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INSIDE

Away With Seasonal Allergies: Butterbur (*Petasites hybridus*)

By David Kiefer, MD

ALLERGY SEASON IS APPROACHING AND CLINICIANS OFTEN FIND themselves in the position of helping their patients negotiate the various pharmacologic and behavioral therapies, balancing side effects and inconveniences along the road to (hopefully) a fall free of runny noses and itchy eyes. Butterbur (*Petasites hybridus*), a plant with an impressive amount of recent laboratory and clinical study, may be another useful treatment for patients suffering from seasonal allergic rhinitis.

History and Traditional Use

Butterbur is a perennial herb native to Europe, northern Africa, and southwest Asia,[1] and was known to be an antispasmodic and analgesic, useful in acute colicky urinary pain such as might result from nephrolithiasis.[2] Homeopathic forms of this plant are documented to be useful for smooth muscle cramps.[3] The German Commission E approved the use of butterbur root for acute spasm pain of the urinary tract, but could not justify the traditional use of butterbur leaf for "cramp states" due to risks associated with the pyrrolizidine alkaloids contained with the all plant parts in varying amounts.[4]

As occurs with other medicinal plants referred to by their common name, butterbur has a confusing array of other names, including blatterdock, bog rhubarb, bogshorns, butterbur, butter-dock, butterfly dock, capdockin, flapperdock, langwort, and umbrella leaves.[3] This information is provided to readers both as a reminder to always confirm a plant's identity with its correct scientific name (in this case, *Petasites hybridus*), and to be aware of herbal medicine combinations that may contain this plant in its unsafe, whole form (see below).

Botany and Pharmacology

Butterbur (*Petasites hybridus*) is a member of the daisy family (Family Asteraceae). The plant grows to 15-40 cm high, and has reddish flowers and large basal (lower) leaves.[3] Interestingly, some texts recommend only harvesting leaves as large as one's hand because they have a higher content of active phytochemicals.[3] These large

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basal leaves were also once used to wrap and carry pieces of butter, partly explaining one of the plant's common names.[5]

All plant parts of butterbur are listed as being used medicinally. Traditionally, above-ground parts such as leaves are collected near the end of the flowering season, and the rhizome (horizontal underground stem) and roots are harvested either in the fall or the spring, a distinction being noted as important in some sources.[3] Currently, most butterbur preparations are ethanolic formulations made from the rhizomes, with further processing to remove the dangerous pyrrolizidine alkaloids.

The compounds thought to be responsible for butterbur's pharmacological activity are referred to as petasins, which fall into the category of eremophilan-type sesquiterpenes;[1] sesquiterpenes are often components of essential oils. The petasins in butterbur occur in a mixture; the three main compounds are petasin, isopetasin, and neopetasin, and they each have unique actions in vitro and in vivo.

Mechanism of Action

There has been a significant amount of in vitro research demonstrating the many actions of butterbur relevant to its use in allergic rhinitis. For example, petasin has been shown to bind to the histamine-H_1 receptor, and an extract of butterbur inhibits cysteinyl-leukotriene synthesis; the release of inflammatory mediators such as histamine and leukotrienes are important in the pathophysiology of allergic rhinitis.[1] Another experiment found that a specific butterbur extract (Ze 339, a carbon dioxide extract standardized to 8.0 mg of total petasin per tablet,[6] also called Tesalin®) blocked leukotriene synthesis in stimulated macrophages, eosinophils, and neutrophils in two in vitro models.[7] The isolated compound petasin was then tested in the same models and was also found to block leukotriene synthesis.

Other studies have begun to delineate the differences between the mechanisms of action of the different phytochemicals in butterbur. For example, in vitro studies have shown that petasin, isopetasin, and neopetasin all inhibit leukotriene generation, but eosinophil cationic protein is only inhibited by petasin.[8] Petasin was also the only compound to prevent an increase in cytosolic phospholipase A2. One of the conclusions that the researchers drew from these and other related experiments is that the different petasin compounds may block different intracellular signaling molecules, and affect different steps in the overall inflammatory cascade.

Clinical Studies

There have been numerous studies examining the use of butterbur in people with allergic rhinitis. One double-blind, crossover trial randomized 20 patients with seasonal allergic rhinitis to receive either 50 mg of a standardized extract of butterbur (Petaforce®, a dry extract of butterbur root) twice daily or placebo for two weeks during the grass pollen season.[9] The researchers measured the nasal response to adenosine monophosphate (AMP), a known irritant and restrictor of nasal airway flow at least partly through a leukotriene mechanism, and found that butterbur attenuated the response to AMP. The researchers then added a subjective component to their research in a double-blind, crossover trial of 16 patients with mild perennial allergic rhinitis who received either 50 mg of a standardized extract of butterbur (Petaforce) twice daily, 180 mg daily of fexofenadine, or placebo for one week.[10] The researchers again measured the nasal response to AMP and found that both butterbur and fexofenadine attenuated the response to AMP, while improving nasal symptoms.

Butterbur also has been compared to cetirizine in a double-blind, parallel-group trial.[11] The researchers randomized 125 patients with seasonal allergic rhinitis to either one tablet of a butterbur extract (Ze 339) four times daily, or 10 mg of cetirizine in the evening, for two

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weeks. The results showed similar improvements in symptoms and global improvement scales between the two groups, and that both butterbur and cetirizine were well tolerated. The cetirizine patients reported sedation as the most common adverse effect; no specific adverse event, such as sedation, was associated with the use of butterbur.

Not all studies with butterbur have been favorable. One double-blind, crossover trial compared butterbur (50 mg twice daily of Petaforce) to placebo in 35 patients with intermittent allergic rhinitis.[12] After two weeks, no difference was detected in objective or subjective outcomes between the two groups. One criticism is that eight of the original 43 patients withdrew and yet were not included in an intention-to-treat analysis.

Another study contributes some information to our understanding of the action of butterbur, but is less clinically useful due to methodological problems.[13] This trial was non-randomized and found that a specific extract of butterbur (Ze 339) in a dose of 16 mg three times daily in patients with allergic rhinitis improved symptoms and quality of life and decreased leukotrienes and histamine in nasal fluids, without affecting generalized leukotriene production. An interesting result, but one that requires controlled study before definitive clinical conclusions can be drawn.

Other Clinical Conditions

Butterbur also has been studied in the context of asthma and allergic skin conditions. In 16 asthmatic patients stable on inhaled corticosteroids, a randomized, double-blind, crossover trial comparing one week of a standardized butterbur extract (Petaforce) 25 mg twice daily to placebo showed that butterbur improved AMP bronchial hyper-responsiveness and several inflammatory markers, apparently acting as a complementary anti-inflammatory for asthmatic patients already on inhaled corticosteroids.[14] In other asthma research, a non-randomized, open trial used a butterbur extract in 80 people (64 adults, 16 children) with asthma.[15] The extract was Petadolex®, softgel capsules with 50 mg of a standardized lipophilic extract of butterbur rhizome with a minimum of 15% petasins and with pyrrolizidine alkaloids removed. Adults were treated with 50 mg three times daily and the children with 50-150 mg daily for two months, with a second month of treatment being optional. The patients' regular asthma medication was continued. The researchers documented improvements in number, duration, and severity of asthma attacks, and some patients were able to lessen the use of their regular asthma medication; an interesting result, but one that needs to be verified by further research.

Testing the hypothesis that the effect of butterbur on inflammatory mediators such as cysteinyl leukotriene and histamine in allergic rhinitis and asthma could also benefit people suffering from atopic skin conditions, researchers conducted a randomized, double-blind, crossover study on 20 atopic patients sensitized to at least one common allergen on skin-prick testing.[15] The patients received either 50 mg twice daily of a standardized butterbur extract (Petaforce), 180 mg daily of fexofenadine plus placebo, 10 mg daily of montelukast plus placebo, or just placebo for one week. Only fexofenadine successfully attenuated the skin wheal response to skin-prick provocation, showing that butterbur had no effect on the immediate histamine and allergen cutaneous response, and suggesting that butterbur's main in vivo effects in this system are via inhibition of leukotriene synthesis rather than through effects on histamine.

Dosage and Formulation

There is little if any dosing information about butterbur in many of the commonly used clinical herbal medicine books. What is clear is that any form of the raw, unprocessed butterbur plant should not be ingested due to the toxicity of pyrrolizidine alkaloids; this includes any teas (decoctions or infusions), capsules of raw herb, or unprocessed tinctures or extracts.

Due to these concerns a number of standardized, patented formulas have been developed which have undetectable levels of pyrrolizidine alkaloids and therefore are presumed free of the related mutagenicity, carcinogenicity, and hepatotoxicity. These formulas (and dosing) include Petaforce (25-50 mg two or three times daily), Petadolex (25-75 mg two or three times daily, maximum 150 mg/d), and Tesalin (or Ze 339, 1-2 tablets two or three times daily). The manufacturers of Petadolex provide a dosing for children 10-12 years of age: 50 mg daily with meals.

Adverse Effects, Contraindications and Drug Interactions

Warnings about the use of butterbur usually are based on preparations from the plant that still contain pyrrolizidine alkaloids, known to be carcinogenic (probably from a genotoxic mechanism) and hepatotoxic; these preparations are dangerous to everyone, but are specifically contraindicated for pregnant and nursing women.[5]

One review article about the safety of butterbur was published by Weber and Weber, the German company that makes one of the standardized butterbur extracts (Petadolex) often used in clinical trials.[16] The authors

mention that butterbur products are under strict regulation in Europe and the standardized extracts have the dangerous pyrrolizidine alkaloids removed. They review the favorable results in animal toxicity testing, and the side effects in humans for using the 25 mg capsule dosed 2-3 capsules twice daily, which include nausea, eructations, and mild stomach pain, though these reactions appear to be very rare as determined by post-marketing surveillance.

As with other plants from the daisy family (Family Asteraceae), some caution is prudent for individuals who wish to try a course of butterbur and who are also particularly sensitive to other plants in the daisy plant family, such as ragweed, marigolds, or echinacea.

Conclusion

Butterbur and, more specifically, its phytochemical complex of petasins (petasin, isopetasin, and neopetasin) have been shown to be effective inhibitors of various stages of the inflammatory cascade relevant to allergic rhinitis. Butterbur extracts inhibit cysteinyl-leukotriene synthesis and the compound petasin has been shown to bind to the histamine-H_1 receptor. These in vitro studies have translated into clinical effects: Double-blind, placebo-controlled trials have demonstrated a benefit with butterbur in allergic rhinitis both in objective signs (through attenuation of the nasal response to the irritant adenosine monophosphate) and subjective symptoms. The effect of butterbur seems to be comparable to cetirizine, or perhaps even better given a lack of side effects (i.e., sedation) as demonstrated by many of the current research trials. Only standardized extracts that are free of pyrrolizidine alkaloids should be used in the treatment of the above conditions.

Recommendation

At this point, based on a significant amount of in vitro research, as well as several small, but high-quality clinical trials, the use of butterbur warrants consideration as a treatment for allergic rhinitis, especially given its excellent tolerability. It is extremely important to recommend only standardized extracts free of pyrrolizidine alkaloids (the three products used in most of the research trials are listed in the Dosage and Formulation Section).

More research is needed to further clarify the use of butterbur in other clinical conditions such as asthma, following up on promising initial research results. ❖

Dr. Kiefer recently completed a fellowship at the Program in Integrative Medicine, College of Medicine, University of Arizona, Tucson.

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Faltering Promise: Vitamin E and Heart Disease

By Howell Sasser, PhD

Understanding of the role of oxidative stress in human health has grown considerably in recent years. With it has grown interest in the potential benefit of antioxidants for disease prevention. As the leading cause of death in the United States, heart disease—and its inflammatory component—have received special attention in this respect. A number of agents, including vitamins C and E, beta-carotene, and selenium, have shown promise in observational studies. As well-controlled clinical trials begin to report results, the likely value of various agents is being re-evaluated. This review summarizes the literature to date on one of the better-studied compounds, vitamin E.

Mechanism of Action

The mechanism of action of vitamin E in processes associated with heart disease is the subject of continuing debate. The most commonly offered explanation focuses on inhibition of low-density lipoprotein (LDL) cholesterol peroxidation.[1] Changes in LDL have been shown to be important both in new atherogenesis and in destabilization of existing plaques. As lipophilic molecules, the various isomers of vitamin E incorporate readily into unsaturated fats, effectively pre-empting the action of free-radical oxidants. However, this property also can have negative consequences. In the right circumstances, vitamin E can also act as a pro-oxidant, prompting the observation that vitamins E and C are more effective together, with vitamin C acting as a restorative agent to return vitamin E to its stable form.[2]

Other potential mechanisms have been suggested, and some have been tested in vitro or in experimental studies in humans. These include a role for vitamin E in suppressing the expression of adhesion molecules that have a role in atherogenesis, and inhibition of endothelial cell proliferation.[3,4] Neither of these possibilities is as well characterized as the oxidative stress hypothesis, which has been the underlying rationale in most of the trials conducted so far.

Commercial Preparations

There is a bewildering variety of commercial preparations of vitamin E available, each with evidence that it is absorbed and mobilized by the body better than the others. The two classes most widely available commercially are the tocopherols and the tocotrienols. Each has eight isomers, of which only four are maintained in human tissue.[5] Both natural and synthetic forms are produced, and esterified forms (α-tocopherol acetate or α-tocopherol succinate) usually are used to improve shelf-life. Animal studies and a few human studies have found that natural forms are more bioavailable than synthetic forms, in a ratio of about 1:1.36.[6] However, it also has been shown that this difference in biological activity does not translate into meaningful differences in antioxidant activity.[7]

The d-α-tocopherol species is the most widely studied and is believed to be the most biologically important.[8] The various forms are not interconvertible in humans and do not have the same metabolic action. Commercial vitamin E supplements commonly advertise that they contain all the natural varieties, but given that only four of eight are maintained in human tissue, presumably about half of what they contain is of little or no value.

Published Trials

On the basis of promising observational data, several large prospective, controlled trials were started in the mid-1990s. The gathering evidence is increasingly negative, but the variety of doses and endpoints used means that the findings published to date still are somewhat confusing and not easily summarized.

The CHAOS trial enrolled 2,002 patients with proven cardiac disease and randomized half to either 400 or 800 IU/d (268 and 536 mg, respectively) of vitamin E.[9] After a median follow-up of 510 days, those taking vitamin E had a significantly lower rate of non-fatal myocardial infarction (MI) (Relative Risk [RR] = 0.53), but not death, as compared to those taking placebo.

The SPACE trial enrolled 196 patients with end-stage renal disease, with random assignment to an 800 IU/d (536 mg) or placebo.[10] Those taking vitamin E had a significantly reduced rate of a composite cardiovascular endpoint (including sudden death) (RR = 0.54) and a reduced rate of MI (RR = 0.45), as compared to the placebo group. It is worth noting that the study population in this case was distinct enough medically to make these results, more than any of the others, of questionable generalizability.

An Australian study of young Type 1 diabetics (n = 41) showed significantly improved flow-mediated vasodilation (FMD)—a measure of vascular endothelial function correlated with cardiac events—after a three-month course of 1,000 IU/d of vitamin E (670 mg).[11] Brachial FMD rose from 2.6 ± 0.6% at baseline to 7.0 ± 0.7% ($P < 0.005$) at study completion. However, there was no significant change in systemic arterial compliance, a generalized measure of arterial stiffness and vascular resistance.

A small number of studies have found benefit specifically with the tocotrienol isomers. A Pakistani study of 90 healthy volunteers found that daily supplementation with tocotrienol in varying doses produced significant reductions in total cholesterol, LDL cholesterol, and apolipoprotein-B.[12] In vitro studies from Asia also have produced evidence that tocotrienol may inhibit endothelial proliferation in the vascular wall, and that it may reduce expression of adhesion molecules (e.g., VCAM-1, E-Selectin) that play a role in atherogenesis.[3,4]

At least as many studies have reported only mild or no apparent benefit, and some suggest the possibility of harm. The GISSI-Prevenzione trial enrolled more than 11,000 Italian patients within three months of an MI.[13] Randomization was factorial, with assignment to vitamin E (300 mg/448 IU daily) or placebo, and to n-3 polyunsaturated fatty acids (PUFA) or not. Neither the vitamin E + PUFA group, nor the vitamin E alone group showed significant improvement in a combined cardiovascular endpoint after an average of 3.5 years. However, there was some indication of potential benefit in the vitamin E alone group with specific cardiac endpoints. Reductions of 20-35% in various categories of cardiovascular death were reported.

The HOPE study randomized 3,654 diabetics, also in a factorial design, to vitamin E (400 IU/268 mg daily) or placebo, and ramipril or placebo.[14] After an average of 4.5 years, there was no significant difference in a composite outcome of MI, stroke, and cardiovascular death, in any of the individual components, or in any secondary outcome by vitamin E status. The results did not change appreciably when those taking ramipril were excluded.

The Primary Prevention Project (PPP) was primarily a low-dose aspirin study that also included vitamin E (300 mg/448 IU daily) with the goal of preventing first cardiac events in those with major risk factors.[15] Both study agents were given on an open-label basis. When the trial was stopped (in response to strong evidence from other trials for the efficacy of aspirin), there were 4,495 patients enrolled with an average of 3.6 years of follow-up. No significant protective effect was noted for vitamin E in the pre-specified cardiac endpoints or death. However, there was a significantly lower incidence of peripheral vascular disease (PVD) (RR = 0.54) in the vitamin E group, as compared to placebo.

The Heart Protection Study (HPS) enrolled 20,536 patients with coronary or vascular disease, or diabetes, and randomized them by a factorial design to simvastatin or placebo, and a cocktail of antioxidants including vitamin E (600 mg/896 IU/d) or placebo.[16] After five years of follow-up, there was no significant reduction in all-cause mortality, deaths due to vascular causes, non-fatal MI, fatal or non-fatal stroke, or need for a revascularization procedure in the vitamin supplement group. There were small and statistically non-significant increases in total mortality and LDL cholesterol. The latter finding is especially important given the concomitant use of a statin in the trial.

The ATBC study randomized 1,862 men to vitamin E (50 mg/75 IU daily), beta-carotene, both, or placebo.[17] All participants were smokers between 50 and 69 years of age. After an average of 5.3 years of follow-up, there were no significant differences in major coronary events (non-fatal MI and fatal coronary heart disease) in any of the supplement groups. There was a non-significant elevation in the risk of death in the vitamin E group (RR = 1.33, P = 0.2).

The ASAP study enrolled 520 patients and assigned them in a factorial design to a relatively low dose of vitamin E (136 IU/91 mg daily) or placebo, and vitamin C or placebo.[18] The main outcome parameter was change in intima-media thickness (IMT) of the common carotid artery, a well-studied marker for atherosclerotic progression. After three years, there was no significant benefit with either supplement alone, although there was with the combination. Change in carotid IMT was significantly less in the combined therapy group, a finding that the authors inferred would translate into reduced clinical events, although these were not counted in this study.

An intriguing mechanistic hypothesis also has been put forward to explain the apparent lack of cardioprotection with vitamin E that has been observed in many trials. This involves a series of small, transient ischemic events in the heart, a phenomenon called preconditioning.[19] It is theorized that the heart's response to these events enables it to better withstand a subsequent major event, such as an MI. There is evidence that antioxidants can interfere with this process.[20] If vitamin E supplementation prevents preconditioning, it would be expected that those taking vitamin E would experience proportionally more fatal cardiac events. As yet, there is little clinical evidence to support or refute this idea.

Strengths and Limitations of the Evidence

Although there appears to be a consensus developing in the trial literature, it still amounts to similar words being sung to different tunes. Several issues should color how the evidence is weighed.

A basic issue is the size of the studies reported to date. The outcome events are very rare, even in very large studies. It is impractical to conduct studies large enough to use a single class of event (i.e., death or MI) as the outcome, so composite endpoints are used. Disparities in the etiology and severity of the component

Table

Clinical studies of vitamin E supplementation and cardiovascular disease

Study	N	Vitamin E/d	Follow-up*	Principal Outcomes	Benefit
CHAOS (1996)	2,002 with CVD	400/800 IU	1.4 yrs	CV death + non-fatal MI, non-fatal MI alone	+
ATBC (1997)	1,862 smokers	50 mg	5.3 yrs	Non-fatal MI + fatal MI	– (Non-significant increased risk of death)
GISSI (1999)	11,253 with recent MI	300 mg	3.5 yrs	Death + non-fatal MI + stroke	– (Possible mitigation of benefit from statins)
ASAP (2000)	520	136 IU	3 yrs	Carotid IMT	– (But with improvements with vitamin E + C)
Skyrme-Jones (2000)	41 Type 1 diabetes	1,000 IU	0.25 yrs	Change in flow-mediated vasodilation	+
SPACE (2000)	196 end-stage renal disease	800 IU	1.4 yrs	MI + ischemic stroke + PVD + unstable angina	+
PPP (2001)	4,495	300 mg	3.6 yrs	CV death + non-fatal MI + non-fatal stroke	– (But decreased PVD)
HOPE (2002)	3,655 with diabetes	400 IU	4.5 yrs	MI + stroke + CV death	–
HPS (2002)	20,536 with vascular disease, CVD, or diabetes	600 mg	5 yrs	Non-fatal MI, coronary death, non-fatal stroke, fatal stroke, revascularization	– (Non-significant increases in total mortality, LDL)

* Length of follow-up is average in most studies.

events may mask genuine effects of the intervention. However, it should also be noted that consistency of the results across most endpoints bolsters confidence in the results for any one endpoint.

With the exception of the Primary Prevention Project, all of the major studies have enrolled patients with confirmed coronary disease or another major health problem. This would be expected to maximize the number of outcome events, but it begins the intervention late in the disease process. Studies of younger and healthier people would have to be larger and last longer (and thus be much more expensive), but would round out the picture with evidence from the pre-acute period.

There also is little similarity across studies in vitamin E dosage or concomitant medication. This observation cuts both ways. On the one hand, it can be difficult to tease out the effect of vitamin E from the noise of other agents. Studies with factorial designs often are not powered to permit analyses of the vitamin E-only arm, and two-way analyses that simply ignore the other active agent seem likely to produce results on which the heterogeneity in both groups has some (unquantifiable) influence. Conversely, the consistency of findings across different dosages and combinations of other medications suggests that the findings of any single study are unlikely to result from conditions unique to it.

Conclusion

Although a few trials have shown clinical benefit from vitamin E supplementation for preventing cardiovascular events, much of the evidence is against it *(see Table)*. Numerous trials, in disparate populations, with varying outcomes and large sample sizes, have produced similar findings: Vitamin E, even in large doses, produces results that are similar to, or not statistically better than, placebo. The preponderance of evidence for the lack of benefit from vitamin E supplementation in those with established cardiovascular disease should motivate clinical researchers to move on to other compounds.

Recommendation

There appears to be little cardioprotective benefit of vitamin E in common supplemental doses once cardiovascular disease is established. However, this should not call into question the value of proper intake of vitamins and minerals as part of a well-balanced diet, or through use of a multivitamin supplement, if necessary. The benefit of a variety of agents in recommended daily amounts—especially from whole-food sources—is well established and should be reinforced. ❖

Dr. Sasser is Director, Research Epidemiology, R. Stuart Dickson Institute for Health Studies, Carolinas HealthCare System, Charlotte, NC.

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Reiki: A Subtle, Vibrational Energy Therapy

By Lynn Keegan, RN, PhD, HNC, FAAN

REIKI (PRONOUNCED RAY KEE), IS A SUBTLE VIBRAtional, energy therapy most commonly facilitated by light touch. Reiki is believed to strengthen the body's ability to heal itself and balance a person's biofield.[1] The biofield is "an energy field that suffuses living bodies and extends several inches beyond the body. There is no consensus on what the biofield is; some say it is spiritual energy, others say it is an electromagnetic field."[2] Some use the term biofield interchangeably with aura, which is described as the human energy field (HEF) that surrounds and blends with the physical field. This HEF consists of distinctive layers of energy corresponding to physical, emotional, mental, spiritual, and subtle aspects of the multidimensional human being.[3] Reiki employs the gentle art of healing touch that is used as a complementary, energy-based healing modality.[4,5]

This ancient healing method has its roots in Chinese medicine.[6] Traditional Chinese medicine is a complete system of medicine and health care based on the concept of balanced *qi*, or "life force," that flows throughout the body. Among the components of traditional Chinese medicine are herbal and nutritional therapy, restorative physical exercises, meditation, acupuncture, acupressure, and therapeutic massage.[7]

History

The technique of Reiki was developed in Japan by Mikao Usui (1865-1926). When people came to Usui, a

Table 1

Chakra energy centers

Number and Name(s)	Location	Function
1. Root or base	Base of spine (coccygeal); relates to basic survival mechanisms and vital life force	If flow of energy is diminished here, then flow to other centers is impaired
2. Sacral center	Sacral area	Function of food, fluids, and endocrine reproductive glands; relates to emotional protectiveness, feelings, and choices
3. Solar plexus or power center	Solar plexus, above umbilicus	Digestion; relates to thinking, control, and power
4. Heart center	Middle of chest	Considered the transformative center; allows shift from gross, more basic energy to higher, more ethereal centers
5. Throat chakra	Middle of throat	Relates to creativity and expression
6. Brow center, intuitive center, or third eye	Middle of forehead	Relates to seeing with intuition and compassion
7. Crown center	Top of head	Relates us to the universe and our connection with a "Higher Power"

practicing Buddhist, he placed his hands on them to offer healing as a part of his spiritual practice. He evolved the technique and initiated fewer than 20 Reiki masters before he died. One of Usui's master students further refined the technique and subsequently trained a woman named Hawayo Takata (1900-1980), a first-generation American who was visiting family in Japan. She originally came to the Japanese clinic for health reasons, but upon regaining her health petitioned the master to teach her the technique. She then was granted permission to take the technique to the West.[8] Reiki began to be used on the U.S. mainland in the early 1970s.[6] Since that time many permutations have evolved, some having nothing to do with the original Usui teachings.[4]

Mechanism of Action

Practitioners and proponents of Reiki contend that we are alive because life force is flowing through us. Life force flows within the physical body though pathways called chakras *(see Table 1)*, meridians, and nadis. It also flows around us in a field of energy called the aura. Life force nourishes the organs and cells of the body, supporting them in their vital functions. Theoretically, when this flow of life force is disrupted, it causes diminished function in one or more of the organs and tissues of the physical body.

The life force also is believed to be responsive to thoughts and feelings. It becomes disrupted when people accept, consciously or unconsciously, negative thoughts or feelings about themselves. These negative thoughts and feelings become attached to the energy field and cause disruption in the flow of life force. If the negative thoughts and feelings are not eliminated quickly, illness results. The negative thoughts and feelings lodged in the subconscious are the greatest problem, as we are not aware of them and thus hampered in changing or eliminating them.

Reiki is believed to offer healing by flowing through the affected parts of the energy field and charging them with positive energy. This causes the negative energy to break apart and fall away. In so doing, Reiki clears, straightens, and heals the energy pathways, thus allowing the life force to flow in a healthy and natural way.[9] As this happens, the unhealthy physical organs and tissues become properly nourished with *qi* and begin functioning in a balanced healthy way, replacing illness with health. The intent of treatment is to gently balance and provide energy that supports the well-being of the recipient in a holistic and individualized manner.

Reiki also has been defined as a spiritually guided life force energy. This is a functional definition that parallels the experience of Reiki practitioners: According to many practitioners, Reiki energy seems to have an intelligence of its own, flowing where it is needed in the patient and creating healing conditions necessary for the patient's individual needs. It cannot be guided by the mind; therefore, it is not limited by the experience or ability of the practitioner. In contrast to conventional thinking where anything that can offer help can also offer harm if applied inappropriately, Reiki practitioners espouse that the practice always creates a healing effect.[9]

Reiki Sessions

Reiki can be used as a complementary treatment to conventional medical protocols. A Reiki treatment generally runs 45-60 minutes. However, sometimes the sessions are given in shorter, more frequent increments of 3-5 minutes. Reiki hand placement positions typically are aligned with the main chakras, or energy pathways, with hands just above the skin surface. Hand positions customarily correspond to the body's endocrine and lymphatic systems and major organs, focusing on the seven main chakras.[10] The chakras are believed to begin at the base of the spine and ascend from there.

Reiki Training

There are four levels of Usui Reiki training *(see Table 2)*, each level building upon the prior. Reiki training is designed to provide support for the practitioner of the therapy as well as benefit those receiving treatment.[5,11] Reiki training programs abound throughout the world. For information on programs, retreat offerings, and continuing education access, see www.reiki.org.

Reiki Research

Although Reiki practitioners and clients believe that the therapy produces positive results, there is little scientific research to substantiate this claim. Most data consist of case reports, descriptive studies, or randomized controlled studies with small numbers of participants.[1]

Twenty-four patients with cancer pain were compared for pain, quality of life, and analgesic use in a small study recently conducted in Canada.[12] Participants received either standard opioid management plus rest (Group 1) or standard opioid management plus Reiki (Group 2). On days 1 and 4, participants either rested for 1.5 hours or received two Reiki treatments one hour after their first afternoon analgesic dose. Visual analogue scale (VAS) pain ratings, blood pressure, heart rate, and respirations were obtained before and after each treatment/rest period. Analgesic use and VAS pain scores were reported for seven days. Quality of life was assessed on days 1 and 7. Participants in the Reiki treatment group experienced improved pain control on days 1 and 4 following treatment compared to the control group, and improved quality of life, but no overall reduction in opioid use. The problem with this small study is that the benefits attributed to Reiki may have been due to human presence and touch.

A larger, more tightly controlled investigation was conducted at Beth Israel Medical Center in New York.[13] The modified double-blind, placebo-controlled clinical trial with an additional historic control-condition design was implemented in the stroke unit of a major rehabilitation hospital. A sample of 50 inpatients with subacute ischemic stroke (31 male and 19 female) was involved. There were four interventions: treatment by a Reiki master, treatment by a Reiki practitioner, sham Reiki, and no treatment (historic control). Subjects received up to 10 treatments over a two-and-a-half-week period, in addition to standard rehabilitation. Outcomes included results of Functional Independence Measure (FIM) and Center for Epidemiologic Studies-Depression (CES-D) measure.

When the results were tallied, no effects of Reiki were found on the FIM or CES-D. Sham Reiki practitioners reported greater frequency of feeling heat in the hands compared to Reiki practitioners. There was no reported difference between the sham and the real Reiki practitioners in their ability to feel energy flowing through their hands. Post-hoc analyses suggested that Reiki may have had limited effects on mood and energy levels. The final conclusion was that Reiki did not have any clinically useful effect on stroke recovery in subacute hospitalized patients receiving standard care rehabilitation therapy.

Results of the most recent published Reiki investigation demonstrated that both hands-on and distance Reiki were effective in reducing symptoms of depression, hopelessness, and stress in 45 treated participants as compared with controls, and that the results were not due to placebo effects.[14] This study supports the hypothesis that Reiki is an effective energetic healing modality treatment, rather than touch being the causative factor. Most importantly, the effects of Reiki were demonstrated to last at least one year after completion of just six hours of treatment.

Safety

The Reiki community contends that there are no negative effects of this therapy and no medical contraindication. A review of the research literature reveals no evidence of negative effects or contraindication. However, one research team did a related investigation.

A Canadian study examined the views of complementary and alternative medicine (CAM) groups on the need to demonstrate the effectiveness, safety, and cost-effectiveness of their therapies and practices.[15] Qualitative interviews were conducted with 22 representatives

Table 2

Four levels of Usui Reiki training

Level	What the student learns
Reiki class one	The history of Reiki How Reiki works How to do Reiki on one's self How to use Reiki on others
Reiki class two	Methods of sending distant Reiki How to incorporate the Reiki symbols into a healing practice How to empower goals
Advanced training	Adds additional tools Demonstrates energy exercises and movements to help the practitioner maintain health and well-being
Reiki Master training	Prepares the practitioner to teach Reiki and to pass attunements

of three CAM groups (chiropractic, homeopathy, and Reiki). There were striking differences in the views of the three sets of respondents. The chiropractors agreed that it was essential for their group to provide scientific evidence that their interventions work and that they are safe and cost-effective. The leaders of the homeopathic group were divided on these points and the Reiki respondents showed virtually no interest in undertaking such research.

Conclusion

Both knowledgeable care givers and recipients alike seem drawn to the practice and the effects of Reiki. Anecdotal reports suggest clinical benefits in certain situations, and many people receiving Reiki experience positive results from the therapy. However, to date, precise scientific validation is lacking for this increasingly popular therapy. Regardless, practitioners must be aware of the various therapies available to their patients, including Reiki, to help guide them through the expanding maze of treatment options.

Recommendation

Reiki is an energy medicine therapy that may offer benefits to those who seek it. Given that it is a non-invasive therapy with no known deleterious effects, it seems reasonable to tell patients and clients about this CAM therapy, especially those experiencing severe pain or debilitating disease. ❖

Dr. Keegan is Director, Holistic Nursing Consultants, Port Angeles, WA.

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CME Questions

CME Instructions: Physicians participate in this continuing medical education program by reading the articles, using the provided references for further research, and studying the CME questions. Participants should select what they believe to be the correct answers, then refer to the list of correct answers to test their knowledge. To clarify confusion surrounding any questions answered incorrectly, please consult the source material.

After completing this activity, participants must complete the evaluation form provided at the end of each semester (June and December) and return it in the reply envelope provided to receive a certificate of completion. When an evaluation form is received, a certificate will be mailed to the participant.

39. Only standardized extracts of butterbur that are free of pyrrolizidine alkaloids should be used to treat seasonal allergies.
a. True
b. False

40. The most commonly offered explanation for the effects of vitamin E on processes associated with heart disease involves inhibition of:
a. high-density lipoprotein cholesterol peroxidation.
b. low-density lipoprotein cholesterol peroxidation.
c. total cholesterol peroxidation.
d. All of the above

41. Although precise scientific validation of Reiki is currently lacking, a Canadian study indicates that Reiki practitioners are committed to providing scientific evidence of this CAM therapy.
a. True
b. False

Answers: 39. a, 40. b, 41. b.

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Clinical Briefs

With Comments from Russell H. Greenfield, MD

Multivitamins and AIDS

Source: Fawzi WW, et al. A randomized trial of multivitamin supplements and HIV disease progression and mortality. *N Engl J Med* 2004;351:23-32.

Goal: To determine whether vitamin and/or micronutrient supplementation has a beneficial effect on disease course in HIV-positive pregnant women.

Study Design: Double-blind, placebo-controlled trial using a factorial design.

Subjects: A total of 1,078 HIV-positive pregnant women in Tanzania.

Methods: Eligible subjects were randomized to receive one of four regimens: vitamin A alone (30 mg beta-carotene + 5,000 IU preformed vitamin A), a multivitamin not containing vitamin A (20 mg B_1, 20 mg B_2, 25 mg B_6, 100 mg niacin, 50 µg B_{12}, 500 mg vitamin C, 30 mg vitamin E, and 0.8 mg folic acid), the multivitamin plus vitamin A, and placebo. Blood tests were performed at study entry and every six months thereafter for measurement of T-cell subgroups. A random sample of 300 women was selected to assess the effects of supplements on viral load. The women were seen monthly at the study clinic, and stage of HIV was assessed according to World Health Organization (WHO) criteria. Survival was the primary outcome. Follow-up occurred for a median of 71 months.

Results: During the period of follow-up 343 women died, of those deaths 243 were deemed to be due to or related to AIDS. Of the 271 women who received multivitamins, 67 progressed to stage 4 disease or died as compared with 83/267 women who received placebo (24.7% vs. 31.1%). Adding vitamin A to the multivitamin regimen reduced some of the aforementioned benefits (26.1% died), while vitamin A alone produced effects not significantly different from those associated with placebo (29.0% died). The multivitamin regimen was also associated with reduced progression to WHO stage 4 disease and reduced progression to stage 3 disease or higher, and resulted in significantly higher CD4+ and CD8+ cell counts, as well as significantly lower viral loads.

Conclusion: Multivitamin supplementation significantly delays HIV disease progression in pregnant women.

Study strengths: Compliance with regimen was determined and was high in all groups (79% over the total follow-up period); excellent follow-up.

Study weaknesses: Cannot extrapolate results to those people already receiving antiretroviral therapy, nor to those who are relatively well nourished.

Of note: All women were offered standard doses of folic acid and iron; antiretroviral therapy was not offered to study participants (at time of study antiretroviral therapy was not available to the majority of women in Tanzania); the effect of multivitamins was strongest during the first two years, but beneficial effects were also observed at four years; multivitamins significantly reduced oral and gastrointestinal manifestations of HIV disease, including painful swallowing and dysentery, and lessened reported fatigue, rash, and acute upper respiratory tract infections; by contrast, vitamin A supplementation increased the risk of painful swallowing, and resulted in significantly lower CD8+ cell counts; dosages used in the multivitamin were multiples of the RDA for specific nutrients in response to the impaired absorption and increased metabolic utilization of nutrients known to be present in people with HIV; the annual retail cost of the multivitamins used in this study was $15 per person.

We knew that: More than 40 million people worldwide are infected with HIV, and less than 8% of the 6 million people with advanced AIDS eligible for antiretroviral treatment are receiving it; a study published earlier this year showed that administration of vitamin A to HIV-positive pregnant women results in a higher rate of transmission of HIV to the baby; observational studies strongly suggest a health benefit from multivitamin supplementation for HIV-positive men; oxidative stress increases HIV replication in vitro.

Comments: This well-done study addresses a low-cost intervention to help slow progression of one of the global scourges of the 21st century, and in a malnourished population of pregnant women, it appears to work. The researchers conclude that in HIV-positive pregnant women multivitamin supplementation delays the need for antiretroviral therapy, a treatment whose very mention brings up issues of cost and morality. The results of the study are compelling, and also speak to the need for supplementation specific to the needs of a given individual, since many multivitamin supplements contain vitamin A, now known to be potentially harmful to HIV-infected pregnant women and their offspring. While we await the results of similar studies performed in industrialized nations, it seems prudent to offer at least B-complex supplementation to people infected by HIV.

What to do with this article: Make copies to hand out to your peers. ❖

Supplement to *Alternative Medicine Alert*
September 2004

ALTERNATIVE MEDICINE ALERT™
A Clinician's Evidence-Based Guide to Alternative Therapies

A New Portrait of CAM Use in the United States

THE MOST COMPREHENSIVE AND RELIABLE FINDINGS TO DATE ON AMERICANS' USE OF COMplementary and alternative medicine (CAM) were released in May 2004 by the National Center for Complementary and Alternative Medicine (NCCAM) and the National Center for Health Statistics (NCHS, part of the Centers for Disease Control and Prevention). They came from the 2002 edition of the NCHS's National Health Interview Survey, an annual study of Americans' health- and illness-related experiences. The 2002 edition included detailed questions on CAM. It was completed by 31,044 adults aged 18 years or older from the U.S. civilian non-institutionalized population. [The full report is available at: http://nccam.nih.gov/news/camsurvey.]

CAM therapies included in the survey

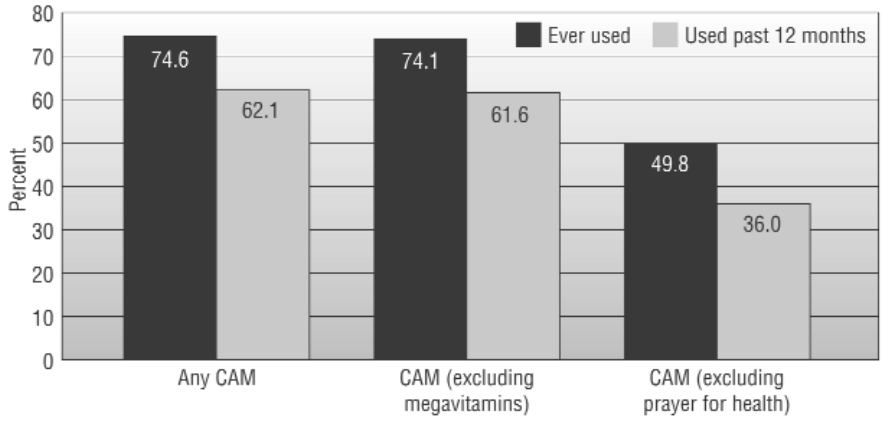
The survey included questions on various types of CAM therapies commonly used in the United States. These included provider-based therapies, such as acupuncture and chiropractic, and other therapies that do not require a provider, such as natural products, special diets, and megavitamin therapy. The results were analyzed including and excluding two therapies: 1) prayer specifically for health reasons and 2) megavitamins—because earlier national surveys did not consistently include these therapies. Unless noted otherwise, the statistics are for CAM use during the 12 months prior to the 2002 survey.

How many people use CAM

In the United States, 36% of adults are using some form of CAM. When megavitamin therapy and prayer specifically for health reasons are included in the definition of CAM, that number rises to 62%. *(See figure 1.)*

Table 1

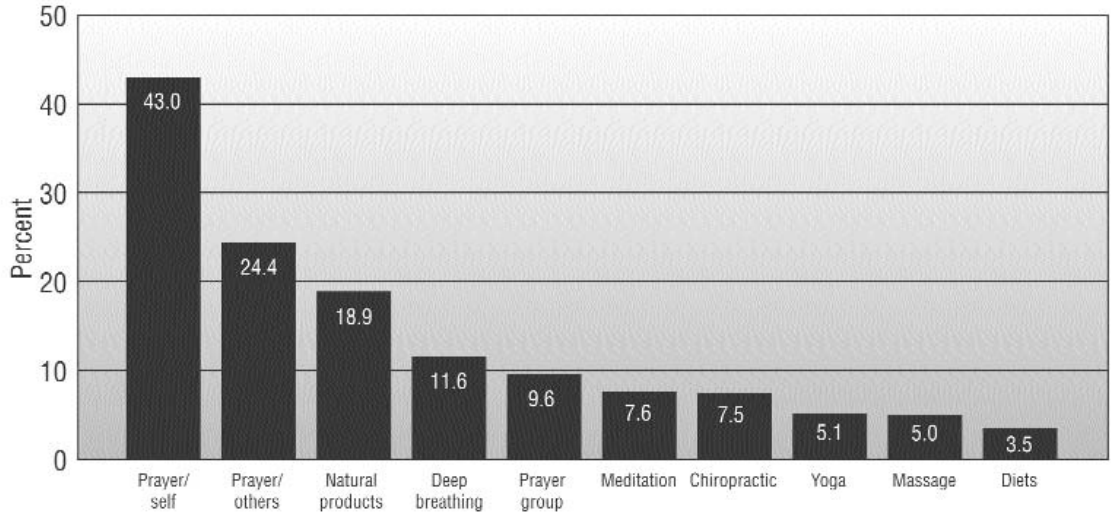
CAM use by U.S. adults—2002



Source: Barnes P, Powell-Griner E, McFann K, Nahin R. CDC Advance Data Report #343. Complementary and Alternative Medicine Use Among Adults: United States, 2002. May 27, 2004

Table 2

Ten most common CAM therapies



Source: Barnes P, Powell-Griner E, McFann K, Nahin R. CDC Advance Data Report #343. Complementary and Alternative Medicine Use Among Adults: United States, 2002. May 27, 2004

Who uses CAM most

Although CAM use spans people of all backgrounds, some people are more likely than others to use CAM. Overall, CAM use is greater by:

- Women than men
- People with higher educational levels
- People who have been hospitalized in the past year
- Former smokers, compared with current smokers or those who have never smoked

CAM domains/therapies used most

When prayer is included in the definition of CAM, the domain of mind-body medicine is the most commonly used domain (53%). When prayer is not included, biologically based therapies (22%) are more popular than mind-body medicine (17%).

Prayer specifically for health reasons was the most commonly used CAM therapy. *(See figure 2.)* Most people who use CAM use it to treat themselves, as only about 12% of the survey respondents sought care from a licensed CAM practitioner.

About 19% (or one-fifth) of the people surveyed used natural products.

Health conditions prompting CAM use

According to the survey, Americans are most likely to use CAM for back, neck, head, or joint aches, or other painful conditions; colds; anxiety or depression; gastrointestinal disorders; or sleeping problems. It appears that CAM is most often used to treat and/or prevent conditions involving chronic or recurring pain.

Reasons for using CAM

The survey asked people to select from five reasons to describe why they used CAM. Results were as follows (people could select more than one reason):

- CAM would improve health when used in combination with conventional medical treatments: 55%;
- CAM would be interesting to try: 50%;
- Conventional medical treatments would not help: 28%;
- A conventional medical professional suggested trying CAM: 26%;
- Conventional medical treatments are too expensive: 13%.

The survey found that most people use CAM along with conventional medicine rather than in place of conventional medicine.

Source: Barnes P, et al. CDC Advance Data Report #343. Complementary and Alternative Medicine Use Among Adults: United States, 2002. May 27, 2004.