REVIEW

Complementary and Alternative Cancer Therapies: Past, Present and the Future Scenario

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Abstract

Use of complementary and alternative therapies is widespread among cancer patients. Throughout the world cancer patients try many questionable or unproven treatment methods. The reasons for adopting these therapies are complex and are related to the social and cultural contexts of their geographical locations. In case of severe illness, the desire to leave no stone unturned is a powerful motivator. In developing countries, ignorance, socioeconomics, and inadequate access to mainstream medical facilities are major factors that play an important role for patients opting for alternative therapies that are replacements for mainstream treatment. Whereas in developed countries a significant proportion of cancer patients try complementary therapies as adjuncts to mainstream care for management of symptoms and to improve quality of life. Many alternative therapies, including pharmacological and biological treatments, remain highly controversial but at the same time are very popular. Evidence from randomized trial supports the value of hypnosis for cancer pain and nausea; relaxation therapy and massage for anxiety; and acupuncture for nausea. This article reviews the different popular alternative cancer therapies practiced in India and neighboring south east Asian countries to project the current international scenario on complementary and alternative cancer therapies.

Key words: Alternative therapies - motivation - social and cultural context - hypnosis - massage - acupuncture

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Introduction

Cancer patients throughout the world use questionable or unproven, complementary and/or alternative methods. They include diagnostic tests, methods of treatment or preventive treatments, which are unproven or have not been scientifically tested (Schraub 2000). The term 'Complementary and Alternative' (CAM) is used by the American Cancer Society and the Union International Contre le Cancer (UICC). Most published terminologies define complementary and alternative medicine simply as anything that is not conventional (Zollman and Vickers, 1999; Pal, 2002 a). An advantage of the phrase 'complementary and alternative' is that it gives the opportunity to make important distinctions between the two. 'Alternative' therapies typically are invasive and biologically active and are commonly promoted for use instead of, rather than an adjunct to, mainstream therapy. Conversely, 'complementary' therapies are used together with mainstream care for management of symptoms and to improve quality of life (Vickers and Cassileth, 2001). One of the major US Cancer Centers has changed the acronym CAM to CIM 'Complementary and Integrative Medicine (Hess, 2002a).

The use of cancer treatments without proven benefits has become a major public health issue, with a substantial number of patients deserting potentially curative conventional therapy in favour of unproven methods (Cassileth et al., 1991). Each decade since the early twentieth century has been associated with a " miracle" cancer therapy that achieved great prominence, only to fade away as new therapies arose (Lerner and Kennedy, 1992). Some of these have found the enthusiastic support of the local public and press. Systematic reviews of surveys from different countries suggests that approximately one-third of all cancer patients try CAM (Cassileth et al., 2001; Richardson et al., 2000; Ernst and Cassileth, 1999). The most commonly employed

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therapies include dietary treatment, herbalism, homeopathy, hypnotherapy, imagery or visualization, meditation, megavitamins, relaxation and spiritual healing (Ernst, 2001). CAM is immensely popular in USA, Australia (Maclennan et al., 1996) and Germany (Ernst and Cassileth, 1999). In a recent survey 75 percent of breast cancer patients of USA reported use of complementary modality to treat their cancers (Morris et al., 2000). The majority of the studies on the use of complementary therapies by cancer patients have been carried out in North America and Northern European countries (Crocetti et al., 1998). Studies on cancer patients sampled from the general population indicate that users are young, of high social class and more likely to be females (Crocetti et al., 1998; Downer et al., 1994), looking for a miraculous cure (Esinberg et al., 1993) tend to be more health conscious (Cassileth, 2002), willing to spend out of pocket (Hess, 2002 a) and treated with chemotherapy (Richardson and Straus, 2002). The reasons for CAM's present popularity most certainly are complex. They are related to the social and cultural context (Ernst and Cassileth, 1998). Patients with acute, serious, life–threatening conditions have different motives for trying CAM than those with chronic, benign diseases. For cancer patients the most powerful motivations are the wish to leave no option untried and dissatisfaction with mainstream oncology (Ernst and Cassileth, 1999). Patients in some areas of the globe may well seek alternative therapies because they do not have adequate access to mainstream cancer treatment (Risberg et al., 1995). The use of 'alternative remedies' or non-proven therapies are either not tested or not proven to be effective in cancer clinical trials, and therefore, not prescribed in public hospitals (Hauser, 1991). However, several randomized trials have shown effect of hypnosis on both procedural and malignant pain. A recent systematic review and a National Institute of Health (NIH) technology assessment panel have supported the use of hypnosis for cancer related pain (Vickers and Cassileth, 2001; Sellick and Zaza, 1998). There is also evidence from a randomized trial that relaxation and imagery decreases cancer pain (Syrjala et al., 1995).

There is voluminous literature on the historical conflict between advocates and critics of CAM for cancer (Hess, 1999). Although the old literature documents the suppression of CAM therapies and advocates, since the 1990s, the politics of CAM have become more complex and subtle. For example, suppression has tended to shift to a politics of integration, that is, of selective uptake of CAM therapies when used as adjuvant modalities. In the late 1990s the Office of the Alternative Medicine (OAM) funded the first center of excellence for CAM research of cancer therapies at the University of Texas Health Sciences Center, Houston, USA. The National Center for Complementary and Alternative Medicine (NCCAM), that replaced the OAM in 1999 with a much-enhanced budget, cooperates with the National Cancer Institute (NCI) for the scientific and systematic investigation of alternative therapies. The NCI has, itself, created an Office of Cancer Complementary and Alternative Medicine (OCCAM) to coordinate and enhance the activity of the NCI in the arena of CAM (Sparber and Wootton, 2001). NCI is currently sponsoring several clinical trials that study complementary and alternative therapies for cancer (NCI website). These trials include enzyme therapy with nutritional support for the treatment of inoperable pancreatic cancer, shark cartilage therapy for the treatment of non-small cell lung cancer, and studies on the effect of diet on prostate and breast cancer. Some of these trials compare alternative therapies with conventional treatments, while others study the effect of complementary approaches used in addition to conventional treatments.

Factors Contributing Growing Interest in Alternative Cancer Therapy

The substantial interest in alternative cancer therapies appears to stem from several sources. The sheer numbers as well as the content of mainstream and alternative magazine articles, books, media, patient reports and the Internet all contributes significantly. There is widespread frustration amongst patients concerning establishment medicine's inability to treat many cancers effectively. The public is distressed by increased cancer incidence and the absence of real treatment gains for major cancers. Adverse side effects of chemotherapy and radiotherapy are still a big concern for patients and their families. A major reason for today's massive public and professional interest in alternative medicine is dissatisfaction with the technology and impersonal nature of modern medicine (Cassileth and Chapman, 1996). Patients complain about insensitive, limited and hurried interactions with oncologists in every setting, from small suburban hospitals to the top comprehensive cancer centers. Provisions frequently are not made for anticipated side effects of chemotherapy, and sometimes patients are not even told to expect these effects. Patients often feel helpless and ignored.

In many respect, alternative cancer therapies represent the antithesis of these perceived values and actions. Patients are simultaneously drawn away from mainstream medicine and towards alternative care as alternative practitioners are viewed as more caring, treating the whole person, and providing more emotionally satisfying, communicative relationships (Cassileth and Chapman, 1996). Many take more time than conventional physicians to develop detailed personal histories of their patients and to talk about concerns other than the disease process viz. "holistic" concerned with the whole person. Because they value quality as well as duration of life, many patients declined care at major cancer centers seek out smaller settings that provide complementary therapies. Some seek alternative care for its more egalitarian approach, for better practitioner-patient relationship, or for enhanced opportunities to make therapeutic decisions and play a major role in their own health care. In a recent survey of cancer patients using CAM suggested that the users were more hopeful about their future and were emotionally stronger and less anxious, even if the cancer remained unchanged (Astin, 1998).

Alternative cancer therapies and conventional Clinicians

Despite broad public acceptance of alternative and complementary therapies, the professional oncology community is hardly unanimous in its approval. It is an area where most oncologists have a certain sense of uncertainty or even discomfort (Curt, 2002). With current efforts to integrate CAM and mainstream medicine, vigorous opposition to CAM as pseudo-science based on absurd beliefs and deviation from basic scientific principles has been voiced (Cassileth, 2002). Many doctors have grave reservations about the ethics and potential health hazards associated with the more extreme unorthodox therapies. The most worrisome aspect is the possibility that patients will have their diagnosis delayed whilst pursuing alternative remedies or they will opt out of conventional care when they could still be effectively treated either curatively or palliatively. The study of Cassileth et al., (1984) has shown that 8 percent of 600 patients never received any conventional treatment but proceeded directly to alternative therapies. A substantial percentage also discontinued conventional treatment entirely in favour of alternative regimens after a mean of 8 months of standard therapy. A similar trend also exists in India (Chaturvedi et al., 2002). Another concern for the clinicians is the needless expenses of the patient and their family incurred by these treatments. It is not uncommon to hear of patients traveling great distances around the world in search of the latest miracle cure, which in itself, may be prohibitively expensive. Although some of the complementary / alternative specialties have professional bodies to govern the standard of training and codes of practice, including the regulation of fees, there is no legislation to prevent any unqualified person from setting up practice and charging whatever they wish (Pal, 2002 a). There is little regulation of mind-body therapies and nutritional counseling in many countries.

A good doctor-patient relationship is well known to enhance compliance with treatment (Jonas, 1998). Patients are often disproportionately alarmed at the thought of radiotherapy and chemotherapy and the 'safe natural' methods of alternative practitioners may seem more appealing in comparison. Thus, it is important to attempt to elicit and dispel any misconception that patients may have in their treatment. Confusion or puzzling aspects of management should be explained. Patients need to know that there are many different types of cancers and many different approaches to treatment. With some of the patients it may not be possible to commence therapy immediately. Nevertheless, they need to be assured by the constant interest and support of the doctors' so that they don't feel abandoned. Attending to the psychological health of cancer patients is a fundamental component of good cancer care. Support groups, good doctor-patient relationships, and the emotional and instrumental help of family and friends are vital. The quality of the patient's relationship with their physicians was related inversely to their propensity to seek unorthodox care (McGinnis, 1991). Crisis intervention technique should be developed. The oncologist remains a key player in this drama, with the patient as the ultimate benefactor. The support system should be emphasized and expanded, and the patient's continual involvement as a team member rather than an object is critical. When patients mention CAM, it is best to demonstrate a willingness to discuss the subject and to present the relevant information as possible. Cancer physicians need to be conversant with the popular forms of CAM and be ready to make inquiries if necessary on behalf of their patients in order to present the facts clearly. Dismissing these treatments out of hand may alienate the patient and make them turn away from conventional medicine. As long as the treatment is not pursued to the exclusion of conventional regimens, there is no reason to object to it, provided that it is not harmful, particularly if it gives the patient hope and improves the quality of life. The patient should be the best judge of these possible benefits. If, after discussion of the advantages and disadvantages of each treatment modality, the patient elects solely for an alternative therapy, an angry judgmental response will only strengthen the patient's resolve and make him or her feel unable to return for conventional therapy in the future if he or she wishes to do so. For many conventional clinicians who are not familiar with different CAM modalities a list of various therapies tried by cancer patients is given in Table 1.

Side Effects of CAM

The emergence of CAM represents a "natural experiment of huge dimension" as million of patients are self-medicating with biological agents (Richardson and Straus, 2002). History indicates people have acted to assist themselves and their ill family members, hence, the existence of a rich folk heritage of healing methods in all cultures. Self-care appears to be an integral component of human instinct and preference. It is well established that a variety of herbal medications may produce serious side effects. The patients should be informed that "natural" does not necessarily mean "safe" (Weiger et al., 2002). Quality control of these preparations can be a major concern (Markman, 2002). Hence, patients using pharmacological / herbal therapies should be warned that some of the adverse effects of these therapies are often similar to symptoms of problem associated with their disease or treatment, thus making it difficult to discern if the disease or the "remedy" is the problem (Winslow and Kroll, 1998). Some of the common side effect experiences with herbal therapies are allergic reactions, ascites, bradycardia, cardiac arrest, congested intestine, dehydration, depression, delirium, dermatitis, diarrhoea, emesis, gastroenteritis, hallucinations, headache, hepatitis, haematochuria, hypertension, insomnia, leucocytosis, muscular contracture, mydriasis, myosis/ myalgia, nausea, negative-inotropic effect, obtundation, pancreatic haemorrhage, pyrexia, seizure, somnolence, vomiting (Winslow and Kroll, 1998; Ernst, 2001). It is also

Table 1. CAM Tested in Cancer Patients

Antineoplastin	Antineoplaston	Aloe vera (** P)	AcupunctureAura
Aromathrapy	Ayurveda	Astrotherapy	Alevizatos treatment
Allium vegetables (e.g. garlic) (* P)	Anti oxidants	Autologous-targeted cytokines	Biofeed back (* Pl)
Bach Flower Remedy	Bio-Electro Magnetic	Bioresonance	Breuss diet
Bitter cucumber	Beljanski treatment	Brujos	Blastofag
The Bristol diet	Biogenics	Black magic	Cancell
Capsicum (*Pl)	Carotenoids	Chinese medicine	Cell-specific cancer therapy 200
Co-enzyme Q 10	Coley's toxins	Coriolus versiculor	Chiropractice
Curcumin	Clelation	Curanderos	Detoxification with enemias
DHEA	Di Bella therapy	Dance therapy	Essiac
Evening Prime oil	Enzyme therapy (* Pl)	Exercise	Electrocrystal therapy
Faith healing	Folk medicine	Fresh Cell therapy	Green tea (* P)
Guar leaf	Guided imagery	Gerson diet	Home remedy
Herbal therapy	Homeopathy	Hydrotherapy	Hydrazine sulphate (* T)
Hypnotherapy (** Pl)	Hyperthermia	Hyperoxygenation	High dose vitamins
Heavy metals	Hoxsey therapy	Hasumi vaccine	Houtsmuller diet
Iridiology	Isoflavones	Immunoaugmentative therapy	Kamateros spring water
Kromba	Laetrile	Lassi	Livingstone-Wheller therapy
Laughter therapy	Mangosteem peel	Mediatiation	Melatonin (* T)
Mind-body therapy	Massage	Mistletoe (Iscador)	Macrobiotic diet
Maharshi Amrit Kalash	Muthu Marunthu	Mantra therapy	Moxibustion
Moerman diet	Maca plant extract	Music therapy (* Pl)	MGN-3 (mushroom & rice bran extract)
Maruyama vaccine	Naturopathy	Nerium Oleander	Noni Juice (Morinda citrifolio)
Ozone	Osteopathy	Obe Mugose	Panax ginseng (** P)
Pancreatic enzyme therapy	Phyto-oestrogen	Pomgranate leaf	Pteris multifida poir
Pulsatilla chinensis	Psorinum	Pranic healing	Pildora de Vibora de Castabel
PC-SPES	Qi gong	Quantum booster	Relaxation (* Pl)
Reiki	Rodent tuber	Reishi mushroom	Royal Agaricus mushroom
Shark cartilage	Selenium	Sho-saiko-to (* Pl)	St. John's wort (* Pl)
Support group (* Pl)	Spirituality	Sun herbal compound	Sidda
Sarvapisti	Scientology	Tantra therapy	Tibetan medicine
Therapeutic touch	Tricosanthes	Tulsi	Tallberg regimen (Calf brain, etc.)
Trace mineral	Teletherapy	Trinivin	Traditional Chinese herbs
Thymus extract	Una de Gato	Unani medicine	Urine therapy
Vegetarian diet	Vitamin A	Vitamin C	Vitamin E
Vipasana	Visualisation	Viral therapy (PV 701)	Wheat grass therapy
Wasam	Yoga	Zen	714 X

* - Encouraging ** - Highly encouraging P - In cancer prevention. T - In cancer treatment. Pl - In palliative care

vital that oncologists provide an environment in which patients feel comfortable talking about alternative in order to learn what the patients are receiving in addition to mainstream treatment. The possible harm, benefits, and interaction of therapies adopted by patients require evaluation. A number of CAM medications have also been revealed to have a potential adverse impact on surgery, due to interactions with anesthetic agents, inhibitions of platelet functions, excessive sedation, or hypertensive effects. As a result, patients scheduled to undergo surgery for cancer should be asked about any nonprescription medications they have taken during the previous several-weeks (Winslow and Kroll, 1998).

Patients and Alternative Therapies

The use of CAM by cancer patients has become widespread. This is a reflection of the many needs and concerns of patients that are not met by conventional medical practice (Pal, 2002 b). Although great advances have been made in managing some tumors, there is little that is new for most. Dramatic technology changes in surgery, radiotherapy and chemotherapy has lead to an increase in cure rates, but at a price that is beyond the reach of many poor cancer patients living in the developing countries (Sikora, 1999). Though a significant proportion of cancer patients use alternative therapies, however, it is likely that many adopt therapies strictly for complementary purpose. However, one of the difficult situations arises in terminal illness when some patients make last-ditch effort to find a cure. Here patients are more susceptible to quackery. They also risk emotional distress, false hope, and wasted money. In addition to failing to experience the promised "cure" patients are not likely to find enhanced quality of life. The

combination of good communication between patients and oncologists and assiduous use of CAM should reduce patients' frustration and dissatisfaction with conventional medicine (Cassileth and Chapman, 1996). With the advent of Internet a wide variety of cancer information as well as treatment options are now available freely. Many sites on cancer are not peer reviewed and may contain mis-information (Biermann et al., 1999). Patients should be aware of this fact and should inform their oncologist regarding the ACT they wish to try. The CancerNet™ Home page (http://cancernet.nci.nih.gov) is an excellent starting point for both patients and clinicians to obtain quality information on cancer prevention, treatment, clinical trials and alternative cancer medicines. Some other sites like http://www.oncolink.com and http://www.cancer.org also provide reliable information. Informative websites on cancer were recently reviewed (Pal et al., 2003).

Complementary Cancer Therapies

A major proportion of cancer patients try complementary therapies to relieve stress and increase quality of life by producing relaxation of muscles. One popular technique, progressive muscle relaxation, involves sequential tensing and relaxing of muscles. Another is hypnosis, the induction of a deeply relaxed state, with increased suggestibility and suspension of critical faculties (Vicker and Cassileth, 2001). Once in this state, sometimes called hypnotic trance, patients are given therapeutic suggestions to encourage change in behavior or symptom relief. Visualisation and imagery technique involved the induction of a relaxed state that followed by a visual image, such as a pleasant scene that enhanced the sense of relaxation. Several randomized trials have shown effects of hypnosis on both procedural and malignant pain. However, hypnosis and relaxation techniques do not seem to be effective for reducing nausea associated with bone-marrow transplant (Syrjala et al., 1992).

There is good evidence that acupuncture reduces nausea and vomiting. A systematic review of acupuncture point stimulation for nausea and vomiting related to chemotherapy, pregnancy, or anesthetics reported that 11 out 12 placebo-controlled, randomized, double-blinded studies favoured acupuncture (Vickers, 1996). Stimulation at P6 (a specific point proximal to the wrist), either alone or in conjunction with stimulation at ST 36 (another point on the lower leg), serve standard antiemetic medication (Weiger et al., 2002). Another potential role of acupuncture in patient with cancer is the palliation of chronic pain. Several case report and series suggest that acupuncture may provide relief when conventional measures fail to control chronic pain resulting from underlying disease or conventional treatment (Singh, 1978; Mann et al., 1973). In a study of the effect of music therapy on the mood of patients with cancer, 50 hospital inpatients were randomly assigned either a live music therapy session or tape-recorded music. Patients receiving live music reported significant lower anxiety scores than the control group (Bailey, 1983). Therapeutic massage involving manipulation of the soft tissue of the whole body or specific areas to induce general improvements in health, such as relaxation or improved sleep, or particular physical benefits, such as relief of muscular aches and pains. Despite many anecdotal reports that massage reduces pain, current research evidence is limited. Only two small-randomized pilot trials have provided preliminary evidence of the massage (Weinrich and Weinrich, 1990) and reflexology (Stephenson et al., 2000) for pain in cancer.

Manual Healing

One of the most popular manual healing methods is therapeutic touch (TT), which, despite its name, involves no direct contact. In TT healers move their hand a few inches above a patient's body and sweep away "blockages" to the patient's energy field. Although scientific study by Rosa et al., (1998) have shown that experienced TT practitioners were unable to detect the investigator's energy field, and despite the unwillingness of main stream scientists to accept its fundamental premises, TT is taught in North American nursing schools and is widely practiced by nurses in the United States and other countries (Cassileth, 2002).

Few oncologists would object to their patients seeking reassurance and comfort from complementary treatments aimed at symptoms control or enhancing the quality of patients' life (Ernst and Cassileth, 1999). In contrast to ' alternative' treatments, adjunctive therapies are minimally or non-invasive, non-toxic, inexpensive, simple to use and often self-administrated. They are soothing and have the added virtue of permitting patients to assume control of some aspects of their care, with all of the psychological benefits.

Alternative Cancer Therapies

Use of Unconventional agents

In the 1940s as radiation therapy for cancer came to public attention, the oscilloclast (a devise to correct electron disharmony) was popular. The 1950s saw an intense regulatory effort involving the Hoxsey treatment (an herbal method with external and internal components), found by the Food and Drug Administration (FDA) to have no antitumour effect. With the development of chemotherapy and its early acceptance as a treatment method in the 1960s, saw the flowering of Krebiozen, reported by the FDA to be creatine and found by the NCI to have no antitumour activity (McGinnes, 1991). Continued interest in chemotherapy in the 1970s saw the development of laetrile (a cyanogenic glucoside) with many advocates, including the John Birch Society. Intense public debate occurred resulting in Dr. Charles Moertel's clinical trial at the Mayo Clinic, and again no antitumour activity was found. The laetrile advocates claimed that the trials were rigged that the real laetrile was not used in the trial. Greek doctors reported that urea can be effective in treatment of skin carcinoma (Danopoulos and Danopoulou, 1974). A liquid medicine made from camphor 714 X is being increasingly used, particularly in patients

with breast and prostate cancer (Kaegi, 1998 a). 714 X contains nitrogen, ammonium salt, sodium chloride and ethanol. It is generally given by injection. The treatment is based on an unusual set of therapy about the biology of cancer, such as the importance of 'somatids,' particles essential to life, which can be seen only in a special microscope, and a substance, called 'cocancerogenic K factor,' which is said to protect cancer cells from immune attack. There is no systematic human research on 714 X (NCI website).

Hydrazine sulphate as an alternative anticancer medicine is still very popular in US and Canada (Ernst and Cassileth, 1999). Based on Warburg's notions that cancer cells are characterized through their anaerobic (rather that aerobic an in normal cells) glucose metabolism, Dr. Joseph Gold, an American research oncologist sought to find a way of blocking this pathway with a view of inhibiting cancerous growth. In his experiment the substance, which apparently proved most effective in achieving this aim, was hydrazine sulphate. Research on hydrazine sulphate as a single agent and in combination with standard chemotherapy regimens continued through the mid-1990s. Hydrazine sulphate has shown only limited anticancer activity in animal and human studies, and the evidence concerning its effectiveness as a treatment for cancer related cachexia by blocking gluconeogenesis, and interfering with the supply of nutrients to tumour is inconclusive. Furthermore, hydrazine sulfate has been shown to increase the incidence of several types of tumour in animals, and the National Toxicology Program of the US Department of Health and human Services has classified it as a potential carcinogen. FDA has not yet approved the use of hydrazine sulphate outside the context of clinical trials (NCI website).

The concept of using oncolytic viruses to treat cancer caught the attention of many scientists. The first published report to establish a link between infection with a virus and the regression of cancer appeared in 1912 (Bergsland and Venook, 2002). Many patients were treated with replication-competent viruses during the 1950s through the 1970s. Wild-type, attenuated, or tissue culture-adapted viruses possessing tumor cell selectivity were used, including adenovirus, mumps virus, NDV, and others. Despite some promising results, the advent of recombinant DNA technology led to the abandonment of these viruses in favour of replicative-incompetent viruses as vectors for gene therapy.

Pharmacological and Biological Agents

Immunology as a cancer control mechanism captured public attention in the late 1970s and 80s. Correspondingly, Dr. Lawrence Burton's immunoaugmentative therapy (IAT) began to flourish in the Bahamas (McGinnes, 1991). Burton' s therapy was based on balancing four protein components in the blood. This injected therapy relied on strengthening the patient's immune system. According to proponent literature, Burton claimed that IAT was particularly effective in treating mesothelioma (Moss, 1992). Documentation of IAT's efficacy remained anecdotal. The clinic has continued to operate following Burton's death but seems to have declined in popularity (Cassileth and Chapman, 1996). As biological therapy entered the scene, the "hot" alternative therapy centered on Dr. Stanislaw Burzynski's antineoplastons, which are medium sized peptides found in human blood and urine. Probably this ACT is one of the most popular pharmacologic therapies today. Despite laboratory investigation by a scientist who concluded that antineoplastons do not exist (Green, 1992), clinical evidence evaluated under NCI found encouraging results of the therapy for pediatric patients with brain tumors. The study did not constitute a clinical trial but, rather, was a retrospective review of medical records, in a best-case series. Investigators at several centers like Memorial Sloan Kettering Cancer Center, the Mayo Clinic, and the Warren Grant Magnuson Clinic Center at the NIH developed protocols for phase II clinical trial with review and input from NCI and Dr. Burzynski. However, because of the small number of patients in these trials, no definitive conclusion could be drawn about the effectiveness of treatment with antineoplaston. Studies of Japanese researchers have now shown that Antineoplaston AS2-1 exhibits cytostatic growth inhibition of human hepatocellular carcinoma (HCC) cells in vitro and showed minimum adverse effect in a phase I clinical trial. Antineoplaston AS2-1 was found to be useful as a maintenance agent after transcatheter arterial embolization in patients with liver cancer (Tusda et al., 1997). Antineoplaston A 10 injection was also found useful in treatment of HCC especially for maintenance therapy (Kubabe et al., 1998). Combination therapy of chemoradiation therapy and antineoplastons AS2-1 and A 10 in phase I clinical trial showed encouraging results and rapid antitumour response in multiple metastatic lung cancer, thalamic glioma and primary lung cancer (Tusda et al., 1998).

A 1992 book written by I William Lane, Shark Don't Get Cancer, followed by a television special that displayed apparent remission in patients with advanced cancer treated with shark cartilage in Cuba, spurred interest in Shark cartilage as a cancer therapy (Cassileth and Chapman, 1996). Two glycoproteins (sphyrnastatin 1and 2) have been isolated from the cartilage of the hammerheaded shark and were reported to have strong antiangiogenesis activity inhibiting tumour neovascularisation (Lee and Langer, 1983) an effect which could be helpful in cancer therapy. According to mainstream scientists, however, the active macromolecules in the "food supplements" shark cartilage sold at health food stores are too large to permit absorption. They decompose into inert ingredients and are excreted. Despite lack of positive evidence shark cartilage pills and suppositories are widely publicized and are available in health food stores throughout the United States (Cassileth and Chapman, 1996). To date, no controlled clinical studies testing the efficacy of shark cartilage have been published. Though 3 randomized control trial are under way (Weiger et al., 2002). Preliminary results have been reported from an US trial: 50% of cancer patients who took 100 mg dried cartilage powder daily reported improvement in quality of life, appetite and relief

of pain (Mathews 1993). More recently, a well-documented trial was published (Miller et al., 1998). No complete or partial response was noted, and the authors concluded that shark cartilage as a single agent was inactive in patients with advanced-stage cancer and had no salutary effect on quality of life. In general, oral shark cartilage seems to be well tolerated. The most common adverse effects are gastrointestinal (Rosenbluth et al., 1999), one study noted possible allergic reaction (Riviere et al., 1998). Bovine cartilage is also under study for its potential anticancer properties. Prudden (1985) claimed response rate of 90% in 31 heterogeneous cases of cancer treated with commercial product known as Catrix. He had studied over 100 cancer patients with Catrix. It is interesting to note that scientists estimate that shark cartilage contains 100,000 times more antiangiogenesis activity than bovine cartilage (Cassileth and Chapman, 1996).

Another well-known biological remedy Cancell/ Enteler is especially popular in the Midwest of USA and Florida. Cancell, also known by the names Sheridan's formula, Jim Juice, Crocinic Acid, JS-114, JS-101, 126F and Cantron was developed in the late 1930s by a chemist, who called it Entelev and provided free of charge to patients with terminal cancer (Cassileth and Chapman, 1996). Proponents claim that it returns cancer cell to a 'primitive state' from which they can be digested and rendered inert. FDA laboratory studies revealed that Cancell is composed of common chemicals, including inositol, nitric acid, sodium sulfuric acid, and catechol. The FDA found no basis for proponent claims of Cancell's effectiveness against cancer. Interest in coenzyme Q 10 as a therapeutic agent in cancer began in 1961, when a deficiency was noted in the blood of both Swedish and American patients, especially in the blood of patients with breast cancer. A subsequent study showed a statistically significant relationship between the level of plasma coenzyme Q 10 deficiency and breast cancer prognosis. Low blood levels of this compound have been reported in patients with other types of malignancies also. A large amount of data showed that coenzyme Q 10 stimulates animal immune systems, leading to higher antibody levels, greater numbers and/or activities of macrophages and T cells and increased resistance to infection. Coenzyme Q 10 has been reported to increase IgG antibody levels and to increase CD4 to CD8 T-cell ratio in humans. Research subsequently, delineated the antioxidant properties of coenzyme. Its primary use now is in complementary modality. The Di Bella regimen, consisting of melatonin, bromocriptine, retinoids and either somatostatin or octreotide, generated intense public interest in Italy in the late 1990s (Pellegrini, 1998). In a rare example of strategically planned and rapid implemented research in alternative medicine, two studies were completed. Neither showed any benefit for this treatment (Italian Study Group, 1999; Buiatti, 1999).

Diet and Nutrition

Advocates of dietary cancer treatment typically extend mainstream assumption about the protective effect of fruits, vegetables, fiber, and avoidance of excessive dietary fat in reducing cancer risk to the idea that food or vitamins can cure cancer. This approach is popular among patients with gastrointestinal malignancies, who are understandably eager to fashion diets that will encourage tumor regression and avoid recurrence (Cassileth, 2002). Dietary fat reduction has received attention in the treatment of both breast and prostate cancer. With regards to breast cancer, reduction of fat intake has been shown to reduce estrogen levels in both premenopausal and postmenopausal women (Wu et al., 1999). Survival of postmenopausal patients with resected breast cancer is greater in Japan, where diets are low in fat, than in the United States (Chlebowski et al.,1992). However, difference between American and Japanese diet go beyond fat content; in particular, soy consumption is higher in Japan. Currently, evidence is inadequate to recommend dietary fat reduction in women with breast cancer. However, it is reasonable to accept fat reduction in well-nourished patients who elect to try this approach (Weiger et al., 2002).

Metabolic therapies continue to draw patients from North America to many clinics in Tijuana, Mexico, that offers practitioner-specific combination of diet plus vitamins, minerals, enzyme and "detoxification". One of the best known is the Gerson clinic. Treatment is based on the notion that toxic products of cancer cell accumulate in the liver, leading to liver failure and death. Treatment aims to counteract liver damage with low-salt, low-fat, high-potassium diet and coffee enemas. This type of therapy can be debilitating and costly, causing enzyme imbalance, perforated colon and sepsis. Proponents claim that caffeine is absorbed in the colon, leading to vascodilation of the liver, which in turn enhances the process of elimination of toxins. These assumptions are unproven (Risberg et al., 1995). The clinic's use of liquefied raw calf's liver injection was suspended in 1997, after sepsis occurred in a number of patients (Cassileth, 2002).

Three of the most influential of the therapeutic diet for cancer in the USA are the Gerson-Kelley group, Asian diets (macrobiotic diet), and low-carbohydrate approach (Hess, 2002 b). Max Gerson first developed his low-salt diet to treat his own migraines, which he later expanded to treat tuberculosis, arthritis, and in 1928, cancer. Later in 1960 dentist William Donald Kelley applied Gerson's dietary approach to treat his cancer patients. The dietary program probably would have passed into obscurity had it not been for the work of oncologist Nicholas Gonzales, who as a medical student at Cornell University in the early 1980s analysed Kelley's cases and found evidence to support the claim of long-term survival for patients. Gonzalez subsequently developed his own nutritional program and after many years of efforts to gain recognition from the establishment, his own support in the late 1990s from the NIH to run a clinical trial of pancreatic cancers at New York' s Columbia Presbyterian Medical Center. Macrobiotic diet is relatively recent creation; it is rooted in the ancient yin-yang principle on which traditional Chinese medicine is based. The macrobiotic diet derives 50% to 60% of its

calories from whole grains, 25% to 30 % from vegetables, and the remainder from beans, seaweed, and soups. The diet avoids all animal meat and certain vegetables and processed foods, and promotes soyabean consumption. There is no evidence, however, that the macrobiotic diet is beneficial for patients diagnosed with cancer. Moreover, versions of this diet are nutritionally deficient and can cause problematic weight loss in patients with cancer (Cassileth, 2002).

Some patients and alternative practitioners believe that large dosage of vitamins-typically hundreds of pills a day-or intravenous infusions of high-dose vitamin C can cure cancer. In 1968, Nobel Laureate Linus Pauling coined the term orthomolecular to describe the treatment of disease with large quantities of nutrients. His claim that large doses of vitamin C could cure cancer, most effectively in patients who had not received chemotherapy were disproved in randomized clinical trial (Creagan et al., 1979; Moertel et al., 1985).

Herbal Therapies

Herbal remedies typically are part of traditional and folk healing processes with long histories of use. Some forms of herbal medicine are found in most areas of the world. Although many herbal remedies are claimed to have anticancer effects, only a few have gained substantial popularity as alternative cancer therapies (Cassileth and Chapman, 1996). Essiac is one of the most popular herbal cancer alternatives in North America. It was popularized by a Canadian nurse, Rene Caisse (Essiac is Caisse spelled backwards) but was developed initially by a Native Canadian healer who reported that it had cured her breast cancer. Essiac comprises of four herbs burdock root (Arctium lappa), Indian rhubarb (Rheum palmatum), Sheep sorrel (Rumex acetosella), and the inner bark of slippery elm (Ulmus fulva or U. rubra) (Kaegi 1998 b). Researchers at the NCI and at Memorial Sloan-Kettering Cancer Centre have found that it has no anticancer effect (Cassileth and Chapman, 1996). For 40 years Rene Caisse gave Essiac to several hundreds of cancer patients. She reportedly administered one of the herbs by injection and others as tea and modified the formula several times on the basis of her experience. During 1959 – 1978 Cassie worked in partnership with a prominent American physician, Dr. Charles Brusch, to modify the recipe and promote its use. As a result of their clinical and laboratory work, they added 4 herbs to the original recipe - water cress, blessed thistle, red clover and kelp – which they believed potentised its action and improved its taste. More importantly, the new mixture did not require injection and could therefore be used at home. The Department of National Health and Welfare placed restriction on the promotion of Essiac for use in the treatment of cancer in 1982. The formula is now manufactured as Eassiac by Essiac Products in New Brunswick and is available in the health Canada's emergency drug release program on compassionate grounds. Another Canadian product-Flor-Essence believed to be the 8-herb recipe is manufactured in British Columbia and is widely available in health food stores. The proponent and manufacturers of Flor-Essence are careful not to make claims that it is useful as cancer therapy; they promote it as a health-enhancement herbal tea. Most people trying Essiac today use it in addition to conventional treatment or as a component of care for terminal disease (Kaegi, 1998 b).

Mistletoe, a parasite plant that grows on the top of trees holds a great interest as a popular cancer remedy in Europe where it has been used as flock treatment for centuries. Mistletoe is available in many mainstream European Cancer clinics (Ernst, 2001a). The Mistletoe extract has been shown to kill cancer cells in vitro and to stimulate immune system cells both in vitro and in vivo and is classified as a type of biological response modifier. Several components of Mistletoe, namely alkaloids, viscotoxins,and lectins may be responsible for these effects. The commercially available products of Mistletoe are marketed under the brand names Iscador, Eurixor, Helixor, Isorel, Vysorel, and ABNOB Aviscum. Despite its fairly widespread use, few clinical trials have been conducted and documented anticancer effects of Mistletoe in humans are sparse. The literature that is available has been published primarily in non-English-language journals and consists of anecdotal reports, case series, and a few clinical trials that have provided inconclusive results (Steuer-Vogt et al., 2001).

Chinese herbs are also used in the treatment of cancer (Normile, 2003), 'Treating Cancer with Chinese Herbs' offers herbal combination for the treatment of specific malignant diseases (Hsu, 1982). Ayurveda for cancer treatment and palliation is popular in India (Singh, 2002; Vaidya et al., 2003), Europe and North America. PC-SPES is one of the most studied herbal therapies in prostate cancer (Oh and Small, 2002). A combination of eight herbal compounds: Ganoderma lucidum, Scutellaria baicalensis, Rabdosia rubescens, Isatis indigotica, Dendranthema morifolium, Seronoa repens, Panax pseudoginseng, and Glycyrrhiza uralensis PS-SPES appeared to have estrogenic activity. Early anecdotes of PS-SPES suggested that this therapy was effective in reducing PSA level in men with prostate cancer who have not been treated with hormonal therapy (Monad, 1999). There have been many clinical and laboratory-based studies of PC-SPES, but no randomized studies (Pandha, 2002). St. John's wort is widely available as over-the-counter herbal product that has gained popularity as a treatment for mild to moderate depression, which can be common among cancer patients (Arnold, 2002). A few studies have reported that green tea and its extracts reduce the metastatic potential of cancer in some animal systems (Kaegi, 1998 c). These findings, together with the evidence that green tea extract suppresses chromosomal abnormalities induced by carcinogens, have generated some interest because they play a role in delaying the cumulative genetic damage necessary for a cell to evolve from normalcy to one with aggressive metastatic capabilities (Sazuka et al., 1995), Pau d'arco tea is said to be an old Inca remedy for many illness including cancer. It is made from the bark of an indigenous South American evergreen tree, and its active ingredient, lapachol, has shown to have anticancer activity

in animal studies, it does not appear to affect human cancer (Vickers and Cassileth, 2001).

Popular Alternative Cancer Therapies in India

Significant proportions of cancer patients in developed countries use complementary therapies as adjuncts to conventional symptom management to improve their quality of life (Vickers and Cassileth, 2001). However, the situation in less-developing countries, for example India, is quite different. Around 80% of cancer patients have late stage incurable disease when first diagnosed (Jones, 1999). This not only complicates the treatment options, but also makes palliation difficult. In the remotest parts of the country, patients are in economically disadvantageous position and have limited access to medical services. Many are compelled to try alternative medicines, such as naturopathy, biopathy, homeopathy, home remedies, wheat-grass therapy, hydrotherapy, acupuncture, auto urine therapy, osteopathy, and vipasana (Das Gupta et al., 1997). An alternative cancer therapy (ACT) called Psorinum is quite popular in Kolkata (Pal, 2002 b). This ACT comprises a combination of homeopathy and natural medicine along with conventional supportive care. Since, the publication of an anecdotal report (Chatterjee et al., 1999) alleging improved survival among many patients with advanced-stage cancer, both the public and many oncologists now regard this approach as effective. Another popular homeopathic approach to treat cancer has been developed by the doctors of PBH Research Foundation in Kolkata. Clinical reports of few of the successfully treated patients were recently presented in the 'NCI Best Case Series' to the Cancer Advisory Panel for Complementary and Alternative Medicine (Vanchieri, 2000). Scientist of the VCP Cancer Research Centre, Dehradun has developed an Ayurvedic approach to treat Acute Myeloid Leukemia (AML). Study on the metal-based formulation has shown complete remission of 15 out of 22 patients suffering from AML within 90 days of treatment (Prakash, 2002). A dietary regimen known as Sarvapisti developed by the scientist of D S Research Centre, Varanasi is also very popular among cancer patients. Sarvapasti was evolved in 1983 from as many as 1621 herbs and plants (Singh 2000). A book published from the center recently, "Cancer is Curable Now," provided documentary evidence of more than 100 patients where marked remission of the cancer / tumor was observed along with substantial increase in the disease free survival time. Proposal of two ACT viz. Antineoplastin (Sharma, 1999; Ghosh, 2001) and Methylglyoxal (Ray, 2001; Pal, 2001) created lot of public interest recently in Kolkata. However, the effectiveness of both these therapies against cancer is yet to be ascertained. Other popular alternative medicines used in India for cancer treatment include, herbal, natural, tribal and folk medicines. Kromba an herbal preparation is popular in Rishikesh. Muthu Marunthu comprising of eight various plant ingredients is popular in South India (Palani, 1999). An Ayurvedic formulation, Maharishi Amrit Kalash, has proved to be effective in controlling the side-effects of chemotherapy (Kher, 1999). Other approaches include nutritional therapy, Tulsi, reiki, religious therapy, meditation, yoga, laughter therapy and black magic (Chaturvedi et al., 2002).

The Future Perspective

In Today's society with its mistrust of authority and in established institutions, and with a prevalent "take-charge, do-it-yourself" attitude, there is the likelihood that usage of ACT will expand (McGinnis, 1991). Moreover, prognostic outcome of the great majority of adult cancer patients, once the disease has developed metastasis spread, is very limited. More than 500,000 people in the United States and even more in Europe and Asia die each year of progressive incurable cancer. Until and unless there is a dramatic improvement in cancer mortality statistics with modern medicine, CAM will continue to be a great attraction for cancer patients. And our best efforts to convince patients to stay away from unproven alternatives will be futile. The world's population is predicted to increase from 6.1 billion to 9.3 billion people over the next 50 years. Cancer burden is also set to increase with the aging population and currently there are about 10.1 million people who have been diagnosed with neoplastic disease. By 2020, this number is expected to increase to 20 million. Perhaps disturbingly, 70% of people are thought to live in the developing world (Sansom and Mutuma, 2002). We do not yet have an effective means for either primary or effective secondary prevention of most malignant visceral tumor types. Hence, most treatment approaches in adult cancer patients are 'palliative', directed to prevent and treat unnecessary suffering of these patients on their way to a premature death. CAM will have a bigger role to play when cure is no longer the realistic objective (Senn, 2001 a).

Cancer is a multifactorial disease, which demands multi-modal therapeutic approaches. CAM seems an important and fruitful area of future research, particularly in the realm of palliative care. We urgently need to know the value of these treatments in comparison with conventional palliative technique. Inadequate pain management, for example, which remains a problem in oncology care, often spurs patients to seek more effective and less toxic alternative to conventional options. Nonsedating techniques, such as acupuncture have shown to be useful (Risberg et al., 1995). In USA complementary cancer therapies are increasingly being " integrated" into mainstream practice (Hess 2002 a). Many research-supported complementary therapies like hypnosis, therapeutic massage, meditation, yoga, herbal tea etc. suggest that these therapies can improve the well being of patients with cancer. Such therapies are increasingly being provided at mainstream cancer centers (Vickers and Cassileth, 2001). New policies are needed to allow for the evaluation of potentially safe and efficacious nontoxic therapies that have "orphaned" because they are not patentable and are therefore unprofitable (Hess, 1999). However, substance used in CAM

cancer treatment are often proprietary and their composition secret, such that the CAM practitioner may be unwilling or unable to share their formula with others. This same secrecy makes quality control and reproducibility problematic (Nahin, 2002). Crude natural products have claimed that the whole is greater than the sum of parts. Certain herbs may be added to a medicinal product with the belief that they counteract the negative effects of other components thus allowing a therapeutic dose of those components to be tolerated. Recent research has begun to investigate the potential validity of some of these concepts (White, 2002). However, of concern is quality of herbal products. Recent analysis has revealed contamination of PC-SPES with conventional medications (DES, warfarin, and indomethacin) (Weiger et al., 2002). Studies found variable amount of DES in most PC-SPES samples tested (Sovak et al., 2002). Because DES has shown clinical efficacy against prostate cancer, the discovery of DES contamination raised the question of whether observed clinical result can be attributed to PC-SPES herbal components. In addition to variable contamination with conventional medication, considerable intersample variation has been found in the levels of potentially active phytochemicals. In February 2002, the FDA warned patients to stop taking PC-SPES. The sole manufacturer issued a recall and subsequently went out of business. This incidence highlights the lack of adequate quality control in the herbal industries today. Complementary approaches to be accepted as viable alternatives to conventional medicine, the same rigorous method of scientific and clinical validations must be applied (Kinsel and Straus 2003).

Conclusion

CAM has become an important component of modern oncology. Despite substantial progress of scientific clinical oncology, the fascination of alternative and especially complementary cancer medicine has not at all declined. On the contrary, in developed countries, CAM is more popular than ever with the patients and their social environment (Senn, 2001 b). In the developing countries the use of alternative cancer therapies are related to socioeconomics and cultural / social differences. In many instances the patients are compelled to try something alternative because of financial constraints and inaccessibility to mainstream cancer treatment. We should therefore acknowledge the patients' need to explore all avenues of treatment, which can benefit the patient. About 50% of the world's cancer burden is carried by the developing world that has access to only 5% of the world's resources to fight the disease. According to some recent estimates, the cancer burden will grow to 70% in these countries in the next two decades (Plesnicar and Plesnicar, 2001). The cancer treatment scenario for the next 20 years is predicted not to change substantially (Cavalli, 1999). CAM if integrated properly with mainstream medicine can play an important role in cancer management in these countries. It is important to understanding on the part of health professionals and policy makers that patients need to play a meaningful role in their own care. Hence, various alternative approaches tried by cancer patients needed to be evaluated and documented so that evidence based useful therapies can be provided to others. The future of complementary and alternative cancer therapies lies in "integration" with conventional medicine, proper integration will ensure better management of cancer.

References

Arnold K (2002). Tests of three herbal therapies yield disappointing results. *J Natl Cancer Inst*, **94**, 649.

Astin JA (1998). Why patients use alternative medicine: results of a national study. *JAMA*, **279**, 1548-53.

Bailey LM (1983). The effect of live music versus tape-recorded music on hospitalized cancer patients. *Music Ther*, **3**, 17- 28.

Bergsland EK, Venook AP (2002). Shedding old paradigms: Developing viruses to treat cancer. *J Clin Oncol*, **20**, 2220-2.

Biermann JS, Golladay GJ, Greenfield MLVH , Baker LH (1999). Evaluation of cancer information on the Internet. *Cancer*, **86**, 381-39.

Buiatti E, Arniani S, Verdecchia A, Tomatis L, the Italian Cancer Registries (1999). Result from a historical survey of the survival of cancer patients given Di Bella Multitherapy. *Cancer,* **86**, 2143 -9.

Cassileth BR (2002). Complementary and alternative medicine. Kelsen D P, Daly J M, Levin B, Kern S E, Tepper J E (Eds.) Gastrointestinal Oncology: Principles and practice (Lippincott Williams & Wilkins, Philadelphia pp. 165–177.

Cassileth BR, Chapman CC (1996). Alternative and complementary cancer therapies. *Cancer*, **77**, 1026-34.

Cassileth BR, Lusk EJ, Guerry D, et al (1991). Survival and quality of life among patients receiving unproven as compared with conventional cancer therapy. *N Engl J Med*, **324**, 1180-5.

Cassileth BR, Lusk EJ, Strouse TB, Bodenheimer BJ (1984). Contemporary unorthodox treatment in cancer medicine: a study of patients treatments and practitioners. *Ann Intern Med*, **101**, 105-12.

Cassileth BR, Schraub S, Ribinson E , Vickers A (2001). Alternative medicine use worldwide. *Cancer*, **91**, 1390-3.

Cavalli F (1999). The future of oncology: more of the same? *Lancet*, 354.

Chatterjee AK , Dutta SK , Bhakta RS, et al (1999). Use of Psorinum in the treatment of cancer. In : Verma A K, eds. Oral Cancer VI. *Macmillan India Ltd*, 297-300.

Chaturvedi P, Chaturvedi U, Sanyal B, (2002). Alternative medicine and cancer patients in less developed countries, *Lancet Oncol*, **3**, 10.

Chlebowski RT, Rose D, Buzzard IM, et al (1992). Adjuvant dietary fat intake reduction in postmenopausal breast cancer patient management. The Women's Intervention Nutrition Study (WINS). *Breast Cancer Res Treat*, **20**, 73-84.

Creagan ET, Moertel CG, O'Fallon JR (1979). Failure of high-dose vitamin C (ascorbic acid) therapy of benefit patients with advanced cancer a controlled trial. *N Engl J Med*, **301**, 687-90.

Crocetti E, Crotti N, Feltrin A, et al (1998). The use of complementary therapies by breast cancer patient attending conventional treatment. *Eur J Cancer*, **34**, 324-8.

Curt GA (2002). Introduction: Complementary and alternative medicine in cancer treatment. *Seminars Oncol*, **29**, 525-30.
Danopoulos ED, Danopoulou IE (1974). Urea treatment of skin malignancies. *Lancet*, **1**, 115-8.
Das Gupta D, Kothari ML, Mehta LA (1997). Cancer pain: An Indian perspective. In : Parris WCV, Foster H W Jr., Melzack R, eds. Cancer pain management principles and practices. *Oxford: Butterworth Heinemann*, 567-74.
Downer SM, Cody MM, McCluskey P (1994). Pursuit and practice of complementary therapies by cancer patients receiving conventional treatment, *BMJ*, **309**, 86-9.
Ernst E, Cassileth BR (1999). How useful are unconventional cancer treatment? *Eur J Cancer*, **35**, 1608-13 .
Ernst E, Cassileth BR (1998). The prevalence of complementary/ alternative medicine in cancer: a systematic review. *Cancer*, **83**, 777-82.
Ernst E (2001). A primer of complementary and alternative medicine commonly used by cancer patients. *Medical J Aust*, **174**, 88-92.
Ernst E (2001a). Mistletoe for Cancer? *Eur J Cancer*, **37**, 9-11.
Esinberg DM, Kessler RC, Foster C, et al (1993). Unconventional medicine in the United States. *N Engl J Med*, **328**, 246-52.
Ghosh T (2001). Can scientist treat cancer patients? The Times of India, Kolkata, June 14, 2001.
Green S (1992). Antineoplastons: an unproved cancer therapy. *JAMA*, **267**, 2924-8.
Hauser SP (1991). Unproven methods in oncology. *Eur J Cancer*, **27,** 1549-51.
Hess DJ (2002a). Complementary or alternative? Stronger Vs weaker integration policies. *Am J Public Health*, **92**, 1579-81.
Hess DJ (2002b). The raw and the organic: Politics of therapeutic cancer diet in the United States. *Annals AAPSS,* **583**, 76-96.
Hess DJ (1999). Suppression, bias and selection in science: The case of cancer research. *Accountability Res*, **6**, 245-57.
Hsu HY(1982). Treating cancer with Chinese herbs (Los Angeles Oriental Healing Arts Institute).
Italian Study Group for the Di Bella (1999). Multitherapy Trials, evaluation of an unconventional cancer treatment (the Di Bella multitherapy): results of phase II trial in Italy. *BMJ*, **318**, 224-8.
Jonas W (1998). Alternative medicine and the conventional practitioner. *JAMA*, **279**, 708-9.
Jones SB (1999). Cancer in the developed world: a call to action. *BMJ*, **319**, 505-9.
Kaegi E (1998 a). Unconventinal therapies for cancer: 6. 714 X. *CMAJ*, **158**, 1621-3.
Kaegi E (1998b). Unconventional therapies for cancer: 3 Iscador. *CMAJ*, **158**, 1157-9.
Kaegi E (1998c). Unconventional therapies for cancer: 2 Green tea. *CMAJ*, **158**, 1033-5.
Kher A (1999). Drug to cure chemotherapy side-effects. The Pioneer, Lucknow November 7.
Kubabe T, Tsuda H, Uchida M, et al (1998). Antineoplaston treatment for advanced hepatocellular carcinoma. *Oncol Rep*, **5**, 1363-7.
Kinsel JF, Straus SE (2003). Complementary and alternative therapies: Rigorous research is needed to support claims. *Annu Rev Pharmacol Toxicol*, **43**, 463-84.
Lee A, Langer R (1983). Shark cartilage contains inhibitors of tumor angiogenesis. *Science*, **221**, 1185-7.
Lerner IJ, Kennedy BJ (1992). The prevalence of questionable methods of cancer treatment in the United States. *CA Cancer J Clin*, **42**, 181-91.
Maclennan AH, Wilson DH, Laylor AW (1996). Prevalence and cost of alternative medicine in Australia. *Lancet*, **347**, 569-73.
Mann F, Bowsher D, Mumford J, lipton S, Miles J (1973). Treatment of intractable pain by acupuncture. *Lancet*, **2**, 87-60.
Markman M (2002). Safety issue in using complementary and alternative medicine. *J Clin Oncol*, **20**, 39S-41S.
Mathews J (1993). Media feeds frenzy over shark cartilage as cancer treatment. *J Natl Cancer Inst*, **85**, 1190-1.
McGinnis LS (1991). Alternative therapies: 1990. An overview. *Cancer*, **67**, 1788-92.
Miller DR, Anderson GT, Stark JJ (1998). Phase I/II trial of the safety and efficacy of shark cartilage in the treatment of advanced cancer. *J Clin Oncol*, **16**, 3649-55.
Moertel CG, Fleming T R, Creagan ET (1985). High-dose vitamin c versus placebo in the treatment of patients with advanced cancer who have had no prior chemotherapy: a randomized double-blind comparison. *N Engl J Med*, **312**, 137-41.
Monad MA, Pienta KJ, Montie JE. (1999). Use of PC-SPES, a commercially available supplement for prostate cancer, in a patient with hormone-native disease. *Urology*, **54**, 319-23.
Morris KT, Johnson N, Homer L, Deb W (2000). A comparison of complementary therapy use between breast cancer patients and patients with other primary tumor sites. *Am J Surg*, 1**79**, 407-11.
Moss RW (1992). Cancer therapy: the independent consumers guide. New York, Equinox Press,.
Nahin RL (2002). Use of the best case series to evaluate complementary and alternative therapies for cancer.: A systematic review. Seminar Oncol, **29**, 552-62.
Normile D. (2003). The new face of traditional Chinese medicine. *Science*, **299**, 188-90.
Oh WK, Small EJ (2002). Complementary and alternative therapies in prostate cancer. *Seminars Oncol*, **29**, 575 -84.
Pal SK (2002a). Complementary and alternative medicine: An overview. *Curr Sci*, **82**, 518-24.
Pal SK (2002b). Use of alternative cancer medicine in India. *Lancet Oncol*, **3**, 394-5.
Pal SK (2001). Use of new cancer drugs in India. *Lancet Oncol*, **2,** 716.
Pal SK, Pandey GS, Kesari A, Choudhuri G , Mittal B (2003). Fighting cancer in the information age: The role of Internet. Ind J Expt Biol, **41**, 189-200.
Palani V, Senthilkumaran RK, Govindasamy S (1999). Biochemical evaluation of antitumor effect of *Muthu Marunthu* (a herbal formulation) on experimental fibrosarcoma in rats. *J Ethnopharmacol*, **65**, 257-65.
Pandha HS, Kirby RS (2002). PC-SPES: phytotherapy for prostate cancer. *Lancet*, **359**, 2213-14.
Pellegrini R (1998). Di Bella's method of curing cancer is becoming popular in Italy. *BMJ*, **317**, 352.
Plesnicar S, Plesnicar A (2001). Cancer: A reality in the emerging world. *Seminars in Oncol*, **28**, 210-6.
Prakash B, Joshi A, Babu R, et al (2002). Ayurvedic approach in the treatment of leukemia, In proceedings of International symposium of Ayurveda, Yoga and Naturopathy, Sevagram 10.
Pruddent J (1985). the treatment of human cancer with agents prepared from bovine cartilage, *J Biol Response Modif*, **4**, 551-81.
Ray M, Ghosh S, Kar M, Dutta S , Ray S (2001). Implication of the bioelectronic principle in cancer therapy: treatment of cancer patient by methylglyoxal-based formulation. *Indian J Phys*, **75B,** 73-7.

Richardson MA, Sanders T, Palmer JL, Greisinger A , Singletary S E (2000). Complementary/ Alternative medicine use in a comprehensive cancer centre and the implication for oncology. *J Clin Oncol*, **18**, 2505-14.

Richardson MA, Straus SE (2002). Complementary and alternative medicine: opportunities and challenges for cancer management and research. *Seminars Oncol*, **29**, 531-45.

Risberg T, Lund E, Wist E, et al (1995). The use of non-proven therapy among patients treated in Norwegian oncology departments. A cross-sectional national multicentric study. *Eur J Cancer*, **31A**, 1785-9.

Riviere M, Alaoni-Jamali M, Falardean P, Blasecki J, Dupont E (1998). Neovastat : an inhibitor of angiogenesis with anti-cancer activity. Proceedings of the American Association of Cancer Research. *New Orleans Louisiana*, **39**, 46.

Rosa L, Rosa E, Sarner L (1998). A closer look at therapeutic touch. *JAMA*, **279**, 1005- 10.

Rosenbluth RJ, Jennis AA, Cantwell S, DeVries J (1999). Oral shark cartilage in the treatment of patient with advanced primary brain tumours. A phase II pilot study. Proceedings of the Annual Meeting of the American Society of Clinical Oncology, Atlanta, Georgia. **18**, A554.

Sansom C, Mutuma G (2002). Kenya faces cancer challenge. *Lancet Oncol*, 3, 456- 8.

Sazuka M, Murakami S, Isemura M, Satoh K , Nukiwa T (1995). Inhibitory effects of green tea infusion on *in vitro* invasion and *in vivo* metastasis of mouse lung carcinoma cell. *Cancer Lett*, **98**, 27-31.

Schraub S (2000). Unproven methods in cancer: a worldwide problem. *Support Care Cancer*, **8**, 10–5.

Sellick SM, Zaza C (1998). Critical reviews of five nonpharmacologic strategies for managing cancer pain. *Cancer Prev Control*, **2**, 7–14.

Senn HJ (2001a). Optimal comprehensive symptom control: an overall strategy. *Eur J Cancer*, **37**, S261– 4.

Senn HJ (2001b). Introduction: Dimension and fascination of complimentary and alternative medicine in oncology. *Eur J Cancer*, **37**, S164.

Sharma DC (1999). India anticancer drug trial halted. *Lancet*, **353**, 735.

Sikora K (1999). Developing a global strategy for cancer, In proceedings of the XV Asia-Pacific Cancer Conference, Chennai, India, 7.

Singh BK (2000). Scientist claims cancer cure. The Times of India, Lucknow, April 12.

Singh CV (1978). Role of acupuncture analgesia for intractable pain in malignancy. *J Indian Med Assoc*, **11**, 108 -9.

Singh RH (2002). An assessment of the ayurvedic concept of cancer and a new paradigm of anticancer treatment in Ayurveda. *J Altern Complement Med*, **8**, 609-14.

Sovak M, Seligson A L, Konas M, et al (2002). Herbal composition PC-SPES for management of prostate cancer: identification of active principle. *J Natl cancer Inst*, **94**, 1275-81.

Sparber A, Wootton J (2001). Survey of complementary and alternative medicine: Part II use of alternative and complementary cancer therapies. *J Altern Compl Med*, **3**, 281-7.

Stephenson NL, Weinrich SP, Tavakoli AS (2000). The effect of foot reflexology on anxiety and pain in patients with breast and lung cancer. *Oncol Nurs Forum*, **27**, 67-72.

Steuer-Vogt MK, Bonkowsky V, Ambrosch P, et al (2001). The effect of an adjuvant mistletoe treatment programme in resected head and neck cancer patients: a randomized controlled clinical trial. *Eur J Cancer*, **37**, 23-31.

Syrjala KL, Cummings C , Donaldson GW (1992). Hypnosis or cognitive behavioral training for the for the reduction of pain and nausea during cancer treatment: a controlled clinical trial. *Pain*, **48**, 137-46.

Syrjala KL, Donaldson GW, Davis MW (1995). Relaxation and imagery and cognitive-behavioural training reduce pain during cancer treatment: a controlled clinical trial. *Pain*, **63**, 189-98.

Tusda H, Sata M, Kumabe T, et al (1998). Quick response of advanced cancer to chemoradiation therapy with antineoplastons. *Oncol Rep*, **5**, 597-600.

Tusda H, Sata M, Saitsu H, et al (1997). Antineoplaston AS2-1 for maintenance therapy in liver cancer. *Oncol Rep*, **4**, 1213-6.

Vaidya ADB, Vaidya RA, Vaidya V, Vaidya G H, Joshi BA (2003). Spontaneous or induced regression of cancer: a novel research strategy for Ayurvidya. *Ancient Sci of Life XXII*, **3**, 75– 83.

Vanchieri C (2000). Alternative therapies getting noticed through best case series program. *J Natl Cancer Inst*, **92**, 1558-60.

Vickers AJ (1996). Can acupuncture have specific effect on health? A systematic review of acupuncture antiemesis trials. *J R Soc Med*, **89**, 303-11.

Vickers AJ, Cassileth BR (2001).Unconventional therapies for cancer and cancer-related symptoms. *Lancet Oncol*, **2**, 226-31.

Weiger WA, Smith M, Boon H, et al (2002). Advising patient who seek complementary and alternative medical therapies for cancer. *Ann Inter Med*, **137**, 889–903.

Weinrich SP, Weinrich MC (1990). The effect of massage on pain in cancer patients. *Appl Nurs Res*, **3**, 140-5.

White JD (2002). Complementary and alternative medicine research: A national cancer institute perspective. *Seminar Oncol*, **29**, 546 – 51.

Winslow LC , Kroll DJ (1998). Herbs as medicines. *Arch Intern Med*, **158,** 2192-9.

Wu AH, Pike MC, Strom DO (1999). Meta-anaysis: dietary fat intake, Serum estrogen Levels and the risk of breast cancer. *J Natt Cancer Inst*, **91**, 529-34.

Zollman C , Vickers A (1999). What is complementary medicine? *BMJ*, **319**, 693– 6.