researchers observed that acupuncture could produce clinically significant surgical analgesia in humans and animals, they sought to elucidate the mechanisms by which acupuncture worked within a scientific schema. While most of the research has focused on mechanisms that might explain the observed effects on pain, little has been done to elucidate the

mechanisms by which acupuncture exerts other observed effects.[13] There now exists a convincing literature that scientifically explains some of the analgesic properties of acupuncture.

Although the theory of qi flow continues to be the guiding principle for most acupuncturists in the United States and abroad, there is evidence that peripheral nerve beds may serve as the anatomic substrate involved in mediating acupuncture's effects.[13,14] Several anatomists have shown that the electrical impedance of the skin is lower at many classical acupuncture points[13,15] and that many of these points of lower impedance correlate with locations where cutaneous nerve beds exist. The decreased electrical impedance is hypothesized to exist secondary to an increased density of nerve-associated gap junctions in the skin. The idea that acupuncture analgesia is mediated through peripheral nerves was further bolstered by the discovery that the systemic analgesia produced by a given acupuncture point could be blocked by the local administration of lidocaine.[16] Regardless of the credibility of the theory of qi, the nervous system now appears to play an essential part in the observed effects of acupuncture.

One mechanism of action warranting further study is that acupuncture exerts systemic analgesia in part by Melzack and Wall's gate theory of pain transmission in the spinal cord.[17] The basic principle of the Melzack and Wall theory is that there are gating mechanisms in the spinal cord that prevent pain fibers from transmitting in the presence of competing sensory information. The anatomical correlates of this have been found in the spinal cord with the discovery of enkephalinergic neurons that inhibit pain fiber transmission (c fiber) in the substantia gelatinosa when activated by mechanoreceptors (Aδ).[13] This mechanism explains both the local analgesic effects of acupuncture and the common observation that people who sustain injuries frequently rub the skin surrounding their injuries as a means of ameliorating the pain.

The distant pain-controlling effects of acupuncture are mediated through a number of physiologic pathways; the most important is the stimulated release of β-endorphin and met-enkephalin.[18-21] Several animal and human studies have demonstrated elevated serum and cerebrospinal fluid levels of endorphins and enkephalins after acupuncture treatment.[22] Their role in pain modulation has been demonstrated in rats, in which antiendorphin antibodies injected into the periaqueductal gray negate the analgesia of acupuncture. In addition, some human studies have shown reversal of analgesic effects of acupuncture from naloxone administration, which is an opioid antagonist.[13,23,24] Although much is known about natural opioids and acupuncture, the relative importance of these hormones compared to neural humoral reflexes is still unclear. Serotonergic[25] and adrenergic[26] systems in the brain are also modulated in acupuncture, but the precise downstream effects of these changes are unclear.

Immune Effects

In addition to its pain-modifying effects, acupuncture appears to have some immunomodulatory properties in animal models including enhancement of splenic interferon gamma (IFN-γ), interleukin-2 (IL-2), natural killer (NK) cell activity,[19,27] and enhanced cortisol production.[24,28,29] A study conducted on mice undergoing electroacupuncture to the ST-36 knee acupoint for 3 consecutive days found an increase in splenic NK cell activity and an immediate increase in splenic IFN-γ compared to sham and no-treatment controls.[19] Another study found an increase in splenic IL-2 in rats with the ST-36 acupoint stimulated by electroacupuncture.[27] Finally, researchers found that electroacupuncture can modulate the immunosuppression of NK cell activity as well as increase IL-2 levels induced by surgical trauma.[30]

Petit and coworkers[31] showed modulation of B and T cell populations that would favor antibody production after acupuncture administration. Furthermore, another study found an increase in CD3+ cells and CD4+ lymphocytes in 77% of patients.[32] Increases in CD8+ cells were found in 60% of the patients. Also, 67% of the patients had an increase in B lymphocytes. They also noted that NK cell activity and phagocytosis of opsonized erythrocytes were increased in a majority of the patients.

While the existence of these biologic changes in animals and humans treated with acupuncture do not prove any important clinical outcome, these changes are surrogate markers for pain control, enhanced hematopoiesis, and immunity. Further research into the physiologic and anatomic underpinnings of acupuncture could provide information that will illuminate the physiologic basis of acupuncture and the general neurophysiology of pain pathways and immune response.

Rationale for Using Acupuncture in Cancer Patients

Patients with cancer represent a fertile population for treatment with and further study of acupuncture for several reasons. First, notwithstanding recent improvements in cancer survival, patients with cancer continue to have side effects from the therapies used to treat their disease as well as from the disease itself. Second, there is a need to produce new ways to decrease the suffering from cancer and treatment side

effects. Nausea, vomiting, neuropathies, pain, malaise, hot flashes, immunosuppression, and mood disturbances are some of the problems that acupuncture may help alleviate. Third, a significant proportion of the patients with malignancies are already using CAM therapies. This inclination to use alternative therapies should improve recruitment into studies that could rigorously examine the therapeutic applications and relative efficacy of CAM therapies, including acupuncture. Finally, the symptom-relieving drugs themselves may also produce significant side effects in many patients. Medications have become available that allow control of emesis, but there are now concerns about the combined use of high-dose chemotherapy agents and new antiemetic agents.[33] Acupuncture may provide a safe adjunct or alternative that will not create complications when combined with high-dose chemotherapy agents.

Uses

In addition to the extensive literature regarding the use of acupuncture as an antiemetic, there are a few studies examining pain, dry mouth, hot flashes, depression and anxiety, fatigue, weight, and quality of life. The therapeutic applications of acupuncture relating to cancer patients, however, remain largely unexplored. The following summaries provide a broad exposure to some of the areas that have been investigated in the hopes of stimulating further, more definitive research.

Antiemetic Effects

In 1997, the NIH produced a consensus statement on the efficacy of acupuncture. The consensus panelists reviewed the current literature and concluded there is evidence to support the use of acupuncture for adult postoperative and chemotherapy-induced nausea and vomiting.[7] The NIH concluded that acupuncture has been well established in placebo-controlled trials to be an effective antiemetic in patients receiving chemotherapy and postoperative dental pain. Also, the NIH has recommended acupuncture as an adjunct treatment or an acceptable alternative to be included in a comprehensive management program in conditions such as addiction, stroke rehabilitation, headache, menstrual cramps, tennis elbow, fibromyalgia, myofascial pain, osteoarthritis, low back pain, carpal tunnel syndrome, and asthma.

One of the first controlled studies, done by Dundee and colleagues,[34] evaluated the efficacy of electroacupuncture in patients with a previous history of cisplatin-induced nausea and vomiting. The control in the study was produced by random crossover treatments to acupuncture at an "inert" or sham position on the elbow, which was expected to have no beneficial effect. In this study, 100% of the patients reported complete or partial symptom relief with real acupuncture versus 10% of the patients reporting benefit from the sham acupuncture ($P < .05$).

Another study, demonstrating efficacy of acupuncture in women with a history of cisplatin-induced nausea and vomiting, was performed in Italy.[35] This pilot study of 26 women looked at the additional benefit of acupuncture over a baseline regimen of dexamethasone, metoclopramide, and diphenhydramine in women receiving cisplatin. The patients received needle acupuncture at the PC-6 point during chemotherapy infusion and then had a "permanent needle" implanted that the patients could stimulate on their own at home if the symptoms recurred. In comparison to historic controls that had received the same antiemetic regimen in the same setting prior to enrollment in the study, the acupuncture group had significantly improved level of complete protection from vomiting, duration of vomiting, and mean nausea score.

The most complete study to date was recently published in the *Journal of the American Medical Association*, and it examined the effectiveness of acupuncture in treating high-dose chemotherapy-related emesis.[33] In this study, 104 women with high-risk breast cancer undergoing myeloablative chemotherapy were randomly assigned to receive electroacupuncture, placebo acupuncture, or no acupuncture in addition to traditional antiemetics. The outcome measured was the number of emesis episodes that occurred over the 5-day study period and the relative proportion of emesis-free days. The electroacupuncture, sham acupuncture, and no intervention groups had 5, 10, and 15 emesis episodes, respectively. The treatment group had significantly fewer emesis episodes than the placebo group did ($P < .001$), and the placebo group had significantly fewer emesis episodes than the no-intervention group ($P = .01$). The antiemetic effects of the acupuncture were limited to the duration of the 5-day study, as the subsequent 3-day follow-up showed no difference between the groups.

Although several studies had shown a definitive effect of acupuncture and acupressure in treating chemotherapy-related nausea and vomiting, the clinical application of the technique seemed limited as the therapeutic benefit of the acupuncture lasted for only 8 to 12 hours. In seeking solutions to this problem, Dundee and colleagues performed follow-up studies to discover if acupressure beads used in an outpatient setting can prolong the antiemetic effects of acupuncture[36] and whether acupuncture and TENS stimulation of the PC-6 acupoint were equally efficacious.[37]

The first study examined the efficacy of stimulating a PC-6 acupressure bead every 2 hours for 24 hours. The results showed that 95% of the patients in the study were able to prolong the antiemetic effect based on 5 minutes of electroacupuncture for 24 hours using bead stimulation. The second study demonstrated that electrical stimulation of PC-6 without a needle was efficacious in reducing symptoms in 88% of study participants, though not as effective as electroacupuncture, which reduced symptoms in 97% of participants. The potential advantage of noninvasive electrical stimulation was that patients could take TENS units home with them and self-administer stimulation to the acupuncture point when nausea recurred.

With the exception of the prospective, randomized, placebo-controlled trial for acupuncture in women with breast cancer, many of the abovementioned studies could be criticized for small study size, lack of adequate control groups, or other problems. Despite these limitations, the efficacy of the treatment emerges from the totality of the literature. This was echoed in 2 reviews of acupuncture and chemotherapy-induced hyperemesis.[38,39] Currently, an ongoing meta-analysis in Cochrane is being conducted to assess the efficacy of acupuncture for chemotherapy-induced nausea and vomiting.[40]

At a minimum, the evidence demonstrates that patients who wish to seek alternative means of treatment for chemotherapy-induced nausea and vomiting should be counseled by their physician regarding the benefits of acupuncture and should receive a referral when appropriate. In addition, for oncologists who are having difficulty controlling nausea and vomiting in patients receiving highly emetogenic chemotherapy, acupuncture should be considered a potentially helpful adjunct treatment. The current literature, while demonstrating some efficacy of acupuncture in treating chemotherapy-related nausea and vomiting, has not provided clear guidelines on the number or length of treatments needed or the ideal acupuncture technique. Generally, patients receive acupuncture once to twice weekly during chemotherapy for 20 to 30 minutes each visit. Acupuncture is typically administered either just prior to chemotherapy and/or within 24 hours after. The acupoints ST-36 (knee) and PC-6 (wrist) are typically stimulated for treatment of nausea and vomiting. Some acupuncturists treat taxane side effects successfully 2 to 3 days after chemotherapy. There are acupuncturists who currently have more than 10 years of experience treating chemotherapy-related side effects. With some acupuncture treatments, regimens can vary due to type of cancer and chemotherapy, as well as other variables.

Pain Control

While there is much literature examining acupuncture in pain treatment, the heterogeneity of pain syndromes has made broad sweeping conclusions about acupuncture's efficacy difficult.[41,42] For example, there is evidence that acupuncture is effective in treating postoperative dental pain[43-45] and limited, but strong, evidence to show that acupuncture is effective in treating menstrual cramps,[46,47] tennis elbow,[48] and fibromyalgia.[49-51] On the other hand, there has been conflicting evidence regarding the efficacy of acupuncture in treating chronic neck and low back pain[52] as well as general chronic pain.[53] One systemic review and 2 Cochrane reviews on acupuncture found inconclusive evidence that acupuncture treatments for pain were more effective than placebo.[54-56]

Western studies examining the efficacy of acupuncture in treating cancer pain are currently limited.[57] A number of Chinese studies have examined acupuncture in cancer pain,[58] but these studies are generally descriptive and lack measurable outcomes, controls, or rigorous statistical analysis. One such Western study, conducted by Filshie and Redman,[59] involved 183 patients with malignant pain referred for acupuncture treatment. Of these patients, an overall amelioration rate of 82% was found. Of the patients who underwent acupuncture, 52% showed significant improvement over baseline pain, and 30% of the patients had some benefit that was short in duration. Muscle spasm and bladder spasm were also helped in these patients. While this study lacks controls and statistical analysis, it was one of the first studies to investigate outcomes for efficacy of acupuncture for malignant cancer pain.

One cancer pain study, which included a control group, examined patients suffering from chronic gastric adenocarcinoma pain.[60] In this study, 48 patients with intermediate- or late-stage gastric cancer were randomly assigned (method of assignment not mentioned) into 2 groups receiving traditional Chinese acupuncture and a third group receiving oral analgesics. The patients were given daily to twice-daily acupuncture treatments depending on their pain severity for 2 months. Although the method of ensuring adequate pharmacologic symptom management was not reported, the study did show comparable analgesic effects between the acupuncture treatment groups and the oral analgesic group. The study also reported measured levels of plasma-leucine enkephalin, which was significantly elevated in the acupuncture groups. The researchers reported fewer chemotherapy-related side effects and less neutropenia in the acupuncture group compared to the medical management groups. While there may be some observer bias, the results of this study warrant further investigation.

One salient study of pain relief and acupuncture examined women with axillary pain after axillary node dissection for breast cancer.[61] In this study, 48 women receiving acupuncture after axillary lymphadenectomy were compared to women who had received the same surgery without specific postsurgical intervention. This study demonstrated that women receiving acupuncture had more complete arm abduction over the first 5 postoperative days compared to women in the control group ($P < .01$). The women receiving acupuncture also showed significantly less pain in the operative field on the fifth postoperative day compared to the control group ($P < .01$). Overall, this study suggests that acupuncture may be an effective treatment to relieve pain and improve arm movement after surgery.

A small study of 3 individuals looked at percutaneous electrical nerve stimulation in patients with opioid-resistant bone pain secondary to cancer.[62] In this study, 2 of 3 patients received good to excellent pain relief using the visual analogue scale (VAS) for 24 to 72 hours following treatment. While this study was too small to draw any conclusions, any therapeutic options would be helpful in these patients with end-stage cancer and opioid-resistant bone pain.

Another small study looked at cancer patients still experiencing pain after treatment with analgesics.[63] The study included 20 patients receiving auricular acupuncture. The results showed that the average pain intensity, measured using the VAS, decreased significantly from day 0 (average of 74 mm on VAS) to day 60 (average of 41 mm on VAS; $P < .00001$). Although this study was small and contained no controls, the promising data have led Alimi and colleagues to design a randomized controlled trial with a double placebo and an independent observer.

A more recent randomized blinded controlled trial by Alimi and colleagues[64] was performed on cancer patients with stable analgesic treatment with neuropathic pain. Ninety patients were randomly divided in 3 groups. One group received 2 courses of auricular acupuncture at points where an electrodermal signal had been found. Pain intensity was reduced by 36% at 2 months. The authors concluded that auricular therapy was effective for cancer pain and that the low cost of the therapy as compared to narcotics argues in favor of its use in cancer patients for the management of pain.

Although research studies demonstrated acupuncture to be ineffective at treating HIV and postherpetic neuropathies,[65] it has not been studied in patients with chemotherapy-related neuropathy. In addition, there were design problems in the HIV study as points were used that may not have been optimum for the problem. In clinical practice, patients have been treated successfully for neuropathy on an individualized basis.

Acupuncture may be an important adjunct treatment for visceral pain, bone pain, and other malignant pain processes and thus should be examined in controlled studies. Cancer pain can often be relieved by oral analgesics; however, 10% to 20% of patients are opioid resistant and require alternative treatment.[66] There are also patients who refuse to use narcotics and suffer untoward side effects from typical pain-control methods. In addition, there are patients who never seem to respond fully to traditional treatment programs. For these patients, and all other cancer patients with pain, acupuncture may be a treatment that is effective, less sedating, and less constipating than conventional treatment and is thus a potentially valuable option. In clinical acupuncture practice, treatment for cancer pain can be of variable effectiveness due to patient heterogeneity. For example, the subgroup of patients with large tumors encroaching on nerves is less likely to respond to acupuncture. Overall, the clinical and research experience suggest that acupuncture for pain seems to be effective in some cases and warrants further investigation.

Fatigue

A phase II pilot study was performed to assess improvement in postchemotherapy fatigue following acupuncture.[67] Vickers and colleagues accrued patients who had completed cytotoxic chemotherapy but continued to experience fatigue. The primary end point was a change in the Brief Fatigue Inventory score between baseline and 2 weeks after the final treatment. Thirty-seven patients were enrolled in 2 cohorts; they had completed chemotherapy on average 2 years prior to the study. The mean improvement following acupuncture was 31.1%. The authors concluded that acupuncture was worthy of further study in the treatment of postchemotherapy fatigue.

Mood Disorders and Quality of Life

Depression often occurs after the diagnosis of cancer. A high level of preexisting depression in cancer patients has also been observed. A comparative study was done using electroacupuncture and maprotiline for treating depression in cancer-free patients.[68] The 2 groups, 31 patients in the electroacupuncture group and 30 patients in the maprotiline group, received their respective treatments and were rated using the Hamilton Depression Rating Scale (HAMD) and the Self-rating Scale for Depression. After treatment, the electroacupuncture group showed an amelioration rate of 96.7%, whereas the maprotiline group showed an amelioration rate of 90.3%, with amelioration de-

fined as a disappearance of psychiatric symptoms and a reduction in HAMD of 8 points. While both groups showed significant improvements over baseline, there was no significant difference between the groups ($P > .05$). This study found that electroacupuncture is just as effective as maprotiline for treating depression.

A single-blind, placebo-controlled study[69] was performed on 70 inpatients with major depressive episodes. The patients were randomized to 1 of 3 groups: acupuncture, placebo acupuncture, or pharmacological treatment with mianserin and clinical care alone. The acupuncture patients also received pharmacological treatment and clinical care. They were treated 3 times per week for 4 weeks at the same points designated by the protocol. Acupuncture, more than drugs, improved the course of depression as assessed by the standard Global Assessment Scale, Bech-Rafaelson Melancholia Scale, Clinical Global Impressions Scale, and self-rating scale. There was, however, no difference between acupuncture and placebo acupuncture. This may have been due to nonspecific effects of treatment or the practitioners or due to the fact that the so-called placebo sites were actually active in depression.

Another study compared electroacupuncture to amitriptyline for depression.[70] The results also showed that electroacupuncture was equal to amitriptyline in treating depression, with significantly fewer side effects ($P < .001$). Electroacupuncture induced a better therapeutic efficacy for anxiety somatization and cognitive process then did amitriptyline ($P < .05$). These studies suggest that acupuncture therapy is an effective treatment for depression, with fewer side effects compared to conventional medical therapies. Although these studies were performed on cancer-free patients, the results are promising and warrant further research to extrapolate the efficacy of acupuncture for cancer-related depression.

The next study used healthy individuals to test auricular acupuncture on the general anxiety levels of a healthy population.[71] Using auricular acupuncture, the anxiety levels of healthy individuals were compared to a placebo group. The researchers found anxiety levels were significantly reduced ($P = .001$) in relation to the placebo group 30 minutes, 24 hours, and 48 hours after treatment. Another study found that patients with generalized anxiety disorders demonstrated significantly reduced anxiety (85.7%) following acupuncture compared to a placebo group ($P < .05$).[72] Overall, studies show that acupuncture therapy is efficacious for the treatment of both anxiety disorders and general anxiety levels. This suggests that acupuncture is potentially efficacious for cancer-related anxiety and needs to be researched further.

Other studies examining such parameters have appeared mostly in the Chinese literature and are frequently descriptive in nature. In clinical practice, acupuncture, especially Five-Element acupuncture, is used routinely to treat anxiety and depression. Further studies looking more specifically at the psychological effects of acupuncture are warranted, and any study of symptom modification with acupuncture should also attempt to assess impact on patient's quality of life.

Breathlessness

Breathlessness, secondary to pleural effusions, mass effect, or lymphangitic spread of tumor, is a common problem in patients with end-stage disease. Filshie and coworkers[73] performed an open pilot study of the efficacy of acupuncture for 20 patients with malignant breathlessness at rest. Respiratory rate, oxygen saturation, pulse rate, and a patient-rated VAS for breathlessness, anxiety, and relaxation were measured. Of the 20 participants in the study, 14 reported marked symptomatic benefit with commensurate changes in the physiologic parameters.

Jobst and colleagues[74] published a randomized controlled trial of acupuncture controlling breathlessness. In this study, 12 matched pairs of patients received traditional Chinese acupuncture or placebo acupuncture for chronic obstructive pulmonary disease (COPD)-associated breathlessness. After 3 weeks of treatment, patients receiving traditional Chinese acupuncture reported significantly improved subjective breathlessness in addition to improved 6-minute walking distance. While these results were shown only in patients with COPD, there is a significant population of patients with lung cancer and cancer with COPD who might benefit from this treatment.

Xerostomia

Several studies in the ear, nose, and throat literature have examined the effect of acupuncture on salivation.[75,76] One study looked at patients with xerostomia (dry mouth) following radiation therapy to the head and neck.[77] In this study, 38 patients who had received salivary gland irradiation were randomized to acupuncture at deep classical points or superficial placebo points (1 cm from classical sites) for 6 weeks of biweekly treatments. The study showed a 68% response rate in the treatment group, which was not statistically significant from the 50% response rate in the placebo group. While the natural history of the problem is such that symptoms will improve over time, the authors felt that the response to treatment was clinically significant in that there was a subgroup of patients who had suffered from xerostomia for years and had failed conventional medical treatment but responded favorably to acupuncture. The authors postulated that over the course of the study, the sham

acupuncture sites may have had some clinical efficacy and that future studies should employ better placebo treatments and a no-treatment group for comparison.

Another study by Johnstone and colleagues[78] used auricular acupuncture for pilocarpine-resistant xerostomia. Researchers found that following acupuncture at 3 points in the bilateral auricles and 1 point in the radial part of the second digit, 50% of the patients showed improvement exceeding 10 points on the Xerostomia Inventory. Another study of 50 patients performed by Johnstone and colleagues[79] found a 70% response rate in patients receiving auricular acupuncture. These findings suggest a significant improvement for patients with xerostomia, although without control groups, placebo effect must be considered. Blom and Lundeberg[80] have also found that the beneficial effects of acupuncture for xerostomia may last up to 6 months. Their trial included 70 patients with xerostomia due to Sjogren syndrome. All patients analyzed 6 months after acupuncture treatments were found to have salivary flow rates that were increased over baseline ($P < .01$). These authors also suggest that additional acupuncture therapy can maintain increased salivary flow rates for approximately 3 years. Wong and coworkers[81] found that Codetron (an acupuncture-like TENS method without invasive needles) improves whole saliva production and related symptoms in patients with radiation-induced xerostomia. While all these studies show beneficial results, the trial sizes are small and often lack control groups. Further investigation is needed to determine the efficacy of acupuncture for xerostomia. Clinical experience of acupuncturists and positive trends in several trials suggest that acupuncture therapy may help alleviate xerostomia complications in some patients.

Flushing

Hot flashes in women are generally treated with hormone replacement therapy. This treatment, however, increases breast cancer risk and is generally inappropriate for patients with hormone-sensitive carcinomas.[82] In a noncancer study, Wyon and colleagues[83] administered electroacupuncture, superficial needle insertion acupuncture, or estradiol treatment to 45 postmenopausal women. All groups improved significantly, with no statistical difference between groups. It is thought that some of the superficial needle insertions may have been active, and the authors do not recommend further use of superficial needle insertion as an inactive control treatment. Overall, acupuncture may be a safe alternative to those hormone replacement therapies with potentially adverse side effects.

One study examined twice-weekly acupuncture in 7 men who experienced significant hot flashes secondary to castration for prostate cancer.[84] Of the 6 men who completed the study, 70% reported fewer symptoms compared to baseline at 10 weeks, and 50% reported fewer symptoms 3 months after the therapy ended. While this study had no control group, the results were interesting. Current treatment options for hot flashes have shown good results but are questioned because of long-term efficacy, safety, and cost.[85] Acupuncture may provide an alternative choice that is relatively safe, inexpensive, and supported by preliminary data. This is an area in which further research is much needed.

Adverse Reactions to Acupuncture

No formal system exists to report adverse events; therefore, a full assessment of the safety of acupuncture in clinical practice is difficult. Despite this, in the available studies, there are very few serious adverse events reported.[86-88] In a prospective study of more than 55 000 acupuncture treatments administered in a college for medically trained acupuncturists, only 63 adverse events, mostly minor, were reported.[89] Despite this, the literature has occasional reports of rare but serious adverse events such as pneumothorax, retroperitoneal hematoma, pericardial tamponade, bacterial meningitis, septicemia, permanent nerve injuries, and subarachnoid hemorrhage.[90,91] Although the rate of infections is extremely low, the increased use of disposable needles has dramatically reduced infections received from acupuncture.[11,91] The relative danger of acupuncture in neutropenic patients has not been studied, but it is generally not recommended that patients receive invasive acupuncture while neutropenic or with severe coagulopathy.

Another study collected data from approximately 1100 medical and nonmedical practitioners in Australia. The findings reported 1 adverse event in every 8 to 9 months of full-time practice (1 adverse event for every 633 consultations).[90] Most of the adverse events, however, were minor, including fainting, increased pain, and nausea and vomiting. This study also found that there was a higher incidence rate for medical practitioners compared to nonmedical practitioners. The authors suggest this difference could be due to the decreased training medical practitioners receive for traditional Chinese medicine and/or the relative condition of the patients being treated, with more severe illnesses possibly being treated by medical practitioners rather than nonmedical practitioners. Although this study provides information on adverse events occurring with acupuncture treatments, the design limits the accuracy of these findings. A

questionnaire was provided to all practitioners requesting that each practitioner recall all adverse events occurring during acupuncture practice. While this study design gives a basic understanding of adverse events and the frequency of occurrence, it is by no means comprehensive. Nevertheless, it is one of the first attempts to determine the occurrences of adverse reactions with numerous full-time practitioners.

Overall, the incidence of significant adverse reactions has been found to be rare. Of the adverse reactions occurring, most are mild and transient. Very few incidences are serious, and most can be eliminated by taking universal precautions, using proper clinical techniques, and having a proper understanding of internal and surface anatomy.

Acupuncture in the Community

Insurance companies traditionally have not covered alternative therapies but are increasingly adding coverage of CAM therapies to their supplemental plans. Some insurance companies have added discounts for visiting the CAM practitioners listed in their catalogue. There are also insurance companies that specifically cater to complementary therapies. Workers compensation policies and accident-related policies typically offer more CAM coverage. In most studies, about 5% of claims for acupuncture treatment are covered by insurance, but this percentage is likely to increase as the efficacy in various disease states is more specifically defined and patient advocacy increases. Insurance may cover physicians who perform acupuncture as a part of the patient encounter. There are state-to-state differences in insurance coverage. For example, Washington State has adopted the Every Category of Provider (ECOP) law.[92] The ECOP law states that every category of licensed provider should be included in private health insurance if their scope of practice encompasses medical conditions that the policy covers. Acupuncturists are licensed providers in Washington State.

Conclusions

In an attempt to review the scientific literature on acupuncture, the NIH convened a panel of experts in 1997 and issued a consensus statement after a 2½-day meeting (see consensus statement).[7] The conclusion of the panel was that there is "clear evidence that needle acupuncture is efficacious for adult postoperative and chemotherapy nausea and vomiting."[7] The panel also found a number of "reasonable studies showing relief of pain."[7] The studies reviewed in this article have supported these findings while offering glimpses into other areas of treatment that may prove fruitful with further research. Clinical experience and/or small studies also suggest that acupuncture may be helpful for treating hot flashes, anxiety, depression, fatigue, low energy, neuropathy, and altered immunity. Acupuncturists also treat cancer patients, constipation, diarrhea, gastritis, alopecia, insomnia, and need for sleep improvement. It should be noted that acupuncturists do not claim to treat or cure the cancer itself. Further research and outcome studies are greatly needed to scientifically document the scope of usefulness for acupuncture.

Although the precise mechanisms through which acupuncture exerts its therapeutic effects are complex and incompletely understood, the scientific demonstration of acupuncture's efficacy has dispelled the earlier belief that acupuncture was a placebo. We now know that the beneficial results of acupuncture are widespread. Acupuncture can be safely used as an adjunct to conventional treatments. Although acupuncture can be efficacious for chemotherapy side effects, it should not necessarily replace Western medical treatment. Instead, it should be used, when appropriate, in conjunction with conventional medical treatments to elicit the best possible response. Acupuncture can also be used as an alternative when conventional therapies no longer elicit a desired response, as is seen with the beneficial results acupuncture had for pilocarpine-resistant xerostomia patients or fatigue.

The list of chemotherapy side effects mentioned above represents a small number of conditions in which acupuncture has been shown to be efficacious. One of the advantages of acupuncture is that multiple symptoms can be addressed at each visit. For example, the patients can potentially be treated each visit for anxiety, depression, fatigue, nausea and vomiting, pain, and constipation. The challenge for the Western clinician investigators is to identify the additional conditions for which acupuncture is efficacious and to evaluate the relative efficacy and safety in comparison to conventional treatments. We recommend that if cancer patients elect to have acupuncture, they see an experienced practitioner with experience (years preferably) in cancer and chemotherapy side effects. There are acupuncturists who specialize in cancer and have developed detailed protocols taking into account type of cancer, stage, and type of chemotherapy.

As a population that is ill and searching for relief and a cure, cancer patients want to participate in studies that may improve their condition or symptoms. Cancer centers should help their patients by providing CAM therapies then examining more scientifically and definitively the questions regarding these CAM therapies. It is helpful when physicians are open minded and candidly discuss CAM use with their

patients. One study found that 50% of patients use CAM therapies without speaking with their physician.[6] By speaking with patients, a physician can determine a proper course of treatment and suggest appropriate acupuncture and CAM usage that can be used in conjunction with conventional therapies. It may also improve the patient-physician relationship when patients are able to discuss integrative therapies.

As for oncologists in the community or in academic centers, in light of our current understanding of acupuncture and its efficacy, it seems reasonable to suggest its use for patients with difficult-to-control chemotherapy-induced side effects such as pain, fatigue, nausea and vomiting, xerostomia, and mood disorders. There may be additional benefits to patients in terms of quality of life, hot flashes, peripheral neuropathy, alopecia, neutropenia, anorexia, constipation, and spiritual connection, but these have not yet been well documented in the literature.

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