

# ALTERNATIVE MEDICINE ALERT™

*The Clinician's Evidence-Based Guide to Complementary Therapies*

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## Yogurt for Vaginitis

*By Nassim Assefi, MD*

**V**AGINITIS IS ONE OF THE MOST COMMON REASONS A WOMAN VISITS a gynecologist, and has been estimated to be the cause of 10 million patient visits each year.<sup>1</sup> Bacterial vaginosis (BV) and yeast infections are the leading etiologies of vaginitis in women of reproductive age, comprising approximately 50% and 25% of cases, respectively.<sup>2</sup> With the availability of over-the-counter topical antifungals and a growing armamentarium of alternative medicines, many women attempt self-treatment of vaginal symptoms before consulting a health care provider.

Yogurt is one of the cheapest and oldest known non-prescription remedies for vaginitis, first advocated by Nobel-laureate Elie Metchnikoff in 1908.<sup>3</sup> While medical professionals have vacillated about the value of yogurt-delivered *Lactobacillus* therapy for vaginitis over the last century, patients have continued to use yogurt (both orally ingested and douches) to treat their vaginal symptoms. An increased understanding of vaginal physiology and pathogens supports the biological plausibility of using exogenous *Lactobacillus* from yogurt to restore vaginal health; however, limited in vitro studies and clinical trials have yet to warm the tepid enthusiasm of conventional practitioners to this common alternative practice.

### Pathophysiology

The estrogenated vagina can be thought of as a fortress fiercely guarded by lactobacilli, which produce lactic acid (to maintain a hostile vaginal pH of 4.0-4.5) and bactericidal metabolites, such as hydrogen peroxide (H<sub>2</sub>O<sub>2</sub>) as weapons against other organisms. Yeast vaginitis occurs when there is disruption of the vaginal ecosystem and overgrowth of candida organisms. BV results from the proliferation of *Gardnerella vaginalis* and anaerobic bacteria.

Successful oral yogurt therapy depends upon the survival of lactobacilli through gastrointestinal processing, as therapeutic vaginal colonization is thought to occur from anal migration. Treatment of vaginitis by *Lactobacillus* recolonization was first described in 1933, and continues to be the rationale for using yogurt, which is a natural source of lactobacilli, for this purpose. Effective topical yogurt treatment (yogurt douching), requires adherence of exogenous lactobacilli to vaginal cells.

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Although knowledge of gram-positive rods dominating the flora of healthy vaginas dates back to the late 1800s,<sup>4</sup> clearly defining the genus *Lactobacillus* continues to be a challenging and arduous process. *Lactobacillus acidophilus*, the predominant *Lactobacillus* species in the normal vagina, generates H<sub>2</sub>O<sub>2</sub>, which correlates with decreased BV and yeast vaginitis when compared to non-H<sub>2</sub>O<sub>2</sub>-producing lactobacilli, and also survives digestion. However, *Lactobacillus* strains from yogurt, including *L. acidophilus*, have been shown to manifest poorer adherence to vaginal epithelial cells than strains derived from the human vagina.<sup>5</sup>

## Clinical Trials

Barriers to accepting yogurt therapy for vaginitis reflect several factors: the ready availability of topical and oral antimicrobials (metronidazole and clindamycin for BV and antifungals for yeast infections); the uneven quality of yogurt products on the market; and the paucity of randomized, double-blinded placebo-controlled trials.<sup>6</sup> Nevertheless, the common use of alternative medicines for vaginitis (42% of chronic vaginitis patients in one study, of which 50% reported using acidophilus pills and 21% used yogurt<sup>7</sup>), the recurrence of symptoms (especially BV) despite antimicrobial therapy,<sup>2</sup> and the

emphasis on avoiding medicines during pregnancy<sup>8</sup> have created interest in the medical community regarding the possibility of *Lactobacillus* replacement by yogurt delivery for vaginitis.

Literature searches of Pubmed, Cochrane Collaboration, CINDAHL, Biosis, Embase, and the *Alternative Medicine Alert* Index using “yogurt,” “yogurt,” “yoghurt,” and “vaginitis” as key words revealed four relevant studies.

In an open, seven-day trial by Neri and colleagues, 64 pregnant women with BV were randomized to twice-daily doses of yogurt douches or acetic acid tampons.<sup>9</sup> Twenty women refusing treatment served as controls. Yogurt douches were made by adding a small amount of water to 10-15 mL of commercially available yogurt (cultures added after pasteurization included more than 10<sup>8</sup> Colony Forming Units (CFU)/mL of *L. acidophilus*) and inserting the syringe of liquefied yogurt 4-6 cm into the vagina. The effect of treatment was evaluated four and eight weeks after completion; BV cure was defined by the absence of Amsel criteria (foul-smelling discharge, pH > 4.5, positive amine test, and clue cells on wet mount).<sup>10</sup> Two months after treatment, 88% of women using yogurt douches versus 38% of women using acetic acid tampons and 5% of women without treatment were free of BV (P < 0.05 between all groups).

Strengths of the study include using both clinical and laboratory outcomes for eradication of BV and a relatively long follow-up period. Weaknesses include choosing non-randomized patients as the no-treatment/natural history controls, as well as the lack of a pasteurized/non-*Lactobacillus* yogurt arm to show that *Lactobacillus* was the active ingredient in the therapy.

A smaller, uncontrolled Japanese study of vaginally delivered yogurt for women with BV showed clinical and laboratory eradication of BV in 55% of cases after three days of douching.<sup>11</sup>

Hilton and associates conducted a crossover study of *Lactobacillus acidophilus*-containing yogurt (8 ounces daily) versus a yogurt-free diet for women with recurrent candidal vaginitis.<sup>12</sup> Infections were defined as clinical vaginal complaints with a Gram-positive stain for budding yeast, pseudohyphae, an acidic vaginal pH, and a positive culture for *Candida* species; colonization was a positive vaginal culture with no clinical evidence of vaginitis.

Of 21 eligible patients, only 13 complied with the protocol (eight patients originally assigned to the yogurt arm refused to enter the control phase six months later due to subjective and clinically confirmed improvement). The resulting one-arm investigation followed 13

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### Questions & Comments

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Table	
Sample fat-free, plain yogurt labeling	
Serving size	8 oz
Calories/serving	110
Calcium/serving	350 mg
Protein/serving	13 g
Carbohydrates/serving	16 g
Live Cultures Added	
	<i>Streptococcus thermophilus</i>
	<i>Lactobacillus bulgaricus</i>
	<i>Lactobacillus acidophilus</i>
	<i>Bifidobacterium bifidum</i>
	<i>Lactobacillus rhamnosus</i>
	<i>Lactobacillus casei</i>
	<i>Bifidobacterium longum</i>
	<i>Bifidobacterium infantis</i>

patients with culture-verified candidal vaginitis for one year: six months with and six months without yogurt ingestion. A significant, threefold decrease in candidal infections was observed in those consuming yogurt, corroborated by a similar decrease in vaginal colonization. Neither patients nor clinical interviewers were blinded to the treatment assignment, although culture results were reported by technicians blinded to identity.

Finally, in a crossover trial, Shalev's group studied the frequency of vaginitis in women with either yeast infections, BV, or both, who were randomized to consuming roughly 8 ounces of yogurt daily either with or without (pasteurized) live *Lactobacillus* cultures (at least  $10^8$  CFU/mL of *L. acidophilus*).<sup>13</sup> Patients were examined on at least monthly intervals by providers blinded to the type of yogurt ingested. Candidal vaginitis was defined as in Hilton's study; BV was defined by Amsel criteria.

After two months, there was no significant difference between candidal vaginitis or colonization in the two groups, but BV episodes were significantly decreased (approximately 50%) in those consuming *Lactobacillus*-containing yogurt. However, of 46 patients randomized to each of the two groups, only seven completed the entire protocol, and the difference in BV infections observed between the two groups decreased with time.

#### Adverse Effects, Allergy, and Drug Interactions

To date, no serious side effects have been reported following ingestion of or vaginal douching with yogurt.<sup>14</sup>

Although there have been a few cases of lactobacillema reported in severely immunosuppressed individuals, all cases have responded to standard antibiotic therapy.<sup>6</sup> Douching, particularly high-pressure douching, has the potential to cause pelvic inflammatory disease, ectopic pregnancy, and peritonitis.<sup>15</sup> *Lactobacillus acidophilus*-containing yogurt should be taken 2-3 hours after an antibiotic dose to prevent the bacteria's death. Lactobacilli also have decreased efficacy in the presence of alcohol.<sup>15</sup> Finally, yogurt that contains milk or milk products added after fermentation (such as many of the yogurt products available in the United States) can produce gastrointestinal disturbance in lactose intolerant individuals.<sup>16</sup>

#### Dosage and Formulation

The delivery of lactobacilli by yogurt is problematic for several reasons. Yogurt is a food that is not regulated in terms of its composition, nor is it even fully understood. Although yogurt must contain *Lactobacillus bulgaricus* and *Streptococcus thermophilus* to be sold,<sup>17</sup> it may contain live bacterial cultures (which may or may not contain *L. acidophilus*, despite advertisements), be pasteurized, or have several added cultures following pasteurization (the most common scenario in today's commercially available yogurt). Furthermore, claims by dairy product manufacturers about the presence of certain *Lactobacilli* species do not always ring true when subjected to microbiological testing.<sup>18</sup>

Yogurt with the greatest therapeutic potential for treating vaginitis should include added cultures of H<sub>2</sub>O<sub>2</sub>-producing lactobacilli after pasteurization, preferably *L. acidophilus*. For lactose-intolerant individuals, yogurt products that are less processed and contain H<sub>2</sub>O<sub>2</sub>-producing lactobacilli, such as Bulgarian yogurt and kefir, will minimize gastrointestinal symptoms. It is unknown, though biologically unlikely, whether the fat content of the yogurt significantly affects *Lactobacillus* colonization.

The high dropout rates in the above studies, patient reluctance to apply messy topical yogurt therapy to the genital area, in vitro studies suggesting decreased adherence of yogurt-derived lactobacilli to vaginal cells, and the potential dangers and medical bias associated with douching suggest daily oral ingestion of yogurt is the optimal mode of delivery. Although there is a paucity of high-quality studies suggesting standardized dosing and duration of treatment, eating 8 oz of yogurt daily for one week for acute vaginitis (and one month for chronic vaginitis) will eradicate BV or candidal symptoms in those women for whom yogurt therapy will be effective.

## Conclusion

Two studies of yogurt douching and one study of orally ingested yogurt suggest clinical benefit for BV.

Oral yogurt ingestion may improve both candidal infections and bacterial vaginosis, and carries very little risk. However, a lack of trials comparing yogurt therapy to conventional treatments, inconsistencies in product quality, the paucity of high-quality studies upon which standardized dosing and duration of treatment can be established, and the fact that a significant portion of women with vaginitis erroneously self-diagnose candida or BV when they instead have gonorrhea, chlamydia, and trichomonas limit its universal recommendation.

## Recommendation

Patients with confirmed diagnoses of yeast vaginitis or bacterial vaginosis may benefit from daily ingestion of 8 oz of yogurt with live H<sub>2</sub>O<sub>2</sub>-producing lactobacilli for treatment of their current and chronic vaginal symptoms; yogurt douching also is likely to be beneficial, but is accompanied by potentially greater risks. ❖

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## References

1. Kent HL. Epidemiology of vaginitis. *Am J Obstet Gynecol* 1991;165:1168-1176.
2. Sobel JD. Overview of vaginitis. *UpToDate Electronic Database (Version 9.2)* 2001.
3. Metchnikoff E. *The Prolongation of Life: Optimistic Studies*. New York: G.P. Putnam; 1908:161-183.
4. Doderlein A. Die scheidensekretuntersuchungen. *Zentralbl Gynakol* 1894;18:10-14.
5. Wood JR, et al. In vitro adherence of *Lactobacillus* species to vaginal epithelial cells. *Am J Obstet Gynecol* 1985;153:740-743.
6. Elmer GW. Probiotics: "Living drugs." *Am J Health Syst Pharm* 2001;58:1101-1109.
7. Nyirjesy P, et al. Over-the-counter and alternative medicines in the treatment of chronic vaginal symptoms. *Obstet Gynecol* 1997;90:50-53.
8. Neri A, et al. Bacterial vaginosis: Drugs versus alternative treatment. *Obstet Gynecol Survey* 1994;49: 809-813.
9. Neri A, et al. Bacterial vaginosis in pregnancy treated with yoghurt. *Acta Obstet Gynecol Scand* 1993;72: 17-19.
10. Amsel R, et al. Nonspecific vaginitis. Diagnostic criteria and microbial and epidemiologic associations. *Am J Med* 1983;74:14-22.

11. Chimura T, et al. Ecological treatment of bacterial vaginosis [in Japanese]. *Jpn J Antibiot* 1995;48: 432-436.
12. Hilton E, et al. Ingestion of yogurt containing *Lactobacillus acidophilus* as prophylaxis for candidal vaginitis. *Ann Intern Med* 1992;116:353-357.
13. Shalev E, et al. Ingestion of yogurt containing *Lactobacillus acidophilus* compared with pasteurized yogurt as prophylaxis for recurrent candidal vaginitis and bacterial vaginosis. *Arch Fam Med* 1996;5:593-596.
14. Udani J. *Lactobacillus acidophilus* to prevent traveler's diarrhea. *Altern Med Alert* 1999;2:53-55.
15. Rosenberg MJ, et al. Vaginal douching. Who and why? *J Repro Med* 1991;36:753-758.
16. Grand RJ, et al. Lactose intolerance. *UpToDate Electronic Database (Version 9.2)* 2001.
17. Food and Drug Administration HHS. Code of Federal Regulations. Office of the Federal Register National Archives and Records Administration. 1991. 21CFR, 131.200 (yogurt).
18. Hughes VL, Hillier SL. Microbiologic characteristics of *Lactobacillus* products used for colonization of the vagina. *Obstet Gynecol* 1990;75:244-248.

## B-Complex Vitamins for Depression

*By Barak Gaster, MD*

WHEN FRIENDS FIND OUT HOW LITTLE TIME IS SPENT learning about diet and nutrition in medical school, they usually are surprised. Patients also come to the clinic with questions about what they should eat and what vitamins they should take, and they may be shocked to find their doctors are not sure what to say.

Among patients suffering from depression, the situation can be more intense. "But what about B-complex vitamins, Doc? I've heard that's all I need to turn me around." Meeting a question like that with a blank stare can put a kink in your therapeutic relationship.

Although depression researchers have been interested in a possible role for B-complex vitamins since the 1960s, few clinical trials have been performed. Thus, although B-vitamin supplementation in patients with depression may be helpful and appears to be safe, there is no good evidence that such treatment is effective.

### Mechanism of Action

The B-complex vitamins are a group of substances that must be obtained from the diet. They serve

Table	
The B-complex vitamins	
<b>B Vitamins Implicated in Depression</b>	<b>Recommended Intake* Males/Females</b>
Thiamin (B <sub>1</sub> )	1.2/1.1 mg/d
Riboflavin (B <sub>2</sub> )	1.3/1.1 mg/d
Pyridoxine (B <sub>6</sub> )	1.3/1.3 mg/d
Cobalamin (B <sub>12</sub> )	2.4/2.4 mcg/d
Folate (B <sub>9</sub> )	0.4/0.4 mg/d
<b>B Vitamins Not Implicated in Depression</b>	
Niacin (B <sub>3</sub> )	16/14 mg/d
Pantothenic acid (B <sub>5</sub> )	5/5 mg/d
* Higher limits for those 14 years and older to reduce risk of deficiency.	
<i>Source: Dietary Reference Intakes 2000: Applications in Dietary Assessment.</i> Washington, DC: National Academy Press; 2000.	

as cofactors for numerous enzymatic pathways in the body. B vitamins have been linked to depression by virtue of their central role in the synthesis of neurotransmitters.<sup>1</sup> Specifically, thiamin (B<sub>1</sub>), riboflavin (B<sub>2</sub>), pyridoxine (B<sub>6</sub>), cobalamin (B<sub>12</sub>), and folate (sometimes referred to as B<sub>9</sub>) all participate in important steps in the synthetic pathways of norepinephrine, dopamine, and serotonin (see Table).

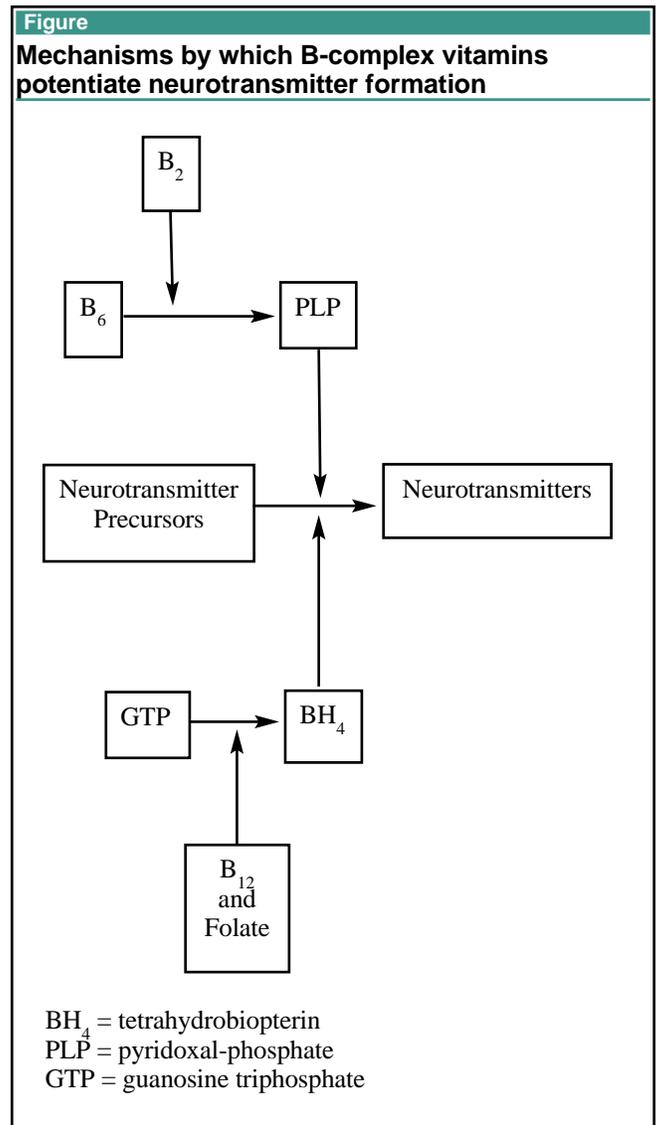
Riboflavin is essential for the biochemical conversion of pyridoxine to pyridoxal-phosphate (PLP) (see Figure). PLP in turn is a co-enzyme for several decarboxylases needed for neurotransmitter synthesis. Cobalamin and folate are required for the formation of tetrahydrobiopterin (BH<sub>4</sub>), which is a hydroxylase cofactor necessary for serotonin synthesis. Thiamin has less of a clear link to depression, although it plays a role in the formation of another neurotransmitter, acetylcholine.

### Pharmacokinetics

All of the B-complex vitamins are water-soluble. They are easily absorbed from the gastrointestinal tract and are metabolized in the liver.

### Efficacy Data

Several studies in the 1980s found that up to 30% of patients with depression have vitamin deficiencies, mostly vitamin B<sub>12</sub> and folate.<sup>2</sup> Studies which used a more accurate test for folate deficiency,<sup>3</sup> red blood cell (RBC) folate concentration, have reported lower rates (10-15%).<sup>4</sup> Whether the vitamin deficiency is primary or secondary to the depression is open to question; however, depressed patients often have poor nutritional intake.



There has been only one randomized placebo-controlled study of a B vitamin for depression. Godfrey et al randomized 24 patients with major depression and RBC folate levels below 200 mcg/L to 15 mg/d of methylfolate (a precursor to folate) or placebo.<sup>5</sup> All patients received standard antidepressants. At six months, there was a significant improvement in the methylfolate patients on a 4-point clinical outcome scale ( $P < 0.01$ ). There were no significant differences in Hamilton Depression Scale score between the groups, although there was a trend in favor of the methylfolate group.

In a trial of patients with unipolar or bipolar mania being treated with lithium, Coppen randomized patients to 200 mcg of folate per day or to placebo.<sup>6</sup> At one year, the patients with unipolar mania who took folate had significantly lower depression scores than those who did not; the patients with bipolar mania who took folate actually had a trend toward worsened depression. The authors did not report aggregate data of the two groups.

## Adverse Effects

Even at very high doses, most of the B-complex vitamins that play a role in depression appear to be safe. Reports of neurotoxicity from pyridoxine have involved doses of 1-6 g/d over several weeks,<sup>7</sup> although doses as low as 200 mg/d may cause such symptoms as well.<sup>8</sup> At very high doses, folate has been reported to cause altered sleep patterns, irritability, nausea, and pruritus.

## Drug Interactions

Anticonvulsants and oral contraceptives may lower folate levels.<sup>9</sup> Pyridoxine can interfere with levodopa's anti-Parkinsonian effects.

## Formulation

B-complex vitamins are available in virtually all multivitamins in doses that are calibrated to meet 100% of the recommended daily intake. In addition, formulations containing B-complex vitamins alone are available.

Folic acid is available in many different tablet dosages: 0.1, 0.2, 0.4, 0.8, and 1.0 mg. The best dietary sources of folic acid are vegetables, especially green leafy vegetables, potatoes, cereal products, fruits, and organ meats (e.g., liver, kidney). Methylfolate is not commercially available in the United States.

## Dosage

Given the lack of clinical trial data, no clear dosing recommendations can be made for B-complex vitamins for depression beyond the recommended daily intakes listed in Table 1.

## Conclusion

Although there are theoretical reasons to think that B-complex deficiency may play a role in depression, the evidence supporting the efficacy of vitamin supplementation in the treatment of depression is lacking. There is no evidence to suggest that supplementation within the range of recommended daily intakes is harmful; however, there are at least theoretical reasons to believe that it may be helpful.

## Recommendation

Given that vitamins are safe, reliably regulated in the United States, and relatively inexpensive, it is reasonable to advise patients with depression to take one or two multivitamins per day that include B-complexes. However, patients should be advised that this should be adjunctive treatment only, and should not be the sole therapy they get for their depression.

Providers should consider checking B<sub>12</sub> and RBC folate levels in patients who are depressed and have poor diets and then treat any specific deficiencies that are

found. Advise patients to steer clear of expensive, megadose formulations of vitamins for the treatment of depression; there is no evidence to suggest that such therapies are effective. ❖

## References

1. Petrie WM, Ban TA. Vitamins in psychiatry. Do they have a role? *Drugs* 1985;30:58-65.
2. Alpert JE, Fava M. Nutrition and depression: The role of folate. *Nutr Rev* 1997;55:145-149.
3. Abou-Saleh MT, Coppen A. Serum and red blood cell folate in depression. *Acta Psychiatr Scand* 1989;80:78-82.
4. Bottiglieri T. Folate, vitamin B<sub>12</sub>, and neuropsychiatric disorders. *Nutr Rev* 1996;54:382-390.
5. Godfrey PS, et al. Enhancement of recovery from psychiatric illness by methylfolate. *Lancet* 1990;336:392-395.
6. Coppen A, et al. Folic acid enhances lithium prophylaxis. *J Affect Disord* 1986;10:9-13.
7. Clinician Fact Sheet: The B vitamins, Part III. *Altern Med Alert* 2001;4(4):S1-2.
8. Parry GJ, Bredesen DE. Sensory neuropathy with low-dose pyridoxine. *Neurology* 1985;35:1466-1468.
9. Schumann K. Interactions between drugs and vitamins at advanced age. *Int J Vitam Nutr Res* 1999;69:173-178.

## Acupuncture for Weight Management

By Judith Balk, MD, FACOG

**O**BESITY IS A MALADAPTIVE INCREASE IN THE AMOUNT of energy stored as fat. The prevalence of obesity in the United States is high. Complications from obesity include insulin resistance, noninsulin-dependent diabetes mellitus, hypertension, atherogenic lipid profile, coronary vascular disease, stroke, gout, exacerbation of arthritis, and many other diseases. The etiology of obesity is multifactorial, and as such, the treatment is often multifaceted.

The main goal of obesity treatment is to lower energy intake below that of energy expenditure. Conservative approaches, such as diet, nutrition education, behavior modification, and exercise, may be used. Self-help groups include Overeaters Anonymous, and commercial programs include Weight Watchers. The attrition rate of commercial programs is very high: 50% at six weeks and 70% at 12 weeks.<sup>1</sup>

Commercial programs do not have high success rates for most participants. Other treatment approaches include pharmacotherapy, surgery, lifestyle modification, and acupuncture. Acupuncture has been used rarely to treat obesity; roughly 1% of acupuncture consultations to British traditional acupuncturists are for the treatment of obesity.<sup>2</sup>

### Traditional Chinese Medicine and Obesity

Traditional Chinese medicine (TCM) differs from Western medicine in its perspective of disease. In TCM, the main causes are due to imbalances of chi, and treatment is based on the particular imbalance.<sup>3</sup> For instance, obesity with shortness of breath, general lassitude, and puffiness of the lower limbs belongs to the category of dampness in the spleen and stagnation of phlegm. Obesity with overeating, strong body composition, and dry stools belongs to excessive heat in the spleen and stomach. Obesity with bulimia, irregular menstruation, and a dark purplish tongue belongs to the qi stagnation and stasis of blood category.

Herbal concoctions are prescribed to treat the appropriate syndrome. Acupuncture also may be used, and points on the body and on the ear are common. Ear acupuncture also is called auricular acupuncture, and may include the use of acupuncture needles, tacks held in place by tape, staples, transcutaneous electrical nerve stimulation units, or acupressure. (*See Table.*)

### Mechanism of Action

Several mechanisms have been proposed to explain acupuncture's anecdotal success in treating weight loss. Acupuncture appears to normalize the sympathetic-adrenal and hypothalamus-pituitary-adrenal systems in overweight adults.<sup>4</sup> The authors suggest that this may regulate the metabolism of carbohydrate, lipid, and protein, and enhance central nervous system excitation.

Appetite and feeding are controlled in a very complex manner by the brain. Two areas in particular are involved: the ventromedial nucleus of the hypothalamus (VMH) and the lateral hypothalamus (LHA). The VMH is thought to be the satiety center, whereas the LHA is thought to be the feeding center. Acupuncture may activate the satiety center in the brain.<sup>5</sup>

A different mechanism may be mediated through the vagus nerve. One author suggests that innervation of the concha by the auricular branch of the vagus nerve may explain the beneficial effects of acupuncture.<sup>6</sup> Dung hypothesizes that mechanical stimulation of the auricular nerve causes a dispatch of neuronal impulses to the central nervous system via the vagus nerve.<sup>6</sup> These impulses can interfere with an appetite signal coming

Table		
Commonly used auricular acupuncture points <sup>16</sup>		
Point	Location	Function
Lung	Inferior concha	Relieves respiratory eating disorders and drug addiction problems such as smoking withdrawal, cocaine addiction, and alcoholism.
Stomach	Conchal ridge	Relieves eating disorders, diarrhea, gastritis, and indigestion.
Hunger (also called appetite control)	Tragus	Diminishes appetite and facilitates weight reduction.
Mouth	Inferior concha	Relieves eating disorders, mouth ulcers, cold sores, and glossitis.
Shen Men	Triangular fossa	Alleviates stress, pain, anxiety, depression, insomnia, and restlessness. Supports all other auricular points.

from the gastrointestinal tract. Thus, the appetite signal may be partially blocked, resulting in less hunger.

Less hunger also could arise if gastric emptying is slowed. A clip that attaches to the tragus prolongs gastric peristalsis time.<sup>7</sup> Gastric peristalsis returned to baseline when the clips were removed.

Another mechanism proposed is via serotonin. Serotonin has been shown to increase tone in the smooth muscle of the gastric wall. Auricular acupuncture points are thought to raise serotonin concentrations and produce endorphins and dopamine.<sup>8</sup>

### Animal Studies

In a controlled study, obese rats were randomized to receive acupuncture or not, and were compared to a non-obese control group.<sup>9</sup> Rats were treated once daily with body acupuncture for 12 days. The animals in the acupuncture group lost weight; the other two groups gained weight. Because the obese control group did not receive body acupuncture, it is possible that the needles caused the weight loss. The second part of the study entailed brain monitoring: Electric activity of the brain satiety center increased with acupuncture. This could translate into greater satiety and lower caloric intake.

Auricular stimulation caused changes in LHA and VMH in obese and normal rats.<sup>10</sup> LHA neuronal activity was depressed and VMH activity was excited

with auricular acupuncture. Satiety was more affected than appetite. Changes in brain activity correlated with the degree of obesity, suggesting that acupuncture would not have much effect in a non-obese population. Another study found that the VMH was stimulated with auricular acupuncture of therapeutic points (e.g., stomach and lung) and the rats lost weight.<sup>5</sup> When non-therapeutic acupuncture points were needled, the VMH was not affected nor did the rats lose weight. Also, after the VMH was lesioned, acupuncture had no effect on body weight. Thus, it appears that the satiety center may be involved in decreasing weight.

### Human Studies

Five clinical trials that utilized a placebo control group were identified. Marked heterogeneity in treatment protocols exists. Also, the outcome variables differ between studies. Ideally, an objective outcome, such as correctly measured weight, is used; using a subjective outcome variable such as hunger or appetite is less ideal. For research purposes, an objective outcome is necessary to make firm conclusions.

One clinical trial included 24 subjects ranging from 5-33% above ideal body weight.<sup>11</sup> Subjects were treated with three different protocols in a random order over a nine-week period. The three groups were treated in the following manners: mouth and stomach points unilaterally; mouth and stomach points bilaterally; or ankle and shoulder points, which were the placebo control points. Both active point groups lowered their percentage above ideal body weight by 0.9; the placebo group had no change. This difference was not statistically significant. Analysis of questionnaires showed variable responses of acupuncture on appetite, ranging from no effect to a sensation of early satiety, with generally decreased hunger. An animal study that ran in conjunction with this clinical trial demonstrated no weight loss with acupuncture.

Allison et al also used weight change as the primary outcome variable.<sup>12</sup> An auricular acupuncture device was studied in a placebo-controlled trial of 96 subjects for 12 weeks. The device was a molded ear piece with six strategically placed bumps. The placebo group wore a wrist acupuncture device. It is not stated which acupuncture points were stimulated with the device. Subjects in the treatment group lost 1.28 kg, and those in the control group lost 0.63 kg. This difference was not statistically significant. Ear problems, such as pain and redness were higher in the treatment group. Self-reported weight loss was higher in the treatment group than in the placebo group ( $P = 0.048$ ).

A different clinical trial enrolled 30 subjects.<sup>13</sup> All subjects were given a 1000 Kcal/d diet. Three groups were formed: bilateral stimulation of the stomach point;

bilateral stimulation of the hunger point; and bilateral stimulation of a placebo point. Subjects were treated for 25 min/d, five days per week, for three successive weeks, and assessed for ability to follow the prescribed diet regimen. The majority of subjects in the active groups (80% and 70% for the stomach and hunger points, respectively) were able to follow the diet regimen; only 20% in the placebo group were able to follow the diet. Among subjects unable to follow the diet, weight did not change. Those that followed the diet lost weight (range: 1-4 kg). The amount of weight loss did not differ for those who were able to follow the diet. The authors concluded that the effect of acupuncture on body weight reduction was secondary to motivating the subject to stay on a diet.

Another randomized, placebo-controlled trial included 120 subjects for six weeks.<sup>14</sup> Subjects were asked not to diet, and if the auricular acupuncture point was not effective after two weeks, it was changed. Of those who failed treatment with the stomach, lung, or placebo points, 70% had abatement of hunger and weight loss when treated with the hunger point. The lack of a true control group, as the control group was changed prior to the end of the study, and the use of a subjective main outcome variable limit the usefulness of this study.

Recently, a pilot study evaluating the effects of minimal acupuncture versus moxibustion and acupuncture was conducted.<sup>15</sup> Forty obese subjects were randomized to one of two weekly acupuncture sessions. A very high dropout rate existed; 30% of patients in the treatment group and 60% of those in the placebo group dropped out. No differences existed between groups for weight loss, but anxiety and depression improved in the treatment group compared to the placebo group. The high dropout rates limit the usefulness of this study.

### Risks

The main risks of auricular acupuncture include tenderness, infection, and chondritis. Long-term application of needles can result in a "cauliflower ear." As with acupuncture elsewhere on the body, some patients become drowsy after auricular acupuncture.

### Conclusion

No firm evidence exists to suggest that acupuncture improves weight-loss efforts; the clinical trials that do exist have methodological issues. If weight loss were as simple as not eating when one was not hungry, then obesity would not be the problem it is today. Thus, even if it is possible to affect the satiety center via acupuncture, weight management must address much more than just the sensation of satiety.

## Recommendation

The current state of knowledge neither supports nor refutes the possibility that acupuncture is beneficial for weight loss. The goal of weight loss efforts should be to lower energy intake below that of energy expenditure. Means of achieving this should be long-lasting and multifaceted. Acupuncture cannot reliably be continued daily or weekly for long periods of time and hence it is not likely to be of long-term benefit. ❖

## References

1. Boeck M. Eating Disorders. In: Leppert P, Howard F, eds. *Primary Care for Women*. Vol. 1. Philadelphia, PA: Lippincott-Raven; 1997:910-918.
2. Wadlow G, Peringer E. Retrospective survey of patients of practitioners of traditional Chinese acupuncture in the UK. *Complement Ther Med* 1996;4:1-7.
3. Qingfu S, Youqiang X. A survey of the treatment of obesity by Traditional Chinese Medicine. *J Trad Chin Med* 1993;13:124-128.
4. Zhicheng L, Fengmin S, et al. Effect of acupuncture on weight loss evaluated by adrenal function. *J Trad Chin Med* 1993;13:169-173.
5. Asamoto S, Takeshige C. Activation of the satiety center by auricular acupuncture point stimulation. *Brain Res Bull* 1992;29:157-164.
6. Dung H. Role of the vagus nerve in weight reduction through auricular acupuncture. *Am J Acupuncture* 1986;14:249-254.
7. Choy D, Eidschenk E. Effect of tragus clips on gastric peristalsis: A pilot study. *J Altern Complement Med* 1998;4:399-403.
8. Richards D, Marley J. Stimulation of auricular acupuncture points in weight loss. *Aust Fam Physician* 1998;27:S73-S77.
9. Mei Z, et al. The time-effect relationship of central action in acupuncture treatment for weight reduction. *J Trad Chin Med* 2000;20:26-29.
10. Shiraishi T, et al. Effects of auricular stimulation on feeding-related hypothalamic neuronal activity in normal and obese rats. *Brain Res Bull* 1995;36:141-148.
11. Mok MS, et al. Treatment of obesity by acupuncture. *Am J Clin Nutr* 1976;29:832-835.
12. Allison DB, et al. A randomised placebo-controlled clinical trial of an acupressure device for weight loss. *Int J Obes Relat Metal Disord* 1995;19:653-658.
13. Shafshak TS. Electroacupuncture and exercise in body weight reduction and their application in rehabilitating patients with knee osteoarthritis. *Am J Chin Med* 1994;23:15-25.
14. Giller R. Auricular acupuncture and weight reduction. A controlled trial. *Am J Acupuncture* 1975;3:151-153.
15. Mazzoni R, et al. Failure of acupuncture in the treatment of obesity: A pilot study. *Eat Weight Disord* 1999;4:198-202.
16. Oleson T. *Auriculotherapy Manual: Chinese and Western Systems of Ear Acupuncture*. Vol. 1. Los Angeles: Health Care Alternatives; 1998:260.

## CME Questions

18. Which of the following is false regarding lactobacilli found in the vagina?
  - a. The predominant species in healthy vaginas is *L. acidophilus*.
  - b. Hydrogen-peroxide-producing species are associated with fewer vaginal infections.
  - c. Lactobacilli create a vaginal ecosystem with an alkaline pH.
  - d. Species found in the vagina adhere to vaginal epithelial cells more tightly than species found in yogurt.
19. The most common cause of vaginitis in a reproductive-age women is:
  - a. candidal vaginitis (yeast infection).
  - b. trichomonas vaginalis (trichomoniasis).
  - c. bacterial vaginosis.
  - d. atrophic vaginitis.
20. Which vitamin has not been implicated in depression?
  - a. Vitamin B<sub>12</sub>
  - b. Vitamin B<sub>6</sub>
  - c. Vitamin B<sub>5</sub>
  - d. Folate
21. How might B vitamins help patients with depression?
  - a. They can act as neurotransmitters.
  - b. They can facilitate the synthesis of neurotransmitters.
  - c. They inhibit the uptake of neurotransmitters.
  - d. They are transformed into neurotransmitters.
22. Which statement best reflects the role of B vitamins in the treatment of depression?
  - a. They are adjunctive therapy to other treatment modalities.
  - b. They are first-line therapy in patients found to have vitamin deficiency.
  - c. They are second-line therapy when other therapies do not work.
23. The main goal of the treatment of obesity is:
  - a. to increase fitness level.
  - b. to lower energy intake below that of energy expenditure.
  - c. to lower body mass index.
24. Which of the following mechanisms of action have been postulated to explain acupuncture's effects on weight loss?
  - a. Acupuncture normalizes the hypothalamic-pituitary-adrenal axis.
  - b. Acupuncture normalizes the sympathetic-adrenal axis.
  - c. Acupuncture is serotonin-mediated.
  - d. Acupuncture is vagus nerve-mediated.
  - e. All of the above

## Cardiovascular Risk and Garlic

**Source:** Ackermann RT, et al. Garlic shows promise for improving some cardiovascular risk factors. *Arch Intern Med* 2001;161:813-824.

TO SUMMARIZE THE EFFECTS OF GARLIC on several cardiovascular-related factors and to note its adverse effects, the authors of this study identified English and non-English citations from 11 electronic databases, references, manufacturers, and experts published between January 1966 and February 2000 (depending on the database searched). Reports of cardiovascular-related effects were limited to randomized controlled trials lasting at least four weeks. Reports of adverse effects were not limited by study design.

From 1,798 pertinent records, 45 randomized trials and 73 additional studies were identified that report adverse events. Two physicians abstracted outcomes and assessed adequacy of randomization, blinding, and handling of dropouts. Standardized mean differences of lipid outcomes from placebo-controlled trials were adjusted for baseline differences and pooled using random effects methods.

Compared with placebo, garlic preparations may lead to small reductions in the total cholesterol level at one month (range of average pooled reductions, 0.03-0.45 mmol/L [1.2-17.3 mg/dL]) and at three months (range of average pooled reductions 0.32-0.66 mmol/L [12.4-25.4 mg/dL]), but not at six months. Changes in low-density lipoprotein (LDL) levels and triglyceride levels paralleled total cholesterol level results; no statistically significant changes in high-density lipoprotein levels were observed.

Trials also reported significant reductions in platelet aggregation and mixed effects on blood pressure outcomes. No effects on glycemically-related

outcomes were found. Proven adverse effects included malodorous breath and body odor. Other unproven effects included flatulence, esophageal and abdominal pain, allergic reactions, and bleeding.

These trials suggest possible small short-term benefits of garlic on some lipid and antiplatelet factors, insignificant effects on blood pressure, and no effect on glucose levels. Conclusions regarding clinical significance are limited by the marginal quality and short duration of many trials and by the unpredictable release and inadequate definition of active constituents in study preparations.

### COMMENT

This highly rigorous meta-analysis of sorts from the University of Texas in San Antonio tried to chew and swallow the garlic literature whole, and emerged with bad breath, but happy. The authors scrutinized "...the internal validity of trials using oral garlic preparations, focused on the importance of differences among various preparations, and comprehensively summarize multiple reported cardiovascular-related effects and potential adverse effects of various oral garlic preparations."

Just the terms used to search the literature give you an idea of how hard they had to look to find everything: "2-propenesulfenic acid," "aglio," "ajo," "ajoene," "alisat," "allicin," "alliinase," "Allium sativum," "allyl mercaptan," "diallyl disulphide," "diallyl sulfide," "diallyl sulphide," "dipropyl disulphide," "dipropyl sulphide," "garlic," "garlic extract," "garlic oil," "knoblauch," "Kwai," "Kyolic," "S-allyl cysteine," "thioallyl derivative," "thiosulfinates," and "vinyl dithiin."

The quality of the 34 trials with double-blind designs was all over the map. Only six studies noted intention-to-treat analyses or reported no dropouts. Different preparations were common (odor-free/odoriferous, dehydrated/not, tablet/powder/oil, standardized/not).

Combining all studies, regardless of garlic preparation, showed that compared with placebo the total cholesterol level and LDL were reduced modestly (see data in the abstract above). Average reductions after 20-24 weeks of treatment were not statistically significant (all garlic preparations, n = 6). The same was true for triglycerides, without 24 week follow-up.

No statistically significant effects were reported for glycosylated hemoglobin, serum insulin and C-peptide levels. Four of 10 trials reported modest but significant decreases in platelet aggregation with garlic treatment compared with placebo.

Approximately half of the trials reported adverse effects—bad breath or body odor (delicately phrased as "malodorous breath or body odor [as perceived by themselves or others]") was the most common.

What makes garlic good medically? From a cardiovascular perspective, many experts think it's the same component (allicin) that gives its bouquet such magic—which is only created and released on smashing, mincing, dicing, crushing, or chewing the clove. Unfortunately, allicin and alliin are unstable, and they cannot be put in a pill reliably, yet. Of course, there also are issues of soil composition, growth conditions, harvesting procedures, and plant processing.

### Recommendation

Without better and better described randomization procedures, adequate (multi-year) trial durations, and thoughtful, opaque blinding to treatment administration and outcome assessments, garlic-as-medicine research cannot bloom.

These authors are experts at evidence-based medicine, and find that some garlic of any kind, if used regularly, likely helps decrease low-density lipoprotein—just a little. Consider it.

It's a good reason to go to [www.garliclife.com](http://www.garliclife.com) for inspiration, and use the stinking rose in cooking happily. ❖

## Perioperative Use of Herbal Products

**Source:** Ang-Lee MK, et al. Herbal medicines and perioperative care. *JAMA* 2001; 286:208-216.

**W**IDESPREAD USE OF HERBAL MEDICATIONS among the presurgical population may have a negative impact on perioperative patient care.

The literature on commonly used herbal medications was reviewed in the context of the perioperative period to attempt to provide rational strategies for managing their preoperative use.

The MEDLINE and Cochrane Collaboration databases were searched for articles published between January 1966 and December 2000 using the search terms “herbal medicine,” “phytotherapy,” and “alternative medicine” and the names of the 16 most commonly used herbal medications. Additional data sources were obtained from manual searches of recent journal articles and textbooks.

Studies, case reports, and reviews were selected that address the safety and pharmacology of eight commonly used herbal medications for which safety information pertinent to the perioperative period was available.

Safety, pharmacodynamic, and pharmacokinetic information was extracted from the selected literature and any discrepancies were resolved.

Echinacea, ephedra, garlic, ginkgo, ginseng, kava, St. John’s wort, and valerian are commonly used herbal medications that may pose a concern during the perioperative period. Complications can arise from these herbs’ direct and pharmacodynamic or pharmacokinetic effects. 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.

During the preoperative evaluation, physicians should explicitly elicit and document a history of herbal medication use. Physicians should be familiar with the potential perioperative effects of the commonly used herbal medications to prevent, recognize, and treat potentially serious problems associated with their use and discontinuation.

### COMMENT

This article received a lot of media attention. Is it, as Dr. Andrew Weil says, “...more herbal alarmism from conventional physicians”? Or is it, as the Tufts University Health and Nutrition Letter claims, “Herbs and Surgery: A Risky Combination”?

Because operative patients appear to use supplements more often than the general population, and because nearly three-quarters of patients have been shown to omit their supplements from pre-op histories and evaluations, there’s more than a little reason to be concerned. These University of Chicago investigators found no randomized, controlled trials about herbs and the perioperative period. So they reviewed everything else they could find, including textbooks and case reports—not the only literature available, but among the best available in the medical literature (the authors didn’t appear to investigate other literatures, which is part of Dr. Weil’s complaint). Here are their (excerpted) take-home points:

1. Patients who may require perioperative immunosuppression, such as those awaiting organ transplantation, should be counseled to avoid taking echinacea.
2. Ephedra’s sympathomimetic effects have been associated with more than 1,070 reported adverse events, including fatal cardiac and central nervous system complications. Ephedra’s elimination half-life is 5.2 hours.
3. Garlic inhibits platelet aggregation in a dose-dependent fashion; patients should discontinue use of garlic at least seven days prior to surgery, especially if postoperative bleeding is a particular concern or other platelet inhibitors are given.

4. Ginkgo appears to inhibit platelet-activating factor; the elimination half-lives of the terpenoids (active compounds) after oral administration are between three and 10 hours. Patients should discontinue taking ginkgo at least 36 hours prior to surgery.
5. Platelet inhibition caused by ginseng may be irreversible; it is probably prudent to recommend that patients discontinue ginseng use at least seven days prior to surgery. Actions are attributed to the ginsenosides that belong to a group of compounds known as steroidal saponins.
6. Kavalactones have dose-dependent effects on the central nervous system; peak plasma levels occur 1.8 hours after an oral dose, and the elimination half-life of kavalactones is nine hours. Kava may potentiate the sedative effects of anesthetics; patients taking kava should discontinue use at least 24 hours prior to surgery.
7. St John’s wort exerts its effects by inhibiting serotonin, norepinephrine, and dopamine reuptake by neurons and by inducing the cytochrome isoform P4503A4. Hypericin and hyperforin, thought to be the active ingredients, have median elimination half-lives of 43.1 and 9.0 hours, respectively. Patients should discontinue use at least five days prior to surgery.
8. Valerian produces dose-dependent sedation and hypnosis, and carries the risk of benzodiazepine-like withdrawal. A several-week, pre-op taper is advised, or benzodiazepines can be used to treat withdrawal symptoms should they develop during the postoperative period.

### Recommendation

Although it’s true that prescription medication likely has much more effect than herbs on most intra- and perioperative adverse effects (with the possible exception of St. John’s wort), an alarm ought to be sounded about these herbs. Herbs are medications. Treat them as such—especially in your patients who may be surgical candidates. ❖

## Nutrient Intake and Risk of Cataract

**Source:** Jacques PF, et al. Long-term nutrient intake and early age-related nuclear lens opacities. *Arch Ophthalmol* 2001;119:1009-1019.

**T**O ASSESS THE RELATION BETWEEN usual nutrient intake and subsequently diagnosed age-related nuclear lens opacities, 478 nondiabetic women ages 53-73 years from the Boston, MA, area without previously diagnosed cataracts were sampled from the Nurses' Health Study (NHS) cohort.

Usual nutrient intake was calculated as the average intake from five food frequency questionnaires that were collected during a 13- to 15-year period before the evaluation of lens opacities. The duration of vitamin supplement use was determined from seven questionnaires collected during this same period. Nuclear opacity was defined as a nuclear opalescence grade 2.5 or higher using the Lens Opacification Classification System III.

The prevalence of nuclear opacification was significantly lower in the highest nutrient intake quintile category relative to the lowest quintile category for vitamin C ( $P < 0.001$ ), vitamin E ( $P = 0.02$ ), riboflavin ( $P = 0.005$ ), folate ( $P = 0.009$ ), beta-carotene ( $P = 0.04$ ), and lutein/zeaxanthin ( $P = 0.03$ ). After adjustment for other nutrients, only vitamin C intake remained significantly associated ( $P = 0.003$  for trend) with the prevalence of nuclear opacities. The prevalence of nuclear opacities was significantly lower ( $P < 0.001$ ) in the highest vitamin C intake quintile category relative to the lowest quintile category (odds ratio [OR], 0.31; 95% confidence interval [CI], 0.16-0.58).

There also were statistically significant trends of decreasing the prevalence

of nuclear opacities with increasing duration of use of vitamin C ( $P = 0.004$  for trend), vitamin E ( $P = 0.03$  for trend), and multivitamin ( $P = 0.04$  for trend) supplements. Only duration of vitamin C supplement use remained significantly associated with nuclear opacities after mutual adjustment for use of vitamin E ( $P = 0.05$  for trend) or multivitamin ( $P = 0.02$  for trend) supplements.

The prevalence of nuclear opacities was significantly lower ( $P = 0.004$ ) for women who used a vitamin C supplement for 10 or more years relative to women who never used vitamin C supplements (OR, 0.36; 95% CI, 0.18-0.72). Plasma measures of vitamins C and E taken at the eye examination also were inversely associated with the prevalence of nuclear opacities.

These results provide additional evidence that antioxidant nutrients play a role in the prevention of age-related nuclear lens opacities.

### ■ COMMENT

The development of most cataracts is now thought to be oxidative in etiology. Though most researchers are uncertain about how much good antioxidant nutrients might do in the prevention of cataract, they're actively trying to make sense of conflicting reports. And well ahead are patients, who generally are not devouring butternut squash, broccoli, and red bell peppers, but are more than willing to try the multivitamin on sale at CVS (which, by the way, can have real merit).

The Nutrition and Vision Project (NVP) is part of the NHS cohort. This huge epidemiological study is retrospective. It calculates usual nutrient intake, including supplements, from five food frequency questionnaires that were collected during a 13- to 15-year period. Exclusions included those with cataract or diabetes. The cohort was significant-

ly more likely to have fewer pack-years of smoking and was slightly more likely to use vitamin E supplements between 1980 and 1995; the cohort was slightly younger and of a slightly lower body mass index than those excluded—all factors which might bias the results in favor of less cataract formation.

But in the study, there were differences. In the quintile with the lowest nutrient intake for vitamin C (mean, 140 mg), there were the most cataracts; those with the highest intake of vitamin C (mean 362 mg) had the fewest cataracts. The low for vitamin E was 6.7 mg; the high for vitamin E was 91 mg: Cataracts were inversely associated. These levels are based on plasma measurements. In fact, these cataract associations for vitamin C were only true for women with the highest (or the lowest) quintile for more than 10 years, and other antioxidants may contribute.

As the authors say, "a significantly lower risk of opacities is not seen until vitamin C supplements are used for 10 or more years... (and) lutein/zeaxanthin intake above 2.4 mg/d may have a lower risk of nuclear cataract. Lutein and zeaxanthin are the predominant carotenoids found in the human eye lens. However, this association was not clearly independent of the relation between vitamin C and nuclear opacities."

### Recommendation

Women at risk for cataract formation may benefit from 300 mg or more of vitamin C daily; given its half-life, it's advisable to take a day's vitamin C in divided doses. Two kiwis have double the vitamin C (148 mg) of an average navel orange (75 mg), but the same number of calories. Red and yellow sweet bell peppers have 4-6 times as much vitamin C as green peppers. And they may well be just as good as tablets for cataract prevention. Or better. ❖

In Future Issues:

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## Potassium and Iodine

**T**HE FOOD AND DRUG ADMINISTRATION NOW PERMITS FOODS THAT ARE HIGH IN POTASSIUM (350 mg/serving) and low in sodium, saturated fat, and cholesterol to include labeling claims that they might reduce the risk of stroke and the risk of developing high blood pressure.

### Intake Recommendations

The normal adult daily requirement and usual dietary intake of potassium is 40-80 mEq.

### Food Sources

Dietary sources of potassium include potatoes, bananas, cantaloupe, grapefruit, oranges, prunes, prune juice, tomato juice and paste, honeydew melon, molasses, bamboo shoots, chard, and cooked spinach.

### Mechanism of Action

- Potassium plays a role in many body functions, including fluid balance, electrodynamic cell activity, isotonicity, and enzymatic reactions.
- Potassium also is involved in nerve impulse transmission; cardiac, smooth, and skeletal muscle contraction; renal function; tissue and carbohydrate synthesis; and gastric secretion.

### Clinical Uses

- Orally, potassium is used to treat and prevent hypokalemia; to produce urinary alkalinization; to reduce blood pressure in people with hypertension; to reduce the risk of stroke; and to treat hypercalciuria.
- Intravenously, potassium is used to treat and prevent hypokalemia; arrhythmias, including atrial tachycardia and ventricular arrhythmias; and myocardial infarction.

### Formulation and Dosage

- Potassium levels should be maintained between 3.5 and 5 mEq/L and should be monitored on an individual basis using serum potassium levels.
- To prevent hypokalemia: 20 mEq/d.
- To treat hypokalemia: 40-100 mEq/d in divided doses.
- To treat hypercalciuria: 1 mEq/kg/d.
- To treat hypertension: 48-90 mEq/d.
- To treat urinary alkalization: 20-30 mEq qid of potassium citrate.
- Intravenous potassium products are available by prescription.

### Adverse Effects/Toxicity

- Oral and intravenous potassium may cause stomach upset, nausea, diarrhea, vomiting, flatulence, ulcerations, and hyperkalemia. Large doses of potassium may cause paresthesias, generalized weakness, flaccid paralysis, listlessness, vertigo, mental confusion, hypotension, cardiac arrhythmias, heart block, and death.

### Interactions/Nutrient Depletion

- Concomitant use of potassium with ACE inhibitors or potassium-sparing diuretics may increase potassium levels and the risk of hyperkalemia.

- Loop diuretics, thiazide diuretics, and stimulant laxatives increase potassium excretion and may cause hypokalemia.
- Bisacodyl may cause potassium loss in patients undergoing bowel-cleansing.
- In patients with renal dysfunction or using ACE inhibitors or potassium-sparing diuretics, potassium-containing foods and salt substitutes may increase potassium levels and the risk of hyperkalemia.
- Potassium supplementation may increase serum and urine potassium concentrations and test results.
- Oral potassium may reduce blood pressure and blood pressure readings.
- Potassium is contraindicated in people with untreated Addison's disease; heat cramps; acute dehydration; hyperkalemia; adynamia episodica hereditaria; severe renal impairment with oliguria, anuria, or azotemia; extensive tissue damage; or GI motility conditions.
- Potassium supplementation should be monitored closely in patients with heart and kidney disease, gastrointestinal bleeding disorders, and sickle cell anemia.

## Iodine

Iodine deficiency is the most common cause of preventable mental retardation and brain damage.

### Recommended Daily Allowance

Infants 0-6 mo: 110 mcg/d; 7-12 mo: 130 mcg/d. Children 1-8 y: 90 mcg/d; 9-13 y: 120 mcg/d. Men and women age 14 y and older: 150 mcg/d.

### Food Sources

The most readily available dietary source of iodine is iodized salt.

### Mechanism of Action

- Iodine kills microorganisms by oxidizing organic substrates.
- Iodine inhibits the release of thyroid hormone and also may increase respiratory secretions.

### Clinical Uses

- Orally, iodine is used to treat thyroid storm, radiation emergency associated with radioactive iodides, cutaneous sporotrichosis, hyperthyroidism, endemic goiter, fibrocystic breast disease, and diabetic foot ulcers.
- Topically, iodine is used as an antiseptic.

### Formulation and Dosage

- A 2% aqueous solution of iodine can be applied topically to affected skin.

- To prevent chemotherapy-induced mucositis, povidone iodine solution can be used as a mouth rinse several times daily.
- To treat fibrocystic breast disease, 0.08 mg/kg/d molecular iodine may be taken orally.

### Adverse Effects/Toxicity

- Oral use of iodine may result in angioedema, cutaneous and mucosal hemorrhage, fever, arthralgia, lymph node enlargement, eosinophilia, urticaria, thrombotic thrombocytopenic purpura, and fatal periarteritis.
- Large doses and/or chronic use can cause metallic taste; soreness in teeth and gums; burning in mouth and throat; increased salivation; coryza; sneezing; eye irritation and swelling; headache; cough; pulmonary edema; swelling of parotid and submaxillary glands; inflammation of the pharynx, larynx, and tonsils; acne; gastric upset; diarrhea; anorexia; and depression.
- Prolonged use of iodides can cause thyroid gland hyperplasia, thyroid adenoma, goiter, and severe hypothyroidism.

### Interactions/Nutrient Depletion

- Concomitant use of iodine with antithyroid drugs or lithium may result in additive hypothyroid activity and hypothyroidism.
- Concomitant use of iodine with potassium-containing products or ACE inhibitors may result in hyperkalemia.
- The di-iodotyrosine form of iodine can reduce thyroid volume in patients with goiter due to iodine deficiency.
- Potassium iodide can reduce serum thyroid hormone concentrations and test results.
- Chronic use or excessive amounts of iodides may cause or exacerbate thyroid gland hyperplasia, thyroid adenoma, goiter, and thyroidism.

### Resources

*International Council for the Control of Iodine Deficiency Disorders.* Available at: [www.tulane.edu/~idec/iddcomm.htm](http://www.tulane.edu/~idec/iddcomm.htm). Accessed September 19, 2001.

*Natural Medicines Comprehensive Database* [database online].

Stockton, CA: Therapeutic Research Center, Inc., 2000.

Pelton R, et al. *Drug-Induced Nutrient Depletion Handbook.*

Hudson, OH: Lexi-Comp; 1999.

*Dietary Reference Intakes for Vitamin A, Vitamin K, Arsenic, Boron, Chromium, Copper, Iodine, Iron, Manganese, Molybdenum, Nickel, Silicon, Vanadium, and Zinc.* Washington, DC: National Academy Press; 2001.