NUTRITION REPORTER

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JAMA Focuses on Alternative Medicine — With Fair and Often Favorable Research

The gulf between conventional and alternative medicine may have narrowed a bit, based on recent reports in the *Journal of the American Medical Association* and several other journals published by the AMA.

JAMA devoted a recent issue to alternative medicine. And while the studies were a mixed bag – some positive, some negative – the overall tone of the reports was balanced and conciliatory.

The lead article, by David M. Eisenberg, MD, of Beth Israel Deaconess Medical Center, Boston, followed up on his 1993 study on the use of alternative therapies. In his latest investigation, Eisenberg estimated that consumers had increased their use of alternative therapies by 47 percent between 1990 and 1997.

In 1997 an estimated four out of ten adults used some form of alternative therapy, including herbal medicine, massage, megavitamins, and homeopathy. In addition, consumers made far more visits to alternative medicine practitioners than to primary-care physicians—an estimated 629 million versus 386 million visits.

During the seven-year period between Eisenberg's two studies, the use of herbal remedies increased by 380 percent and high-dose vitamins by 130 percent, he wrote.

"Total 1997 out-of-pocket expenditures relating to alternative therapies was conservatively estimated at \$27.0 billion, which is comparable to the projected 1997 out-of-pocket expenditures for all US physician services," Eisenberg noted.

In other articles in *JAMA*, researchers reported both positive and negative findings in alternative medicine studies.

- A controlled study tested whether the chinese herb *Artemisia vulgaris*, when burned near the acupuncture point of a pregnant woman's little toe, would encourage a fetus to rotate away from a breech-birth position. Among the women undergoing the practice, called moxibustion, 30 percent more fetuses moved out of the breech position, compared with untreated women.
- A Chinese formula containing 20 herbs resulted in a significant improvement in irritable bowel syndrome, according to both subjects and attending physicians.
- A review of published studies found that the herb saw palmetto (*Serenoa repens*) improved symptoms of enlarged prostate and had fewer side effects than the drug finasteride. (See following article.)

- Acupuncture failed to improve peripheral neuropathy (nerve damage) in patients with HIV infections.
- A study of chiropractic manipulation found that the technique did not reduce tension headaches.
- The herb *Garcinia cambogia* turned out to be less effective than placebo in promoting weight loss.

In a letter to *JAMA*, researchers from the University of Florida and Case Western Reserve University reported that, in a survey of faculty members at six science center schools, more than half of the respondents had used one or more types of alternative medicine. Seventy-six percent of health profession (allied health) faculty members had used alternative medicine, followed by 74 percent of nursing, 65 percent of dentistry, 56 percent of pharmacy, and 52 percent of medicine faculty members.

Reference: Eisenberg DM, Davis RB, Ettner SL, et al., "Trends in Alternative Medicine Use in the United States, 1990-1997," *JAMA*, 1998;280:156—1575. The entire Nov. 11, 1998, issue of *JAMA* was devoted to alternative medicine.

Saw Palmetto Gets 'Thumbs Up' for BPH in Two Journal Reports

Two studies in major medical journals have acknowledged that, while more research would be great, the herb saw palmetto (*Serenoa repens*) does a fine job of reducing symptoms from benign prostatic hyperplasia (BPH). The condition, which typically affects men over the age of 50, interferes with urinary flow, resulting in nighttime urination and dribbling. Based on the evidence, saw palmetto is also safer than the drug finasteride.

Glenn S. Gerber, MD, of the University of Chicago Pritzker School of Medicine asked 50 men with BPH to take 160 mg of saw palmetto extract twice daily for six months. Four of the men, with severe urinary problems, dropped out of the study before it was completed. Of the remaining men, 10 reported urinary improvements after two months and 14 after four months.

After six months, 21 (46 percent) of the men described having improvements in urinary flow. Despite the reported improvements from the men in the study, Gerber was not able to document any objective improvements in bladder obstruction.

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In the other study, Timothy J. Wilt, MD, of the Minneapolis Veterans Affairs Medical Center and colleagues from other institutions pooled the results of 18 controlled trials of saw palmetto in almost 3,000 men. All but two of the studies were double-blind, and the length of treatment ranged from four to 48 weeks.

The evidence suggested that "extracts from the saw palmetto plant, *S. repens*, improve urinary tract symptoms and flow measures in men with BPH," Wilt wrote. "Compared with finasteride, *S. repens* produces similar improvements in urinary tract symptoms and flow measures, has fewer adverse treatment effects, and costs less."

Saw palmetto caused impotence in only 1.1 percent of the men in the studies, whereas finasteride caused impotence in 4.9 percent of men taking it.

The risk of BPH increases with age, and it may affect 40 percent of men over the age of 70. The annual cost of treating the condition is estimated at \$2 billion in the United States.

"Phytotherapeutic agents represent nearly half the medications dispensed for treatment of BPH in Italy...In Germany and Austria, phytotherapy is the first-line treatment for mild-to-moderate lower urinary tract symptoms and represents more than 90% of all drugs prescribed for the treatment of BPH," noted Wilt.

References: Gerber GS, Zagaja GP, Bales GT, et al., "Saw palmetto (*Serenoa repens*) in men with lower urinary tract symptoms: effects on urodynamic parameters and voiding symptoms," *Urology*, 1998;51:1003-1007. Wilt TJ, Shani A, Stark G, et al., "Saw palmetto extracts for treatment of benign prostatic hyperplasia," *JAMA*, 1998;280:1604-1609.

Low B Vitamins, High Homocysteine Levels Linked to Alzheimer's

Homocysteine, a byproduct of protein metabolism, is established as an independent risk factor in heart disease and in multi-infarct dementia, the type of senility caused by mini-strokes. Now, British researchers have provided strong evidence that homocysteine may play a major role in the development of Alzheimer's disease, the major type of dementia.

Alzheimer's disease is generally characterized by a tangle of amyloid protein choking brain cells. It does, however, often coexist with multi-infarct dementia.

Robert Clarke, MD, of Oxford University, England, compared levels of homocysteine, folic acid, and vitamin B12 in 164 patients diagnosed with Alzheimer's (of whom 76 had histologically confirmed disease) and 108 healthy subjects.

Subjects with the highest blood homocysteine levels (more than 14 micromoles/liter) were 4.5 times more likely to develop Alzheimer's disease than those with

lower homocysteine levels (less than 11 micromoles/liter). People with low levels of folic acid and vitamin B12 were 3.3 and 4.3 times, respectively, more likely to develop Alzheimer's disease.

Many studies have shown that folic acid, vitamin B12 (and vitamin B6) can lower homocysteine levels in people.

In 43 patients with Alzheimer's disease, brain scans over three years showed a strong relationship between the disease and elevated homocysteine levels.

Reference: Clark R, Smith AD, Jobst KA, et al., "Folate, vitamin B12, and serum total homocysteine levels in confirmed Alzheimer's disease," *Archives of Neurology*, 1998;55:1449-1455.

Coenzyme Q10 Necessary When Taking 'Statin' Cholesterol Drugs

Coenzyme Q10, a vitamin-like nutrient found in foods and produced by the body, plays a crucial role in shuttling around electrons and protons in the mitochondria, the energy-producing organelles of cells. When CoQ10 levels are inadequate, cellular energy levels suffer and affect cell function. High doses of supplemental CoQ10 (~400 mg daily) are well established as a therapy for cardiomyopathy and heart failure and show promise as an immune-enhancing anti-cancer compound.

Yet a common class of cholesterol-lowering drugs, called statins, can interfere with CoQ10 synthesis in the body, according to an article by Emile G. Bliznakov, MD, and David J. Wilkins, PhD.

Statins limit cholesterol production by inhibiting the body's production of HMG-CoA reductase, an enzyme involved in cholesterol synthesis. But by blocking HMG-CoA reductase, statin drugs (e.g., lovastatin, simvastatin, and pravastatin) also interfere with downstream CoQ10 synthesis.

The irony, according to Bliznakov and Wilkins, is that by trying to lower cholesterol and reduce the risk of heart disease, statins may cause mitochondrial injury and increase the risk of heart failure, cancer, and other diseases.

"A survey of the abundant literature indicates strongly that some adverse effects result from inhibition of CoQ10 biosynthesis associated with statin administration and consequent CoQ10 deficiency," the researchers wrote. "Adjunctive CoQ10 support therapy should be considered for such patients...We also hope for the development of a new generation of cholesterol-reducing drugs that...do not inhibit CoQ10 biosynthesis."

Reference: Bliznakov EG and Wilkins DJ, "Biochemical and clinical consequences of inhibiting coenzyme Q10 biosynthesis by lipid-lowering HMG-CoA reductase inhibitors (statins): a critical overview," *Advances in Therapy*, 1998;15:218-228.

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Vitamin B3 Can Lower Fibrinogen Levels, Provide Vascular Benefits

Fibrinogen, a blood protein involved in clotting, is a major risk factor in peripheral vascular disease and likely coronary artery disease. A recent study, however, has shown that the B-vitamin niacin can lower fibrinogen levels.

Claire S. Philipp, MD, of the MDNH Robert Wood Johnson Medical School, New Brunswick, N.J., studied 35 subjects who had been given 1.5 to 3 grams of niacin, a form of vitamin B3, daily or an antioxidant formula for 48 weeks. "Niacin is a highly effective agent for increasing high-density lipoprotein (HDL) cholesterol and decreasing low-density lipoprotein (LDL) cholesterol and triglyceride levels," Philipp wrote.

Subjects taking niacin "exhibited significant decreases in fibrinogen and LDL levels and an increase in HDL levels after 48 weeks compared with subjects not taking niacin," Philipp found.

High levels of LDL, the so-called bad cholesterol, are associated with greater risk of heart disease, whereas high levels of HDL are linked with a low risk of disease.

The researchers suggested that niacin decreases the liver's production of LDL, which lowers fibrinogen levels.

Editor's note: Niacin triggers the release of histamine, which causes a temporary but intense bodywide flushing sensation. This flush decreases in intensity with regular niacin use. Niacinamide does not cause this flush; nor does it reduce cholesterol levels.

Reference: Philipp CS, Cisar LA, Saidi P, et al., "Effect of niacin supplementation on fibrinogen levels in patients with peripheral vascular disease," *American Journal of Cardiology*, 1998;82:697-699.

Higher Dietary Intake of Vitamins Associated with Healthier Lungs

Eating diets rich in vitamins can maintain good lung function and reduce the risk of lung cancer, two recent studies have shown.

In one study, U.S. and Chinese researchers compared diet and lung function in 3,000 people living in different rural communities in China. They sought to identify nutrients that might be protective against chronic obstructive pulmonary disease, which includes emphysema and chronic bronchitis.

People who ate foods containing about 151 mg of vitamin C daily – and had relatively high blood levels of the nutrient – had better lung function than people with lower vitamin C levels. Lung function was measured by forced expiratory volume in one second (FEV1) and forced vital lung capacity.

An additional increase of 100 mg of vitamin C daily was associated with still greater increases in FEV1 and forced vital lung capacity. No other nutrients in this

study were associated with lung function, according to Patricia A. Cassano, PhD, of Cornell University, Ithaca, N.Y.

In a separate study, David C. Christiani, MD, of the Harvard School of Public Health, analyzed the relationship between diet and upper lobe lung cancers in 328 surgical patients. Most lung cancers occur in the organ's upper lobes, which may be the result of less efficient delivery of nutrients through circulation, compared with the lung's lower lobes.

Using several statistical methods, Christiani found that vitamin E and yellow-orange vegetables reduced the risk of lung cancer. "Our data show that subjects who consumed fewer yellow-orange vegetables or less vitamin E are more likely to develop upper lobe tumors than lower lobe tumors," he wrote. Furthermore, the risk of upper lobe cancers was greater among people who smoked more and consumed relatively less vitamin E or fewer yellow-orange vegetables.

References: Hu G, Zhang X, Chen J, et al., "Dietary vitamin C intake and lung function in rural China," *American Journal of Epidemiology*, 1998;148:594-9. Lee BW, Wain JC, Kelsey KT, et al., "Association between diet and lung cancer location," *American Journal of Respiratory Care Medicine*, 1998;158:1197-1203.

Low Blood Magnesium Levels Raise Heart Risk – Mostly in Women

Low blood levels of magnesium are associated with an increased risk of coronary heart disease, according to a study of almost 14,000 middle-age adults.

Aaron R. Folson, MD, of the University of Minnesota, Minneapolis, analyzed blood and dietary levels of magnesium in men and women initially free of heart disease. Over four to seven years of follow up, 319 of the study participants developed heart disease.

Folson found that high blood levels of magnesium were strongly associated with a low risk of heart disease. Women with the highest blood magnesium levels were 56 percent less likely to develop heart disease. However, the apparent protective effect of magnesium was considerably weaker in men. Those with the highest blood magnesium levels had a 27 percent lower risk of developing heart disease.

Meanwhile, there was a weak association between dietary magnesium and protection against heart disease, and the correlation appeared only in men.

"Our strongest finding was that low serum magnesium is an independent predictor of coronary heart disease in women," Folson wrote.

Reference: Liao F, Folson AR, Brancati FL, "Is low magnesium concentration a risk factor for coronary heart disease? The Atherosclerosis Risk in Communities (ARIC) study," *American Heart Journal*, 1998;136:480-490.

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Quick Reviews of Recent Research

• Ketogenic diet helpful in epilepsy

The ketogenic diet, developed in the 1920s to control epileptic seizures, is a high-fat, low-protein, and low-carbohydrate regimen. The diet fell into disfavor with the advent of anticonvulsive drugs. Doctors placed 51 children, with 10 or more seizures monthly and unresponsive to drug therapy, on individualized ketogenic diets. After three months, the frequency of seizures decreased by more than half in 54 percent of the children. After one year, 40 percent of the children on the diet had more than a 50 percent decrease in seizures. Also after one year, five of the patients were completely free of seizures.

Vining EPG, et al., Archives of Neurology, 1998;55:1433-1437.

• Horse chestnut helpful in venous insufficiency

Chronic venous insufficiency is often caused by blood vessel blockages in the legs and results in lower leg cramps, pain, and edema in the calf and ankles. Extracts of the seeds of horse chestnut (*Aesculus* spp) have been a popular remedy for chronic venous insufficiency in Europe. In a review of double-blind studies, researchers found that horse chestnut seed extract was superior to placebo in all studies. Typically, leg circumference, leg pain, itching, and other symptoms declined.

Pittler MH, et al., Archives of Dermatology, 1998;134:1356-1360.

• Vitamin E helpful in diabetic neuropathy

Diabetics have a high risk of developing neuropathies, characterized by nerve numbness or pain. High levels of free radicals, possibly generated by the auto-oxidation of glucose, contribute to these neuropathies. Researchers asked 21 adult diabetics to take 900 mg of vitamin E or placebo daily for six months. During the study, they measured the speed of nerve signals, which typically slow down in diabetics. By the end of the study, nerve conduction speed improved significantly in two of the 12 diagnostic measures used to assess the patients. Tutuncu NB, et al., *Diabetes Care*, 1998;21:1915-1918.

Antioxidants good for the skin

In a comprehensive review of antioxidants in dermatology, researchers concluded that vitamin A, beta-carotene, vitamin C, and vitamin E can be helpful in preventing and treating sun damage to skin, skin cancer, and many other skin disorders.

Keller KL and Fenske NA, Journal of the American Academy of Dermatology, 1998;38:611-25.

• Cell study confirms alpha-lipoic acid's benefits

Alpha-lipoic acid, an antioxidant, is used in Germany to treat diabetic neuropathy. In a cell-culture

study, researchers found that alpha-lipoic acid enabled human red blood cells to metabolize glucose at twice the rate of untreated cells. Alphalipoic acid also reduced glycosylated hemoglobin (a marker of diabetic control) and increased levels of glucose-burning enzymes.

Jain SK and Lim G, Free Radical Biology and Medicine, 1998;25:S94, Abst #268.

• Review finds ginkgo helpful in Alzheimer's

Extracts of *Ginkgo biloba* are a popular treatment for poor memory and Alzheimer's disease. In a review of studies on ginkgo, researchers found that the herb did have a "modest" effect on cognition, based on Alzheimer's disease assessment tests. Many of the studies used 120 to 240 mg of ginkgo extract for three to six months.

Oken BS, et al., *Archives of Neurology*, 1998;55:1409-1415.

• Walking reduces risk of prostate problems

Walking two to three hours per week reduced the risk of benign prostatic hyperplasia (BPH) by 25 percent in a study of more than 3,700 men, ages 40 to 75 years. In general, physical activity reduced the risk of benign prostatic hyperplasia, surgery for BPH, and BPH symptoms by 25 percent.

Platz EA, et al., Archives of Internal Medicine, 1998;158:2349-2356.

• Vitamin B12 deficiency common, linked to pain

Researchers evaluated vitamin B12 levels in 303 veterans over the age of 65. Nineteen (6 percent) of the subjects were vitamin B12 deficient by strict laboratory definitions, and 49 (16 percent) were deficient as measured by broader definitions (including elevated levels of methyl malonic acid and homocysteine). Of nine symptomatic measures of B12 deficiency, only body pain was associated with low levels of the nutrient.

Bernard MA, et al., Journal of the American Geriatrics Society, 1998;46:1199-1206.

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