



Integrative oncology for comprehensive cancer centres: definitions, scope, and policy

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1. INTRODUCTION

Integrative oncology combines the discipline of modern science with the wisdom of traditional healing. It is an evolving evidence-based specialty that uses complementary therapies in concert with medical treatment to enhance efficacy, improve symptom control, alleviate patient distress, and reduce suffering. Many of these therapies are used to improve coping and to help patients adhere to their medical treatment program.

Integrative oncology focuses on the roles of massage and other touch therapies, acupuncture, music therapy, botanicals, meditation and other mind–body approaches, nutrition, fitness therapies, and more. Its goal is to increase the efficacy of conventional cancer treatment programs, to reduce symptoms, and to improve quality of life for cancer patients.

The therapies employed are wide-ranging. For example, botanicals from ancient Chinese medicine are being evaluated for their pharmacologic activity in enhancing the anticancer effects of chemotherapy and radiotherapy and in improving symptom control. Meditation and exercise techniques from Ayurvedic medicine are being shown in scientific studies to improve mental state and to control some adverse side effects during cancer treatment.

When used wisely in a regulated cancer care program, integrative therapies can transform the physical, emotional, and spiritual dimensions of patients' lives and contribute to their rehabilitation following cancer treatment.

Integrative oncology is part of a wider definition of integrative health care. Integrative health care seeks—through a partnership of patient and practitioner—to treat the whole person, to assist the innate healing properties of the individual, and both to promote health and wellness and to prevent disease. It is an interdisciplinary blending of conventional medicine with complementary health care that should provide a seamless continuum of decision-making and patient-centred care. It should employ a collaborative team approach guided by consensus-building, during which the various practitioners and the patient contribute their particular knowledge and skills.

It avoids medical paternalism, but encourages evidence-based advice that is consistent with the patient's values. It aims to provide a more effective and cost-efficient care plan by synergistically combining therapies and services in a manner that exceeds the collective effort of the individual practices^{1,2}.

1.1 Complementary or Alternative?

The term “complementary therapy” (or “complementary medicine”) is to be distinguished from “alternative medicine.” Historically, the two are bundled together under the term “complementary and alternative therapies” (CAM). Alternative therapies are typically promoted as viable treatment options: “alternatives” to so-called mainstream therapies such as chemotherapy, radiation, and surgery. Alternative therapies are unproved, rarely based on credible scientific rationale, and potentially harmful—especially when patients are led away from effective, proven therapies by the lure of false promises and an emphasis on a lack of adverse side effects as compared with conventional therapies (see Table 1)^{3–6}.

There is no alternative to scientifically evaluated, evidence-based medicine. Most patients who use unconventional therapies (all but 2%) do so to complement rather than to replace mainstream treatment⁷. However, because of desperation or fear, or because of inadequate support and communication, patients may seek alternative therapies. Integrative oncology provides an opportunity to evaluate techniques that fall outside the conventional medical domains of surgery, pharmaceuticals, radiotherapy, and conventional psychological support. If proven effective and capable of adding value, then these additional techniques should be incorporated into comprehensive cancer management programs.

1.2 Making the Choice for Integrative

The Society for Integrative Oncology (SIO) was founded in 2003, and its inaugural annual conference was held in New York City in December 2004. The conference was sponsored by multiple cancer

TABLE 1 Alternative therapies promoted for cancer treatment that have been researched and shown to be ineffective or to lack credible evidence⁴⁻⁶

Dietary “cures”

These “cures” falsely extend mainstream evidence of risk reduction for cancer initiation and promotion to actual treatment of cancer after it has developed. Many of the diets can cause dietary insufficiencies. Some diets involve the addition of so-called detoxification techniques (such as coffee enemas) that aim to remove unspecified “toxins” from the body.

- No-dairy diet
- Macrobiotic diet (vegetarian diet plus minimum fish)
- Gerson diet (low salt, high potassium, massive intake of juiced fruit and vegetables, coffee enemas, injectable crude liver extract)
Treatment is based on the belief that cancer is a symptom of the accumulation of toxins. Research that purportedly showed a survival benefit of the Gerson regimen was flawed by nonrandomised comparisons and subgroup analysis. A more recent case series of 11 patients that included pancreatic enzymes (Gonzalez regimen) reported encouraging findings and is the basis of a randomised controlled trial.
- Individualised metabolic therapies or orthomolecular therapies (high-dose vitamins, minerals, enzymes, and detoxification regimens, such as colonic cleansing with laxatives)

Biologic treatments

These invasive treatments are based on biologic extracts, often associated with fantastic claims that have not been confirmed by appropriate scientific clinical trials. (If they had been confirmed, they would already have been incorporated into the mainstream medical system.) Promoters usually provide the treatments through expensive clinics that are often offshore or in Tijuana, Mexico, where they are exempt from U.S. and Canadian regulations.

- Antineoplastons (Burzynski Clinic, Houston, Texas)
The active agent in this treatment was originally derived from blood and urine and is now thought to be phenylacetate. Research efforts by the Office of Alternative Medicine of the National Institutes of Health (NIH) and by the National Cancer Institute (NCI) have failed to demonstrate tumour regression. Further research by the Burzynski Institute was permitted under an investigational new drug permit. The initial report from a single-arm study of 12 patients showed a 50% response rate, but that finding has not been confirmed by a randomised controlled trial.
- Immunoaugmentation therapy (Burton Clinic, Bahamas)
This therapy involves subcutaneous injections of sera derived from the blood of healthy donors. Documentation of efficacy is anecdotal.
- Shark cartilage (William Lane)
Advocates of shark cartilage base their therapeutic claims on the misconception that sharks don’t get cancer and on the putative antiangiogenic properties of the cartilage. A phase I/II trial found no clinical benefit. A nonrandomised trial of cartilage extract (Neovastat: Aeterna Zenatris, Québec, QC, Canada) for renal cell cancer showed a survival benefit. Two large NIH-sponsored phase III trials continue to evaluate the clinical benefits of cartilage extracts.
- 714-X (Cerbe, Rock Forest, Canada)
This product is an aqueous solution that consists of camphor, salts, and alcohol. It is applied by injection into the lymphatics (often in the inguinal region). The treatment is based on a theory that emphasises the importance of “somatids” (particles claimed to be essential to life that can be seen only with the researcher’s special microscope). Evidence for any clinical efficacy is anecdotal and based on testimonials.
- Cancell
This mixture of chemicals, including nitric acid and potassium hydroxide, claims to return cancer cells to a primitive state from which they are digested and rendered inert.
- Oxygen therapies
In these therapies, the tumour or the entire body is infused with oxygen, thereby allegedly killing or returning cancer cells to normal. Variations include intravenous hydrogen peroxide, hyperbaric oxygen, and ozone. Theories emphasise that cancer cells thrive in a low-oxygen environment, and it is true that hypoxia can result in gene mutations that can increase metastasis. However, no randomised trials have been conducted to support these therapies.
- Electrotherapies
Various devices are alleged to produce an electric charge that resonates with and destroys cancer cells. Magnetic or bioresonance therapies, radio-wave treatment, and Rife machines work on similar principles, sending waves of energy to resonate with cancer-cell frequencies and thus destroy tumour.
- Hulda Clark’s Cure for All Cancers
On the belief that cancers are caused by parasites, toxins, and pollutants, this program of treatment aims to destroy intestinal flukes.
- Insulin potentiation

Botanical treatments

- Essiac (Flor-essence)
This substance is a mixture of four herbs (burdock, turkey rhubarb, sorrel, slippery elm) given by a Native American healer to nurse Renee Caisse (Essiac being her name spelled backward). Despite a lack of research confirming the mixture’s value, it is promoted for all forms of cancer.
- Laetrile (amygdalin)
This substance is derived from the pits of apricots. It contains cyanide, which was thought to exert antitumoural effects. It shows little anticancer activity in animals and none in human trials. A phase II study showed some toxicity, but no benefit⁶.

continued

TABLE 1 *continued*

- Iscador (Mistletoe)
This herbal treatment is advocated mainly in Europe. Despite having some activity on cancer *in vitro*, no phase III trial is available to support its clinical utility. Randomised clinical trials in patients with head-and-neck cancers and melanoma were negative.
- Pau d'arco tea
This ancient Incan remedy for cancer is made from the bark of an indigenous South American evergreen tree. Its active ingredient, lapachol, showed antitumour activity in animal studies. There is no systematic clinical evidence that it helps. In 1985, it was banned by Health Canada pending proof from distributors that it is safe and effective. The federal *Food and Drug Act* does not allow pau d'arco to be advertised or sold as a treatment, prevention, or cure for any disease, including cancer. Side effects include nausea, vomiting, anaemia, and bleeding.
- Chaparral tea
This tea is an old Indian remedy for cancer. The principal lignin component is nordihydroguaiaretic acid (NDGA). Despite studies showing that NDGA has an anticancer effect *in vitro*, research by the NCI found no such effect *in vivo*. Some reports suggest that NDGA may stimulate certain malignancies such as renal cell carcinoma. It can cause severe liver toxicity, with cholestasis and hepatocellular injury. Chaparral is considered to be an unsafe herb; in 1970, it was removed by the U.S. Food and Drug Administration from the "generally recognised as safe" list.
- Noni
There is no evidence that noni helps cancer patients. This substance has been associated with bacterial contamination.
- Hoxsey regimen (poke root, burdock root, barberry root, buckthorne bark, stillinga root)
This compound was used in 1924 by Harry Hoxsey after an observation that a horse can cure itself of cancer after eating these plants. No supporting data have been forthcoming.

Energy therapies

Energy therapies include healing touch, therapeutic touch, Reiki, Qi Gong, and many other variants. Although randomised trials have provided some evidence that these practices can reduce symptoms and improve quality of life, no evidence that they can cure cancer or influence its course has been forthcoming. The studies that demonstrated improvement of symptoms were not well controlled, and factors other than the "exchange of energy" no doubt contributed to the apparent benefits. The patient's awareness of focused attention may have a significant mind-body effect.

Mind-body techniques

The potential to influence health with the mind affirms personal power and is an extremely appealing concept. Mind-body techniques are important for symptom alleviation, coping, and quality of life. Also, by influencing health-related behaviour, such techniques can help to prevent cancer (for example, through smoking cessation). However, no definitive evidence currently exists that mental attributes and mind-body work can cure cancer. David Spiegel's study findings of an increase in survival in advanced breast cancer patients participating in support groups was not confirmed in larger prospective randomised trials. An analysis of all the studies addressing this issue does not confirm an increase in survival. Nonetheless, many patients turn to Bernie Siegel's approach: attitude and responsibility for one's own health and understanding why patients "need" their cancers can help to correct unhealthy emotional patterns and thereby effect cancer remission or cure. However, a study coauthored by Siegel found no difference in length of survival for his support group patients and a control group. The idea that patients can influence the course of their cancer by mental or emotional work is not substantiated and can evoke feelings of guilt and inadequacy when disease continues to advance despite patients' best spiritual or mental efforts. A caring, empathic, and attentive practitioner who allows hope in the moment within a supportive environment is most important.

organisations including the American Cancer Society, the American Society of Clinical Oncology (ASCO), and the American Society for Therapeutic Radiology and Oncology (ASTRO). A non-profit, multidisciplinary organisation, SIO attracts health professionals committed to the study and application of complementary therapies and botanicals for cancer patients. Many members come from major international academic cancer centres. These professionals are dedicated to studying and facilitating the cancer treatment and recovery process by using integrated evidence-based complementary therapies.

The SIO's mission is to educate oncology professionals, patients, caregivers, and relevant others about state-of-the-art integrative therapies, including scientific validity, clinical benefits, toxicities, and limitations. The forum that SIO provides encourages presentation, discussion, and peer review of evidence-based research and treatment modalities in the discipline known as integrative medicine. Because a

constantly growing number of cancer patients throughout the world turn to both alternative and complementary therapies as part of their cancer treatment plan, oncologists must have ready access to information about research, existing treatment programs, and the benefits and the dangers alike of the wide range of complementary therapies available today. Members of SIO are individuals and organisations dedicated to optimising cancer treatment. The organisation itself promotes the scientific evaluation of complementary therapies, shares results, and encourages symptom control using therapies found to be beneficial. More information can be found at SIO's Web site (www.integrativeonc.org/).

2. USE OF CAM BY CANCER PATIENTS IN NORTH AMERICA

Data on the use of CAM by patients vary according to the definition of CAM therapies⁸⁻¹⁵. We believe that

spirituality or prayer should not be defined as CAM. Some of the population data on CAM is inflated by including prayer.

Some studies concluded that the use of CAM is associated with depression^{16,17}; in general, however, use of CAM by cancer patients is not associated with perceived distress or poor compliance with medical treatment but with active coping behaviour^{18,19}. Nevertheless, some patients suffering psychological distress may turn to CAM in desperation¹⁵.

Patients seem to consider CAM to be supplementary to standard medical methods; they see it as one way to avoid passivity and to cope with feelings of hopelessness. According to one major study, 83.3% of the population have used CAM at some time in their life^{20–22}. Use was greatest for spiritual practices (80.5%), vitamins and herbs (62.6%), and movement and physical therapies (59.2%). After excluding spiritual practices and psychotherapy, 68.7% of the population had used CAM.

A systematic review of relevant published data located 26 surveys of cancer patients from 13 countries¹⁴. In the United States, the prevalence of CAM use ranged from 7% to 50%. Another systematic review found that 33% of the population in the United States had used CAM in the preceding 12 months²³. Recent studies in women with breast cancer and men with prostate cancer revealed use of some form of CAM in up to 53% and 25% of those two populations respectively^{24–27}. Some studies show that herbal remedies were combined with prescription medicine in 16% of the population^{13,22,28}. Overall, up to 77% of cancer patients use CAM, including high-dose vitamins in up to 63%. Up to 72% do not inform their physician about their use of CAM^{29–31}. A study in Canada determined that 66.7% of breast cancer survivors used CAM (vitamins and minerals, green tea, herbal medicines, and dietary supplements)³². Alternative practitioners (traditional Chinese medicine and acupuncture, naturopathy, chiropractic, herbal) were visited by 39.4%. Only 50% informed their physicians. In view of the published statistic that more than 100,000 deaths annually in North America are attributable to drug interactions, the potential for concealed toxicity gives cause for concern³³.

Given the number of patients using CAM, and especially the number combining vitamins and herbs with conventional therapies, the oncology community must improve communication, offer reliable information and education, and initiate research to determine efficacy and potential adverse effects. No longer can patients be left to the perils of dubious Web sites and publications sponsored by certain irresponsible commercial enterprises that promote and sell the products they report, often using irrelevant testimonials³⁴. After a critical mass of evidence-based data is accumulated, practice guidelines for CAM and cancer need to be developed. That task is one of the responsibilities of integrative oncology.

3. COMPLEMENTARY THERAPIES FOR SUPPORTIVE CARE

3.1 Natural Health Products (Botanicals, Vitamins, and Minerals)

The role of botanicals in enhancing the effectiveness of conventional cancer therapies and reducing adverse effects remains to be defined. However, with new regulations to establish quality and proof of efficacy, the phytochemical constituents of botanicals may have an expanding role to play in cancer treatment³⁵.

In Canada, the federal government now regulates all botanical medicines. This step was taken to ensure that all Canadians have ready access to natural health products (NHPS) that are safe, effective, and of high quality, and that freedom of choice and philosophical and cultural diversity are simultaneously respected. The regulations for NHPS have recently undergone extensive modification, and the new regulations took effect in January 2004 under the authority of the Natural Health Products Directorate of Health Canada.

Under the new regulations, all NHPS sold in Canada require product licences. The regulations set out the requirements for submitting an application for a product licence, including quantity of the medical ingredients, purpose for which the NHP is intended, and safety and efficacy data that support the intended purpose. A “standards of evidence” framework is being developed to ensure that the product claims are supported by appropriate evidence that can be both scientific and traditional, depending on the type of claim being made.

Many patients entering a cancer treatment program are already self-administering herbal remedies for a variety of ailments (Table II)^{36,37}. Oncologists need to be aware of the potentially serious toxic effects of some herbal remedies (Table III)⁵.

Historically, herbal remedies have not been formally evaluated for safety, and few have been tested for side effects, quality control, or efficacy^{38,39}. Some herbal remedies are contaminated with heavy metals that can cause serious long-term toxicity. Ayurvedic medicinal products may deliberately contain high levels of heavy metals such as lead, mercury, and arsenic⁴⁰.

Many botanicals interact with the hepatic cytochrome P450 (Cyp) metabolic pathways involved in drug metabolism³⁷. The levels of some drugs, including chemotherapy agents, will be increased by botanicals that inhibit Cyp. Herbal inhibitors of Cyp include proanthocyanidin (grape seed extract), ginseng, quercetin, valerian, grapefruit, goldenseal, echinacea, red clover, cat’s claw, chamomile, liquorice, rosemary, and some Chinese herbs⁴¹. Conversely, Cyp inducers such as hypericin (St. John’s wort) and kava kava will reduce the activity of drugs such as indinavir, oral contraceptives, digoxin, cyclosporin, and coumadin.

A variety of natural health products require caution if taken near the time of surgery. The risk of bleeding can be increased by vitamin E, feverfew, garlic,

TABLE II Top 15 self-administered botanicals³⁶

Rank	Name	Indication
1	Garlic	Hypercholesterolaemia
2	Ginkgo	Dementia, intermittent claudication
3	Echinacea	Prevention of common cold
4	Soy	Menopausal symptoms
5	Saw palmetto	Benign prostate hyperplasia
6	Ginseng	Physical and mental fatigue
7	St. John's wort	Mild depression
8	Black cohosh	Menopausal symptoms
9	Cranberry	Urinary tract infection
10	Valerian	Insomnia, stress
11	Milk thistle	Alcoholic cirrhosis, hepatitis
12	Evening primrose	Premenstrual syndrome
13	Kava	Anxiety
14	Bilberry	Diabetic retinopathy
15	Grape seed	Allergic rhinitis, cardio-cancer prevention

ginger, saw palmetto, destagnation Chinese herbs, dong quai, and ginkgo used at high doses or in combination. Ginseng can potentiate insulin and precipitate hypoglycaemia. Valerian and kava may potentiate anaesthetic and sedative drugs, and liquorice may result in hypokalaemia and cardiac arrhythmias during anaesthesia. St. John's wort and ginseng are monoamine oxidase inhibitors (MAOIS) and may increase the toxicity of serotonin and catecholamine reuptake inhibitors such as phenelzine and various antidepressants.

The activity of chemotherapy may be reduced by free-radical scavenging (ginkgo, grape seed extract), Cyp induction (echinacea, St. John's wort, kava, grape seed extract), and anti-oestrogen inhibition (soy, ginseng). On the other hand, chemotherapy toxicity may be enhanced by Cyp inhibition (ginseng, ginkgo, valerian). In general, no significant interactions with chemotherapy are expected with saw palmetto, black cohosh, cranberry, silymarin (milk thistle), evening primrose, or bilberry.

Antioxidants such as alpha-lipoic acid, vitamin E, ginkgo, or grape seed extract could reduce the efficacy of radiotherapy by scavenging free radicals. However, the interaction is a complex one. For example, ginkgo can also increase perfusion and oxygenation, thereby increasing radiosensitivity⁴². On the other hand, the results of a recent randomised trial confirmed that vitamin E might reduce tumour control⁴³.

In general, long-term administration of vitamin E and beta-carotene do not seem to prevent cancers; in fact, they may be associated with an increased risk of death^{44,45}. Selenium shows more promise for cancer prevention.

Reduction of radiation toxicity by antioxidants and vitamins is emerging as a more promising area for research—for example, vitamin E to counteract radiation fibrosis⁴⁶ and vitamin A to counteract chronic radiation proctopathy⁴⁷. Some classes of botanicals, such as Chinese destagnation herbs, may have beneficial radiosensitising activity through a multitude of physiologic pathways that include anti-angiogenesis and anticoagulant activity⁴⁸. A randomised trial of radiotherapy plus or minus destagnation herbs for nasopharyngeal cancer demonstrated a doubling of tumour control and survival for the interventional arm⁴⁹. However, more research needs to be done on quality assurance and therapeutic gain.

Some botanicals are promising for cancer treatment: for example, PC-SPES for prostate cancer^{50–53}. Other emerging candidates for clinical trials include turmeric (curcumin)^{54,55}, maitake mushroom^{56,57}, and *Ganoderma lucidum*^{58,59}. Botanicals are often found to inhibit cancer cells by multiple pathways such as apoptosis induction, adhesion prevention, invasion reduction, and antagonism of the Cox-2 enzyme (Table IV)⁶⁰.

The herbal complex PC-SPES also illustrates the importance of quality assurance and supply from a reputable manufacturer. Originally distributed by Botanic Labs, PC-SPES consists of eight herbs, all but

TABLE III Herbal products with serious toxic effects⁵

Product	Expected effect	Toxic effect
Chaparral tea	Promoted as cancer treatment	Liver failure
Chaste tree berry	Premenstrual syndrome	Pro-dopamine activity; may potentiate antihypertensives and lithium; may potentiate diuretics and increase the risk of hypokalaemia; can interfere with and reduce the effectiveness of oral contraceptives and sex hormones
Coltsfoot	Expectorant	Liver failure
Comfrey	Digestive/lung problems; trauma and bruises	Liver thrombosis and failure
Jin bu huan	Sedative/analgesic	Bradycardia; hepatitis
Kava kava	Sedative/hypnotic	Hepatotoxicity; liver failure
Senna, cascara, aloe	Laxative	Hypokalaemia; arrhythmias with digitalis
Liquorice	Peptic ulcers/expectorant	Hypokalaemia; arrhythmias with digitalis
Lobella	Antiemetic	Tachyarrhythmias
Ma huang or ephedra	Weight loss/stimulant	Hypertension; myocardial infarction; cerebrovascular event
Yohimbe	Male performance enhancer	Seizures; kidney failure; death

two from traditional Chinese medicine: *Serenoa repens* (saw palmetto), *Panax pseudoginseng* (ginseng), *Chrysanthemum morifolium* (chrysanthemum), *Ganoderma lucidum* (reishi mushroom), *Glycyrrhiza glabra* (liquorice), *Isatis indigotica* (dyer's woad), *Rabdosia rubescens* (rubescens), and *Scutellaria baicalensis* (skullcap). Ingredients were chosen to produce multifactorial activity.

Serenoa repens can reduce the symptoms of benign prostatic hypertrophy. A systematic review of 18 randomised trials involving more than 2000 patients concluded that saw palmetto improves urologic symptoms and urine flow as effectively as finasteride, but with less toxicity⁶¹. *In vitro* studies suggest moderate antiproliferative activity against prostate cancer cell lines⁶². *Scutellaria* contains baicalin, a compound with known antiproliferative activity⁶³. *Ganoderma lucidum* has multiple activities that include inhibiting cell adhesion, cell migration, and cell invasion *in vitro*, and stimulation of immunity *in vivo*^{58,59,64,65}. Liquorice contains oestrogenic compounds that can inhibit prostate cancer⁶⁶.

Laboratory research supports the activity of PC-SPES against prostate cancer. Antiproliferative and proapoptotic effects have been demonstrated on tumour cell lines *in vitro*⁵⁰⁻⁵². In rat models, PC-SPES reduced the incidence of spontaneous tumours and the weight of implanted tumours⁵³. It also demonstrated oestrogenic activity⁵¹. Phase II studies showed that prostate specific antigen (PSA) decreased in most patients evaluated, including those with androgen-independent cancer^{51,67,68}. Significant improvements in pain and quality of life have also been reported⁶⁹. A phase II trial in 70 patients with prostate cancer showed a more than an 80% decline in PSA in all androgen-dependent patients, with PSA becoming undetectable in 82%⁷⁰. At a median follow-up of 64 weeks, none of the patients had progressed. In

addition, more than half of the patients with androgen-independent disease had a PSA response of more than 50%, with a median duration of 18 weeks.

Some endocrine side effects were associated with PC-SPES, including decreased libido, erectile dysfunction, gynecomastia, hot flushes, and increased thrombotic events⁷¹⁻⁷³. An NCI phase III study was planned to determine whether PC-SPES caused an increase in survival, but that study was terminated when quality assurance procedures showed that the clinical preparation, which was manufactured in China, contained diethylstilbestrol, coumadin, indomethacin, and alprazolam⁷⁴. Those findings prompted the U.S. Food and Drug Administration to issue a recall of PC-SPES in 2002. The manufacturers of PC-SPES, Botanic Labs, ceased operations and will no longer manufacture or market the compound. There are currently no other known North American sources of this combination botanical product.

Chinese herbs have many potential roles in the support of cancer patients. Various components in a botanical may have synergistic activities. Clinical studies from China are not usually methodologically sound, and quality control poses significant challenges^{75,76}; however, they indicate that specific herbs can increase immunity, reduce fatigue, improve mental alertness, and increase appetite⁷⁷⁻⁸⁰.

The Radiotherapy Oncology Group is developing a randomised controlled trial to determine the effect of American ginseng (*Panax quinquefolium*) derivatives in preventing radiotherapy-induced fatigue. There is preliminary evidence that the ginsenosides (saponins) and polysaccharides found in the various varieties of ginseng can reduce fatigue and increase immunity⁸¹⁻⁸³. A quality-assured derivative of North American ginseng, CVT-E002 (COLD-fX: CV Technologies, Edmonton, AB, Canada), which mainly contains the polysaccharide component, has been shown in a randomised controlled trial to reduce colds and influenza⁸⁴. Another Chinese herb that has potential anti-fatigue activity is *Cordyceps sinensis*^{85,86}. Many NIH-supported research programs encourage collaboration between American and Chinese institutions to evaluate traditional Chinese herbs for cancer patients in a methodologically sound context.

A randomised double-blind controlled trial has shown that the homeopathic medication Traumeel S significantly reduces the severity and duration of chemotherapy-induced stomatitis in children undergoing bone marrow transplantation⁸⁷. Traumeel S is a homeopathic complex remedy that has been sold through pharmacies in Germany, Austria, and Switzerland for more than 50 years. It contains highly diluted extracts (10⁻¹ to 10⁻⁹ of the stem solution) from the following plants and minerals: *Arnica montana*, *Calendula officinalis*, *Achillea millefolium*, *Matricaria chamomilla*, *Symphytum officinale*, *Atropa belladonna*, *Aconitum napellus*, *Bellis perennis*, *Hypericum perforatum*, *Echinacea angustifolia*,

TABLE IV Natural health products that inhibit Cox-2 activity⁶⁰

Ginger
Aloe vera
Epigallocatechin gallate (green tea)
Resveratrol (red wine, grapes)
<i>Glycyrrhiza glabra</i> (liquorice)
Garlic
<i>Scutellaria baicalensis</i>
Bilberry
Proanthocyanidins (pine bark and grape seed extract)
Panax ginseng
Milk thistle
Omega-3 fatty acids [eicosapentaenoic acid (EPA), fish oils]
Green-lipped mussel
Antioxidants (A, C, E, Se, Zn, carotenoids, flavonoids, coenzyme Q10, N-acetylcysteine, α-lipoic acid)
<i>Boswellia serrata</i>
Bromelain (pineapple)
Curcumin (turmeric)
Quercetin (ubiquitous plant bioflavonoid)

Echinacea purpurea, *Hamamelis virginica*, *mercurius solubilis*, and *hepar sulphuris*. Patients used the solution to rinse their mouths and then swallowed it five times each day. Traumeel S, with its multiple constituents and high dilution level, contrasts with conventional pharmaceutical products, which are often single agents utilised at a relatively high dose. The therapeutic paradigm of low doses of multiple agents requires further evaluation. The Children's Oncology Group is currently conducting a larger randomised controlled trial of Traumeel S.

Phytochemicals offer a smorgasbord of potential anticancer therapies and agents for symptom control. Government regulation will encourage quality assurance and clinical trials to determine efficacy. Pharmaceutical production standards are required, and companies should be rewarded with appropriate patents based on quality assurance and evidence that the refined products have efficacy and that any adverse reactions are documented and made explicit.

3.2 Acupuncture

Acupuncture is the stimulation of specific points on the skin using needle, pressure, electrical, or laser sources⁸⁸. The points are specified by traditional Chinese medicine and lie along lines called "meridians" that are alleged to transfer energy (*qi*). Although *qi* has not been defined scientifically, stimulation of acupuncture points has been found to induce neurologic reflexes that correspond with release of neuropeptides and other neurotransmitters⁸⁹⁻⁹¹, with modulation of cerebral blood flow⁹², and with balancing of the autonomic nervous system⁹³.

Clinical trials are proving that acupuncture can improve some of the more common side effects of cancer and its treatment, such as nausea and vomiting, anxiety, pain, fatigue, depression, xerostomia, and hot flushes. The efficacy of acupuncture for anaesthetic- and chemotherapy-induced nausea and vomiting has been proven by a series of randomised controlled trials, systematically reviewed by Vickers before 1996⁹⁴, and further reviewed from 1997 onward here in Tables v and vi⁹⁵⁻¹⁰⁹. A Cochrane database systematic review concluded that stimulation of the Pericardium 6 acupoint is effective for postoperative nausea but not for vomiting¹¹⁰. In 1997, the NIH issued a consensus statement supporting the efficacy of acupuncture for adult postoperative and chemotherapy-associated nausea and vomiting¹¹¹.

Some patients still suffer chemotherapy-related nausea and vomiting despite modern pharmacological interventions¹¹². Although some negative studies exist (possibly related to poor technique or inappropriate patient selection), acupuncture is a viable adjunct to drugs for controlling postoperative or chemotherapy- and radiotherapy-induced nausea or vomiting^{113,114}. It can be conveniently administered using devices such as the Codetron (EHM Re-

habilitation Technologies, Toronto, ON, Canada)¹¹⁵ or ReliefBand (Abbott Laboratories, Abbott Park, IL, U.S.A.)¹⁰⁷ to deliver transcutaneous electrical stimulation at specific acupoints. However, a more recent study did not support the hypothesis that acustimulation bands are efficacious as an adjunct to pharmacologic antiemetics for control of chemotherapy-related nausea in female breast cancer patients¹⁰⁹.

Acupuncture may also be used to reduce anxiety prior to procedures¹¹⁶⁻¹¹⁹. Randomised controlled trials have confirmed that acupuncture is effective for some types of cancer-related pain¹²⁰⁻¹²⁷. A phase II study of acupuncture in patients suffering post-chemotherapy fatigue at Memorial Sloan-Kettering Cancer Center (MSKCC) in New York showed a clinically important degree of improvement¹²⁸. Acupuncture may also alleviate depression^{129,130}. Three phase II studies have indicated a partial reversal of xerostomia or dry mouth secondary to radiotherapy¹³¹⁻¹³³. Studies of acupuncture for hot flushes secondary to hormonal therapies and menopause are promising¹³⁴⁻¹³⁷. Phase III trials of acupuncture for fatigue and hot flushes are in progress at MSKCC and for xerostomia at the Juravinski Cancer Centre (Hamilton, ON, Canada). Further indications for acupuncture and Chinese medicine for cancer patients are reviewed elsewhere¹³⁸.

3.3 Mind-Body Therapies

The psychosomatic connection between distress and physical illness and the effects of physical illness on mental suffering are increasingly being recognised¹³⁹⁻¹⁴². However, the proposal that mental distress may cause cancer or its relapse is not proven¹⁴³⁻¹⁴⁶. Currently, no level III evidence that psychological interventions can increase survival (apart from indirect effects such as increased adherence to conventional therapies)¹⁴⁷ has been found.

Mind-body therapies certainly can help with coping and with reduction of symptoms, smoothing the patient's path through conventional therapies, reducing pain, and increasing quality of life¹⁴⁸. Mind-body interventions aim to utilise the reciprocal relationship between body and mind to help patients relax, reduce stress, and relieve symptoms associated with cancer and cancer treatments.

Several randomised trials have shown effects of hypnosis on pain^{149,150}, anxiety, depression, and mood in newly diagnosed cancer patients¹⁵¹⁻¹⁵³. On the other hand, a recent randomised trial of hypnosis on non-selected patients undergoing radiotherapy showed no influence on anxiety or quality of life¹⁵⁴. Selection of appropriate patients seems to be necessary.

Trials have generally found hypnosis and relaxation training to be beneficial against chemotherapy-induced nausea^{155,156}, although some studies showed no differences¹⁵⁷. Mindfulness meditation improves

TABLE V Evidence for acupuncture in the treatment and prevention of postoperative nausea and vomiting, 1997 – 2005

Study	Acupuncture technique	Patients (n)	Comparator	Outcome
Al-Sadi <i>et al.</i> 1997 ⁹⁵	Needle	81	Sham	Pos
Schlager <i>et al.</i> 1998 ⁹⁶	Laser	40	Sham	Pos
Somri <i>et al.</i> 2001 ⁹⁷	Needle	90	Sham	Pos
			Ondansetron	Equivalent
Kotani <i>et al.</i> 2001 ⁹⁸	Needle	175	Sham	Pos
Wang and Kain 2002 ⁹⁹	Needle	187	Sham	Pos
			Droperidol	Equivalent
White <i>et al.</i> 2002 ¹⁰⁰	ReliefBand (transcutaneous electrostimulation)	120	Sham	Pos
			Ondansetron	Equivalent
Alkaissi <i>et al.</i> 2002 ¹⁰¹	Acupressure	410	Sham	Pos
			Reference	Pos
Kim <i>et al.</i> 2003 ¹⁰²	Auricular	100	Sham	Pos
Streitberger <i>et al.</i> 2004 ¹⁰³	Needle	220	Sham	Pos
Butkovic <i>et al.</i> 2005 ¹⁰⁴	Laser	120	Metoclopramide	Equivalent

TABLE VI Evidence for acupuncture in the treatment and prevention of chemotherapy-induced nausea and vomiting, 1997 – 2005

Study	Acupuncture technique	Patients (n)	Comparator	Outcome
Shen <i>et al.</i> 2000 ¹⁰⁵	Needle (electrostimulation)	104	Placebo (all subjects received ondansetron)	Pos
Josefson and Kreuter 2003 ¹⁰⁶	Needle (auricular)	39	All subjects received ondansetron	Pos
Treish <i>et al.</i> 2003 ¹⁰⁷	ReliefBand (transcutaneous electrostimulation)	49	Placebo (all subjects received ondansetron)	Pos
Streitberger <i>et al.</i> 2003 ¹⁰⁸	Needle	80	Placebo (all subjects received ondansetron)	Neg
Roscoe <i>et al.</i> 2005 ¹⁰⁹	Acupressure band	96	Sham	Neg
			Reference	Neg

mood and reduces stress during cancer treatment¹⁵⁸. Tibetan yoga improves sleep¹⁵⁹. Chanting the rosary prayers or yoga mantras may induce relaxation¹⁶⁰. Expressive art therapy may improve coping skills¹⁶¹.

Professional musicians who are also music therapists are trained to deal with both the psychosocial and clinical issues faced by patients and family members. Music therapy is particularly effective in the palliative care setting, with randomised trials indicating benefit for reducing anxiety^{162–166}, depression,^{167–169} and pain^{170,171}. Immunity may also be increased¹⁷². A randomised controlled trial at MSKCC concluded that music therapy is a non-invasive and inexpensive intervention that appears to reduce mood disturbance in patients undergoing high-dose therapy with autologous stem cell transplantation¹⁷³.

Several randomised trials suggest that massage reduces anxiety^{174–176}. In a high-quality trial, massage was found to be superior to the control treatment in reducing anxiety, nausea, and fatigue, and in improving general well-being¹⁷⁶. In another randomised study, pain and anxiety scores were both lower with massage, and the differences between groups achieved both statistical and clinical significance¹⁷⁷. The largest report to date on massage comes from MSKCC¹⁷⁸. That study analysed before-and-after data from the initial massage session of 1290 cancer patients during a 3-year period. Swedish and foot mas-

sage were the most common interventions. Anxiety, pain, and fatigue were significantly reduced.

In the United Kingdom, aromatherapy is often used for relaxation and coping with medical procedures. The smell of lavender seems to reduce anxiety through the olfactory nerves^{179–181}. A systematic review from the Cochrane Library concludes that massage and aromatherapy confer short-term benefits on psychological well-being¹⁸².

3.4 “Energy” Therapies

We mention energy therapies here because of their increasing popularity in some health care institutions. The practitioners’ theory is that they manipulate an energy field around the patient. This energy field has never been detected by objective scientific methodology.

The effectiveness of the so-called energy therapies is controversial^{183,184}. Studies are complicated by various confounding factors, so that the underlying process by which the therapist entrains the patient into a relaxed state is unclear. Nevertheless, there are published reports of therapies such as therapeutic touch (which, unlike massage, does not use actual touch), Reiki, and polarity therapy influencing the autonomic nervous system¹⁸⁵, affecting biologic markers and inducing relaxation^{186–188}, reducing

pain¹⁸⁹, and having a positive influence on cancer-related fatigue and health-related quality of life¹⁹⁰. The quality of these outcome studies is generally poor, and they lack scientific validity. Confounding variables include awareness of the practitioner, the patient's belief system, actual touching (which occurs in Reiki and polarity therapy), and subtle environmental influences such as background music.

4. AN ACADEMIC FUTURE FOR INTEGRATIVE ONCOLOGY

Not all mainstream physicians are pleased with CAM, with current efforts to integrate CAM with mainstream medicine, or with a separate NIH research entity for "alternative" medicine^{191–194}. Alternative medicine is a quintessential example of the sociopolitical force behind medical change. However, as this brief review demonstrates, evidence is increasing that some complementary therapies help cancer patients cope and also reduce adverse effects of conventional therapies. Appropriate scientific methodology is "sorting the wheat from the chaff" and preventing the proverbial "throwing out the baby with the bathwater." Further challenges include developing practice guidelines, performing economic evaluations, and determining whether an integrative oncology program provides added value to a comprehensive cancer centre. It is essential that programs incorporate evaluation practices such as audit and randomised controlled trials.

A consortium of academic health centres for integrative medicine aims to transform medicine and health care through scientific studies, new models of clinical care, and innovative education programs that integrate biomedicine, the complexity of human beings, the intrinsic nature of healing, and the rich diversity of therapeutic systems¹⁹⁵. Many North American medical schools now have introductory courses on CAM, and universities are providing postgraduate education. In the United States, Congress initiated the National Center for Complementary and Alternative Medicine with a mandate to fund research programs. The NCI has an Office of Cancer Complementary and Alternative Medicine that provides ad-

vice and some funding for research. Mainstream medical journals are increasingly publishing good-quality studies of CAM therapies. Scholarly journals such as *Focus on Alternative and Complementary Medicine* provide critical reviews of published studies on CAM. The Society for Integrative Oncology will be publishing its own peer-reviewed journal that will focus on high-quality research and reviews. On its own Web site, MSKCC provides guidelines for integrative oncology, including a resource for herbs and botanicals. In addition, the M.D. Anderson Cancer Center and the British Columbia Cancer Centre also provide Internet resources. Table VII lists the Internet addresses of these credible Web sites. Further data-based information on useful complementary therapies used in integrative oncology may be found in the book *PDQ Integrative Oncology*¹⁹⁶.

5. IMPLICATIONS FOR ONCOLOGISTS

Many cancer patients are using CAM therapies^{8–16}. Patients appear increasingly willing to discuss the use of these remedies, especially when asked by their oncologists. To encourage open communication about CAM use by their patients, oncologists should be knowledgeable about the most commonly used remedies, or at least be able to direct patients to reliable sources of information and to help them avoid bogus sources³⁴. In a receptive, evidence-based atmosphere, patients should be advised to avoid questionable alternative therapies. Many unproved alternatives are promoted in very appealing and convincing fashions. Brushing the topic aside categorically without open discussion may not dissuade use by the patient.

On the other hand, complementary therapies that help manage pain, nausea, fatigue, anxiety, and other symptoms should be integrated into the patient's overall care. In some cases, patients feel that the problems they perceive as important fail to receive sufficient attention. When complementary therapies are integrated into an evidence-based program of supportive care, those therapies can improve patients' quality of life, may increase satisfaction, and can strengthen the physician–patient relationship.

TABLE VII Credible Web sites for evaluation of complementary and alternative (CAM) therapies for cancer patients

Organisation	Web site
Consortium of Academic Health Centers for Integrative Medicine	www.imconsortium.org
National Center for Complementary and Alternative Medicine	nccam.nih.gov
NCI Office of Cancer Complementary and Alternative Medicine (OCCAM)	www.cancer.gov/cam/
Focus on Alternative and Complementary Medicine (FACT)	www.ex.ac.uk/FACT/about.htm
Society for Integrative Oncology	www.integrativeonc.org/
Memorial Sloan Kettering Cancer Center	www.mskcc.org/aboutherbs
MD Anderson Cancer Center	www.mdanderson.org/departments/CIMER/
BC Cancer Centre	www.bccancer.bc.ca/PPI/UnconventionalTherapies/EvaluatingAlternativeComplementaryTherapyInformation.htm

Anticancer technology is extremely important, but it needs to be softened. Integrative oncology is humanistic and empathetic, but it is also scientific. In addition to providing support, some botanicals may effectively treat symptoms and prevent complications, avoiding certain adverse effects of the more potent drugs. Such may be the case for black cohosh, used for menopausal symptoms and the prevention of osteoporosis¹⁹⁷. Other evidence-based and quality-assured botanicals and their derivatives are in the pipeline¹⁹⁸.

We believe that integrative oncology will provide added value to standard cancer treatment. The aim of integrative oncology should be one medicine, not alternatives; it should be patient-focused; it should be evidenced-based; and it should provide the best care for cancer cure and prevention, for symptom control, and for quality of life.

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