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*Vitamin E Stays in the News...*

# Two New Studies Find Natural Vitamin E Better Absorbed, Retained Than Synthetic

Researchers have long known that natural vitamin E, milligram for milligram, is about 36 percent more potent than the synthetic form of the vitamin. In fact, the "international unit," or IU, standard was developed to compensate for these differences.

But two new studies using different groups of people – not laboratory animals – have found that natural vitamin E is utilized twice as efficiently as the synthetic form.

"Natural vitamin E may cost twice as much , but you get twice as much bang for your buck," Graham W. Burton, PhD, told THE NUTRITION REPORTER. Burton, a researcher at the National Research Council of Canada, Ottawa, directed one of the studies.

In the study, Burton and his American colleagues gave five healthy men and women a single 30 mg dose of vitamin E, which was half natural and half synthetic. A month later, the same people took an identical vitamin E supplement for eight days.

Another five subjects took a single 300 mg dose of vitamin E, which was also half natural and half synthetic. A month later, they took an identical vitamin E supplement for eight days.

By chemically labeling the natural and synthetic vitamin E supplements, Burton and his colleagues were able to tell them apart and to also distinguish dietary vitamin E.

While natural and synthetic vitamin E were absorbed equally well through the digestive tract, the liver selected for the natural form over the synthetic: blood levels of natural vitamin E were consistently twice those of the synthetic form.

"What we found was that blood and organ levels of natural vitamin E were almost double those of synthetic vitamin E, and they were consistently so," Burton explained. "The beauty of this study design is that each participant, by taking both natural and synthetic vitamin E, served as both a control and experimental subject."

A similar trend was found in the blood of 22 surgical patients given the half-natural, half-synthetic vitamin E supplements for up to six weeks and in two terminally ill patients given the supplements for one to two years.

Tissue levels of natural vitamin E – based on organs removed during surgery – also increased compared with the synthetic. However, it appeared to take at least a year or two for the 2:1 natural-to-synthetic ratio to develop in tissues.

In the other study, Robert V. Acuff, MD, of East Tennessee State University, Johnson City, gave vitamin E supplements – again, half natural and half synthetic – to 15 pregnant women five days before giving birth. At delivery, natural vitamin E levels in the mothers' blood were consistently double those of the synthetic vitamin. Furthermore, natural vitamin E levels in the placental cords was almost 3.5 times higher than the synthetic form.

References: Burton GW, Traber MG, Acuff RV, et al., "Human plasma and tissue a-tocopherol concentrations in response to supplementation with deuterated natural and synthetic vitamin E," *American Journal of Clinical Nutrition*, 1998;67:669-684. Acuff RV, Dunsworth RG, Webb LW, et al., "Transport of dueterium-labeled tocopherols during pregnancy," *American Journal of Clinical Nutrition*, 1998;67:459-464.

## Vitamin E, Beta-Carotene Can Lower Risk of Prostate Cancer

Relatively low supplemental doses of vitamin E can substantially reduce the risk of prostate cancer, according to a new analysis of data from the Finnish Alpha-Tocopherol, Beta-Carotene (ATBC) Prevention Study.

The findings, reported in the *Journal of the National Cancer Institute*, also found that beta-carotene supplements reduced the risk of prostate cancer, but only if men did not regularly drink alcohol. If they did, their risk of prostate cancer increased, though the increase was not statistically significant.

This year, an estimated 184,500 American men will be diagnosed with prostate cancer and 39,200 will die.

Ollie P. Heinonen, MD, DSc, and his colleagues at the University of Helsinki, tracked 29,000 male smokers for an average of 6 years. Some of the men took 50 IU of vitamin E, 20 mg of beta-carotene, or both daily.

Men taking vitamin E were 32 percent less likely to develop prostate cancer and 41 percent less likely to die from the disease. Beta-carotene supplements conferred a

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similar benefit, so long as the smokers did not also consume alcohol.

A combination of vitamin E and beta-carotene seemed to negate the benefits somewhat, reducing the incidence of prostate cancer by only 16 percent.

The supplements also slightly reduced the risk of benign prostatic hyperplasia, known also as enlarged prostate. Vitamin E reduced the incidence of benign prostatic hyperplasia by 4 percent, and beta-carotene reduced its risk by 6 percent.

An earlier study by Harvard University researchers found that beta-carotene supplements reduced the risk of prostate cancer by 36 percent. Another Harvard study reported a 45 percent lower risk of prostate cancer among men regularly eating lycopene-rich tomato sauces.

Reference: Heinonen OP, Albanes D, Virtano J, et al., "Prostate cancer and supplementation with a-tocopherol; and b-carotene: incidence and mortality in a controlled trial," *Journal of the National Cancer Institute*, 1998;90:440-446. □

## Low Vitamin B6 Again Linked to Carpal Tunnel Syndrome

A study of 441 people from a variety of industries and a university has found that, among men, carpal tunnel syndrome (CTS) is strongly associated with low blood levels of vitamin B6.

CTS is characterized by numbness or pain in the wrist and hand. People who perform repetitive hand movements, such as typists and supermarket clerks, have an above-average risk of developing the condition.

"What is clear is that vitamin B6 may not be effective for everyone with CTS but that some patients benefit from this therapy," wrote Richard C. Keniston, MD, in the *Journal of Occupational and Environmental Medicine*.

Keniston, of the Portland Hand Surgery and Rehabilitation Center, Portland, Ore., diagnosed CTS based on patient descriptions of hand and wrist numbness, tingling, and pain – and confirming the condition by measuring abnormal nerve conduction.

Many of the subjects were already taking vitamin B6 because they had heard it might help relieve CTS. So, focusing on 137 men not taking supplements, Keniston found a significant inverse correlation between tingling and other symptoms and low levels of pyridoxal 5'-phosphate (PLP), the biologically active form of B6.

"We found that higher plasma PLP concentration, particularly in unsupplemented males, appeared to be associated with less frequent pain/discomfort, tingling, and nocturnal awakening," he wrote.

Keniston also found that a "relative" deficiency of B6 – low B6 relative to high vitamin C levels – was also associated with an increased risk of CTS.

"Many medical conditions (eg, diabetes, thyroid disease, and rheumatoid arthritis) requiring chronic medications and many drugs, including hormones and nontherapeutic legal drugs such as tobacco and alcohol, are associated with increased risk of CTS," he wrote. "These same medical conditions and drugs are also associated with impaired vitamin B6 and/or vitamin C metabolism."

More than 25 years ago, John Ellis, MD, of Mt. Pleasant, Texas, began recommending 200 mg of vitamin B6 daily to treat patients with carpal tunnel syndrome. Ellis noted that it generally took three months for vitamin B6 levels to normalize.

Reference: Keniston RC, Nathan PA, Leklem JE, et al., "Vitamin B6, vitamin C, and carpal tunnel syndrome," *Journal of Occupational and Environmental Medicine*, 1997;39:949-959. □

## More Evidence that Folate, B6 Protect Against Heart Disease

Two new studies have found that high blood levels of folate (folic acid) and vitamin B6 lower blood levels of homocysteine – and likely reduce the risk of cardiovascular disease. However, the amount of folate currently added to enriched cereals is not enough to protect against heart disease.

Killian Robinson, MD, a cardiologist at the Cleveland Clinic Foundation, along with European researchers, compared homocysteine and vitamin levels in 750 people with cardiovascular disease and 800 healthy subjects.

"Increases in plasma concentrations of homocysteine are common in patients with stroke, coronary disease, and peripheral vascular disease and confer an independent risk of atherosclerosis," Robinson wrote in *Circulation*. "Independent risk" means that a person's homocysteine levels are unrelated to other risk factors, such as smoking and elevated cholesterol.

In the study, high levels of homocysteine and low levels of folate and vitamin B6 were strongly associated with a high risk of cardiovascular disease. Low vitamin B12 levels were also linked to increased risk of disease, but not significantly.

People with the highest homocysteine levels had more than twice the risk of cardiovascular disease, compared with those with low levels. In addition, people with the most severe blood-vessel blockages had the lowest levels of folate and vitamin B6.

Robinson wrote that folate and homocysteine levels were inversely related, but vitamin B6's benefits appeared unrelated to any effect on homocysteine, suggesting that the vitamin may protect against vascular disease through other mechanisms.

In a related editorial, Gilbert S. Omenn, MD, PhD, of the University of Michigan, wrote, "We believe it is desirable to bring tHcy [homocysteine] levels down to

the range of 9 to 10 mmol/L. Diet alone is unlikely to be sufficient to increase circulating folate levels and decrease tHcy levels." Omenn recommended that "everyone" consume at least 400 mcg of folic acid daily, as well as some vitamin B6 and B12.

In a separate study, Manuel R. Malinow, MD, of Oregon Health Sciences University, Portland, reported that recommended levels of folate in enriched cereal (~127 mcg/serving) decrease homocysteine levels by only 3.7 percent, too small a change to reduce heart disease risk. Higher amounts – between 499-665 mcg/serving – would reduce homocysteine levels by 11 percent.

References: Robinson K, Arheart K, Refsum H, et al., "Low circulating folate and vitamin B6 concentrations," *Circulation*, 1998;97:437-443. Malinow MR, Duell PB, Hess D, et al., "Reduction of plasma homocyst(e)ine levels by breakfast cereal fortified with folic acid in patients with coronary heart disease," *New England Journal of Medicine*, 1998;338:1009-1015. ▯

## Creatine Increases Strength in Sedentary Women

Loading up on creatine can increase muscle strength and fat-free muscle mass, according to a placebo-controlled study of young, sedentary women.

Creatine, a component of protein, has been known for more than 20 years to promote protein synthesis in skeletal muscle. It also plays a key role in regenerating adenosine triphosphate (ATP), the chemical that stores and releases energy in cells.

Dutch researchers gave 10 women supplements containing 20 mg of creatine monohydrate daily for four days, followed by 5 mg of creatine monohydrate daily for 10 weeks. Nine other women were given supplements containing inert ingredients. Both groups underwent supervised weight training—including leg presses, bench presses, squats, and shoulder presses—for three days each week.

After four days, women taking creatine supplements had a 6 percent increase in muscle phosphocreatine, a level maintained with lower doses of supplements.

By the end of the study, the creatine users had a 20-25 percent increase in maximum strength (in the muscle groups trained), a 10-25 percent increase in the exercise capacity of forearm muscles, and a 60 percent increase in fat-free muscle mass, compared with women taking the placebo. Much of the increase in muscle mass, however, was the result of increased water content in the muscles.

Within four weeks of ceasing creatine supplements, phosphocreatine levels in the women returned to pre-study levels.

The researchers wrote that "our findings suggest that creatine supplementation might allow optimal training to continue for a longer period before overtraining develops."

Reference: Vandenberghe K, Goris M, Van Hecke P, "Long-term creatine intake is beneficial to muscle performance during resistance training," *Journal of Applied Physiology*, 1997;83:2055-2063. ▯

## Breast Feeding Reduces Respiratory Ills as Children Grow

Breast-fed infants are less likely than bottle-fed babies to develop respiratory illnesses as children, according to a study by Scottish researchers.

J. Stewart Forsyth, MD, and his colleagues at Ninewells Hospital and Medical School, Dundee, tracked the eating habits and health of 545 children. They found that infants breast fed exclusively for 15 weeks after birth had only a 17 percent risk of later having respiratory illness, compared with 32.2 percent for bottle-fed infants.

"One of the explanations for these findings is that nutritional deficiencies at critical periods of fetal and infant growth may induce permanent changes in physiological function," Forsyth wrote in the *British Medical Journal*.

There were other differences as well. Systolic blood pressure was higher in children who had been bottle fed as infants, compared with those who had been breast fed. In addition, infants who received solid food during their first 15 weeks of life were more likely to wheeze and have a higher percentage of body fat.

Reference: Wilson AC, Forsyth JS, Greene SA, et al., "Relation of infant diet to childhood health: seven year follow up of cohort of children in Dundee infant feeding study," *British Medical Journal*, 1998;316:21-5. ▯

## Prescription Drugs Kill 106,000 Hospitalized Patients Each Year

While questions sometimes arise about the safety of vitamins and other supplements, few doctors have addressed the broad issue of prescription drug safety. That makes an analysis of adverse drug reactions and deaths, published in the *Journal of the American Medical Association*, all the more significant.

Researchers at the University of Toronto estimated that 2,216,000 patients in the United States annually suffer serious adverse drug reactions and 106,000 deaths. This number would make prescription drug deaths the fourth or six leading cause of death, depending on the method of calculation – a number than does not account for prescription drug deaths among nonhospitalized patients.

Reference: Lazarou J, Pomeranz BH, and Corey PN, "Incidence of adverse drug reactions in hospitalized patients," *JAMA*, 1998;279:1200-1206.

No deaths from vitamin supplements, in or outside of hospitals, have been reported in years. —*Editor*. ▯



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# Quick Reviews of Recent Research

**• Lycopene reduces lung cancer risk in mice**

Researchers exposed laboratory mice to several cancer-causing compounds, then provided some of them with supplemental lycopene, a carotenoid found in tomatoes. Lycopene reduced the number of lung cancers in male but not female mice.

Kim DJ, et al., *Cancer Letters*, 1997;120:15-20.

**• Melatonin prevents ischemia-reperfusion injury**

Melatonin, an antioxidant and hormone, can prevent free radical damage after injury. In the study, researchers blocked and restored blood flow to a major gastric artery. Lipid peroxidation, a marker of free radical activity, increased. However, this increase was inhibited with melatonin.

De La Lastra CA, et al., *Journal of Pineal Research*, 1997;23:47-52.

**• Pycnogenol® reduces DNA damage**

In a series of laboratory experiments, Pycnogenol® (a complex of flavonoids from French maritime pine trees) reduced the release of free radicals by white blood cells, prevented the oxidation of the low-density lipoprotein form of cholesterol, and prevented free radical damage to DNA.

Nelson AB, et al., *Drug Development and Industrial Pharmacy*, 1998;24:139-144.

**• Carotenoids lessen free radical damage**

Nine women were placed on a low-carotenoid diet and/or were given supplements of beta-carotene and mixed carotenoids. Women eating the low-carotenoid diet had high blood levels of malondialdehyde-thiobarbituric acid (MDA-TBA), a marker of lipid peroxidation. After receiving supplements of beta-carotene or mixed carotenoids, MDA-TBA levels declined.

Dixon ZR, et al., *Journal of the American College of Nutrition*, 1998; 17:54-58.

**• Beta-carotene protects against DNA damage**

Fourteen sedentary young men, were given 30 mg of beta-carotene daily for one month, and six others were given a placebo. After the period of supplementation, all of the men were asked to exercise until exhaustion. Beta-carotene levels increased 17-fold among the men taking supplements, but levels of this nutrient decreased in both groups after exercise. While beta-carotene did not reduce exercise-induced free radical damage to DNA, levels of DNA damage in general tended to be lower among men taking beta-carotene supplements.

Sumida S, et al., *Free Radical Research*, 1997;27:607-618.

**• Phosphatidyl choline and B12 enhance brains**

Both phosphatidyl choline and vitamin B12 have been sometimes been found helpful in brain disorders. In an experiment with laboratory rats, Japanese researchers found that a combination of these two nutrients – but neither by itself – enhanced learning and memory.

Masuda Y, et al., *Life Sciences*, 1998; 62: 813-822.

**• Genistein may help prostate**

Asian men who eat soy-based diets have a relatively low risk of enlarged prostate and invasive prostatic cancer compared with American men. Soy is rich in genistein, a hormone-like substance that also functions as an antioxidant. Using tissues obtained from men who had undergone prostate surgery, researchers found that genistein slowed the growth of benign prostatic hyperplasic cells. Genistein also inhibited the growth of prostate cancer cells.

Geller J, et al., *Prostate*, 1998; 34:75-79.

**• Lycopene and vitamin E protect cholesterol**

Lycopene, a carotenoid found in tomatoes, can team with vitamin E to prevent the oxidation of the low-density lipoprotein form of cholesterol. In experiments with LDL obtained from healthy human subjects, researchers found that the ability of lycopene and beta-carotene to inhibit LDL oxidation was enhanced by vitamin E. In mice, lycopene enhanced resistance to LDL oxidation, but tomato oleoresin (a fatty extract of tomato that contains lycopene and other antioxidants) was more effective.

Fuhrman B, et al., *Nutrition Metabolism and Cardiovascular Disease*, 1997; 7: 433-443.

**• Vitamin E Eases Hot Flashes**

Women treated for breast cancer cannot take estrogen-replacement therapy because it can stimulate the growth of breast cancers. However, vitamin E may service as a substitute. In a study of 120 breast cancer survivors, 800 IU of vitamin E daily slightly decreased hot flashes.

Barton DL, et al., *Journal of Clinical Oncology*, 1998; 16: 495-500.

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