

# The Nutrition Reporter™

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## The Vitamin D Dilemma: Is the Danger Too Much or Too Little of this Nutrient?

Frightened by periodic warnings that too much vitamin D is toxic, many people may be avoiding the broad health benefits of this essential vitamin.

Vitamin D certainly aids calcium uptake into bones and teeth, and a growing body of research suggests that adequate amounts may reduce the risk of diseases as diverse as cancer and diabetes.

Researchers have been developing a variety of vitamin D-like drugs for the treatment of cancer. But a recent study, published in the *British Journal of Cancer*, shows that a common defect in a gene responsible for vitamin D utilization is strongly associated with an increased risk of breast cancer.

According to Kay W. Colston, MD, of St. George's Hospital Medical School, London, the VDR gene controls the activity of the vitamin D receptor (VDR), which in turn helps regulate a number of hormone-responsive genes. However, common variations (called polymorphisms) in the structure of the VDR gene can limit the activity of vitamin D.

In analyzing genetic patterns in 181 women with breast cancer and 241 women without the disease, Colston and her colleagues found that two of three specific variations in the VDR gene more than doubled a woman's risk of developing breast cancer.

This finding, combined with the anti-cancer effect of vitamin D-related compounds, builds a strong case for the role of low vitamin D levels in breast cancer. Based on similar research with other vitamins (such as folic acid), supplements may compensate for the genetic defect.

In a separate study, Elina Hypponen, PhD, of the Institute of Child Health, London, and Finnish researchers, reported that childhood supplementation with vitamin D significantly reduced the risk of juvenile-onset (type 1) diabetes.

The study, which tracked more than 10,000 infants and children, found that regular consumption of vitamin D-containing supplements reduced the risk of diabetes by 88 percent, compared with no supplementation. Inconsistent supplementation also

helped, lowering the risk by 84 percent.

The dosage was important as well. Infants and children who received the Finnish recommended amounts each day, were 78 percent less likely to develop diabetes, compared with children who took lower amounts of the vitamin.

Recent studies have found that many people may not have adequate vitamin D levels. One American study, published in 1999, found that women hospitalized for hip fractures were consistently low in vitamin D and half were clearly deficient. Another study, published in the *Journal of Pediatrics*, noted an increase in vitamin D-deficiency rickets in infants.

Years ago, it was common for mothers to give their children cod liver oil, which is rich in both vitamins A and D. Dietitians and physicians often urge caution with vitamin D supplements, because long-term daily intake of about 2,000 IU may be toxic.

However, supplements may not be necessary. Brief exposures to sunlight (15-30 minutes daily) stimulate the body's production of vitamin D. People working outdoors in sunny climates may produce more than 10,000 IU daily – 25 times the U.S. recommended daily intake.

In fact, the value of even brief exposure to sunlight may be greatly underestimated. A study by Turkish researchers has shown that veiled Muslim women who wore veils outdoors had significantly lower vitamin D levels compared with women who did not wear veils.

References: Bretherton-Watt D, Given-Wilson R, Mansi JR, et al. Vitamin D receptor gene polymorphisms are associated with breast cancer risk in a UK caucasian population. *British Journal of Cancer*, 2001;85:171-175. Hypponen E, Laara E, Reunanen A, et al. Intake of vitamin D and risk of type 1 diabetes: a birth-cohort study. *Lancet*, 2001;358:1500-1503. Guzel R, Kozanoglu E, Guler-Uysal F, et al. Vitamin D status and bone mineral density of veiled and unveiled Turkish women. *Journal of Women's Health and Gender-Based Medicine*, 2001;10:765-770. □

**Perspectives...****Questions with Statins and Antioxidants**

A widely reported study in the Nov. 29, 2001, *New England Journal of Medicine* found that a combination of antioxidants – vitamins E and C, beta-carotene, and selenium – slowed the progression of coronary artery disease, but not by as much as a combination of the drug simvastatin (Zocor) and niacin (vitamin B3). Furthermore, the antioxidants actually interfered with the statin/niacin combo.

How does one make sense of this study – and help us maintain more faith in antioxidants and, perhaps, less in newspaper headlines?

First, the study included relatively few people, only 40 in each of the four treatment groups. Second, all of the subjects had serious coronary artery disease, reflecting the effect of treatment, not prevention. Third, all of the patients had low levels of HDL, the so-called good cholesterol. Low HDL is found in only 40 percent of heart patients, so this was not a “typical” group of heart patients.

Is this simply rationalizing? Not necessarily. A soon-to-be-published British study, almost identical except that it included more patients and for a longer duration, found no negative effect from antioxidants.

The researchers also downplayed the role of niacin, while emphasizing the benefits of statin drugs. Niacin has been known to lower cholesterol levels for more than 50 years, but pharmaceutical companies don't promote it unless it is combined with a patentable drug. A far more interesting study would have also looked at the effect of niacin combined with antioxidants. – *Jack Challem*

**Is the “Sulfate” Doing More than the Glucosamine in Osteoarthritis?**

Considerable research shows that supplements of glucosamine sulfate reduce pain and often maintain joint cartilage in people with osteoarthritis. Until now, many people have believed that the glucosamine increases synthesis of glycosaminoglycans (GAG), a group of compounds that form “articular,” or joint, cartilage.

However, new research strongly suggests that the sulfate portion of the molecule, and not the glucosamine, may be responsible for improvements in osteoarthritis.

The problem with glucosamine *per se*, points out L. John Hoffer, MD, PhD, of Jewish General Hospital, Montreal, is that oral glucosamine supplements do not lead to increases in glucosamine. Without absorption into the bloodstream, glucosamine cannot be transported to the joint space, where cartilage synthesis occurs.

So, Hoffer and his colleagues gave seven healthy men and women a 1-gram of glucosamine sulfate supplement, then measured their blood and synovial joint levels of sulfate. Three hours later, their blood levels of sulfate increased by an average of 13 percent. Levels of sulfate in the synovial joint and blood were almost identical, and synovial sulfate levels increased accordingly after supplementation.

Hoffer noted that GAG production is very sensitive to sulfate deficiency, and human levels in the joint are lowest among mammals. Sulfate levels decrease rapidly when people eat low-protein diets.

In an interesting twist, Hoffer confirmed earlier researching showing that acetaminophen (Tylenol) lowered blood sulfate levels by about 11 percent, even when given along with 1 gram of glucosamine sulfate. This might suggest that taking acetaminophen might increase the risk of osteoarthritis.

“These results do not prove that glucosamine sulfate improves osteoarthritis, but considered with other data, they do provide a plausible biochemical mechanism for its reported beneficial effects,” wrote Hoffer and his colleagues.

Reference: Hoffer LJ, Kaplan LN, Mamadeh MJ, et al. Sulfate could mediate the therapeutic effect of glucosamine sulfate. *Metabolism*;2001;50:767-770. □

**Two Studies Provide Additional Support that Antioxidants Can Prevent Cataracts**

Two teams of researchers, one from England and the other from the United States, have reported that various antioxidant nutrients are associated with a relatively low risk of developing cataracts. The condition, a clouding of the eye's lens, is believed to result in large part from free radical damage from ultraviolet rays in sunlight.

Catherine R. Gale, PhD, of the University of Southampton, investigated the relationship between three types of cataracts and blood levels of carotenoids and vitamins E and C among 372 elderly men and women. Two-thirds of the subjects had at least one type of cataract.

Gale found that high levels of specific carotenoids seemed to protect against particular types of cataracts. For example, people with the highest blood concentrations of either beta- or alpha-carotene were 30 and 50 percent less likely, respectively, to develop nuclear cataracts, which are located in the central part of the lens.

Similarly, high blood levels of lycopene were associated with a 60 percent lower risk of cortical cataracts, located in the outer layer of the lens. And people with high lutein concentrations were 50 percent less likely to develop posterior subcapsular cataracts, located toward the bottom rear of the lens

and causing significant impairment of vision.

Although the researchers did come out and say it, the study's take-home message was fairly simple: a diet with a diverse supply of carotenoids can greatly reduce the overall risk of developing cataracts. That's important because no one knows what type of cataract they might develop.

Although Gale's study did not find any protective effect from vitamin antioxidants, Paul F. Jacques, ScD, of Tufts University and his colleagues reported that long-term use of vitamin C or multivitamin supplements did reduce the risk of nuclear cataracts.

Jacques tracked the dietary habits and health of 478 nondiabetic middle-age and elderly women. Those who took vitamin C supplements for more than 10 years had a two-thirds lower risk of developing cataracts. Multivitamin supplements were almost as beneficial, lowering the risk by 57 percent. Vitamin E supplements showed a slight protective trend, but the benefit was not statistically significant because of the small number of people taking the vitamin.

References: Gale CR, Hall NF, Phillips DI, et al. Plasma antioxidant vitamins and carotenoids and age-related cataract. *Ophthalmology*, 2001;108:1992-1998. Jacques PF, Chylack LT Jr, Hankinson SE, et al. Long-term nutrient intake and early age-related nuclear lens opacities. *Archives of Ophthalmology*, 2001;119:1009-1019. □

## Ginkgo Supplements May Reverse Sudden Loss of Hearing

A condition known as sudden deafness, which is often accompanied by tinnitus (a ringing in the ears), is the most common functional (noninfectious) disorder of the inner ear. Supplements of an extract of *Ginkgo biloba* may speed recovery.

Sudden deafness, which is also known as acute hearing loss, often has no apparent cause, such as a loud noise. It is believed to be caused by a microcirculatory disorder in the ear, and it is often treated with medications used in peripheral artery disease.

In a study conducted at the University of Heidelberg, Germany, researchers treated 72 patients with sudden deafness, based on an average 30-dB (decibel) hearing loss. Almost half of them also had tinnitus. They received either 200 mg of ginkgo extract or the drug pentoxifylline daily for ten days.

Both ginkgo and the drug treatment resulted in a similar, substantial restoration of hearing over the ten-day treatment period, with a recovery of about 13 dB in hearing. In addition, more than one-third of the patients reported that their tinnitus had ceased, with slightly more in the drug group. Overall, the patients' subjective impressions suggested that ginkgo was slightly more effective.

Reference: Reisser C, Weidauer H. *Ginkgo biloba* extract EGb761® or pentoxifylline for the treatment of sudden deafness: a randomized, reference-controlled, double-blind study. *Acta Otolaryngologica*, 2001; 121:579-584. □

## Researchers Identify Details of Feverfew's Anti-Inflammatory Effects

Herbal remedies have often been discredited – even with positive clinical studies – because scientists lack an understanding of how they work. The herb feverfew (*Tanacetum parthenium*) is one such example. It has been used for centuries to treat migraine headaches and fevers, and studies have found that regular supplementation does reduce the frequency of migraines.

Recently, Craig M. Crews, Ph.D., of Yale University, New Haven, Conn., and his colleagues investigated the anti-inflammatory properties of parthenolide, the principal active chemical in feverfew. Inflammation is involved in the blood vessel disturbances leading to migraine.

In studying the molecular biology of feverfew, Crews found that parthenolide binds to and inhibits the activity of "I $\kappa$ B kinase beta" (IKKB), which is closely related to "nuclear factor kappa beta" (NF $\kappa$ B), a protein that activates many genes involved in inflammation. By blocking the activity of IKKB, parthenolide inhibited the activity of NF $\kappa$ B.

Parthenolide is part of a family of compounds known as sesquiterpene lactones, believed to be the active components of many herbal medicines.

Reference: Kwok BHB, Koh Ndubuisi MI, et al. The anti-inflammatory natural product parthenolide from the medicinal herb feverfew directly binds to and inhibits I $\kappa$ B kinase. *Chemistry & Biology*, 2001;8:759-766. □

## Diets High in Carbohydrates Can Deplete Vitamin B1 Levels in the Body

Does a diet high in carbohydrates deplete your body's vitamin and mineral reserves? Nutritionally oriented physicians have been saying so for years, and a new study has found that they are correct.

Ibrahim Elmadfa, PhD, and his colleagues at the University of Vienna, Austria, studied how increased consumption of carbohydrates affects levels of thiamin, or vitamin B1, in the body.

Almadfa focused on vitamin B1 because the activity of numerous enzymes, including dehydrogenases, depend on it. Dehydrogenases are primarily involved in the metabolism of carbohydrates.

Nutrition experts have long applied "absolute," or fixed, recommendations for vitamin B1 intake

Continues on next page

## Quick Reviews of Recent Research

### • Low folic acid implicated in male infertility

Low levels of the B-vitamin folic acid increase the risk of birth defects in women. But new research shows that a lack of the vitamin may reduce a man's ability to father children. In this study, researchers found that men with low sperm counts have low levels of the vitamin in their semen.

Wallock LM, et al. *Fertility and Sterility*, 2001;75:252-259.

### • Antioxidants help asthmatics breathe easier

Ozone, a component of urban air pollution, injures the respiratory system, and people with asthma are particularly sensitive to its effects. With this in mind, researchers measured the lung function of 17 adult asthmatics who ran on a treadmill while being exposed to ozone. The researchers then re-

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based on the overall number of calories in the diet. However, they have ignored the source of those calories, such as carbohydrate, fat, or protein.

It stands to reason, Elmadfa noted, that a higher intake of carbohydrates might place additional stresses on vitamin B1-dependent dehydrogenases. To determine if this was the case, he asked 12 healthy men and women to eat a diet in which carbohydrates comprised 55 percent of the total calories. He then increased their carbohydrate intake to 65 percent and then 75 percent over four-day periods.

As the percentage of carbohydrate increased, vitamin B1 levels decreased significantly in the subjects' blood and urine. However, activity of erythrocyte transketolase, another vitamin B1-dependent enzyme, remained steady, which the researchers believed was due to the study's short duration.

In their conclusion, Almadfa and his colleagues noted that people eating large amounts of carbohydrates may not be receiving sufficient vitamin B1 unless they take supplements.

It is worth noting, as well, that carbohydrate-rich foods tend to be calorie dense, meaning that they provide a large amount of calories relative to other nutrients. In contrast, nutrient-dense foods, such as fish, lean meats, and low-starch vegetables and fruit provide greater concentrations, calorie for calorie, of other nutrients.

Elmadfa I, Majchrzak D, Rust P, et al. The thiamine status of adult humans depends on carbohydrate intake. *International Journal for Vitamin and Nutrition Research*, 2001;71:217-221. □

peated the experiment after the subjects took 400 IU of vitamin E and 500 mg of vitamin C daily for one week. After taking the vitamins, the subjects experienced less breathing difficulty and some had improvements in lung function.

Trenga CA et al. *Archives of Environmental Health*, 2001;56:242-249.

### • Vitamin E can prevent ataxia

Research has found that vitamin E supplements can relieve some forms of hereditary ataxia, a neurological disorder that impairs walking and causes uncontrollable physical movements. Researchers bred mice without a gene needed to maintain normal vitamin E levels. The mice had no vitamin E, and they consequently developed ataxia symptoms after one year. However, some of the mice were given vitamin E, and their brain levels of the vitamin rose to 10-20 percent of normal. These modest levels of vitamin E prevented ataxia.

Yokota T, et al. *Proceedings of the National Academy of Sciences*, 2001;98:15185-15190.

### • N-acetylcysteine may help in Alzheimer's

Researchers gave 43 patients with Alzheimer's disease supplements of approximately 3,500 mg N-acetylcysteine daily or placebo for almost six months. The subjects' ability to perform daily activities did not improve, but the patients taking NAC did benefit from improvements in short-term memory and reasoning skills.

Adair JC, et al. *Neurology*, 2001;57:1515-1517.

### • Alpha-lipoic acid may help prevent diabetes

In an article reviewing the use of alpha-lipoic acid in treating diabetes, researchers concluded the antioxidant's greatest benefit may be in preventing the development of full-blown diabetes. Alpha-lipoic acid improves insulin sensitivity and protects nerves from free-radical damage.

Coleman MD, et al. *Environmental Toxicology and Pharmacology*, 2001;10:167-172.

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