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Little-Known Nutrients Play Major Roles in Bone Density, Preventing Osteoporosis

Based on advertising for dairy products, you might think that calcium is the only nutrient needed to build strong bones. But your body requires many other nutrients for normal bone development and density, and recent studies have highlighted two of them: vitamin K and hesperidin.

In recent years, increasing evidence has pointed to vitamin K playing a key role in bone health. An essential nutrient, it is needed for the normal clotting of blood. However, vitamin K is also required for the body's synthesis of several bone proteins, including osteocalcin. Contrary to common opinion, bone is a matrix of minerals and proteins, not solid minerals.

A team of researchers from the University of Maastricht, Netherlands, studied 155 women who were divided into three groups, with each group given a different supplement daily for three years. One supplement contained calcium, zinc, magnesium, and vitamin D. Another was identical except that it also contained 1 mg of vitamin K (phylloquinone, which is also found in leafy green vegetables). The third supplement was a placebo.

All of the women were between ages 50 and 60 and postmenopausal. The researchers measured their bone density in the femoral neck and lumbar spine before and after three years of supplementation.

The supplement containing vitamin K reduced bone loss in the femoral neck the most, by 1.7 percent compared with the placebo. The other supplement slowed bone loss by only 1.3 percent. However, neither supplement appeared to reduce bone loss in the lumbar spine, which the researchers wrote might have been because of technical difficulties in measuring bone density at that location.

In a separate study, Japanese researchers removed the ovaries of mice, a technique that mimics postmenopausal osteoporosis in women, and bone-mineral density decreased. But when mice were given supplemental hesperidin, an antioxidant flavonoid found in oranges and lemons, bone loss was largely prevented and normal bone levels of calcium, phosphorus, and zinc were maintained. In addition, total blood fats were lower in mice receiving supplemental hesperidin.

"These results suggest a possible role for citrus flavonoids in the prevention of lifestyle-related diseases because of their beneficial effects on bone and lipids," wrote Hiroshige Chiba, PhD, currently with Seitoku University, Japan.

References: Braam LA, Knapen MH, Geusens P, et al. Vitamin K1 supplementation retards bone loss in postmenopausal women between 50 and 60 years of age. *Calcified Tissue International*, 2003;73:21-26. Chiba H, Uekara M, Wu J, et al. Hesperidin, a citrus flavonoid, inhibits bone loss and decreases serum and hepatic lipid in ovariectomized mice. *Journal of Nutrition*, 2003;133:1892-1897.

Cooking Methods Can Raise or Lower Levels of Hazardous AGEs in the Body

Advanced glycation endproducts do exactly what their acronym – AGEs – suggests: they accelerate the aging process. Also known as "glycotoxins," AGEs are formed as a byproduct of eating diets high in sugars and refined carbohydrates, as well as high-temperature cooking. They consist of proteins that have become permanently bound with sugars, preventing the protein from functioning.

Not surprisingly, AGEs levels are usually elevated in people with diabetes. AGEs also promote inflammation, which is involved in heart disease, cancer, and many other diseases. They are also elevated in people with kidney disease and undergoing dialysis, partly a consequence of the standard diet recommended for such patients as well as from the dialysis process itself.

In a recent study, Jaime Uribarri, MD, of the Mount Sinai School of Medicine, New York City, tested whether certain cooking methods might boost or lower levels of AGEs in people. He asked 18 patients with kidney failure, and undergoing regular

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dialysis, to eat either a high- or low-AGE diet for four weeks. The high-AGE diet included foods that were roasted, broiled, and oven fried. The low-AGE diet consisted of foods that were boiled, poached, stewed, or steamed, with avoidance of fried foods.

After four weeks, tests indicated that the low-AGE diet reduced AGE levels by about one-third, while the high-AGE diet increased AGE levels by a little more than one-fourth over initial values.

Uribarri wrote that "dietary glycotoxins contribute significantly to the elevated AGE levels in renal failure patients. Moreover, dietary restriction of AGE is an effective and feasible method to reduce excess toxic AGE and possibly cardiovascular associated mortality."

He also noted that the diet can be a significant source of preformed AGEs, which in turn boost levels of AGEs in the body.

Reference: Uribarri J, Peppa M, Cai W, et al. Restriction of dietary glycotoxins reduces excessive advanced glycation end products in renal failure patients. *Journal of the American Society of Nephrology*, 2003;14:728-731.

Borage Oil, an Anti-Inflammatory, Reduces Periodontal Symptoms

Taking supplemental borage oil, rich in gamma-linolenic acid (GLA), can reduce periodontal inflammation and pocket depth, according to a recent study.

In an article in *Prostaglandins, Leukotrienes and Essential Fatty Acids*, Elliot D. Rosenstein, MD, and his colleagues from the St. Barnabas Medical Center, Livingston, N.J., and the New York Veterans Medical Center, New York City, noted that GLA has been shown to reduce inflammation in people with rheumatoid arthritis. They wanted to test whether GLA and eicosapentaenoic acid (EPA) might reduce symptoms of periodontal disease.

They asked 24 patients to take one of four supplements daily for 12 weeks: 3,000 mg of borage oil; 3,000 mg of fish oils; a combination of 1,500 mg of both oils; or placebos. The seriousness of their periodontal disease was assessed through examination of gum tissues, the amount of plaque, and probing to measure pocket depth. Deep pockets frequently become infected, which erodes the bone.

The greatest benefits occurred in patients receiving 3,000 mg of borage oil daily. Both gingival inflammation and pocket depth were significantly reduced compared with placebos. Patients taking fish oils had some improvements, but they were not statistically significant, and the combined lower dosage of borage oil and EPA did not led to any significant improvement either.

"Traditional treatment of periodontal disease has been based on the concept that inflammation and tissue destruction are the direct consequences of bacterial infection," Rosenstein and his colleagues wrote. "Although clearly initiated by bacteria, host defense [immune] responses have more recently been recognized as having a critical role in periodontitis."

In a separate study, Walter J. Loesch, DMD, of the University of Michigan School of Dentistry, reported that extensive professional cleaning (root planing and scaling), combined with oral antibiotics and topical nonantibiotic antibacterial compounds, greatly reduce the risk of periodontal surgery and tooth extraction.

Loesch reported – in his fourth study along these lines – that his treatment plan, over five years, spared 87 percent of the teeth original recommended for periodontal surgery or extraction. The treatment plan is also relatively inexpensive compared with dental surgery.

References: Rosenstein ED, Kishner LJ, Kramer N, et al. Pilot study of dietary fatty acid supplementation in the treatment of adult periodontitis. *Prostaglandins, Leukotrienes and Essential Fatty Acids*,2003;68:213-218. Loesche WJ, Giordano JR, Soehren S, et al. The nonsurgical treatment of patients with periodontal disease: results after five years. *Journal of the American Dental Association*, 2003;133:311-320.

Diets High in Isoflavones and Lignans Reduce Cancer Risk in Women

Two new studies add strong evidence to the belief that soy isoflavones might reduce the risk of breast and endometrial cancers.

In the first study, Seiichiro Yamamoto, PhD, of the National Cancer Center Research Institute, Japan, analyzed dietary data obtained from almost 22,000 women, ages 40 to 59 years, in 1990. By 1999, 179 of the women had been diagnosed with breast cancer.

Yamamoto found that women who consumed the most isoflavone-rich miso soup – generally at least once a day – had about half the risk of developing breast cancer. Overall isoflavone intake (from foods) was similarly associated with a lower risk of breast cancer. However, specific soyfoods other than miso soup were not associated with a reduced risk.

In the other study, Pamela L. Horn-Ross, PhD, of the Northern California Cancer Center, Union City, compared the diets of 500 women in the San Franciso Bay area and 470 healthy women and their risk of developing endometrial cancer.

"The development of endometrial cancer is largely related to prolonged exposure to estrogens without cyclic exposure to progesterone," Horn-Ross wrote. Isoflavones and related compounds called

lignans are weak plant-based estrogens that block the effect of more powerful estrogen hormones.

High intake of isoflavones was associated with a 41 percent lower risk of endometrial cancer, and high intake of lignans was associated with a 32 percent lower risk.

"These associations were slightly stronger in postmenopausal women," Horn-Ross reported, with isoflavones decreasing the risk by 56 percent and lignans by 43 percent.

Soy foods are the richest dietary source of isoflavones, whereas lignans are found in whole grains, seeds, and dried fruit. Overall, Japanese women consume about 700 times more isoflavones than do American women.

References: Yamamoto S, Sobue T, Kobayashi M, et al. Soy, isoflavones, and breast cancer risk in Japan. *Journal of the National Cancer Institute*, 2003;95:906-913. Horn-Ross PL, John EM, Canhola AJ, et al. Phytoestrogen intake and endometrial cancer risk. *Journal of the National Cancer Institute*, 2003;95: 1158-1164.

Antioxidant Supplements Reduce Chromosome Damage

Damage to DNA, genes, and chromosomes is part of the normal aging process, and such damage can also lead to cancer-causing mutations. But a new study shows that a combination of antioxidant supplements can significantly reduce chromosome damage.

Norwegian and Slovakian researchers asked 57 healthy men and 28 who had recovered from a heart attack to take an antioxidant combination – 100 mg (149 IU) of vitamin E, 100 mg of vitamin C, 6 mg (10,000 IU) of beta-carotene, and 50 mcg of selenium – or placebos daily for 12 weeks.

The researchers obtained lymphocyte cells from the blood of subjects before and after supplementation, then analyzed the number of cells with chromosome damage. DNA damage in lymphocytes generally reflects exposure to potential carcinogens, not a consequence of other DNA damage in the body.

Among the healthy men, "chromosome aberrations" declined by more than half. And among smokers, chromosome damage decreased by almost seven times.

The supplements did not alter chromosome damage in the men who had survived a heart attack, possibly because the antioxidant dosages were too low.

Reference: Dusinska M, Kazimirova A, Barancokova, M, et al. Nutritional supplementation with antioxidants decreases chromosomal damage in humans. *Mutagenesis*, 2003;18:371-376.

More Research Adds to Coenzyme Q10 Benefits in Parkinson's Disease

Recent research has shown that coenzyme Q10, a vitamin-like nutrient, slows the development of Parkinson's disease. In a new study, German researchers report that CoQ10 supplementation led to a significant improvement in visual function and color discrimination among patients with Parkinson's disease.

Thomas Müller, MD, and his colleagues at Ruhr University Bochum, treated 28 Parkinson's patients with either 360 mg of CoQ10 or placebos daily for four weeks. The patients ranged from 49 to 81 years of age, and all had been receiving conventional treatment and were considered stable.

Using a clinical test to determine sensitivity to color variations, Müller found that the CoQ10 led to an average 30 percent improvement, compared with placebos. In addition, overall disease symptoms – scored by another test – improved, but motor function did not.

Müller noted that patients with genetic defects affecting CoQ10 metabolism often have altered vision. He speculated that CoQ10 supplements might free up some tyrosine, so it could be used for L-dopa production by the body.

Reference: Müller T, Büttner, Gholipour AF, et al. Coenzyme Q10 supplementation provides mild symptomatic benefit in patients with Parkinson's disease. *Neuroscience Letters*, 2003;341:201-204.

Vitamin E and Selenium May Help in Prevention, Treatment of Urinary Stones

Urinary stones, which include those of the kidney and bladder, are common and painful. One in every thousand Americans will at some time in his or her life be hospitalized because of them. Elevated levels of oxalate (hyperoxaluria) are a key risk factor for developing urinary stones, but the balance between free radicals and antioxidants may be a powerful influence on oxalate.

Researchers from the University of Madras, Chennai, India, fed laboratory rats a diet designed to increase the risk of urinary stones. As expected, activity of oxalate-producing enzymes increased. In addition, urinary levels of free radical levels were elevated and antioxidants were low.

However, rats given supplemental vitamin E and selenium (a component of the antioxidant glutathione peroxidase) had lower levels of oxalate-synthesizing enzymes, including glycolic acid oxidase, lactate dehydrogenase, and xanthine oxidase. Levels of several endogenous antioxidants – includ-

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Quick Reviews of Recent Research

• Copy machines are a source of free radicals

Ozone, a generator of free radicals, is released during the operation of photocopy machines. Researchers assessed blood levels of free radicals and antioxidants in 67 people operating copiers and 67 subjects not working around copiers. Copier operators had significantly higher levels of lipoperoxide, a marker of free-radical activity. They also had low levels of all antioxidants measured, including vitamins E and C, beta-carotene, glutathione peroxidase, catalase, and superoxide dismutase. The researchers wrote that "there exist a series of free radical chain reactions and pathological oxidative stress induced by high dose ozone in the operators, thereby causing potential oxidative and lipoperoxidative damages in their bodies."

Zhou JF, et al. *Biomedical and Environmental Sciences*, 2003;16:95-104.

• Low-dose vitamins lower heart-attack risk

Researchers investigated whether a low-dose daily multivitamin might lower the risk of a heart attack. They studied 1,685 healthy Swedish men and women and 1,296 Swedish men and women who had survived a heart attack. The population was unique in that they ate relatively few fruits and vegetables and did not eat foods fortified with folic acid. Women were 34 percent less likely to have a heart attack if they regularly took multivitamin supplements. Men who supplemented had a 21 percent lower risk than those who did not.

Holmquist C, et al. *Journal of Nutrition*, 2003;133:2650-2654.

• Cherries may reduce symptoms of gout

A medical report in 1950 found that eating cherries reduced uric acid levels and symptoms of gout. In a new study, researchers asked 10 healthy women, ages 22 to 40, to consume two servings of cherries. Blood urate levels decreased by 15 percent five hours after eating the cherries. In addition, C-reactive protein levels decreased slightly. The researches wrote, "The decrease in plasma urate after cherry consumption supports the reputed anti-gout efficacy of cherries. The trend toward decreased inflammation…adds to the in vitro evidence that compounds in cherries may inhibit inflammatory pathways."

Jacob RA, et al. *Journal of Nutrition*, 2003;133:1826-1829.

• St. John's wort has anti-inflammatory properties

Long before the herb St. John's wort became a popular remedy for depression, it was used to treat burns, bruises, and infections – all conditions involving inflammation. Researchers tested the effects of *Hypericum perforatum* and two other species of St. John's wort on myeloperoxidase levels in human white blood cells. The herb reduced myeloperoxidase levels after just a few minutes. This mode of action is similar to many anti-inflammatory drugs.

Pabuccuoglu A, et al. *Journal of Ethnopharmacy*, 2003;87:89-92.

• Calcium and vitamin D boost bone density

Researchers asked 192 elderly women with diagnosed vitamin D deficiency to take either 1,000 mg of calcium and 800 IU of vitamin D or placebos daily for one year. Bone mass increased significantly at the lumber spine, femur, trochanter, and whole body with supplementation. In addition, blood markers of bone health also returned to normal.

Grados F, et al. *Joint Bone Spine*, 2003;70:203-208.

• Ellagic acid and quercetin have anti-leukemia effect

In a study using human leukemia cells, quercetin's anticancer properties were potentiated with the addition of ellagic acid, an antioxidant polyphenol found in strawberries. Quercetin is an antioxidant flavonoid found in onions and apples.

Jertens-Talcott SU, et al. *Journal of Nutrition*, 2003;133:2669-2674.

Urinary Stones, Vitamin E, Selenium...

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ing glutathione peroxidase, catalase, and superoxide dismutase – increased. So did vitamin E and C concentrations.

Although human studies remain to be conducted, the researchers concluded that the "combination of these antioxidants may be therapeutically advocated for the treatment of urolithiasis."

Reference: Kumar MS, Selvam R. Supplementation of vitamin E and selenium prevents hyperoxaluria in experimental urolithic rats. *Journal of Nutritional Biochemistry*, 2003;14:306-313. □

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