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Vitamin D and Calcium Supplements Lower Cancer Risk, Reduce Risk of Death

People who take supplements of vitamin D and calcium not only strengthen their bones – they also significantly reduce their risk of some cancers and decrease their risk of death from any cause.

Joan M. Lappe, PhD, of Creighton University, Omaha, Nebraska, and her colleagues studied 1,179 postmenopausal women, some of whom were given 1,400 to 1,500 mg of calcium, a combination of calcium and 1,100 IU of vitamin D₃, or placebos daily for four years.

Overall, women taking vitamin D and calcium had a 60 percent lower risk of developing cancer, chiefly leukemias, myelomas, and breast, colon, lung, and lymph cancers.

When the researchers excluded cancers diagnosed during the first 12 months of the study (to rule out previously unidentified cancers), women taking the supplements had a 77 percent lower risk. Calcium supplements also reduced the risk of cancers, but not to the same extent as vitamin D and calcium together.

In a separate study, Cedric F. Garland, MD, of the University of California, San Diego, analyzed the combined results of two previous studies on vitamin D and breast cancer prevention. The studies together involved 1,760 women. Those with the highest blood levels of vitamin D – 52 ng/ml – had one-half the risk of developing breast cancer, compared with women who had low levels of the vitamin – less than 13 ng/ml."

Garland pointed out that blood levels of 52 ng/ml correspond to about 4,000 IU daily. This vitamin D level "could be maintained by intake of 2,000 IU/day and, when appropriate, about 12 minutes/day in the sun, equivalent to oral intake of 3,000 IU of vitamin D₃."

Another study, by Jennifer Lin, PhD, of Brigham and Women's Hospital, Boston, tracked the health of more than 31,000 pre- and postmenopausal women for an average of 10 years. Lin found a similar pattern relating to dietary intake of vitamin D and

calcium. Premenopausal women consuming the largest amounts of vitamin D had a 35 percent lower risk of breast cancer; those with the highest calcium intake had a 39 percent lower risk of breast cancer. High levels of the two nutrients did not appear to influence the risk of breast cancer among postmenopausal women in this study.

"The likely apparent protection in premenopausal women may be more pronounced for more aggressive breast tumors," wrote Lin.

Finally, Philippe Autier, MD, of the International Agency for Research on Cancer, Lyon, France, analyzed 18 controlled studies with a total of 57,311 women and men. Over an average follow-up of almost six years, people who took vitamin D supplements were 7 percent less likely to die from any cause – and were 8 percent less likely to die if they had been taking vitamin D supplements for at least three years.

More than 200 human genes get turned on and off in response to vitamin D, and many of these genes code for proteins involved in regulating cell proliferation and differentiation. Low vitamin D impairs the activities of these genes.

References: Lappe JM, Travers-Gustafson D, Davies KM, et al. Vitamin D and calcium supplementation reduces cancer risk: results of a randomized trial. *American Journal of Clinical Nutrition*, 2007;85:1586-1591. Garland CF, Gorham ED, Mohr SB, et al. Vitamin D and prevention of breast cancer: pooled analysis. *Journal of Steroid Biochemistry & Molecular Biology*, 2007;103: 708-711. Lin J, Manson JE, Lee IM, et al. Intakes of calcium and vitamin D and breast cancer risk in women. *Archives of Internal Medicine*, 2007;167: 1050-1059. Autier P, Gandini S. Vitamin D supplementation and total mortality. A meta-analysis of randomized controlled trials. *Archives of Internal Medicine*, 2007;167:1730-1737.

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Perspectives...

A New Role for Vitamin K

Osteocalcin is best known as a protein needed to make bone. After all, bone is more than a collection of calcium, magnesium, and other minerals. It is a living tissue that consists of a matrix of proteins, such as osteocalcin, and minerals. To make osteocalcin, however, your body needs vitamin K. If you don't get enough vitamin K, you cannot make enough osteocalcin or healthy bone.

The osteocalcin story recently took an interesting twist. Researchers reported in the journal *Cell* (2007; 130:456-469) that osteocalcin is also a hormone – one that plays a previously unknown role in regulating insulin, blood sugar, and fat cells. Osteocalcin increases the secretion of insulin, improves insulin sensitivity (a good thing, as opposed to insulin resistance), and reduces fat stores. A long story in the October 16 *New York Times* discussed these newly discovered and important roles for osteocalcin. But the article failed to mention that osteocalcin production depends on vitamin K.

The problem? Nine of every 10 Americans do not eat enough vegetables, especially leafy greens, the major source of dietary vitamin K. In addition, more than 2 million Americans take Coumadin (warfarin), a blood-thinning drug that reduces vitamin K activity. As a consequence, Coumadin interferes with osteocalcin production and increases the risk of fracture.

But if you connect the dots, low intake of dietary vitamin K and the common use of Coumadin and related anticoagulant drugs, might also contribute to the epidemics of overweight and prediabetes. Two-thirds of Americans are overweight or obese, and upwards of 100 million have prediabetes.

What do you do? Eat your leafy greens, the best dietary source of vitamin K, or consider taking vitamin K2 supplements. If you're taking Coumadin, ask your doctor if you can switch to an anticoagulant that does not interfere with vitamin K. –*JC*

Researchers Clearly Link Food Additives to Hyperactive Behavior

More than 30 years ago, Benjamin Feingold, MD, argued that food additives were often a cause of hyperactivity in children. Although many parents agreed – their childrens' behavior improved after they began eating additive-free foods – medical researchers had difficulty confirming Feingold's findings. As a result, the role of food additives in behavioral problems was officially dismissed.

In September, a well-controlled study, published in the journal *Lancet*, finally confirmed what Feingold and thousands of parents had found: some food additives can in fact increase hyperactive behavior in children.

Donna McCann, PhD, of the University of Southampton, England, and her colleagues fed mixes of food additives, including sodium benzoate (a preservative) and various artificial food colorings, or placebos to a mixed group of 153 three-year-old and 144 eight- and nine-year-old children – in other words, not just children who had been previously judged as hyperactive.

The additives were in the form of drinks, but the amounts were the same as found in two 2-ounce (56 gram) bags of sweets. The test drinks and placebos were given daily for six weeks.

Using several measures of hyperactivity, McCann and her colleagues found that the food additives significantly increased hyperactive behavior – overactivity, impulsiveness, and inattentiveness – while decreasing attention span. In effect, normal children became more hyperactive, and previously hyperactive children became more hyper.

McCann and her colleagues added, "We have completed a pilot study showing that changes in hyperactivity in response to food additives can be produced within about one hour."

Reference: McCann D, Barrett A, Cooper A, et al. Food additives and hyperactive behaviour in 3-year-old and 8/9-year-old children in the community: a randomised, double-blinded placebo-controlled trial. *Lancet*, 2007; epub Sept 7: doi:10.1016/S0140-6736 (07)61306-3.

Vitamin C Supplements Reduce Long-Term Pain After Wrist Fractures

Moderate doses of vitamin C supplements can reduce the chances of long-term pain following a fractured wrist, according to a new study.

Paul E. Zollinger, MD, of the department of orthopedic surgery, Ziekenhuis Rivierenland, Netherlands, and his colleagues treated 328 fracture patients with either vitamin C or placebos. The subjects were asked to participate in the study while in the emergency room, and if they agreed, they immediately began receiving either vitamin C or placebos. Patients receiving vitamin C were given 200 mg, 500 mg, or 1,500 mg daily for 50 days.

The end point of the study was the presence of "complex regional pain syndrome" at any time within 12 months of the fracture. Patients were evaluated at various times during the study up to one year. Complex regional pain syndrome was diagnosed based on several criteria related to ongoing pain, edema, limited range of motion, and other factors.



Overall, complex regional pain syndrome affected 2.4 percent of people in the vitamin C group and 10.1 percent of those taking placebos. The greatest benefits from vitamin C occurred at the 500 mg and 1,500 mg dosages, in which only 1.8 and 1.7 percent of patients, respectively, developed complex regional pain syndrome. In effect, patients taking these daily doses of vitamin C were 83 percent less likely to experience long-term pain, compared with patients in the placebo group.

The researchers wrote that "a daily dose of 500 mg for 50 days is recommended."

Reference: Zollinger PE, Tuinebreijer WE, Breederveld RS, et al. Can vitamin C prevent complex regional pain syndrome in patients with wrist fractures? A randomised, controlled, multicenter dose-response study. *Journal of Bone and Joint Surgery*, 2007;89A;1424-1431.

N-Acetylcysteine May Help People Overcome Gambling Addictions

N-acetylcysteine (NAC), which was recently found to reduce the urge to use cocaine, appears to also help people who suffer from an addiction to gambling.

John E. Grant, MD, of the University of Minnesota, Minneapolis, and his colleagues treated 23 patients who had been diagnosed with obsessivecompulsive gambling disorder. Before the study began, the subjects lost an average of \$456 weekly on slot machines, blackjack, or internet sports betting sites.

They were given 600 mg of NAC daily for two weeks, which was increased to 1,200 mg daily for two weeks, and then to 1,800 mg daily for four weeks. Of the 16 patients who responded favorably to NAC supplements, almost two-thirds reported abstinence from gambling activities. The patients' average scores on clinical tests to assess gambling addiction decreased by an average of 40 percent during the first phase of the study.

Thirteen of the patients who responded to treatment then agreed to enter a double-blind phase of the study in which they were given either 1,800 mg of NAC or placebos for six weeks. Of these people, about 83 percent of those taking NAC continued to respond. In contrast, almost 72 percent of those who started taking placebos resumed gambling.

The researchers wrote that NAC likely influences neurotransmitter activity, particularly the brain's glutamate pathways.

In hospitals, NAC is the treatment of choice for treating acetaminophen (Tylenol®) overdose. It is

also commonly used to break up mucous in the lungs. Reference: Grant JE, Kim SW, Odlaug BL.

N-acetylcysteine, a glutamate-modulating agent, in the treatment of pathological gambling: a pilot study. *Biological Psychiatry*, 2007;62:652-657.

New Study Finds that Alpha-Lipoic Acid Reduces Diabetic Nerve Pain

Alpha-lipoic acid, an antioxidant, has been used for decades by German physicians to treat diabetes and, in particular, neuropathy. A recent study looked at whether alpha-lipoic acid improved blood flow in the skin as well as clinical symptoms of neuropathy, including pain and numbness.

Tae Sun Park, MD, PhD, of the Chonbuk National University Medical School, South Korea, and his colleagues treated 19 patients with 600 mg of alphalipoic acid, which was administered daily for 14 days. The patients had diabetes for an average of 12.5 years. Thirteen patients were used as a control group for comparison sake.

Although blood flow in the skin improved, the changes were very modest. However, symptoms of neuropathy, decreased significantly – by almost 75 percent.

Reference: Jin HY, Joung SJ, Park JH, et al. The effect of alpha-lipoic acid on symptoms and skin blood flow in diabetic neuropathy. *Diabetic Medicine*, 2007;24:1034-1038. □

Modest Vitamin/Mineral Supplement Improves Depression in Seniors

Researchers in England have found that giving seniors a low-dose multivitamin and multimineral supplement improves mood – in both patients who are depressed and those who are not.

Salah Gariballa, MD, and Sarah Forster, PhD, researchers at the University of Sheffield, provided 225 seriously ill hospitalized older patients with the standard hospital diet plus either a vitamin-enriched beverage of placebos each day for six weeks. The drink contained 100 percent of the official recommended daily amounts of vitamins and minerals (an amount that many experts consider too low for health).

"The effect of the supplement was seen in all patients groups, including those with no symptoms of depression, mild depression and those with severe depression," wrote Gariballa and Forster.

The researchers used a standardized questionnaire for depression screening in seniors. Overall, they found a 26 percent difference in depression scores between the supplement and placebo groups.

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Quick Reviews of Recent Research

Vitamin supplements lower breast cancer risk

Researchers at Vanderbilt University in Nashville, Tennessee, compared the use of dietary supplements among 3,454 women who had been diagnosed with breast cancer and 3,474 women without the disease. Women who had a low dietary intake of vitamin E, but took supplements of the vitamin, had a significant 20 percent decrease in the risk of breast cancer. Similarly, women with a low dietary intake of B-complex vitamins had a 20 percent lower risk of breast cancer if they took those vitamins as supplements, though this particular finding was not statistically significant. Nonetheless, the researchers wrote that both vitamins may "confer protection against breast cancer among women who have low dietary intake of those vitamins."

Dorjgochoo T, et al. *Breast Cancer Research and Treatment*, 2007; October 5: epub ahead of print.

Green tea extracts ease cold and flu symptoms

In a study of 52 men and 72 women, researchers from the University of Florida found that proprietary extracts of green tea, which are sold as supplements,

Vitamin, Minerals, and Depression...

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The number of patients with severe depression decreased from 16 to three, and the number of patients with mild depression decreased from 50 to 21 after taking the supplements for six months.

"Improvement of micronutrient status would be the most plausible explanation for the results presented here," wrote Gariballa and Forster. They also noted that the "clinical benefits were observed despite [only a] modest degree of compliance with the supplements."

The researchers concluded that their study "demonstrated that nutritional supplementation of hospitalized older people does lead to a clinically important benefit."

In a separate publication, they wrote that the supplements also led to improved physical and social functioning in the patients.

Reference: Gariballa S, Forster S. Effects of dietary supplements on depressive symptoms in older patients: a randomised double-blind placebo-controlled trial. *Clinical Nutrition*, 2007; July 25: epub ahead of print. Gariballa S, Forster S. Dietary supplementation and quality of life of older patients: a randomized, double-blind, placebo-controlled trial. *Journal of the American Geriatrics Society*, 2007; October 18: epub ahead of print.

can prevent symptoms of colds and flus. The researchers gave study participants supplements containing L-theanine (Suntheanine®) and epigallocatechin gallate (EGCG) twice daily for three months. During this time, the subjects had increased immune cell activity accompanied by greater resistance to cold and flu symptoms. People taking the supplements were 32 percent less likely to have symptoms, had 23 percent fewer illnesses lasting two or more days, and had almost 36 percent few days with symptoms.

Rowe CA, et al. *Journal of the American College of Nutrition*, 2007;26:445-452.

NAC lowers lung complications, death

Swiss researchers administered high-dose NAC (approximately 10,000 mg daily) post-operatively to 22 patients with esophageal cancer and compared their responses to patients treated without NAC. Patients receiving NAC had better lung function at two, eight, and 12 hours after surgery, though the benefits equalized after 36 hours. However, the risk of death among patients receiving NAC was about 45 percent lower over the next several years, compared with untreated patients.

Zingg U, et al. *Diseases of the Esophagus*, 2007; 20:399-405.

Supplements improve nutrient levels

U.S. Department of Agriculture researchers investigated nutrient levels in 4,384 middle-age and older men and women. Fewer than 50 percent of both supplement users and nonusers obtained recommended amounts of most vitamins and minerals from their diets. However, supplements improved the nutritional intake of middle-age and older adults, so that 80 percent of them met recommended amounts.

Sebastian RS, et al. *Journal of the American Dietetic Association*, 2007;107:1322-1332.

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