

# The NUTRITION REPORTER™

THE INDEPENDENT NEWSLETTER THAT REPORTS VITAMIN AND MINERAL THERAPIES © NOVEMBER 1998 VOL 9 NO 11 BY JACK CHALLEM

## Magnesium, Potassium Help Reduce Blood Pressure, Lower the Risk of Stroke

Magnesium and potassium, often overshadowed by antioxidants, play key roles in heart function and in the health of the cardiovascular system.

Yuhei Kawano, MD, and his colleagues at the National Cardiovascular Center, Japan, used magnesium supplements to treat 60 patients with hypertension. The patients, ages 33-74, had an average blood pressure of 140/90 mmHg. All were monitored while taking daily magnesium supplements (480 mg of elemental magnesium as part of 800 mg of magnesium oxide) for eight weeks and also while abstaining from supplements for an equal length of time. Most of the patients were also taking blood-pressure-lowering drugs.

Kawano found that "blood pressures were significantly lower during the magnesium supplementation period, although the differences were small." On average, blood pressures declined by 2.7/1.5 mmHg.

In a separate study, Frank M. Sacks, MD, of the Harvard School of Public Health, explored whether supplemental minerals could lower blood pressure in people with normal blood pressures, but who generally had low mineral intake. Previous studies had shown limited blood pressure-lowering effects when minerals were given to people with normal blood pressures.

Sacks and his colleagues gave daily supplements of calcium (1,200 mg), magnesium (336 mg) and potassium (1,600 mg), together or individually, or placebos to 300 women for 16 weeks. Neither calcium nor magnesium lowered blood pressure, but potassium did have a "modest" blood pressure-lowering effect.

In another Harvard study, Alberto Ascherio, MD, found that men consuming large amounts of potassium from foods or supplements had a 38 percent lower risk of stroke, compared with men consuming relatively little potassium.

Ascherio and his colleagues analyzed the diets of almost 44,000 men, ages 40-75 years old. During eight years of follow up, 328 of the men suffered strokes. While high levels of potassium stood out for their apparent protective properties, high intake of magnesium and cereal fiber were also linked to a lower risk of stroke.

Ascherio and his colleagues wrote, "although these data do not prove a causal relationship, they provide strong support for a preventive effect of diets rich in potassium and magnesium, and cereal fiber on stroke,

particularly among men with high blood pressure. Increased intake of potassium alone may decrease the risk of stroke, and perhaps potassium supplements for hypertensives should be more broadly considered."

References: Kawano Y, Matsuoka H, Takishita S, et al., "Effects of magnesium supplementation in hypertensive patients," *Hypertension*, 1998;32:260-265. Sacks FM, Willett WC, Smith A, et al., "Effect on blood pressure of potassium, calcium, and magnesium in women with low habitual intake," *Hypertension*, 1998;31:131-138. Ascherio A, Rimm EB, Hernan MA, et al., "Intake of potassium, magnesium, calcium, and fiber and risk of stroke among US men," *Circulation*, 1998;98:1198-1204. □

### More Findings Further Support the Heart Benefits of Vitamin E

Approaching the relationship of free radicals and coronary heart disease from a new angle, researchers have confirmed the protective effects of vitamin E.

In recent research, Garret A. FitzGerald, MD, of the University of Pennsylvania, Philadelphia, focused on measuring isoprostanes in the blood and urine of mice bred to develop a form of heart disease similar to that found in people. Isoprostanes are chemicals produced by free radical reactions, and high levels indicate lipid peroxidation (free radical damage to cholesterol and other fats) and overall oxidative stress.

The mice were given either a standard laboratory diet or a diet supplemented with 2,000 IU of vitamin E per kilogram (2.2 pounds) of food for 16 weeks.

Although vitamin E did not affect cholesterol or triglyceride levels, it did significantly reduce isoprostane levels in both blood and urine. Vitamin E supplementation also reduced the size of cholesterol deposits in the aortas of the mice, compared with untreated animals.

FitzGerald and his colleagues noted that their experiment confirmed the role of free radicals in heart disease and the protective effect of vitamin E, adding that "oral vitamin E significantly reduces disease progression, despite the continued presence of high cholesterol levels."

FitzGerald's findings could eventually lead to a simple urine test for isoprostanes – and thus, free radical stress – in people.

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Meanwhile, in a review article, Alvin C. Chan, PhD, of the University of Ottawa, Canada, summarized research supporting the role of vitamin E in treating heart disease. He noted that Evan Shute, MD, was the first physician to report, in 1946, vitamin E's benefits to the heart.

Chan outlined the steps involved in the development of heart disease, beginning with an injury to heart cells and the body's inflammatory response. The inflammation generates free radicals that, in turn, oxidize cholesterol. Next, byproducts of oxidized cholesterol trigger the activity of cell growth factors, which then promote the growth of smooth muscle cells. As the number of smooth muscle cells increases, they narrow blood vessels and restrict blood circulation.

"Vitamin E enrichment has been shown to retard LDL oxidation, inhibit the proliferation of smooth muscle cells, inhibit platelet adhesion and aggregation ...collectively, these biological functions of vitamin E may account for its protection against the development of atherosclerosis," Chan wrote.

References: Pratico D, Tangirala RK, Rader DJ, et al., "Vitamin E suppresses isoprostane generation in vivo and reduces atherosclerosis in ApoE-deficient mice," *Nature Medicine*, 1998;4:1189-1192. Chan AC, "Vitamin E and Atherosclerosis," *Journal of Nutrition*, 1998;128:1593-1596. □

## Vitamin C May Help in Hypertension, Coronary Spasms as Well

Two studies have underscored the benefits of vitamin C in preventing heart disease.

In one study, Christopher J. Bates, PhD, of the Dunn Nutrition Unit, Cambridge, England, found that high blood levels of vitamin C were associated with lower blood pressures and slower pulse rates.

Bates and his colleagues compared blood levels of various nutrients and blood pressure and pulse among 541 subjects. "The only nutrient found to be consistently inversely related to both blood pressure and pulse rate was vitamin C," Bates wrote.

Large quantities of vitamin C, from foods, were associated with a 5 percent decrease in systolic blood pressure and a 4 percent decrease in pulse rate.

In the other study, Kiyotaka Kugiyama, MD, of the Kumamoto University School of Medicine, Japan, investigated the effects of vitamin C on 32 patients with heart spasms, known also as coronary spastic angina. During coronary catheterization, Kugiyama and his colleagues infused acetylcholine into the hearts of these patients and 34 controls (patients without the condition) to induce heart spasms. Fifteen minutes later, some of the patients were then infused with vitamin C (directly into heart tissue).

Patients receiving vitamin C had a reduction in heart spasms and lower levels of thiobarbituric acid, a marker of free radicals.

References: Bates CJ, Walmsley CM, Prentice A, et al., "Does vitamin C reduce blood pressure? Results of a large study of people aged 65 or older," *Journal of Hypertension*, 1998;16:925-932. Kugiyama K, Motoyama T, Hirashima O, et al., "Vitamin C attenuates abnormal vasomotor reactivity in spasm coronary arteries in patients with coronary spastic angina," *Journal of the American College of Cardiology*, 1998;32:103-109. □

## Does Vitamin C Damage DNA? Researchers Do About Face—Sort Of

In April, THE NUTRITION REPORTER criticized a study claiming to have found that vitamin C supplements resulted in DNA damage. At the time, Ian D. Podmore, PhD, and his colleagues at the University of Leicester, England, reported that vitamin C supplements significantly increased damage to 8-oxoadenine and reduced damage to 8-oxoguanine, both markers of DNA damage. For the most part, newspapers reported the study without any critical evaluation of its findings.

Recently, *Nature* published two letters critical of Podmore's research. In his response, Podmore defended his research and the accuracy of his findings. However, in his conclusion, Podmore emphasized the overall benefits of vitamin C. In referring to the increase in damage to 8-oxoadenine, he concluded that such damage is "at least ten times less mutagenic than 8-oxoguanine, and hence our study shows an overall profound protective effect of this vitamin."

Podmore ID, Griffiths, HR, Herbert KE, et al., "Does vitamin C have a pro-oxidant effect?" *Nature*, 1998, 395:232. □

## Beta-Carotene, Related Nutrients May Reduce Risk of Heart Disease

Researchers have documented a strong association between high dietary intake of beta-carotene and associated nutrients and a low risk of heart disease.

Stephen B. Kritchevsky, PhD, of the University of Tennessee, Memphis, and his colleagues investigated the relationship between intake of dietary carotenoids and the occurrence of carotid artery plaques, a marker of heart disease, in almost 13,000 men and women.

In both men and women, high intake of carotenoid-rich foods were associated with a substantially lower prevalence of plaques. But after the researchers accounted for variables, women benefited the most from high dietary intake of carotenoids. In general, women had a 16 percent lower risk of developing blood vessel plaques. Women smokers benefited the most from a high-carotenoid diet, specifically with a 33 percent reduction in plaque risk.

Kritchevsky attributed most of the benefits to provitamin A carotenoids, chiefly beta-carotene. However, he acknowledged that other carotenoids, such as lutein, found in the same foods, may also contribute to a lower prevalence of plaque. The findings of the study, he wrote, "support the hypothesis that carotenoids or some other compound found in high-carotenoid foods may play a role in atherosclerotic plaque."

Reference: Kritchevsky SB, Tell GS, Shimakawa T, et al., "Provitamin A carotenoid intake and carotid artery plaques: the Atherosclerosis Risk in Communities Study," *American Journal of Clinical Nutrition*, 1998;68:726-733. □

## **Folic Acid Supplements May Reduce Risk of Developing Colon Cancer**

People can reduce their risk of colon cancer by 75 percent – just by taking a multivitamin with the B-vitamin folic acid for at least 15 years. That's the latest finding from Harvard University researchers, based on their analysis of data from the ongoing Nurses Health Study.

Edward Giovannucci, MD, ScD, compared vitamin intake and supplement use among 442 women with newly diagnosed cases of colon cancer and more than 88,000 women who did not develop the disease.

Giovannucci and his colleagues were able to distinguish between the effects of dietary folic acid, supplemental folic acid, and other vitamins and minerals found in multivitamin supplements.

Folic acid donates carbon and hydrogen molecules to a process called methylation, which is essential for the synthesis of DNA. Low folic acid levels lead to decreases in methylation and abnormalities in DNA synthesis and repair, which can set the stage for colon cancer.

"The inverse association between colon cancer and folate was stronger with supplemental folate than with dietary folate," Giovannucci wrote. "This may reflect the high level of folic acid in a typical supplement (400 mcg) and the high bioavailability of supplementary folate..."

Reference: Giovannucci E, Stampfer MJ, Colditz GA, et al., "Multivitamin use, folate, and colon cancer in women in the Nurses' Health Study," *Annals of Internal Medicine*, 1998;129:517-524. □

## **Low Doses of the Carotenoid Lutein May Curb Breast Cancer Growth**

Building on earlier studies, researchers have reported that small supplemental doses of lutein can inhibit the growth of breast cancers in mice. Lutein, a carotenoid related to beta-carotene, is found in kale and spinach.

Boon P. Chew, PhD, of Washington State University, Pullman, fed different groups of laboratory mice various supplemental dosages of lutein. The animals received lutein as 0.002, 0.02, 0.2, or 0.4 percent of their diet or no

lutein at all. After two weeks, the mice were injected with breast cancer cells.

The animals receiving lutein developed breast cancer later than did untreated animals. They also had a lower incidence of breast tumors, and their tumors were smaller than those of untreated mice.

However, a little lutein provided greater benefits than a lot of the nutrient. Animals consuming a diet with 0.002 percent lutein, the lowest amount, were the slowest to develop tumors. They also had the lowest incidence of tumors and the smallest tumors of all the mice.

Most of the unsupplemented mice developed tumors by 50 days after cancer cells were injected. In contrast, none of the mice fed 0.002 lutein had tumors by that time. "This suggests, for the first time, that lutein is not only capable of inhibited mammary tumor growth but possibly of preventing tumor initiation," Chew wrote.

In a separate study, British researchers reported that egg yolk and corn provided the highest percentage of lutein and zeaxanthin – more than 85 percent of the carotenoids in those foods. Corn contained the greatest amount of lutein and orange pepper provided the largest amount of zeaxanthin relative to other carotenoids. Kiwi fruit, grapes, spinach, orange juice, zucchini and other types of squash also provided large amounts of lutein and zeaxanthin.

Reference: Park JS, Chew BP, Wong TS, "Dietary lutein from marigold extract inhibits mammary tumor development in BALB/c mice," *Journal of Nutrition*, 1998;128:1650-1656. Sommerburg O, Keunen JE, Bird AC, et al., "Fruits and vegetables that are sources for lutein and zeaxanthin: the macular pigment in human eyes," *British Journal of Ophthalmology*, 1998;82:907-910. □

## **Women With Breast Cancer Lack CoQ10, a Vitamin-Like Nutrient**

Several clinical reports have found that large daily doses (390 mg) of coenzyme Q10 can prevent the recurrence of breast cancers in women. A team of French researchers have confirmed that women with breast cancer and other types of breast disease have low blood levels of CoQ10.

CoQ10, the core of the 1978 Nobel prize in chemistry, is a vitamin-like nutrient that plays a key role in producing energy in cells. Numerous studies have shown that it can increase the energy output of heart cells, and some researchers believe that it can also increase the activity of immune cells.

In the study, researchers analyzed blood levels of CoQ10 and vitamin E in 80 patients with carcinomas, 120 patients with noncancerous breast lesions (adenofibromas, dystrophies, and lipomas), and 253 healthy women.

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## Quick Reviews of Recent Research

### • Pycnogenol® enables blood vessels to relax

Nitric oxide (NO), the basis of the 1998 Nobel prize in medicine, can function as both a free radical and antioxidant. In the cardiovascular system, NO promotes relaxation of blood vessel walls, which in turn stimulates blood flow and reduces the risk of coronary artery disease. In a recent experiment, using blood vessels from laboratory rats, researchers found that Pycnogenol®, an extract from French maritime pine bark, increased NO levels and promoted blood vessel relaxation.

Fitzpatrick DF, et al., *Journal of Cardiovascular Pharmacology*, 1998;32:509-515.

### • Proanthocyanidins beneficial in UTIs

Cranberries have long been recommended for the prevention of urinary tract infections (UTIs). These berries contain flavonoids that prevent bacteria from adhering to the urinary tract. In a recent study, researchers found that related berries, including blueberries, contain a specific group of flavonoids, called proanthocyanidins, which account for this antibacterial activity. In laboratory experiments, both cranberries and blueberries showed similar effects in preventing bacterial adhesion.

Howell AB and Corsa N, *New England Journal of Medicine*, 1998;339:1085.

### • Red yeast lowers cholesterol levels

In a double-blind study, researchers asked 83 healthy subjects to take either 2.4 grams/day of a proprietary red yeast product (Cholestin-3) or a placebo for eight weeks. Both cholesterol and triglyceride blood levels declined significantly among subjects taking the red-yeast product. On average, cholesterol levels decreased from 254 to 208 mg/dl.

Heber D, et al., *FASEB Journal*, 1998;12(5):1201.

### • Cancer patients often use alternative treatments

In an analysis of 26 surveys from 13 countries, researchers found that a range of 7-64 percent of adult cancer patients used some type of alternative therapy, often in conjunction with conventional therapies. On average, 31 percent of adult cancer patients used some type of alternative therapy. The therapies included

## Coenzyme Q10 and Breast Cancer...

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They found that women with breast cancers or lesions consistently had low blood levels of CoQ10, but normal levels of vitamin E. "This suggests that even benign mammary cell growth is associated with decreased relative ubiquinone [CoQ10] plasma levels," the researchers wrote.

Reference: Jolliet P, Simon N, Barre J, et al., "Plasma coenzyme Q10 concentrations in breast cancer: prognosis and therapeutic consequences," *International Journal of Clinical Pharmacology and Therapeutics*, 1998;36:506-509. □

meditation, visualization, dietary changes, supplements, and herbal remedies.

Ernst E and Cassileth BR, *Cancer*, 1998;83:777-782.

### • Genistein plus zinc promotes bone development

Dietary genistein, a component of soy, increased bone development in elderly female laboratory rats. A combination of genistein and zinc further enhanced bone development.

Gao YH, et al., *General Pharmacology*, 1998;31:199-202.

### • B vitamins help relieve pain

Vitamins B1, B6, and B12 exert analgesic effects when given individually and especially when given in combination. They can be helpful in musculoskeletal pain and seem to potentiate the effects of nonsteroidal antiinflammatory drugs (NSAIDs).

Jurna I, *Schmerz*, 1998;12:136-141.

### • Soy foods associated with lower cholesterol

In a study of almost 5,000 Japanese men and women, researchers noted a significant relationship between high intake of soy foods and relatively low blood levels of total cholesterol.

Nagata C, et al., *Journal of Nutrition*, 1998;128:209-213.

### • Trace minerals improve burn recovery

Serious burns depress immunity, and infections are the leading cause of death after burns. In a study of burn patients, researchers found that intravenous supplementation of extra zinc, copper, and selenium resulted in a significant decrease in bronchopneumonia infections and in shorter hospital stays.

Berger MM, et al., *American Journal of Clinical Nutrition*, 1998;68:365-371.

### • Bilberry powerful antioxidant

Bilberry is a traditional remedy for eye and vascular disorders. In an experiment, the berries were found to quench hydroxyl and superoxide radicals and to inhibit the oxidation of fats.

Martin-Aragon S, et al., *Phytotherapy Research*, 1998;12 (Suppl):S104-S106.

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