

A SCIENTIFIC LOOK AT ALTERNATIVE MEDICINE

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February 14, 2006

Cancer and AIDS Therapies; Chelation Therapy; Allergy and Arthritis Treatments; Other Miscellaneous Topics

COMPLEMENTARY AND ALTERNATIVE CANCER TREATMENTS

Background

Estimated costs: \$28 billion/year (1990)

About half of practitioners are M.D.'s. Others are chiropractors, homeopaths, naturopaths, nutrition advisors, etc.

A study of Austrian cancer patients (*Cancer* 89, 873-880 (2000)) found that most who used CAM methods were highly compliant with conventional therapy; the seeking of alternatives was part of an active coping mechanism. However, Burstein et al. (*New Engl. J. Med.* 340, 1733-9 (1999)) concluded that in breast cancer patients, "new use of alternative medicine was a marker of greater psychological distress and worse quality of life."

Earlier estimates of use among cancer patients range from 6 to 23%. More recent surveys found 43% usage in prostate cancer (but 3/4 of them did not inform their doctors!), 24% in brain tumor patients, 75% in breast cancer, and 31-84% in children with cancer. (However, some of these may be complementary methods for relief of symptoms, rather than intended as cures.)

Many Americans go to clinics near Tijuana, Mexico, where they can obtain treatments that are illegal in the U.S. In 2001, Mexican officials began enforcing tighter regulations, and many of these clinics were closed temporarily or permanently (however, as of Feb. 2002, an estimated 30 to 70 were in operation).

OAM and NCCAM have funded several studies of alternative cancer methods, as well as a university-based research center at M.D. Anderson Cancer Center in Texas. The National Cancer Institute also has its own Office of Cancer Complementary and Alternative Methods. There are 6 NCI-designated cancer centers with major programs in researching CAM methods.

Vickers et al. (*J. Clin. Oncol.* 24, 136-140) reviewed clinical trials of unconventional cancer treatments and concluded that they "have not been subject to appropriate early-phase trial development." "Of the 27 different agents tested in phase III, only one agent had a prior dose-finding trial, and only for three agents was the definitive study initiated after the publication of phase II data."

Schmidt and Ernst (*Annals Oncology* 15, 733-742 (2004)) evaluated 32 popular web sites dealing with CAM for cancer, and concluded: "Most sites issued recommendations for a plethora of treatments, which are typically not supported by sound scientific evidence. Three sites had the potential for harming patients through the advice issued."

Another survey of commercial websites dealing with cancer found that “92% claimed that a supplement could prevent cancer; 89% claimed that a supplement could be used to treat cancer; and 58% referred to the supplement as a cure for cancer...less than 40% recommended that users should consult their doctor” (news report by Charatan, *BMJ* 323, 827 (2001)). (Such claims of prevention and treatment are illegal in the U.S.) Matthews et al. (*Psychosomatics* 44, 100-103 (2003)) concluded that “There is a staggering amount of medical misinformation on the internet.”

In an American Cancer Society survey (2005), 27% agreed (and another 14% thought it might be true) that the medical establishment was suppressing a cure for cancer.

Major categories of CAM used by patients, as classified by Wieger et al. (*Ann. Intern. Med.* 137, 889-903 (2002)): “dietary modification and supplementation, herbal products and other biological agents, acupuncture, massage, exercise, and psychological and mind-body therapies.” However, some of these are sought for their putative benefits in dealing with the effects of the disease or the side effects of treatments, rather than with the intent of curing the cancer. The therapies discussed below are those that are promoted as cancer treatments or cures.

Some prominent types of treatment

| <u>Therapy</u> (numbers refer to clinical or laboratory studies listed below) | <u>Problems and comments</u> (other than lack of effectiveness, lack of conventional treatment, expense) |
|---|---|
| LAETRILE (amygdalin, "vitamin B17") - cyanide released from compound said to kill cancer cells in preference to normal. Later claimed to be a vitamin. ① | Cyanide toxicity. Flawed biochemical logic behind use. |
| METABOLIC THERAPY (Harold Manner): "the use of natural food products and vitamins to prevent and treat disease by building a strong immune system" (Manner, quoted in Barrett, <i>Health Schemes, Scams and Frauds</i>). Immune system thought to be weakened by toxins, stress, or poor nutrition. Includes vegetable juices, natural foods, Laetrile, coffee enemas, high colonic irrigation, vitamins, minerals, enzymes, glandulars. | Colonic irrigation has led to deaths from electrolyte imbalance, bowel necrosis or perforation, toxic colitis, amebiasis, hypokalemia, and sepsis. Dehydration, renal failure have been produced. Enzymes and glandular given in diet are digested rather than reaching target organs or cells. |
| GERSON THERAPY (Max Gerson; Charlotte Gerson Straus). Metabolic therapy featuring large amounts of fresh fruit and vegetable juices, vitamins, minerals, other supplements, Laetrile, coffee enemas. Intravenous glucose-potassium-insulin. Ozone, hydrogen peroxide. "Staphage lysate" vaccine. ② | Infections from raw liver. See “metabolic therapy” above. |
| KELLEY METABOLIC THERAPY (William Kelley, Nicholas Gonzalez) - pancreatic enzymes, colonic irrigation or coffee enemas, diet, supplements. ⑦ | See above concerning colonic irrigation and enzymes. (See also p. 5) |
| FRESH CELL THERAPY (Live cell therapy) (Paul Niehans, Switzerland). Intramuscular or subdural injection of fresh embryonic animal cells from organ which, in patient, is cancerous. Said to be transported to target organ, where they repair function. | Infections, allergic reactions, anaphylactic shock; some deaths have occurred from these. Chronic progressive neurological damage. Animal cells would be rejected, unlikely to reach organ and function. |

CONTRERAS METHOD (Ernesto Contreras). Metabolic therapy with Laetrile, coffee enemas, colonic irrigation, proteolytic enzymes. Live cell therapy, oxygen therapy, shark cartilage, herbs. Spiritual and psychological components, with worship and Bible study, humor and laughter, etc.

IMMUNOAUGMENTATIVE THERAPY (IAT) (Lawrence Burton - clinic in Bahamas) - proteins prepared from blood of cancer patients or healthy donors; injected into patients.

LIVINGSTON VACCINE (Virginia Livingston-Wheeler) - "Immuno-Shield" program. Attributes cancer to a bacterial infection. Vaccines prepared from cultures from patient. Also special diet, supplements, visualization. ③

REVICI SYSTEM (lipid therapy, "biologically guided chemotherapy") (Emanuel Revici). Treatment guided by analysis of single sample of patient's urine for acidity and specific gravity. Correction of "imbalances" with: lipid alcohols, zinc, iron, caffeine ("anabolic"); fatty acids, sulfur, selenium, magnesium ("catabolic"). ⑨

HERBAL TEAS (e.g., pau d'arco)

HOXSEY METHOD (Harry Hoxsey; Mildred Nelson) - tonics with herbal components to stimulate elimination of toxins, balance pH of body, bring DNA "back to its more normal state," etc. Key component is potassium iodide. External powders, pastes and solutions. Special diet. ⑥

GREEK CANCER CURE (Hariton Alivizatos, Athens) - Secret blood tests to measure severity of cancer. Treatment with intravenous injection of "serum"; said to contain "a combination of organic substances such as sugars, vitamins, amino acids, and other factors" to boost immune system. Diet low in salt and acids.

MACROBIOTIC DIET (George Ohsawa; Michio Kushi) - based on Eastern yin-yang philosophical principles. Foods (yin or yang) to balance the yin or yang of the cancer. Includes whole grains, vegetables, fruits, miso; almost no animal foods. Recommends avoiding conventional treatment except in emergency. ⑨

OTHER DIETS - Grape diet (grapes and other "raw foods"); plant materials containing chlorophyll (alleged "detoxifying" agent)

MEGAVITAMINS - to enhance body's capacity to destroy malignant cells. Vitamin C promoted by Linus Pauling. ④

Literature contains dubious biochemical statements.

Spread of AIDS, hepatitis.
Stated preparative procedure inconsistent with purification of the proteins.

No evidence of the postulated bacterium.

Acidity and specific gravity of urine too variable to be meaningful.

Dubious biochemistry.

May contain toxic compounds.

Toxic effects of excess iodide.
Corrosive, disfiguring external agents.

Analysis of a sample of "serum" revealed it to be a solution of nicotinic acid.
Formula now marketed as METBAL and CellBal.

Malnutrition (protein, vitamins, iron). May be too bulky to meet high caloric needs of cancer patients.
Invalid diagnoses based on external appearances.
Guilt: patient/family feels poor diet responsible for cancer.

No known role of chlorophyll in human metabolism.

Toxic levels of vitamins.

MENTAL IMAGERY; SIMONTON METHOD (O. Carl Simonton) - relaxation, stress reduction, mental imagery (visualize destruction of cancer cells; brain said to stimulate endocrine system, which enhances immune system)

ANTINEOPLASTONS (Stanislaw Burzynski) - substances which allegedly "normalize" cancer cells. Synthetic or extracted from urine. ⑨

CANCEL (Entelev, "Jim's Juice") - claimed to "digest" cancer cells by adjusting their "vibrational frequency," causing them to reach a "primitive state." Composed of inositol, catechol, and inorganic chemicals. (11)

HYPEROXYGENATION THERAPY - based on finding (Warburg) that tumor cells have increased anaerobic metabolism, leading to hypothesis that oxygen is toxic for them. HYDROGEN PEROXIDE, GERMANIUM sesquioxide, and OZONE are used.

HYDRAZINE SULFATE - developed by Joseph Gold. Supposedly blocks liver gluconeogenesis, depriving tumors of glucose (needed for anaerobic glycolysis). ⑧

SHARK CARTILAGE, SHARK OIL - Based on presence of angiogenesis inhibitors in cartilage, and allegation that sharks don't get cancer. Sales of \$50 million/year. ⑨ ⑩ Alkylglycerols in the oil are claimed to kill tumor cells, stimulate the immune system, and reduce side effects of conventional treatments.

MEDICINAL MUSHROOMS (Ganoderma/reishi, shiitake/lentinan) - used in Oriental herbal remedies. Contain polysaccharides thought to enhance immune system.

CAT'S CLAW - prepared from bark of a Peruvian vine. (13)

ESSIAC - herbal remedy promoted by Canadian nurse Rene Caisse. ⑤ (12)

ELECTRONIC DEVICES - various devices are alleged to diagnose and treat cancer.

Guilt from thinking stressful lifestyle responsible for cancer.

Chemical properties inconsistent with Burzynski's description. (See also below, p. 5)

Rationale involves bizarre concepts inconsistent with scientific knowledge. Distributed free (patients may donate to offset costs).

Increased anaerobic metabolism does not mean enhanced susceptibility to oxygen. Claimed to be effective for many other diseases. Possible damage from free radicals.

Glucose needed for brain and other tissues, and normally is tightly controlled - patients suffer many side effects.

Sharks do get cancer - even in cartilage. Lower incidence likely due to immune system, not the anti-angiogenesis factor. Only negligible amounts of factor would be ingested, and would be broken down in digestion.

Also used in AIDS treatments.

Also promoted for AIDS, arthritis, other conditions.

Also promoted for many other conditions.

See below (p. 16) under Miscellaneous Topics.

Some clinical studies:

① *Laetrile* - Because of widespread interest and public pressure, has been subjected to many scientific investigations. Animal studies, several retrospective case studies, and one prospective clinical trial (by the National Cancer Institute) were carried out. None supported the usefulness of Laetrile.

② *Gerson therapy* - cases reviewed by National Cancer Society and New York County Medical Society in 1947; no evidence of effectiveness found. Austin (1983-8): 20 of 21 patients died within 5 years (see Barrett,

The Health Robbers, p. 88).

- ③ *Livingston vaccine* - Univ. Pennsylvania Cancer Center - no enhanced survival for patients with advanced untreatable cancer.
- ④ *Vitamin C therapy* - two double-blind studies, of patients with or without prior chemotherapy, at Mayo Clinic found no benefit.
- ⑤ *Essiac* - Canadian federal health department reviewed 86 patients, found no benefit (Barrett, p. 87).
- ⑥ *Hoxsey treatment* - Univ. of British Columbia study (1957) - followup of Hoxsey patients revealed no benefit.
- ⑦ *Kelley Metabolic Therapy* - Office of Technology Assessment reviewed 50 "best cases" of Kelley; no evidence of effectiveness.
- ⑧ *Hydrazine sulfate* - three double-blind trials published in 1994 (*J. Clin. Oncol.*) found no evidence of effectiveness.
- ⑨ The NIH Office of Alternative Medicine funded a major study of antineoplastons, as well as small exploratory grants for shark cartilage, Revici therapy, magnets, and macrobiotics. However, earlier reviews of patients treated with antineoplastons found no evidence of effectiveness. In 2000, the Mayo Clinic concluded, based on a small study, that Burzynski's method was useless and potentially harmful.
- ⑩ *Shark cartilage* - two studies of advanced cancer patients found no benefit (Miller et al. (1998) *J. Clin. Oncol.* 16, 3649-55; Loprinzi et al. (2005) *Cancer* 104, 176-182).

Other tests

- (11) *Cancell* - tested by National Cancer Institute (animal studies, 1978, 1980; *in vitro* studies, 1990, 1991). Negative results.
- (12) *Essiac* - no anticancer activity in animal tests.
- (13) *Cat's Claw* - tested by National Cancer Institute; activity in initial screening insufficient to merit more detailed study.

Some currently prominent promoters and methods

Nicholas Gonzalez (see *Kelley Metabolic Therapy*, p. 2) obtained promising results in a pilot study of 11 pancreatic cancer patients, and a larger study (funded by NCCAM) is now in progress. A network television story on Gonzalez revealed that he follows the progress of patients' cancer using hair analysis, and was unable to explain the basis of the test (which involved an invalid method, radionics).

Stanislaw Burzynski was acquitted in 1997 on charges of using an unapproved drug in interstate commerce. His gross income from antineoplastons was \$40 million from 1988 to 1994. Although the FDA had approved clinical trials, Burzynski enrolled and treated only six patients in his trials from 1983 to 1995. More recently he enrolled hundreds of patients, but the trials were so poorly designed that they were unlikely to yield any useful information.

Hulda Clark, in *The Cure for All Cancers*, claims that cancer (and AIDS) is caused by an intestinal parasite, and can be cured with plant materials within three weeks. She also promotes a device called the "Zapper" that is claimed to kill parasites, viruses, and bacteria with radio waves tuned to the correct frequencies. Another device, the "Syncrometer," is used in diagnosis. In 2001 and 2003 the FTC took action against promoters of these devices for claims related to cancer and other diseases; a 2004 settlement forbids the companies from making unsubstantiated health claims.

PC-SPES is a mixture of Chinese herbs; it had shown some promise as a treatment for prostate cancer. However, in 2002 it was discovered that the product was adulterated with several conventional drugs. One of these, diethylstilbestrol, is known to have antitumor effects, which could account for the apparent benefits of PC-SPES.

In 2000 the FDA took action against several *Laetrile* marketers, including three Internet sites selling "Vitamin B17." One leading promoter was convicted in 2003 of violating a court order against selling or promoting laetrile. The FDA and FTC also acted against *shark cartilage* products in 1999-2000. In 2005 Lane Labs agreed to refund millions of dollars to customers who bought shark cartilage products for cancer treatment.

714-X is a mixture of a modified form of camphor and other chemicals. In 2001 the National Cancer Institute agreed to review claims of cures.

Mistletoe (marketed as the product *Iscador*) has been the subject of considerable interest, especially in Germany. Research studies and reviews have come to conflicting conclusions as to whether there is evidence of effectiveness.

Characteristics of pseudoscience

Claims of proponents to be visionaries (ahead of their time) or persecuted

Claim burden of proof is on opponents to show that therapies don't work

May employ dubious diagnostic methods (e.g., iridology) - "cured" patients may not have had cancer

Lack of documentation: improper or inadequate diagnosis; lack of followup studies. Reliance on patients to report back with claims of success. Survival estimates based on subjective evaluation of departing clinic patients.

Anecdotal evidence of success. "Cured" patients may be in remission or having progressive cancer.

Use of secret formulas (Hoxsey, Greek Cancer Cure). Dr. Alivizatos was invited to submit material to National Cancer Institute for testing of antitumor activity, but did not respond.

Declare test protocol invalid after completion of study (Revici)

Rationale for use is changed when previous rationale shown to be invalid (Laetrile)

Nonscientific (yin-yang) or nonmeasurable (detoxification) concepts

Attribute failures to effects of previous conventional therapy in poisoning body.

Wide-ranging claims to heal all cancer, whereas there are many types of cancer with different characteristics and sensitivities to established therapies.

"They frighten patients away from proper therapy by referring to surgery as cutting, to radiation as burning, and to chemotherapy as poisoning." (S. Bertolone, (1991), *Louisville Medicine* 10(5), 40-42.)

If condition worsens, patient told this is a "healing crisis" due to removal of toxins

Groups that promote questionable methods (Barrett, pp. 97-98):

International Association of Cancer Victors and Friends
 Cancer Control Society
 National Health Federation
 Foundation for Alternative Cancer Therapies

Committee for Freedom of Choice in Medicine
 People for Cancer
 Project Cure

(Health Resource, World Research Foundation, and CANHELP provide information on both conventional and "alternative" methods.)

Cancer Treatment Centers of America use some questionable methods.

Psychological aspects

Holland ("Why Patients Seek Unproven Cancer Remedies: A Psychological Perspective," American Cancer Society (1982)): "Psychologically, the patient with cancer is apt to feel the worst when it becomes clear that medical treatment can no longer control his disease. As soon as traditional medicine is perceived as being unable to offer either control or cure, both patient and family are likely to begin considering unorthodox and unproven methods for curing cancer...Well-meaning friends and colleagues exert enormous pressure...to 'leave no stone unturned' and to explore all known unproven methods of cancer therapy...The result, however, is a barrage of information that the patient hears at a time of great personal anxiety and uncertainty."

Appeal to patients to take control over dealing with illness.

Other points

No drug that has failed lab tests has been demonstrated to be effective against cancer.

Cases of claimed cures who later died of cancer.

Credit may be given to unorthodox therapy when conventional therapy was also being employed.

Variability in survival times may lead to credit being attributed to unorthodox treatment. Some studies have found that prognoses for survival tend to be too pessimistic. Some patients have long survival times with *no* treatment.

Spontaneous remissions occur in nearly all types of cancer and at all stages. The overall incidence is estimated to be between 1 in 10,000 and 1 in 100,000. These cases can lead to stories of miraculous cures, attributed to whatever treatment the patient was receiving.

Study of Cassileth et al. (*N. Engl. J. Med.* 324, 1180-1185 (1991): patients with advanced cancer had poorer quality of life when treated with unorthodox methods.

If patient feels a need to go beyond conventional therapy, an option is to participate in a clinical trial of an investigative therapy.

"...Pursuit of questionable remedies can deprive the patient of the time and resources needed to adjust to the realities of the situation...Reinforcing the illusion of the denial stage prevents the normal psychological adjustments from taking place and thus removes the potential for some satisfaction in the final days." (Jarvis, *CA* 36, 293-301 (1986))

Freedom of choice: can patients make informed decisions based on misinformation provided in much of the literature for the lay public?

Ethical/legal considerations: what are the rights of minors and their parents to choose unorthodox treatment? In general, courts may protect the rights of children to conventional treatment if there is a reasonable chance for a cure. A mature, well-informed older adolescent may be given more rights to choose an alternative.

Undisclosed use of CAM methods by participants in clinical trials is widespread and may complicate research findings.

COMPLEMENTARY AND ALTERNATIVE HIV/AIDS THERAPIES

(This section is based partly on a talk by Ardis Hoven, M.D., of Lexington, at the Kentucky Health Fraud Conference, Nov. 18, 1994, and on an article by William Templeton, M.D., in *Louisville Medicine*.)

General points:

Like cancer patients, HIV patients are desperate, vulnerable, and willing to take risks. Some wish to avoid unpleasant side effects of conventional therapy, and want to try more "natural" remedies.

Studies in the mid- to late-1990s reported CAM usage of 30% to 68% among HIV patients. One study (based on 1996-7 surveys) found that "One quarter of patients used CAM with the potential for adverse effects, and one-third had not discussed such used with their health care provider...Three percent of patients substituted CAM for conventional HIV therapy" (Hsiao et al., *J. Acquir. Immune Defic. Syndr.* 33, 157-165 (2003)).

Some alternative therapies for cancer and other diseases have been promoted as AIDS therapies. Some of the Mexican cancer clinics (see p. 1) now treat AIDS as well.

Many HIV patients are highly organized, with self-help groups, buyers' clubs, and other sources of information, leading to the dissemination of information on obtaining unorthodox therapies. Project Inform has developed access to unapproved drugs. By 1988 there were over 200 "alternatives" being promoted. One company listed 120 mail order items.

With increasing effectiveness of conventional treatments, much of the use of CAM now is for improved quality of life while standard drugs are being taken. St. John's wort, garlic, and vitamin C can potentially reduce the effectiveness of conventional drugs.

Clinical studies of conventional therapies may be compromised if patients are secretly taking other agents.

Examples

Alleged immune enhancers - vitamins A, C, E; fatty acids, iron, zinc, selenium, amino acids, bee pollen, garlic, blue-green algae, Immunex (low-dose α -interferon), PCM4 (pig spleen protein plus Siberian ginseng), other Chinese herbal remedies, "immunity soup" (major component is from mushrooms), Cat's Claw

Metabolic therapy

Diets - Immune Power Diet (avoids cow's milk, wheat, corn, yeast, soy products), macrobiotic diet, yeast-controlled diet (avoids yeast, sugar, food additives)

Live cell therapy

Alleged antiviral compounds - compound Q, AL727, St. John's wort, ribovirin, shark cartilage, dextran sulfate, hypericin, DHEA, aloe vera juice

Cancel

Oxygen therapies. Ozone administered to blood (after removal from patient), rectally, IM, or IV. Treatments in Germany may cost \$4000/week.

Malarial therapy - inject with malarial parasites; fever allegedly kills HIV

Meditation, imagery, massage, yoga, therapeutic touch, etc.

Crystals (to stimulate chakras related to AIDS), magnets, etc.
 Homeopathy, acupuncture, chiropractic
 Gregory Method - hydrotherapy, saunas, sunshine, colonic irrigation, etc.
 Hyperthermia - body temperature raised to 108° (potentially serious complications)

CHELATION THERAPY

Principles

Ethylenediamine tetraacetic acid (EDTA) binds strongly with metal ions having two positive charges (it *chelates* them). There is a legitimate use in removing heavy metals like lead in cases of metal toxicity (approved by FDA for heavy metal poisoning and for Wilson's disease, in which there is excess copper storage). By extension, alternative practitioners use it to remove supposed toxic metals underlying other conditions.

An early rationale was to remove Ca²⁺ from calcified plaques in arterial disease. Also, deactivation of calcium channels to prevent hypertension. "The lowering of serum calcium during and immediately after a treatment stimulates the release of parathyroid hormone, resulting in the partial removal of metastatic calcium deposits, including those from atherosclerotic plaque." (L. T. Chappell (1997) *Alt. Med. Rev.* 2, 426-432)

Newer rationale sees free radicals as being responsible for most chronic illnesses. EDTA is supposed to prevent this. Also alleged to lower LDL and VLDL, inhibit platelet aggregation, and relax vascular tone.

What do chelationists do, and why?

Intravenous injection of EDTA to remove metals (Thus, practice is limited to physicians and others under their supervision who are allowed to give IV's. Note that physicians can use approved drugs for unapproved purposes!)

Claimed to be effective in a wide range of diseases, including heart disease, kidney disease, arthritis, Parkinson's disease, Alzheimer's disease, diabetes, emphysema, and multiple sclerosis, as well as the aging process itself. Claimed to help 75 to over 90% of patients.

Compounds to be taken orally are also marketed as alleged chelating agents.

Supported by anecdotal evidence, studies in obscure medical journals, nondocumented studies described in books

Arguments against chelation:

Basic science:

No way for EDTA to remove "bad" but not "good" calcium.

"This rationale [deblocking of arteries] is (at best) based on an outdated understanding of arterogenesis. There is reason to believe that proponents of chelation therapy adhere to pathophysiological models of arteriosclerosis, which are in overt discordance with our present knowledge." (E. Ernst (1997) *Circulation* 96, 1031-1033)

No evidence that EDTA prevents free radical damage. Free radicals are produced as a side-product of normal metabolic reactions, and removing the metals that cause these would prevent vital cellular processes.

Moreover, while iron is bound to EDTA and still in the circulation, it remains capable of forming free radicals.

Clinical trials:

No controlled trials support above uses (except possibly in cases of true metal toxicity).

Clinical trials for arterial disease showed no benefit. A randomized, double-blind trial for ischemic heart disease found no benefits (Knudtson et al. (2002) *JAMA* 287, 481-486) (see below for a planned larger trial).

Clinical trial for intermittent claudication (a problem of circulation to the legs) showed no effect (1992).

Reviews:

Meta-analysis by Ernst (*Am. Heart J.* 140, 139-141 (2001)): "The most striking finding is the almost total lack of convincing evidence for efficacy...Given the potential of chelation therapy to cause severe adverse effects, this treatment should now be considered obsolete."

Cochrane Review (2002): "At present, there is insufficient evidence to decide on the effectiveness or ineffectiveness of chelation therapy in improving clinical outcomes of patients with atherosclerotic cardiovascular disease."

Review by Seely et al. (*BMC Cardiovasc. Dis.* 5, 32 (2005)): "The best available evidence does not support the therapeutic use of EDTA chelation therapy in the treatment of cardiovascular disease."

Side effects:

Dangerous if used instead of proper medical treatment for these diseases.

"Furthermore, the serious side effects of EDTA chelation are worrisome. Toxic effects include renal toxicity, cardiac arrhythmias, bone marrow depression, exfoliative dermatitis, histamine-like reactions, insulin shock, and thromboemboli. Fortunately, few adverse effects have been reported when the guideline of 50 mg/kg per infusion is used, as specified by the American College of Advancement in Medicine." (N. Elihu et al. (1998) *J. Clin. Pharmacol.* 38, 101-105)

Guldager et al. (*Dan. Med. Bull.* 40, 627-630 (1993)) found that EDTA treatment was accompanied by bone loss.

In 2005, a 5-year-old died after chelation therapy for treatment of autism.

Other points

Expensive (about \$100 per treatment, up to \$3000 for a course of treatments), usually not covered by insurance.

Treatment may also include exercise and diet, which could lead to improvement being attributed to chelation.

Advocate groups: American College of Advancement in Medicine (ACAM), American Board of Chelation Therapy. ACAM estimates that there are 800,000 chelation visits per year.

In 2002, NCCAM and the National Heart, Lung, and Blood Institute announced a \$30 million, 5-year study of chelation therapy, to include 2400 patients at 100 sites.

In 1998, the FTC reached a consent agreement with ACAM, prohibiting it from “representing that EDTA chelation therapy is an effective treatment for atherosclerosis without possessing and relying upon competent and reliable scientific evidence to substantiate the representations.”

In 10 states, “Access to Medical Treatment Acts” have been passed in response to lobbying by supporters of ACAM.

ALLERGY TREATMENTS

40 million Americans suffer from allergies, making it a profitable area for alternative treatments.

Food allergies - These are relatively rare (5 percent of children, 2 percent of adults) (should not be confused with food *intolerance*, which is much more common), but are frequently "diagnosed" by mail order labs and some allergists.

Invalid methods of diagnosis and treatment include:

1. Provocation and neutralization - food extract is injected in arm or placed under tongue, and symptoms such as drowsiness or fatigue are looked for. A weaker *neutralizing* dose is then used to treat the disorder (either before or after an episode with the offending food). However, double-blind studies show that provocation and neutralization methods are invalid.
2. Cytotoxic testing (Bryan's test) - leukocytes are mixed with suspected allergens *in vitro* and examined under microscope for changes.
3. Urine autoinjection - uses preparation from patient's own urine. Potentially dangerous complications.
4. Sublingual testing - foods placed under tongue.
5. Applied kinesiology - see below, p. 15.
6. Nambudripad's Allergy Elimination Technique (NAET). According to Stephen Barrett's critique (Quackwatch), "NAET is a bizarre system of diagnosis and treatment based on the notion that allergies are caused by 'energy blockage' that can be diagnosed with muscle-testing and permanently cured with acupressure and/or acupuncture treatments."
7. IgG testing for food allergies.
8. Vegatest - see below (p. 16, "Devices")

A survey found that 42% of *asthma* and rhinosinusitis patients used alternative methods, with the most popular being herbs, caffeine-containing products, homeopathy, and acupuncture (Blanc et al. (2001) *Chest* 120, 1461-1467). Markham and Wilkinson (*J. Asthma* 41, 131-139 (2004)) reviewed 15 studies on CAM for asthma, and concluded that they "show a tendency to little or no significant differences between placebo or sham therapy."

Clinical ecology ("environmental medicine") - treatment of alleged "environmental illness" or "multiple chemical sensitivity." Hypersensitivity to common foods and chemicals said to cause "depression, irritability, mood swings, inability to concentrate or think clearly, poor memory, fatigue, drowsiness, diarrhea, constipation, sneezing, runny or stuffy nose, wheezing, itching eyes and nose, skin rashes, headache, muscle and joint pain, urinary frequency, pounding heart, muscle incoordination, swelling of various parts of the body, and even schizophrenia" (Barrett, *Skeptical Briefs* 2(4), 5, 7 (1992)). Standard and nonstandard (e.g., provocation and neutralization) tests given. Treatments range from simple avoidance of implicated substances to severe life-style changes (moving to a new location, special diet with only organically grown food, specially constructed housing units). Nutritional supplements, drugs, and other measures may be prescribed. American Academy of Allergy and Immunology feels that evidence in support of the tenets of clinical ecology is lacking. Many

patients may actually suffer from psychosomatic diseases. However, a 1994 meta-analysis (Davidoff and Fogarty, *Arch. Environ. Health* 49, 316-325) found major flaws in studies concluding a psychological basis. Other patients may have respiratory infections, etc., which cause similar symptoms. One paper suggested a genetic link to panic disorder (Binkley et al. (2001) *J. Allergy Clin. Immunol.* 107, 887-890)).

ARTHRITIS TREATMENTS

About 40 million Americans suffer from arthritis, many of them having frequent pain. Thus, this is another popular area for alternative remedies. Estimated \$1 to \$3 billion per year.

A study of rheumatology patients (Rao et al., *Arthritis Care & Res.* 49, 619-625 (2003)) found that the most popular CAM therapies were dietary supplements, herbs, special diets, chiropractic, electrical stimulators, and vitamins and minerals. Other remedies that have been popular include copper bracelets, magnets, golden raisins soaked in gin, bee venom (also promoted for multiple sclerosis), acupuncture, massage, biofeedback, and lubricants.

An NCCAM report on CAM for rheumatoid arthritis (2005) noted that "None of the CAM therapies discussed in this report have been proven to be of benefit for RA."

Glucosamine and chondroitin sulfate; and *methylsulfonylmethane (MSM)* are discussed in the handout on dietary supplements. Other dietary supplements and herbs taken for arthritis include vitamin E, fish oil, gamma linolenic acid, ginger, turmeric, Thunder God root (a Chinese herbal product), devil's claw, and boswellia.

DMSO (dimethylsulfoxide) - has local analgesic properties, but conflicting results on overall effectiveness. Potential toxicity. (Also used as cancer treatment)

Black Pearl (Chinese Black Balls, chufong tuokuwan) - contains several powerful (and dangerous) drugs. Illegal in US, but sold surreptitiously.

Some evidence that *dietary administration of proteins* may be effective in treating rheumatoid arthritis and other autoimmune diseases. Antibiotic therapy has also been supported by some studies. A study indicated reduction of symptoms with a Mediterranean diet. Fish oil, with omega-3 fatty acids, may be beneficial.

Periods of remission are a natural feature of the disease; if one of these corresponds to the time of use of an alternative therapy, it might be given credit.

ALZHEIMER'S TREATMENTS

As another area of growing concern and no effective treatment, Alzheimer's disease is a popular area for "alternative" treatment. According to *NCAHF Newsletter*, summarizing Coleman et al. (1995) *J. Am. Geriatr. Soc.* 43, 747-750: "Interviews with caregivers of 101 Alzheimer's patients found that 55% had used at least one 'unconventional' remedy; 20% had tried 3 or more. Among those who used such remedies, the leading choices were: vitamins 84%, health foods 27%, herbal medicines 11%, smart pills 9%, and home remedies 7%." DHEA and hyperoxygenation therapy (see below, p. 13) are also marketed for Alzheimer's. **Ginkgo biloba** is discussed in handout on herbs.

MERCURY AMALGAM

100 Million Americans have "silver" dental fillings, which are actually made of an amalgam of silver, copper, tin, and mercury. The mercury is allegedly released in dangerous amounts. Therefore some dentists recommend replacing all such fillings with newer plastic composites (which are more expensive and less durable). Mercury toxicity claimed to be responsible for multiple sclerosis, immune deficiency, epilepsy, leukemia, arthritis, and other conditions. In my assessment, whether mercury in amalgams is dangerous is a genuine controversy within the scientific community. However, some dangerous and pseudoscientific practices are associated with anti-amalgamist dentists.

In 2001, Maine passed a law requiring dentists to provide information on mercury toxicity. More recently, class-action suits have been filed in Maryland and California on behalf of patients allegedly harmed by amalgam fillings, and charging the American Dental Association with unfair trade practices, fraud, and conspiracy.

The case for toxicity:

1. Mercury is a highly toxic element that can damage the nervous system.
2. Studies showing mercury vapor can be released during chewing.
3. Human and animal studies of dangers of exposure to mercury vapor (reproductive problems)
4. Despite rejections of the toxicity claims by some experts (see below), some toxicologists and physiologists feel that the amalgams are dangerous, and both sides agree that more study is needed.
5. A 1995 review (Lorscheider et al. *FASEB J.* 9, 504-8) concluded that "Recent research does not support the notion of amalgam safety."
6. Reportedly causes 2/3 of human body load of mercury.

The case for safety of amalgam:

1. Mercury in fillings is combined with copper, tin, and silver in an inert state.
2. Amounts released during chewing are extremely small, may not be harmful.
3. NIH panel - concluded not toxic (August, 1991). PHS report (January 1993) - no evidence that it is a problem, though more study needed. FDA Consumer Update (Feb. 2002): "...no valid scientific evidence has ever shown that amalgams cause harm to patients with dental restorations." Life Sciences Research Office report (requested by NIH and other agencies) (2004): "...there is little evidence to support a causal relationship between mercury fillings and human health" (though it also stated that "many research gaps existed").
4. American Dental Association - feels that amalgams are safe
5. Study showing people with mercury-containing fillings had normal blood levels of mercury (though rapid storage in tissues may make blood levels a poor indicator).
6. Two studies from the University of Kentucky found no effect on brain function or Alzheimer's.
7. Replacing fillings might produce more exposure than leaving them in. Lorscheider (see above) did not recommend removing existing fillings.
8. Review by Clarkson et al. (*New Engl. J. Med.* 349, 1731-7 (2003)): "Patients who have questions about the potential relation between mercury and degenerative diseases can be assured that the available evidence shows no connection...There is no clear evidence supporting the removal of amalgam."

A study found that patients convinced that they were adversely affected by their amalgam fillings had no higher mercury levels than controls (Bailer et al. (2001) *Psychological Med.* 31, 255-263). The authors concluded, "The findings suggest that self-diagnosed 'amalgam illness' is a label for a general tendency toward somatization."

Two major NIH-funded studies, to end in 2006, are examining effects of amalgam fillings in children. To date, oversight boards have not noticed harmful effects.

CANDIDIASIS HYPERSENSITIVITY (Yeast Syndrome)

Candida albicans is often found in the digestive tract and vagina; normally harmless, but may cause occasional or chronic vaginal infections (which can be treated with antifungal drugs). However, it is alleged that many Americans (30%) suffer from various diseases as a result of sensitivity to the normal low levels of the organism. Consequences are said to include fatigue, depression, headaches, infections, weight gain, indigestion, AIDS, arthritis, multiple sclerosis. Often diagnosed with a questionnaire (won't show up on lab tests). Treated with strict diets (no foods made from or containing yeast, as well as many other prohibitions), vitamins, herbs, antifungal drugs, provocation/neutralization and possibly other therapies such as chiropractic or acupuncture. Promoted by C. Orian Truss and by William Crook (author of *The Yeast Connection*, which sold 800,000 copies).

Executive Committee of American Academy of Allergy and Immunology (1986): "The concept is speculative and unproven." Pointed out possible development of resistant strains as a result of inappropriate use of oral antifungal drugs.

OXYGENATING THERAPIES

Various methods attempt to provide oxygen or oxygenating compounds to the body. Supposedly aids in metabolism (giving more "energy"), fights cancer and AIDS (see above), helps weight loss, and assists in numerous other conditions. Promoters make false claim that Earth's atmospheric oxygen has declined, or that pollution prevents people from getting enough oxygen. In fact, hemoglobin is nearly completely saturated by breathing normal air. Several means of delivery:

Oxygen bar - a recent fad in which patrons breathe pure oxygen. (Dispensing oxygen without a prescription violates FDA regulations.) In some cases aromatherapy oils are used to produce "flavored oxygen." This presents a risk of lung inflammation.

Hyperbaric oxygen - patient breathes pure oxygen at higher than atmospheric pressure. Considered effective for various problems. However, use for others (e.g., strokes, multiple sclerosis, cardiovascular disease, Alzheimer's disease) is unsupported. (Since most stroke patients will improve to some extent, hyperbaric oxygen may be given undeserved credit.) A Canadian study found ineffective in treating cerebral palsy.

Ozone - administered by treatment of blood and reinjection; topically as gas or solution; rectally as gas or solution; etc. Treatments are more readily available in Europe than in U.S.

Hydrogen peroxide - can be administered topically, orally, or intravenously; all present dangers if levels too high. The president of the International Oxidative Medicine Association "estimates as many as 200 physicians nationwide administer more than 100,000 hydrogen peroxide infusions annually" (A. Breed, Associated Press, 2005).

Other - undefined oxygen-delivering molecules or solutions (e.g., "'Vitamin O' contains stabilized oxygen molecules in a liquid solution..."). The FTC has taken action against some of these products.

MAGNET THERAPY

Unlike pulsating electromagnetic fields, which may have some medical use, magnets with *static* fields are marketed for pain relief. A variety of shapes and configurations are available (e.g., to strap on affected parts of the body, or as mattress pads).

A review of the literature by NCCAM (<http://nccam.nih.gov/health/magnet/magnet.htm>) concluded, "Scientific research so far does not firmly support a conclusion that magnets of any type can relieve pain...Clinical trials in

this area have produced conflicting results...Many concerns exist regarding the quality and rigor of the studies conducted to date, leading to a call for additional, higher quality, and larger studies.” In contrast, Eccles (*J. Altern. Complement. Med.* 11, 495-509 (2005)) concluded that “The weight of evidence from published, well-conducted controlled trials suggests that static magnetic fields are able to induce analgesia.”

In newer studies not included in these reviews, Harlow et al. (*BMJ* 329, 1450-1454 (2004)) found relief of hip and knee pain from magnetic wrist bracelets, but could not rule out placebo effects, while Winemiller (*Mayo Clin. Proc.* 80, 1138-1145) found no benefits for magnetic insoles.

There are strong reasons for skepticism concerning claimed benefits. The magnets are too weak to have any conceivable effects within tissues, and proposed mechanisms (e.g., increasing blood circulation) are implausible. Nerves and blood vessels are almost randomly oriented, so any directional effects would cancel out. It should be possible to demonstrate relevant effects in laboratory or animal models, but this has not been done. Several animal studies and two human studies show no effects on circulation. Much larger fields used in MRI seem to have no effects on tissues.

A general problem with clinical studies is difficulty in blinding, since it is often possible to tell if a real magnet is being used.

There is a possible danger of magnets interfering with pacemakers or implantable defibrillators unless these are sufficiently shielded.

MISCELLANEOUS TOPICS

Anti-aging remedies - include antioxidant supplements and DHEA (see handout on dietary supplements), HGH (see below) and others. In 2002, 51 leading researchers in the field of aging denounced such products, noting that none had been shown effective. It was also noted that “two so-called scientific ‘journals’ (*Journal of Longevity* and *The International Journal of Anti-Aging Medicine*) that appear on the surface to be traditional refereed publications are in fact little more than advertisements for a pseudoscientific anti-aging industry” (de Grey et al. (2002) *Science* 296, 656) [they note that *Journal of Anti-Aging Medicine* is a legitimate scientific journal].

Applied kinesiology - method of diagnosis involving testing of muscle weakness. May be used to assess condition of internal organs supposedly related to the muscles. Two different rationales: 1. alleged “neurolymphatic reflexes,” with changes in internal organs affecting (via lymphatic drainage) the peripheral nervous system and muscles. 2. connections according to meridian theory in traditional Chinese medicine. Using before and after comparisons, may be used to test for allergies or nutritional deficiencies when subject holds a food item, places under tongue, etc. Several studies have demonstrated that it is not a valid diagnostic procedure. Likely involves stage trickery (perhaps unintentional) to make muscle strength appear to respond to the treatment.

Aqua Detox - subjects place feet in a basin of salt water through which electrical current is passed. Allegedly removes “toxins” and balances “energy.” Water discoloration is taken as evidence of the toxins. However, it actually comes from rusting of the electrodes.

Bioidentical hormones - estrogen and progesterone (made synthetically, but identical to human forms) are given in individualized doses by compounding pharmacists. Taken by women who are concerned about risks, or lack of optimum benefits, of standard hormone replacement therapy. However, there is no evidence that these are less risky. Moreover, saliva tests used to prescribe doses maybe unreliable, and there are concerns over quality control.

Biological terrain assessment - “a computerized analysis of blood, urine and saliva specimens used to recommend nutritional programs, vitamin and mineral supplements, homeopathic products, and/or herbs”

(Barrett, Quackwatch article). The pH, resistivity, and oxidation-reduction potential of samples are measured.

Cold laser therapy - also known as *low-level light therapy*. Lasers (also referred to as “soft” lasers) with wavelengths of 600-2000 nm and power too low to produce heat are used to treat various types of pain and for wound healing. Some evidence in support, though many experts are skeptical. FDA has approved for treatment of carpal tunnel syndrome and back and shoulder pain.

Colloidal silver - marketed for both topical and sublingual use. Claimed to be an antibiotic and antiviral agent, as well as a treatment for AIDS, cancer, and numerous other diseases. Danger of argyria (deposits of silver salts in skin, eyes, and other sites), seizures, and kidney damage. Case of myoclonic status epilepticus and coma reported, 2004. In 1999 the FDA declared that OTC silver products are not recognized as safe and effective, with additional actions by FDA and FTC in subsequent years to stop illegal marketing.

Colonic irrigation - based on theory of autointoxication (accumulation of toxins in the colon). May involve as much as 20 gallons of liquid, possibly pumped in by machine. Other substances (e.g., coffee) may be included to assist in removal of toxins. Used in some cancer treatments, as well as for other conditions or general maintenance of health. See dangers, p. 2. In 2003, Texas filed several lawsuits against promoters.

Devices - over the years a variety of bizarre electrical and mechanical devices have been marketed for diagnosis and treatment of disease. The *Rife Frequency Generator* supposedly treats cancer by detecting “auras” of bacteria and destroying the bacteria with radio waves of the proper frequency. (See also Hulda Clark’s “Zapper” and “Synchrometer,” p. 5) Various *electrodiagnostic devices* (e.g., electroacupuncture, electrodermal screening, Vegatest) use electric probes placed on the skin to diagnose “energy imbalances,” various diseases, allergies, nutritional deficiencies, etc. Double-blind tests of these devices found them ineffective in diagnosing allergies. The FTC took action against the Q-Ray Ionized Bracelet in 2003, and a 2002 controlled study found that such bracelets provided no benefits for muscle or joint pain.

Ear candling - candle is placed in ear and lit; allegedly creates suction that removes wax and other impurities from ear, sinuses, and even the brain. Drippings are used as evidence of the removed material. Popular at health expos. Can cause ear injuries. FDA has taken action against distributors.

Full body scans - CT scans are offered to detect diseases in early stages. However, there is not evidence that the benefits outweigh the risks of surgery or further testing to deal with detected abnormalities that may be benign. In addition there is risk from the radiation. Several professional groups have recommended against such screening. According to the FDA, this is an unapproved use for the device (it is only approved when there are disease symptoms or other reasons for testing). Many full body scanning clinics went out of business in 2005.

Genetic testing - some companies are now performing genetic tests in order to recommend supplements, etc. There is legitimate research interest in identifying genetic markers that might indicate susceptibility to disease, guide appropriate doses of drugs, etc. However, many of the current tests being marketed are inappropriate, since there is not reliable evidence connecting the genes identified to benefits of the products being sold.

Hair analysis - Used to diagnose deficiencies or excesses of minerals and deficiencies of vitamins. May be of some use in screening for heavy metal exposure, but otherwise unsupported. Problems include lack of correlation of hair levels with tissue levels, unknown normal levels, inaccurate and inconsistent analyses by various labs, and inappropriate interpretations and recommendations. Dyes, shampoos, and other environmental factors can alter mineral levels in hair. An investigation (*JAMA* 285, 67-72 (2001)) documented numerous problems with commercial hair analysis.

HGH (human growth hormone) - is being injected as an anti-aging remedy (estimated usage, 25,000-100,000, with \$2 billion in annual sales). However, there are numerous risks associated with elevated IGF-1 levels (which increase in response to GH). Prescription of GH for adults is illegal except for individuals who meet

diagnostic criteria for GH deficiency. A 2002 paper reported increased lean body mass and decreased body fat, but there were also significant adverse effects. Growth hormone supplements and sprays are also being marketed, but significant absorption is unlikely. Some supplements contain other chemicals alleged to stimulate the release of GH, but effects are likely to be insignificant. FTC took action against marketers of sprays and other products in 2005.

Hypoglycemia - True hypoglycemia is relatively rare; primarily due to certain enzyme deficiencies and endocrine disorders. *Reactive hypoglycemia* (oversecretion of insulin following meal) is also relatively uncommon. However, some practitioners claim that hypoglycemia affects tens of millions of Americans, and causes depression, fatigue, schizophrenia, criminal behavior, and other disorders. Special diets, supplements, and herbs are prescribed.

Ion generators - based on idea that negative ions in the air can improve mood, overcome depression, etc. Thought to act by increasing serotonin levels. Being tested for treatment of seasonal affective disorders. Also advocated for counteracting excess positive ions generated by video displays. Supported by a number of studies (e.g., Terman & Terman (1993) *J. Alternative Complementary Med.* 1, 87-92; Terman et al. (1998) *Arch. Gen. Psychiatry* 55, 875-882 (here bright light was also used)); I am unaware of a recent scientific critique.

Live cell analysis - invalid diagnostic technique in which blood is viewed with dark field microscope connected to video display. Appearance of cells and other particles used to diagnose nutritional deficiencies, excess fat, presence of yeast or other "parasites," and other conditions.

Multiple sclerosis - some patients are using *bee venom* (a form of "apitherapy"). 2005 study found no benefit. A product named Procarin (or Prokarin) is being marketed, but there is no good evidence that it is effective.

Progesterone creams, yam creams - creams marketed for premenstrual and menopausal symptoms. Such products are becoming more popular with recent research showing possible dangers of hormone replacement therapy. Some actually contain progesterone (referred to as "natural" because it is the same compound as the natural hormone, even though it is synthetic). To the extent that this is absorbed, it has the same potential for adverse side effects as oral hormone therapy. Some products are based on Mexican wild yams. While a compound in these can be converted to progesterone in the laboratory, this conversion does not occur in humans.

Prolotherapy - injection of fatty acids and other compounds into injured tissues with the aim of stimulating healing of cartilage and ligaments. Does not appear to be supported by solid evidence of effectiveness.

Sugar - claimed to cause hyperactivity in children. Disputed in 1994 article in *N. Engl. J. Med.*, as well as 1995 meta-analysis in *JAMA*.

Thermography (infrared imaging) - heat produced at the body's surface is used to screen for health problems. Proposed as an alternative to mammography. Controversial whether this is useful.