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Major Study Finds Good News About Vitamins E and C's Cardiovascular Benefits

A new study has found that regularly taking natural vitamin E and vitamin C can significantly reduce the risk of several cardiovascular diseases. The study was published in the August 13, 2007, issue of *Archives of Internal Medicine*, published by the American Medical Association.

Nancy R. Cook, ScD, of the Harvard School of Public Health, and her colleagues asked 8,171 women to take 500 mg of vitamin C daily, 600 IU of natural-source vitamin E or 50 mg of beta-carotene every other day, placebos, or various combinations of these supplements for about of nine and one-half years.

When Cook and her colleagues analyzed data from people who consistently took their supplements, they found several specific benefits. Vitamin E supplements reduced the risk of heart attack by 22 percent, stroke by 27 percent, and death from cardiovascular disease by 9 percent. Vitamin E also led to a 23 percent lower combined risk of heart attack, stroke, and cardiovascular-related death.

In addition, vitamin E and vitamin C together lowered the risk of stroke by 31 percent.

Despite these positive findings, newspaper and television reports on the study tended to be negative, stating that the benefits were marginal or that there were no benefits at all. The negative media spin originated with a news release from Brigham Women's Hospital in Boston, where the research was conducted, as well as from an equivocal news release from the American Medical Association.

Cook and her colleagues reported that, overall, vitamin E supplements led to a "marginally significant" 11 percent lower risk of combined cardiovascular disease events, including heart disease and stroke.

The researchers identified that small benefit after combining data from people who infrequently took supplements with those who consistently took them, which in effect diluted the benefits.

However, when the researchers focused only on people who regularly took supplements, the benefits of vitamins E and C were strengthened.

Beta-carotene did not have any clear cardiovascular benefits, and the researchers also pointed out there were no signs of harm from any of the supplements. Other studies have pointed out that beta-carotene may have benefits in preventing cancer among people who do not eat many fruits and vegetables.

Reference: Cook NR, Albert CM, Gaziano M, et al. A randomized factorial trial of vitamins C and E and beta carotene in the secondary prevention of cardiovascular benefits in women. *Archives of Internal Medicine*, 2007;167:1610-1618. □

Perspectives...

Selenium Causes Diabetes? Not Likely

We live in an era of headline-driven medical news in which the latest study invalidates everything that came before. Consider a recent study, in the *Annals of Internal Medicine*, suggesting that selenium supplements increase the risk of type 2 diabetes.

First, is it biochemically plausible that selenium supplements increase the risk of type 2 diabetes? I doubt it. The four antioxidant and detoxification glutathione peroxidase molecules (of which selenium is part) are essential. Numerous clinical studies have found benefits from selenium in HIV infection and cancer – diseases in which glucose intolerance is common. If selenium increased glucose intolerance, the progression of these diseases would get worse with selenium supplements, not better.

Second, anyone who bothered to read the *Annals* report would have found that the researchers were extraordinarily cautious about their findings. They admitted that the diabetes cases were self-reported, meaning that they may have been under-reported at the beginning of the study. In addition, diabetes was a secondary endpoint, which is not regarded as being as strong as a primary endpoint in such studies.

Third, the researchers acknowledged that they

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did not have data on body-fat distribution (e.g., apple vs. pear shape), family history of diabetes, or physical activity, all of which would influence risk. Nor did they have data on dietary intake; most of the subjects were from what I call the “grits belt,” where there would be a high background risk of type 2 diabetes.

Fourth, the researchers admitted that they “cannot rule out the role of chance...” and they added that their numbers were shaky: “...a few more cases of diabetes in the placebo group would attenuate the main effect of selenium treatment and produce null findings.”

Fifth, the researchers glossed over the fact that selenium supplements had no negative effect on the most overweight subjects, people who would have had the highest risk of developing diabetes (and were most likely to be prediabetic when the study began). That alone should have invalidated the study.

It’s also important to consider the bigger picture: it’s difficult to conduct clinical trials that test individual nutrients as if they were drugs.

All diseases are multifactorial in origin. When one nutrient helps, odds are that multiple nutrients will help even more because they strengthen multiple biochemical pathways. However, reductionist single-nutrient studies seek the equivalent of a pharmaceutical silver bullet. Unlike drugs, nutrients function as part of a network. Although many individual supplements do shine in clinical trials, multinutrient studies generally shine brighter.

No sensible person would try to prevent or treat a disease with just one nutrient or drug. Supplements are always best when combined with good eating habits, physical activity, and healthy lifestyles. – JC

Supplement Eases Symptoms in Patients with Fibromyalgia

People with fibromyalgia often have a variety of debilitating symptoms, including pain, problems with sleep, mood disturbances, and fatigue. Treatment can be frustratingly difficult and recovery slow.

Recently, Italian researchers reported that acetyl-L-carnitine supplements can help many patients with fibromyalgia. Acetyl-L-carnitine is a form of carnitine, a nutrient needed to transport fats within cells so they can be burned (or oxidized) for energy.

Silvano Adami, MD, of the University of Verona, and his colleagues at several rheumatology centers treated 102 fibromyalgia patients with either acetyl-L-carnitine (ALC) or placebos. All but three of the patients were women. The patients took two 500 mg capsules of ALC daily for two weeks, and also received one intramuscular injection of 500 mg of ALC. The patients then took three 500 mg capsules of

ALC daily for eight weeks. Placebos were given in a similar fashion.

For the first six weeks, the patients’ “total myalgic score,” based on clinical and self-perceived symptoms, improved in both the ALC and placebo groups. By the tenth week, patients taking acetyl-L-carnitine continued to improve, with significant improvements in depression and musculoskeletal pain. Meanwhile, people in the placebo group did not improve after six weeks.

Reference: Rossini M, Di Munno O, Valentini G, et al. Double-blind, multicenter trial comparing acetyl-L-carnitine with placebo in the treatment of fibromyalgia patients. *Clinical and Experimental Rheumatology*, 2007;25:182-188. □

Magnesium Reduces Signs of Inflammation in Heart Failure Patients

Heart failure is characterized by reduced cardiac output, and presenting symptoms often include breathlessness, fatigue, and fluid overload. Approximately half of patients die less than five years after diagnosis. The immediate cause of death is often arrhythmias related to an imbalance of electrolytes, including sodium, potassium, and magnesium.

Researchers compared 68 patients hospitalized with heart failure and 65 patients hospitalized for other reasons. Patients with heart failure had lower blood levels of magnesium and three times higher levels of C-reactive protein (CRP), a marker of inflammation.

Seventeen of the heart failure patients were given 300 mg of magnesium citrate daily. CRP levels in these patients decreased by about 40 percent after five weeks of magnesium supplementation. The researchers did not report whether there were any changes in clinical symptoms of heart failure.

Reference: Almozni-Sarafian D, Berman S, Mor A, et al. Magnesium and C-reactive protein in heart failure: an anti-inflammatory effect of magnesium administration? *European Journal of Nutrition*, 2007;46:230-237. □

Magnesium Intake Also Influences the Risk of Developing Arrhythmias

Magnesium has long been known to control some types of irregular heart rhythms. Studies have also found that people with diabetes tend to have lower blood levels of magnesium, compared with people who don’t have diabetes.

Forrest H. Nielsen, PhD, and his colleagues at the U.S. Department of Agriculture’s Nutrition Research Center, Grand Forks, North Dakota, conducted a magnesium-deprivation study on 13 postmenopausal women.

The study was designed to provide the women with a very low magnesium diet (101 mg magnesium daily) for 78 days, followed by a moderately higher magnesium diet (200 mg magnesium for 58 days). However, if women experienced magnesium-related health problems before the 78th day, they would immediately receive larger amounts of magnesium.

Five of the women developed either heart flutters or a type of heart-rhythm abnormality known as atrial fibrillation between the 42nd and 64th day of the study. Their symptoms disappeared after they received larger amounts of magnesium.

In addition, during the low-magnesium phase of the study, the subjects' blood sugar levels increased. Inexplicably, their total cholesterol level decreased; other research has associated elevated cholesterol with low magnesium.

According to U.S. Department of Agriculture data, 68 percent of Americans do not obtain the recommended daily amounts of magnesium, which are 310 mg for women and 420 mg for men.

Reference: Nielsen FH, Milne DB, Klevay LM, et al. Dietary magnesium deficiency induces heart rhythm changes, impairs glucose tolerance, and decreases serum cholesterol in post menopausal women. *Journal of the American College of Nutrition*, 2007;26:121-132. □

Coenzyme Q10 Supplements Reduce Muscle Pain Side Effects from Statins

Statin-class cholesterol-lowering drugs, such as Lipitor, Crestor, and Vytorin, inhibit the activity of 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA), which in turn reduces cholesterol production. However, lower HMG-CoA also interferes with the body's production of coenzyme Q10 (CoQ10), a vitamin-like nutrient involved in cellular energy production.

Many statin side effects, including muscle pain and liver problems, have been attributed to CoQ10 depletion.

Giuseppe Caso, MD, and his colleagues at Stony Brook University, New York, treated 32 patients with statin-induced muscle myopathy and pain. They were given either 100 mg of CoQ10 or 400 IU vitamin E daily for 30 days. By the end of the study, CoQ10 reduced pain severity by an average of 40 percent. It also reduced the impact of pain on daily activities by 38 percent. Vitamin E had no effect.

CoQ10 was the basis of the 1978 Nobel prize in chemistry.

Editor's note: The role of CoQ10 in offsetting statin side effects has long been recognized, though not widely publicized. In 1990, Merck was granted two patents for the use of CoQ10 in treating statin-related myopathies. You can search for patent

numbers 4,929,437 and 4,933,165 at <http://patents.uspto.gov/>

Reference: Caso G, Kelly P, McNurlan MA, et al. Effect of coenzyme Q10 myopathic symptoms in patients treated with statins. *American Journal of Cardiology*, 2007;99:1409-1412. □

Current Recommendations for Choline Intake May be Far Too Low

Choline was recognized as an essential B vitamin by the National Academy of Science relatively recently – in 1998 – and the recommended daily intake was set at 550 mg for men and 425 mg for women. The vitamin helps build chemical compounds known as methyl groups, needed in the synthesis of DNA and phospholipids. Choline is also the precursor to the neurotransmitter acetylcholine.

Steven H. Zeisel, MD, PhD, of the University of North Carolina, Chapel Hill, and his colleagues, conducted a choline-deficiency study of 57 people, including men and pre- and postmenopausal women. For 10 days, the subjects were fed a diet containing 550 mg of choline daily, followed by a choline-deficient phase (less than 50 mg daily) for 42 days.

During the choline-deprivation phase, 77 percent of men, 80 percent of postmenopausal women, and 44 percent of premenopausal women developed subclinical biochemical signs of fatty liver and muscle damage. In most cases, increasing choline to 550 mg daily restored normal organ function.

However, six of the men developed signs of organ dysfunction despite consuming 550 mg of choline daily. A total of 11 (19 percent) subjects needed 825 mg of choline daily to completely reverse the signs of organ dysfunction.

Supplemental lecithin granules and egg yolks are excellent sources of choline.

Reference: Fischer LM, daCosta KA, Kwock L, et al. Sex and menopausal status influence human dietary requirements for the nutrient choline. *American Journal of Clinical Nutrition*, 2007;85:1275-1285. □

Low Vitamin D Levels Appear to Boost Risk Factors for Heart Disease

Vitamin D is essential for strong bones, fighting infections, and preventing cancer. A new study now links low blood levels of vitamin D to a higher risk of risk factors for heart disease.

Keith Norris, MD, of the Drew University of Medicine and Science, Los Angeles, and his colleagues analyzed data on blood vitamin D levels and specific cardiovascular risk factors among more than 15,000 men and women participating in the Third National Health and Nutrition Examination Survey.

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Quick Reviews of Recent Research

• Dietary oils may impact bone health

Researchers from the University of Texas fed laboratory mice diets rich in either corn oil (high in omega-6 fats) or fish oils (high in omega-3 fats). After six months, the researchers found that mice eating fish oils had high bone mineral density, compared with mice fed corn oil. In addition, mice fed fish oils had lower levels of inflammation-causing chemicals.

Bhattacharya A, et al. *Journal of Nutritional Biochemistry*, 2007;18:372-379.

• Alpha-lipoic acid May help with arterial disease

Researchers from the University of Virginia used 600 mg of alpha-lipoic acid or placebos daily to treat 28 patients with peripheral artery disease. Patients taking alpha-lipoic acid had striking improvements in initial claudication time and walking distance after three months. However, their findings were influenced by the fact that five regular walkers had been inadvertently included in the group receiving alpha-lipoic acid. As a result, the researchers concluded that

Vitamin D and Heart Disease

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Low vitamin D levels were associated with a 30 percent greater risk of high blood pressure, double the risk of diabetes, and almost a 50 percent greater likelihood of elevated triglycerides. Low levels of the vitamin were also related to more than twice the risk of obesity, though the researchers wrote that this particular link might be related to less physical activity outdoors.

Although the study analyzed associations, not direct cause and effect, Norris cited research showing clear biochemical links between low vitamin D and glucose intolerance, blood pressure, heart failure, and inflammation.

"This is the first study, to our knowledge, to demonstrate a significant association between low vitamin D levels and CVD [cardiovascular disease] risk factors in a nationally representative sample," wrote Norris.

He added, "The current recommended levels of... [vitamin D] are primarily based on levels needed to maintain optimum bone health and prevent rickets but do not address the levels of vitamin D that may be necessary to minimize the prevalence of CVD risk factors...[blood] levels of 37 ng/mL or greater (≥ 92 nmol/L) may confer additional health benefits."

Reference: Martins D, Wolf M, Pan D, et al. Prevalence of cardiovascular risk factors and the sum levels of 25-hydroxyvitamin D in the United States. *Archives of Internal Medicine*, 2007;167:1159-1165. □

a combination of alpha-lipoic acid and walking might be better than the supplement alone.

Vincent HK, et al. *Journal of Alternative and Complementary Medicine*, 2007;13:577-584.

• Supplement might protect hearing

Researchers at the University of Michigan tested several individual nutrients, a combination of nutrients, and placebos to determine whether they would prevent hearing loss in guinea pigs. The individual nutrients did not have any significant effect, but a combination of vitamins A, C, and E, plus magnesium had a significant protective effect, even when provided just one hour before exposure to loud noise.

Le Prell CG, et al. *Free Radical Biology and Medicine*, 2007;42:1454-1463.

• Prenatal vitamins reduce cancer risk

Researchers at the University of Toronto, Canada, analyzed data in seven previous studies of pregnant women who took multivitamin supplements. Multivitamins led to significant reductions in cancer risk for children of the women. The risk of leukemia decreased by 39 percent. Brain tumors decreased by 27 percent, and neuroblastoma decreased by 47 percent.

Goh YI, et al. *Clinical Pharmacology & Therapeutics*, 2007;81:685-691.

• Magnesium may influence metabolic syndrome risk

Researchers from the U.S. Centers for Disease Control and Prevention analyzed the relationship between magnesium intake and the risk of metabolic syndrome. The syndrome consists of insulin resistance, abdominal obesity, elevated blood fats, and hypertension – and increase the risk of diabetes and heart disease. The researchers found that people with the lowest magnesium intake were 44 percent more likely to have metabolic syndrome. Magnesium is involved in glucose control, but it might also be a marker of healthy eating habits.

Ford ES, et al. *Obesity*, 2007;15:1139-1146.

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