A SCIENTIFIC LOOK AT ALTERNATIVE MEDICINE

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January 17, 2006

Herbs; Mind-Body Medicine; Approaches Related to Mental Health

HERBS (BOTANICALS)

Overview

Rapidly growing (18% per year) business in late 1990's, but sales leveled off in 2000. Estimated annual sales of $4 billion. Estimated fraction of Americans using herbs rose from 16% to 40% in 1996-8. In a survey covering 1998-9, 14% used herbs in the preceding week.

Sold by major pharmaceutical companies. A recent trend is the selling of snacks and drinks containing herbal ingredients (e.g., ginkgo, St. John's wort). In 2001 the FDA began warning companies that such herbal additives may be illegal. Use of herbs by children has increased (to an estimated 28-40%).

About 250 herbs are on the FDA's "Generally Recognized as Safe" list. However, some of these are for use as flavors and spices, and medical uses may not be safe. Marketed for a wide variety of medical conditions. Most of these are self-limiting or mild conditions, but some remedies are promoted for cancer and other serious illnesses.

Regulated as for dietary supplements (1994 DSHEA). Thus, unlike over-the-counter drugs, they do not need to have demonstrated safety and effectiveness. A survey of Internet retail sites for herbs found that 55% made claims to treat or prevent disease (which is illegal under DSHEA).

There has been an increase in independent testing to verify ingredients.

In 1999-2000 NIH began funding four university centers to study botanicals. In 2002 the National Institute of Standards and Technology was asked by NIH to develop standard reference materials for use in quality control during manufacture of botanicals.

The German government (*Commission E*) conducted a systematic review of herbs from 1978 to 1994. Its monographs have been translated and are available in the U.S. However, the scientific status of these reports is questionable; they have relied heavily on uncontrolled studies, historical evidence, and anecdotal reports. With respect to safety, they are more trustworthy. Overall, 380 herbs were considered, with 254 approved as safe and reasonably effective.

Some pharmacies have programs to ask customers concerning herb use, and to link to databases with potential drug interactions.

Vickers and Zollman (*BMJ 319*, 1050-1053 (1999)) pointed out three important differences between herbal medicine and conventional pharmacy:

- Use of whole plants or unpurified extracts - ingredients are alleged to work synergistically and with

lower toxicity ("buffering")
- Herb combining - "This contrasts with conventional practice, where polypharmacy is generally avoided whenever possible."
- Unconventional diagnostic principles are used by many herbalists.

Pro

Herbs have been sources of useful drugs. Many remain to be scientifically examined; likely that some traditional herbal remedies may contain pharmacologically useful compounds.

Value of several herbs supported by controlled studies (see table below)

Often less expensive than prescription drugs.

Con: toxicity

Tyler, "Hazards of Herbal Medicine," specific hazards
Carcinogens
Tumor promoters
Photosensitizers (e.g., psoralens)
Allergens (e.g., chamomile, arnica)
Hormone-like compounds (e.g., glycyrrizin in licorice; ginseng)
Teratogens
Respiratory inhibitors (glycosidic compounds, such as Laetrile, that yield cyanide)
Cathartics (e.g., aloe)
Abortifacients and irritants
Other toxic effects

Some ***dangerous herbs*** (from *Consumer Reports*, May 2004):
- definitely hazardous: aristolochic acid
- very likely hazardous: comfrey, chaparral, germander, kava
- likely hazardous: bitter orange, lobelia, pennyroyal oil, scullcap, yohimbe

Chaparral and comfrey have been banned in Canada; germander in France and Germany. FDA issued a warning against comfrey in 2001, while FTC took action against marketing of comfrey products. Toxicity of chaparral has been disputed; FDA issued warning in 1992. California requires warnings on herbal laxative products. *Sassafras oil* is banned in the U.S. as a food additive, but the herb is available. *Fenugreek* and comfrey are popular among nursing mothers but are potentially hazardous to their infants. Fenugreek may have interactions with diabetes and clotting drugs. In 2004, the FTC warned a seller of a dietary supplement containing yohimbe for unsubstantiated claims as well as for its risks.

Ephreda (ma huang) has been marketed as an appetite suppressant and/or metabolic stimulant. Sometimes promoted as an alternative to illegal drugs such as "ecstasy." More recently has been promoted for use in children with attention deficit hyperactivity disorder. Active component is ephedrine, which can raise blood pressure, cause strokes and heart problems, and have other effects. *Blamed for at least 54 deaths and hundreds of illnesses since 1993.* After growing concern over its safety, the FDA banned sale of dietary supplements containing ephedra in 2004 (the ban did not apply to traditional Asian medicines containing ephedra). In 2005, a federal judge ruled that the FDA cannot ban products containing 10 mg or less of ephedra; the status of more potent products (which allegedly would be needed for weight loss benefits) is unclear. Meanwhile, other herbs (such as Citrus aurantium (bitter orange), which contains synephrine) are now being substituted, and they may present similar hazards.

Some other examples of hazards:

- Liver damage due to chaparral ingestion (1995)
- Cases of adulteration of Chinese and Ayurvedic remedies with conventional drugs. These may also contain heavy metals (see handout on Eastern approaches).
- Contamination of a shipment of plantain (subsequently used in various dietary supplements) with digitalis
- Four deaths due to injections of aloe vera (1997)
- Two infants suffered multiple organ failure from pennyroyal in tea.
- An herbal sedative, "Sleeping Buddha," was recalled by the FDA after being found to contain a strong sedative drug, estazolam.
- Kidney failure in about 100 Belgian women 1990-1 (as well as more recent British cases) from aristolochic acid in Chinese herbal remedies. Even though the FDA issued a warning in 2001, a 2003 survey found many aristolochic acid-containing products available on the Internet.
- A researcher found heavy bacterial contamination in common herbal products, which could present a risk for people with weak immune systems (2001).
- Colchicine found in placental blood of women taking ginkgo (2001).
- More than 25 cases of liver damage in foreign users of kava (2001). FDA issued advisory in 2002.Herbal allergy product found to contain excessive levels of lead (2002).
- Autoimmune hepatitis from black cohosh (2003).
- FDA warns against teas containing star anise (2003).
- Herbal products for erectile dysfunction found to be contaminated with sildenafil (Viagra) and tadalafil (Cialis) (2004).
- FDA warned against “Green Hornet,” marketed as an herbal version of “Ecstasy,” for containing diphenhydramine and dextromethorphan (2004).
- Neonatal seizures and stroke after mother took blue cohosh tea to induce labor (2004).
- Case of ventricular tachycardia after ingestion of herbal tea containing aconite (2005).
- Muscle damage from black cohosh (2006).

Ang-Lee et al. (*JAMA 286*, 208-276 (2001)) reviewed the hazards of presurgical use of common herbs. “Direct effects include bleeding from garlic, ginkgo, and ginseng; cardiovascular instability from ephedra; and hypoglycemia from ginseng. Pharmacodynamic herb-drug interactions include potentiation of the sedative effect of anesthetics by kava and valerian. Pharmacokinetic herb-drug interactions include increased metabolism of many drugs used in the perioperative period by St. John’s wort.”

A 2002 study found that two herbs used for menopausal symptoms, dong quai and ginseng, stimulated growth of cultured breast cancer cells.

A survey of web sites dealing with ginseng, gingko, and St. John’s wort found that 25% “contained statements that could lead to direct physical harm if acted upon” (Walji et al. (2004) *J. Med. Internet Res. 6(2)*:e2).

<u>Con: other</u>

Pharmacologically active chemicals from herbs can be isolated in pure form; these then can be subject to controlled studies of their safety and effectiveness. If a useful drug results, this can then be prepared with high standards of purity and administered in a known dosage, free of possible side effects of other compounds in the herbal preparation.

Herbs may be selected and administered by laypersons, or on the advice of health food store personnel or others without medical expertise.

Names on products may not indicate which species they come from (particularly for imported herbs)

Plants differ widely in content of effective ingredients, making dosages inconsistent. A 1998 study of St. John's wort products found more than 10-fold differences in the concentrations of the presumed active ingredients (see also below concerning standardization). Similar studies dealing with other herbs have also found wide variation in contents among commercial preparations.

Some herbal remedies may be spiked with real drugs, or have other herbal products substituted for expensive ones (e.g., ginseng) (one study found that only 25% of commercial ginseng products actually contained ginseng!).

Substitution for effective treatments: “Many oncologists have seen patients with early-stage cancers who eschewed curative conventional care in favor of herbal medicines.” (Winslow and Kroll (1998) *Arch. Int. Med. 158*, 2192-2199)

Attribution of protective effects: “Patients may also continue detrimental behaviors, such as smoking tobacco or drinking large amounts of alcohol, with the rationalization that the herbal remedy they are taking will be protective.” (*ibid*)

Some herbs can interfere with certain laboratory tests based on immunoassays.

Some scientific considerations

A review of the ergogenic properties of ginseng (Bahrke and Morgan (1994) *Sports Med. 18*, 229-248) illustrates the complexities in evaluating some herbal remedies. Ginseng is advocated for enhanced energy in general as well as for numerous specific conditions. Its active ingredients are at least 13 saponins, which can have opposing effects and be present in different amounts in different preparations. This could explain why "...in animal research, hypertensive and hypotensive effects, histamine- and antihistamine-like actions, and both stimulant and depressant activity on the central nervous system (CNS) have been reported." Sengupta et al. (*Circulation 110*, 1219-1225 (2004)) identified one component of ginseng that has an angiogenic effect, and another that has an anti-angiogenic effect.

Manufacturers attempt to control for variability by making *standardized preparations*, blended to contain consistent amounts of the presumed active ingredients. However, this presumption may be inaccurate. St. John's wort has been standardized to hypericin and pseudohypericin, but some studies suggested that another component, hyperforin, is actually most important. Also, studies with feverfew suggest that its actions may not be from the commonly presumed active ingredient. A study of echinacea preparations (2003) found that less than half of standardized preparations met the standards on their labels.

Even if the active ingredient is standardized, other ingredients may affect its absorption or metabolism.

Nonscientific aspects

Reliance on undocumented claims, sometimes dating back centuries.

Claim that herbs are safe and effective because they have been used for thousands of years.

Reliance on anecdotal evidence

Reference to mystical concepts of "energy"

Claims of conspiracy by medical establishment and pharmaceutical industry to suppress use of herbs.

Unsupported claim that the whole herb is more effective and less toxic than its isolated components. Related to idea that the herb is present for human benefit (scientific view: plant makes compounds for its own benefit; occasionally one is of pharmacologic use in humans)

Concerning the idea that different constituents of an herb work together, V. Tyler wrote: “Synergism occasionally occurs, but for every case where a desirable action is enhanced, there are several where undesirable actions are produced. For example, cinchona bark contains some 25 closely related alkaloids, but the only one recognized as useful in the treatment of malaria is quinine. A person who took powdered cinchona bark would also ingest the alkaloid quinidine, a cardiac depressant, and cinchotannic acid, which would induce constipation.”

Claim that a natural chemical is superior to its synthetic counterpart

"Doctrine of Signatures" - ancient magical idea that the shape or appearance of an herb guides its application (e.g., eyebright, having a spotted flower and resembling an eye, for treatment of eye diseases)

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Some Popular Herbs [note: garlic is covered in dietary supplements handout]

herb	*uses*	*presumed active agent(s)*	*presumed mechanism of action*	*possible toxic effects**	*notes*
black cohosh (*Actaea racemosa* = *Cimicifuga racemosa*)	premenstrual distress, postmenopausal symptoms, breast enhancement	triterpene glycosides (including actein and cimicifugo-side)	Central dopaminergic activity. Affects hypothalamic-pituitary axis; estrogenic effects are controversial.	GI disturbances, hypotension, nausea, headaches, drowsiness. Possible interference with cancer drugs such as tamoxifen. May decrease iron absorption. Possibly unsafe for women who have had breast cancer. Concern over possible liver damage.	Review (2002) concluded that efficacy "has not been convincingly demonstrated" [1]. A 2003 review [2] was favorable, but acknowledged that "clinical trials are of insufficient quality to support definitive statements." More recent negative [3] and positive [4] studies have been reported. A recent large controlled trial reportedly showed no benefits.
echinacea (coneflower) (*Echinacea purpurea*, *E. angustifolia*, *E. pallida*)	prevent and treat cold and flu symptoms; general immune enhancement	echinaco-sides, poly-saccharides, isobutylam-ides, cichoric acid	proliferation of macrophages and other immune cells, enhanced cytokine production and phagocytic activity	Possible immunosuppression and hepatotoxicity with long-term use; little toxicity if taken orally, but several risks if injected. Severe allergic reactions have been reported. Gastrointestinal side effects were common in clinical trials. Rashes observed in trial with children. May interfere with protease inhibitors for HIV.	Six controlled trials (1998-2005) found no benefit [5-10], while one gave positive results [11].
feverfew (*Tanacetum parthenium*)	relieve migraine; treat fevers, menstrual problems	parthenolide, mono-terpenes	inhibition of prostaglandin production, spasmolytic effects on cerebral vessels	mouth ulcers from fresh leaves; reduced blood clotting; rebound headaches if suddenly discontinued	1998 review on prevention of migraine found data supportive, but effectiveness "not established beyond reasonable doubt" [12]. A 2002 study on migraine [13] found results that overall were not supportive, though indications of usefulness for one subgroup.

herb	*uses*	*presumed active agent(s)*	*presumed mechanism of action*	*possible toxic effects**	*notes*
ginger (*Zinziber officinale*)	reduce nausea; reduce inflammation; hypoglycemic effects	gingerol, shogaol	increase GI motility, affecting signals to CNS; cause vagal stimulation leading to decreased blood pressure and heart rate	heartburn	Appears to work for nausea of gastrointestinal origin but not other types (e.g., motion sickness). 1999 review [14] concluded it was "promising" but data "insufficient to draw firm conclusions." Two more recent studies supported usefulness for nausea of pregnancy. Some evidence that it might be useful for arthritis.
Ginkgo biloba (maidenhair tree)	improve circulation: treat stroke, improve memory, lessen Alzheimer's symptoms; treat heart disease, impotence, blindness	flavonoids, proanthocyanidins, terpenoids (ginkgolides, bilobalide), other	promote vasodilation and improve blood flow to brain; antioxidant effects (flavonoids); platelet-activating factor antagonists (ginkgolides)	May inhibit clotting, cause GI disturbance, headache, nausea, vomiting. May interact with several drugs.	Widely used in Europe. 1997 study [15] supported use in Alzheimer's (slightly slows progression); also 1998 meta-analysis [16] supported use. 2002 and 2003 studies found no effect on memory [17-18].
ginseng (*Panax ginseng*)	enhanced energy and well-being; aphrodisiac; enhance learning; enhance immune function; sedative; demulcent; other	ginsenosides (see p. 4)	vasodilation; antioxidant; increased production of acetylcholine	Nervousness, excitation, headache, insomnia, palpitations, hypoglycemia; estrogenic effects, vaginal bleeding. Reduces effects of warfarin and some other drugs.	Reviews (1994, 2000, 2003) concluded a lack of research in support of claims [19-21]. No effect in 2001 trial for psychological well-being [22] and 2003 study of exercise performance [23]. Some studies indicated that it might reduce blood glucose. NIH panel (2005) concluded that it "may help with some menopausal symptoms" (but not hot flashes). (Note: *Siberian ginseng* (*Eleutherococcus senticosus*) is a much different plant.)
goldenseal (*Hydrastis canadenis*)	relieve cold and flu symptoms; treat gastritis	hydrastine, berberine		nausea, vomiting, diarrhea, CNS stimulation, respiratory failure, increased blood pressure, diuretic effects	effectiveness not demonstrated

herb	*uses*	*presumed active agent(s)*	*presumed mechanism of action*	*possible toxic effects**	*notes*
kava kava (*Piper methysticum*)	relaxation, reduce anxiety, treat insomnia	kava pyrones	enhanced GABA receptor activity	potential for abuse; drowsiness; muscle weakness; skin discoloration, eye disturbances; allergic reactions; may be risky if combined with alcohol; liver problems (see p. 3)	2000 meta-analysis indicated useful in treatment of anxiety [24]. 2005 study found ineffective for anxiety and insomnia [25].
St. John's wort (*Hypericum perforatum*)	treatment of depression (also promoted to fight viral infections)	Hypericin, pseudo-hypericin, hyperforin. One study indicates that hyperforin is most important, not hypericin.	inhibition of reuptake of serotonin, dopamine, norepinephrine; some preparations may contain MAO inhibitors; effects on GABA receptors	Dangerous drug interactions possible: *appears to increase metabolism of numerous commonly used drugs.* Photodermatitis, stomach upset, allergy, dizziness, dry mouth, restlessness, fatigue. Suggested that in bright sunlight could lead to cataracts. High blood pressure when taken with foods containing tyramine.	1996 meta-analysis [26]: "more effective than placebo for the treatment of mild to moderately severe depressive disorder." 2000 review [27] reached similar conclusions. 1999 and 2000 studies [28, 29] provided stronger support. 1997 study [30] supported used in severe depression, but two others (2001, 2002) did not [31, 32]. 2005 study supported use in moderate to severe depression [33]. Long-term studies lacking.
saw palmetto (*Serenoa repens*)	treatment of benign prostate hyperplasia and urinary problems	β-sitosterol and other steroid-like compounds	possibly antiandrogenic effects via inhibition of 5-α reductase and of binding of dihydrotestosterone to receptors; anti-inflammatory effects via inhibition of cyclooxygenase and lipoxygenase	stomach upset, headache, diarrhea; controversial whether it can interfere with PSA tests for prostate cancer	Placebo effects of 50% seen in some trials, which can account for anecdotal reports of success. 1998 review [34] concluded that it appeared useful, and compared favorably with the standard drug treatment. But a 1999 review [35] noted that the drug effects might be placebo effects; it concluded that the efficacy “has yet to be conclusively determined.” 2001 study was supportive [36]; 2003 was not [37].

herb	*uses*	*presumed active agent(s)*	*presumed mechanism of action*	*possible toxic effects**	*notes*
silymarin (a crude preparation from milk thistle, *Silybum marianum*)	treatment of liver and gallbladder problems, reduction of cholesterol, treatment of diabetes and cancer	silybin and other flavono-lignans	protection of liver cells (antioxidant activity); acceleration of liver cell regeneration (stimulation of ribosomal RNA polymerase)	diarrhea, nausea, allergic reactions	2005 review found a lack of evidence of effectiveness for liver problems [38].
tea (green, black) (*Camellia sinensis*)	prevention of cancer and heart disease, treatment of arthritis	flavonoids	Flavonoids as antioxidants; the catechin EGCG is thought to inhibit tumor growth and cartilage breakdown. Tea may also enhance insulin action. L-Theanine may stimulate immune system		Support is from epidemiological and lab studies. Studies indicated protection against atherosclerosis [39], improvement in endothelial function [40], increased bone density [41], and reduced mortality after heart attacks [42]. However, did not appear to protect against gastric cancer [43]. FDA has concluded that it is highly unlikely that green tea reduces the risk of breast and prostate cancer.
valerian (*Valeriana officinalis*)	promote sleep; treat depression, anxiety, convulsions, ADHD, other.	valepotriates (valtrate, isovaltrate, dihydroval-trate), others	may increase GABA levels at synapses	increased morning drow-siness, lack of coordination, fatigue; possible depression with long-term use	2000 review [44] concluded that evidence was inconclusive; NIH-ODS agrees. 2005 study found ineffective [25]. May need two weeks of use to become effective.

*In general, herbs should be avoided in *pregnancy and lactation* (an estimated 40% of pregnant women use herbs!). Some herbs affect blood glucose and should be avoided in *diabetes*. Also a general danger of interactions with other drugs. American Society of Anesthesiologists recommends discontinuing herbs 2-3 weeks prior to surgery.

Key points for physicians: herbs are drugs, with contraindications and potentially dangerous interactions with other drugs. Patients may not inform you that they are using herbs unless asked specifically.

Some other herbs

Butterbur (*Petasites hybridus*) - trials have found evidence of effectiveness for migraine prevention (Lipton et al. (2004) *Neurology 63*, 2240-2244) and allergic rhinitis (Schapowal et al. (2005) *Phytotherapy Res. 19*, 530-537).

Cat's Claw (*Uncaria tomentosa*) - Peruvian herb used for many disorders, including arthritis and cancer.

Dong quai (*Angelica sinensis*) - used for menstrual and menopausal problems. Only one randomized clinical trial for the latter, which did not support effectiveness.

Fenugreek (*Trigonella foenum-graecum*) - used to increase milk supply during lactation, as well as for various other purposes. Considered unsafe to use during pregnancy.

Hawthorn (*Crataegus oxyacantha*) - used for chronic heart failure, ischemic heart disease, other. Meta-analysis (Pittler et al. (2003) *Am. J. Med. 114*, 665-674) concluded that the results "suggest that there is a significant benefit from hawthorn extract as an adjunctive treatment for chronic heart failure."

Horse chestnut (*Aesculus hippocastanum*) - used for chronic venous insufficiency. A 1998 review (Pittler & Ernst, *Arch. Dermatol. 134*, 1356-1360) concluded that it was as effective as compression therapy.

Licorice (*Glycyrrhiza glabra*) - used for coughs, hoarseness, ulcers, other. Numerous potentially serious side effects due to mineralocorticoid action.

Peppermint oil (*Menta piperita*) - used for irritable bowel syndrome and dyspepsia. Meta-analysis (Pittler & Ernst (1998) *Am. J. Gastroenterol. 93*, 1131-1135) gave support for use in IBS.

Siberian ginseng (*Eleutherococcus senticosus*) - claims are similar to those for *Panax ginseng*.

Stinging nettle (*Urtica diocia*) - used for a variety of conditions, including as a diuretic and for benign prostate hypertrophy.

Thunder God Vine (*Tripterygium wilfodii* Hook F) - used for rheumatoid arthritis and other immune and inflammatory diseases.

Turmeric (*Curcuma longa*) - part of traditional medicine of India. Used for many conditions, including inflammation and indigestion.

MIND-BODY MEDICINE

Theory

Emotional and mental states can influence body's ability to fight disease; usually thought to involve the *immune system.*

Immune surveillance theory of cancer - cancer cells are periodically being generated but are usually destroyed by the immune system. However, Garssen and Goodkin (*Psychiatry Res. 85*, 57-61 (1999)) concluded that "The role of immunosurveillance seems modest overall." In immunosuppressed individuals, the incidence of some, but not the most common, types of cancer are increased. The most important component of the immune surveillance system that may be decreased in response to stress is thought to be NK cell activity.

Stress may cause or contribute to various diseases:

1. The body naturally turns down the immune system in a stressful situation in order to conserve resources. If done chronically, this could reduce the ability to fight disease.
2. Other physiological responses that are useful in stress (increased pulse and blood pressure, increased blood glucose, decreased GI tract activity) can be harmful if continued chronically.

Thus, relief of stress may relieve an underlying cause or contributing factor for various conditions.

"Complex stimuli such as social and physical stressors influence susceptibility to disease by activating a variety of CNS pathways simultaneously." (E. Sternberg (1997) *Nature Medicine 3*, 264-7) Such overstimulation can cause the release of *glucocorticoids* (via the *hypothalamic-pituitary-adrenal axis*) to down-regulate the immune system and lead to increased disease susceptibility.

In a review, McEwen (*New Engl. J. Med. 338*, 171-179 (1998)) discussed "the long-term effect of the physiologic response to stress, which I refer to as allostatic load." "One speculation is that allostatic load over a lifetime may cause the allostatic systems to wear out or become exhausted. A vulnerable link in the regulation of the HPA axis and cognition is the hippocampal region. According to the 'glucocorticoid-cascade hypothesis,' wear and tear on this region of the brain leads to dysregulation of the HPA axis and cognitive impairment." "...inadequate responses by some allostatic systems trigger compensatory increases in others. When one system does not respond adequately to a stressful stimulus, the activity of other systems increases, because the underactive system is not providing the usual counterregulation. For example, if cortisol secretion does not increase in response to stress, secretion of inflammatory cytokines (which are counterregulated by cortisol) increases."

A 2003 study found that stress increased levels of interleukin-6, which is in turn associated with heart disease, arthritis, osteoporosis, diabetes, and some forms of cancer.

<u>Techniques</u>

- *Meditation* or *visualization* of soothing scenes to reduce stress, induce relaxation. A study found activation of the "left prefrontal cortex - the locus of positive, optimistic emotions" during meditation (M. Robbins (2004) *Discover*, Jan., 45). In *Transcendental Meditation*, "practitioners repeat a silent word or phrase (a mantra) with the goal of quieting (and ultimately transcending) the ordinary stream of internal mental dialogue" (Astin et al. (2003) *J. Am. Board Fam. Pract. 16*, 131-147).
- Silent repetition of a neutral word or phrase (as in transcendental meditation), or of a meaningful word or phrase (possibly associated with one's religious belief). Slow, rhythmic breathing. Herbert Benson - *relaxation response.*
- Repetition of positive affirmations
- *Guided imagery* (may be guided by therapist or tape). Said to help deal with chronic pain, tumors, infections. Patients may visualize harmful cells being killed by antibodies or white cells.
- *Relaxation*. In progressive muscle relaxation, muscles are sequentially tensed and relaxed.
- *Mindfulness* - "involves focusing on whatever a person happens to be experiencing at the time - and learning to experience anything calmly, whether it is pleasant or not" (*Consumer Reports*, Feb. 1993). Promoted by Jon Kabat-Zinn, Univ. Massachusetts Medical Center Stress Reduction Clinic.
- *Prayer, spirituality, religious observation*
- *Support groups*
- *Psychotherapy*
- *Music therapy* - certain types of music appear capable of lowering heart rate and blood pressure, reducing need for anesthesia, etc. Can also be used to assist in physical or neurological therapy.
- *Toning* - chanting of vowel sounds
- *Laughter therapy* - humor may enhance levels and activities of immune cells and endorphins, and decrease stress hormones. (It is speculated that laughter is linked to the emotions of social connections.)
- *Yoga* (discussed in handout on Eastern approaches)
- Pet therapy

Some promoters (through books, lectures, workshops, etc.)

- Deepak Chopra - endocrinologist, promoter of ayurvedic medicine. Author, *Creating Health; Perfect Health; Quantum Healing; Ageless Body, Timeless Mind*.
- Bernie Siegel - surgeon; author, *Love, Medicine and Miracles* and *Peace, Love and Healing.*
- Jon Kabat-Zinn - stress reduction (see above). Author of *Full Catastrophe Living*.
- Herbert Benson - cardiologist, Harvard Medical School. Founded Mind/Body Medical Institute. Relaxation response (see above). Author of *The Relaxation Response*; co-author of *Timeless Healing.*
- Larry Dossey - promoter of effects of prayer and spirituality. Author, *Healing Words*.
- Candace Pert - researcher in psychoneuroimmunology. Author, *Molecules of Emotion*.
- James Gordon - Director, Center for Mind-Body Medicine.
- Templeton Foundation - funds work related to religion and spirituality.

Arguments in favor

Evidence for connections between brain and *immune system* has produced an area of research called ***psychoneuroimmunology***.

Communication between the brain and the immune system:
- The brain can release peptide hormones (neuropeptides) that can affect the immune system.
- There are also nerves connecting the brain directly to some cells of the immune system.
- The immune system can release hormones (e.g., the cytokine *interleukin-1*) that affect the brain and other organs.

Animal studies showed that disruptions in these communications (by mutation, pharmacological intervention, or surgery) increases the susceptibility to inflammatory disease, as the brain does not properly down-regulate the immune system.

Studies on animals and people indicate that stress can affect the immune system (however, effects are complex, and do not always suppress the immune system). Stressful lifestyle associated with increased infection and poorer health in general (disputed by some studies). Hostility associated with more heart attacks.

However, it should be noted that "large, well-controlled studies do not support the widespread belief that emotional factors...lead to cancer or accelerate its spread" (Holland (1996) *Scientific American*, Sept., 158-161). Garssen and Goodkin (*op cit.*) concluded that “The role of psychological factors is more convincingly demonstrated for cancer progression...than for cancer initiation.”

Studies on recovery from, or susceptibility to, various diseases and conditions:
- M. Friedman - better recovery with reduced hostility
- D. Spiegel - study of breast cancer patients - support group, self-hypnosis for pain control doubled survival time (but see below)
- Study of hypertension - lower blood pressure with relaxation techniques
- Study of minor surgery - guided imagery prior to surgery produced faster recovery, less pain
- Correlation of increased survival time with more optimistic attitude in studies of leukemia and heart attacks; with social support in study of leukemia
- Evidence that muscle relaxation can reduce stress-related pain, including headache and back pain
- R. Surwit - improved glucose control in Type II diabetes with muscle relaxation
- F. Fawzi - increased survival with support groups in study of melanoma
- J. Blumenthal (1997) - reduced heart attack risk in heart patients under stress management program.
- S. Cohen (1997) - people involved in social activities less likely to catch colds.
- J. Barefoot (1997) - depression correlated with increased risk of stroke.

- Sephton et al. (Spiegel group) - abnormal cortisol rhythm associated with increased breast cancer mortality.
- Depression linked to heart disease (2004).
- Stress linked to obesity (2004)
- Stress linked to DNA damage in immune cells (2004)

NIH panel (1995) recommended meditation, hypnosis, relaxation, biofeedback and cognitive-behavioral therapy for chronic pain and insomnia.

Astin et al. (*op cit.*) concluded that the evidence of effectiveness of mind-body medicine was strong for treatment of myocardial infarction, cancer symptoms, incontinence disorders, surgical outcomes, insomnia, headache, and chronic low back pain.

May improve quality of life for patient even if disease not overcome

Some reasons for caution concerning the claims of mind-body medicine:

Study of advanced cancer patients (Cassileth, 1985) found no relationship between mental attitude and survival or reoccurrence.

Patients may blame themselves for causing the disease or for failing to get well

May raise false hopes of recovery

In some studies, techniques were combined with other factors (diet, exercise) so difficult to evaluate effect of mental aspect

For subjective outcomes (e.g., perception of pain), placebo effects are possible.

Correlation of recovery or survival with attitude or social support may be misleading - patients with better attitude and support may comply better with medication, recommended exercise, etc.

Tesman and Tesman (*Science 276*, 369-370 (1997)) found serious flaws in the evidence used by Herbert Benson in support of his "relaxation response."

W. Sampson (*Semin. Oncol. 29*, 595-600) criticized Spiegel's study of breast cancer patients, noting that the survival rates for the patients in the support groups were no better than those typical of the time (i.e., Spiegel's controls had abnormally *low* survival times). More recently, Goodwin et al. (*New Engl. J. Med. 345*, 1719-1726 (2001)), attempting to replicate Spiegel's results, found no effect on survival. A 2004 study found no connection between optimism and lung cancer survival.

A review by Petticrew et al. (*BMJ 325*, 1066-1075 (2002)) concluded that "There is little consistent evidence that psychological coping styles play an important part in survival from or recurrence of cancer."

O'Malley et al. (*New Engl. J. Med. 343*, 1298-1304 (2000)) - study of Army personnel found no relationship between stress and coronary artery calcification.

A meta-analysis of effects of psychological intervention on the immune system (Miller and Cohen (2001) *Health Psychol. 20*, 47-63) concluded that there was "only modest evidence that interventions can reliably alter immune parameters."

Adverse psychological effects from meditation have been reported.

Prayer, spirituality

Spirituality is defined by NCCAM as "an individual's sense of purpose and meaning to life, beyond material values. Spirituality may be practiced in many ways, including through religion." (*CAM at the NIH 12*(1), 1-4 (2005))

Various studies show beneficial effects of religious faith, prayer, and church attendance in health and recovery from illness, especially in elderly. This need not involve a supernatural explanation, but could be due to effects of positive attitude and social support discussed above.

Sloan et al. (*Lancet 353*, 664-667 (1999)) charged that these studies were seriously flawed; their points were rebutted by Koenig et al. (*Int. J. Psychiatry Med. 29*, 123-131 (1999)). A later review (Sloan and Bagiella, *Ann. Behav. Med. 24*, 14-21 (2002)) concluded that "there is little empirical basis for assertions that religious involvement or activity is associated with beneficial health outcomes." Again, there was a rebuttal: Weaver et al., *Altern. Ther. Health Med. 9*, 42-46 (2003). King et al. (*Social Science & Medicine 48*, 1291-1299 (1999)), found that stronger religious belief was associated with *poorer* outcome in hospitalized patients.

Intercessory prayer will be discussed in another handout, along with faith healing.

The placebo effect

Many studies show positive results in 30 to 70% of patients receiving placebos. However, in a reexamination of the literature, Kienle and Kiene (1997) *J. Clin. Epidemiol. 50*, 1311-1318, stated: "Having analyzed a total of 800 articles on placebo, we have not found any reliable demonstration of the existence of placebo effects...There can be no doubt that the extent and frequency of placebo effects as published in most of the literature are gross exaggerations."

A widely-publicized meta-analysis (Hróbjartsson and Gøtzsche (2001) *New Engl. J. Med. 344*, 1594-1602) found little evidence for the placebo effect, except possibly in pain and other subjective responses. However, numerous criticisms of their analysis have been raised (e.g., letters in *New Engl. J. Med. 345*, 1276-1279 (2001)). For example, the analysis pooled results from many different types of studies, which likely differ in the importance of placebo effects.

Recent research studies have identified changes in activity in certain regions of the brain in response to placebos.

"Now, research has shown that placebo responses are mediated by conditioning when unconscious physiological functions such as hormonal secretion are involved, whereas they are mediated by expectation when conscious physiological processes such as pain and motor performance come into play, even though a conditioning procedure is carried out.

"Positron emission tomography (PET) scanning of the brain is providing evidence of the release of the endogenous neurotransmitter dopamine in the brain of Parkinson's patients in response to placebo." (NCCAM, "Mind-Body Medicine: An Overview")

More recently, Zubieta et al. (*J. Neurosci. 25*, 7754-7762 (2005)) used imaging techniques to show involvement of the endogenous opioid system (using μ-opioid receptors) in the placebo effect.

We can divide placebo effects into two types:
1. Patients may perceive subjective improvement (e.g., in pain) in the absence of objective improvement in the condition.
2. Mind-body interactions as discussed above could produce objective improvement.

These effects may be involved in successes of some alternative practitioners.

Ethical questions: should doctors give placebos on purpose? Should we condone alternative methods that "work" only via placebo effects, since they may be helping patients?

Other points

NIH has established ten centers for mind-body medicine research.

SUMMARY: A growing body of evidence indicates that mental attitudes can affect the incidence and progress of disease, though many results need to be confirmed with more research. Applying the various techniques described above may help patients, as long as they do not have unrealistic expectations.

HYPNOSIS

Background

Can be broadly defined as an altered state of mind associated with greatly increased suggestibility; exact definition is controversial. New research is attempting to identify changes in the brain associated with the hypnotic state. “Brain scans show that the control mechanisms for deciding what to do in the face of conflict become uncoupled when people are hypnotized. Top-down processes override sensory, or bottom-up information” (S. Blakeslee, *New York Times*, Nov. 22, 2005).

Hypnotherapy practiced by 15,000 health professionals. However, it is also taught to, and practiced by, nonprofessionals (one can get a "Ph.D." in hypnotherapy in a 2-week course!).

How is hypnosis performed? What is it used for?

Hypnotic state induced by having subject focus on mental image, object, or soothing voice. Therapist then gives suggestions relating to the desired change in behavior.

Advocated for smoking cessation, weight control, stress management, motivation, pain control, etc.

“The pain-relieving effect of hypnosis is often substantial, and in a few cases the degree of relief matches or exceeds that provided by morphine.” (M. Nash (2001) *Scientific American*, July, 47-55)

“Hypnosis can boost the effectiveness of psychotherapy for some conditions...patients who received cognitive behavioral therapy plus hypnosis for disorders such as obesity, insomnia, anxiety and hypertension showed greater improvement than 70 percent of the patients who received psychotherapy alone.” (Nash)

“...a task force of the American Psychological Association validated hypnosis as an adjunct procedure for the treatment of obesity. But the jury is still out on other disorders with a behavioral component. Drug addiction and alcoholism do not respond well to hypnosis, and the evidence for hypnosis as an aid in quitting smoking is equivocal...there is strong, but not yet definitive evidence that hypnosis can be an effective component in the broader treatment of other conditions...these include a subgroup of asthmas; some dermatological disorders, including warts; irritable bowel syndrome; hemophilia; and nausea associated with chemotherapy...claims that hypnosis increases immune function in any clinically important way are at this time unsubstantiated.” (Nash)

Hypnosis is also used as a tool to help recall repressed or "lost" memories. This is sometimes used in psychotherapy. However, *hypnosis is not a magic route to the truth*; subjects can (and do) recall things incorrectly and construct fantasies. (See also “Recovered memories,” p. 19)

Two pseudoscientific applications of hypnosis

1. *Past-life therapy* - under hypnosis, patient is "regressed" through childhood and then back to alleged previous lives. (Some practitioners even claim to be able to "progress" the subject through *future* lives!) Events in these lives are held to underlie psychological problems in the present life. As in psychoanalysis, the reliving of these traumatic events is held to be therapeutic.

Arguments against:
- The concept of reincarnation is unsupported by scientific evidence, and, if true, would present important philosophical problems.
- Hypnosis is a state of relaxation and compliance, leading to increased suggestibility and desire to please the hypnotist. Under such conditions fantasization can occur. Using fragments of old memories, elements of books and stories, learned historical and geographical information, etc., the subject may create a convincing story. The subject may be unaware of the source of these "hidden memories" (*cryptomnesia*).
- Careful examination of cases of alleged past lives has revealed either historical inaccuracies or inconsistencies, or information which the subject could have obtained readily earlier in life.
- As with hypnosis in general, the techniques can be applied by people who have no training in psychotherapy, and may therefore be subject to abuse.

2. *UFO abductee regression* - it has been claimed that thousands of Americans have been abducted by aliens; often they allegedly have been subjected to sexual and reproductive experimentation. These instances are usually "remembered" only after the victims are hypnotically regressed, often many years later. This allegedly can lead to resolution of psychological problems. Promoted by author Budd Hopkins and Harvard psychiatrist John Mack (died 2004).

Arguments against:
- Problems with the general idea of alien visits include lack of corroborating physical evidence and the vast distances to other stars.
- If aliens did visit, why would they contact and abduct obscure individuals rather than government leaders or scientists?
- Idea that aliens could interbreed with humans is scientifically preposterous (and if they are so advanced, why would they want to?).
- Hypnosis does not necessarily lead to truthful reports; it can be a medium in which fantasy-prone individuals are encouraged to generate stories which will please the hypnotist.
- *Hypnogogic* (when falling asleep) and *hypnopompic* (when waking up) hallucinations may provide the bases for some reports.
- Some individuals may generate the reports to gain the fame (e.g., talk-show appearances) and possible financial rewards which go to "victims." Others may simply find it rewarding to have their normally secretive fantasy lives validated by the investigator.
- With the huge numbers of people allegedly abducted, there should have been many witnesses, unless the aliens have mastered such supernatural powers as making people invisible and allowing them to pass through walls.

BIOFEEDBACK

Definition

"*Biofeedback* employs electronic sensors to inform people of variations in physiological processes whose activities are not normally accessible to consciousness (e.g., brain or muscle electrical activity, blood pressure, etc.)." (Beyerstein, *Skeptical Inquirer 10*, 42-59 (1985)) Subjects then use mental state to manipulate the process in the desired direction.

Two major types:

1) One type includes measurement of muscle tension and skin temperature (higher temperature associated with relaxation). These techniques are *not* controversial (at least for some applications) and have been incorporated into many treatment programs. Used for treatment of chronic pain and migraine headaches, to help regain movement of limbs, and incontinence.

Allen (*Ped. Annals 33*, 241-245 (2004)) wrote, “Research demonstrated that biofeedback can be an effective treatment for a variety of stress-related disorders, including chronic headaches, hypertension, Raynaud’s disease, irritable bowel syndrome, and fibromyalgia.” (The article advocates the use of biofeedback for children with recurrent headaches.)

A meta-analysis by Nakao et al. (*Hypertens. Res. 26*, 37-46 (2003)) concluded that biofeedback “was more effective in reducing blood pressure in patients with essential hypertension than no intervention. However, the treatment was only found to be superior to sham or non-specific behavioral intervention when combined with other relaxation techniques.”

2) *Brain wave biofeedback* (or *neurofeedback)*. Sensors on scalp and earlobes detect brain waves. Subject is given feedback through earphones or video display. Generally, subject tries to maximize alpha and theta waves, associated with resting, meditation, and creativity, in contrast to beta waves, associated with excitation, stress, or narrowly focused states. (Thus, other techniques such as meditation, guided imagery, or psychotherapy may achieve the same results.)

Uses include inspiration of creativity in corporate settings; reduction of stress; improved attention span (and reduced hyperactivity) in children with attention-deficit disorder (here the goal would be to reduce alpha); reduction of depression; recall of repressed memories (memories associated with intense emotional states are held to be linked to theta waves); overcoming addictions; and dealing with insomnia and phobias; dealing with head injuries, cerebral palsy, autism, epilepsy.

Many of these applications are controversial, and benefits are not well documented.

According to psychologist Joel Lubar, there are 2000 practitioners using neurofeedback for ADHD, with 40-80% of children showing benefit.

Various *electronic devices* are also used to induce relaxation and produce desired brain states. These may be used in practitioners' offices, in stress-reduction salons, or in the home. The FDA has taken action against some of these. They can produce seizures in some individuals, even with no prior history of epilepsy or seizures.

A critical evaluation was provided by B. Beyerstein (1985), "The Myth of Alpha Consciousness," *Skeptical Inquirer 10*, 42-59. Some of his points:

- Just because alpha is associated with a certain state doesn't mean that it causes it.
- An increase in alpha during a session may simply be due to decrease in the novelty of the initial situation, in addition to the relaxation that occurs with time in the quiet, monotonous setting.
- About 10-15% of normal subjects did not produce any alpha, yet seemed no more stressed than others. Conversely, some very anxious individuals had high alpha.
- In one study, subjects could be induced to *increase* alpha under stressful conditions (threat of electric shock)
- Lack of controls for placebo effect in some studies. Patients may simply believe the treatment will help them.
- Possibly distractive effect in pain control.
- Subjects reported transcendent experiences when given feedback to *suppress* alpha.

OTHER UNCONVENTIONAL PRACTICES RELATED TO MENTAL HEALTH

(Quotes are from S. Barrett, "Mental Help: Procedures to Avoid."
http://www.quackwatch.org/01QuackeryRelatedTopics/mentserv.html)

Autism - surveys have found that 30% to 75% of autistic children are treated with alternative methods. One is treatment with *secretin*. However, controlled trials found no benefits. More recently, *vancomycin* has been used. A preliminary study found temporary benefits, but symptoms soon reappeared. Other approaches include *Auditory Integration Training (AIT)* and the supplement *dimethylglycine (DMG)*; controlled studies found neither was useful. *Gluten-free diets* and *chelation* (to remove mercury) have also been employed (in 2005 a 5-year-old died after chelation). FDA took action in 2002 against a marketer of *taurine* for treatment of autism.

Attention deficit hyperactivity disorder - dietary supplements are being marketed to treat this condition. In 2000 and 2002 the FTC took action against marketers of essential fatty acids, pycnogenol, and other products for unsupported claims.

Brain mapping - promoted by Daniel Amen. Uses single-photon emission computed tomography (SPECT) brain imaging “to diagnose and treat attention deficit disorder and other behavioral problems” (S. Reiss (2005) *Technology Review*, June, 27).

Down syndrome - nutritional therapy (with vitamins, minerals, amino acids, antioxidants, and other components) has been advocated as a treatment. However, there is no evidence of benefit.

Eye Movement Desensitization and Reprocessing (EMDR) - "promoted for the treatment of post-traumatic stress, phobias, learning disorders, and many other mental and emotional problems. The method involves asking the client to recall the traumatic event as vividly as possible and rate certain feelings before and after visually tracking the therapist's finger as it is moved back and forth in front of the client's eyes...Recent reviews have concluded that the data claimed to support EMDR derive mostly uncontrolled case reports and poorly designed controlled experiments and that the theory of EMDR clashes with scientific knowledge of the role of eye movements." According to promoters, 60,000 therapists have been trained worldwide, and they have treated 1 million patients.

Facilitated communication - used to help an autistic or otherwise disabled person communicate. A "facilitator" helps the subject spell out messages. However, controlled studies show that the messages are actually produced unintentionally by the facilitator.

Feingold diet - based on idea that hyperactivity and many other conditions arise from salicylates, artificial colors, and artificial flavors in the diet. However, blinded tests show that food additives have little effect on behavior.

Neural Organization Technique - developed by a chiropractor; purports to realign skull bones to heal mental disorders.

Neuro Emotional Technique (NET) - based on releasing emotional blocks which produce adverse health effects. Involves applied kinesiology, chiropractic adjustments, and other invalid methods in diagnosing and dealing with these blockages.

Neurolinguistic programming - "a variable system of procedures purported to enable people to communicate more effectively and influence others. Proponents claim that NLP has cured phobias, allergies, and other problems in one or a few brief sessions. Its core postulates are: (a) people are most influenced by messages that reflect how they internally represent whatever they are doing; and (b) this representation is reflected by eye-gaze patterns, posture, tone of voice, and language patterns... A National Research Council committee has found no significant evidence that NLP's theories are sound or that its practices are effective."

Optometric Visual Training - "based on the idea that learning can be improved by exercises that improve coordination of the eye muscles or improve hand-eye coordination. Its proponents assume that the basic problem that leads to reading disability is some deficit in the visual system. The American Academy of Pediatrics and the American Academy of Ophthalmology have criticized this approach and cautioned that no eye-muscle defects can produce the learning disabilities associated with dyslexia."

Patterning (psychomotor patterning; Doman-Delacato Treatment) - for treatment of mental retardation, learning disabilities, etc. Based on scientifically discredited idea that putting patient through series of passive motions (e.g., crawling) can stimulate brain development to more advanced stages. Trials in the 1960's and 1970's showed little or no value.

Recovered memories - during therapy (possibly involving hypnosis), subject "remembers" early events (e.g., childhood sexual abuse). There have been many cases of alienation within families or even criminal prosecution as a result of such "memories." However, many of them are false, created in response to the promptings of the therapist. Elizabeth Loftus received the 2005 University of Louisville Grawemeyer Award for Psychology for her work on the unreliability of “recovered” memories. (see also past-life regression and UFO abductee regression above)

Thought Field Therapy (TFT) - psychological problems are alleged to involve disturbances in “energy fields” (or “thought fields”) in the body. These are supposedly corrected through sequences of tapping on various acupressure points, plus other sensory activities. No controlled studies in support.