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Folic Acid and Vitamin B12: Can These Nutrients Help Prevent Hearing Loss?

Can high levels of some vitamins reduce the risk of age-related hearing loss? According to a new study, they just might.

An estimated 28 million Americans have some form of hearing impairment, and hearing loss is one of the top four chronic health problems experienced by the elderly. (The others are heart problems, hypertension, and arthritis.)

The cause of hearing loss may be related, in part, to poor circulation resulting from low levels of some vitamins, according to Mary Ann Johnson, PhD, of the University of Georgia, Athens. The cochlea, the principal structure of the inner ear, contains a complex network of small blood vessels, which are fed by a single artery.

Like the body's other arteries, this one may be subject to damage from high levels of homocysteine, a toxic substance formed during the metabolism of methionine (an amino acid). Other studies have determined that high levels of homocysteine, which damages blood vessel walls, are a key risk factor for coronary heart disease and stroke.

The link between homocysteine and hearing loss was strengthened by the findings of Johnson's most recent study: elderly women were more likely to suffer from hearing loss if their blood levels of folic acid and vitamin B12 were below normal. Both vitamins are known to reduce homocysteine levels.

In the study, Johnson tested the hearing of 55 healthy women ages 60-71. Based on the results of the test, they were determined to have either normal or impaired hearing. Next, Johnson measured blood levels of folic acid and vitamin B12 and assessed the women's dietary intake of the vitamins.

Women with impaired hearing had 31 percent lower levels of folic acid and 38 percent lower levels of vitamin B12 in their blood, compared with women who had normal hearing. Among women who did not take any supplements containing these vitamins, folic acid levels were 43 percent lower and vitamin B12 levels were 48 percent lower.

In addition, women with normal hearing were eight times more likely to consume the Recommended Dietary Allowance (RDA) for folic acid and three times more likely to consume RDA levels of

vitamin B12. The strongest correlation was between normal hearing and adequate folic acid intake.

Further analysis confirmed that normal hearing was most strongly associated with folic acid intake. Johnson did not measure homocysteine levels in her volunteer subjects.

Johnson suggested that low folic acid and vitamin B12 levels could reduce blood flow to the cochlea. She also noted that inadequate vitamin B12 might affect the myelination of nerve cells in the cochlea.

Reference: Houston DK, Johnson MA, Nozza RJ, et al., "Age-related hearing loss, vitamin B12, and folate in elderly women," *American Journal of Clinical Nutrition*, 1999;69:564-571. □

B Vitamins Reduce Homocysteine in Patients with Heart Disease

Relatively modest levels of folic acid, combined with vitamins B6 and B12, work just as well as higher doses of folic acid in reducing homocysteine levels.

Killian Robinson, MD, of the Cleveland Clinic gave 95 elderly patients with heart disease one of four supplement regimens for three months: (1) 400 mcg of folic acid, plus 12.5 mg of vitamin B6 and 500 mcg of B12; (2) 1 mg of folic acid, plus B6 and B12; (3) 5 mg of folic acid, plus B6 and B12; or (4) a placebo.

Homocysteine levels in each of the treatment groups declined about 30 percent, from about 13-14.8 micromoles per liter of blood to 9.6-9.8 micromoles per liter. There was no significant change in the placebo group.

Robinson wrote that "a daily dose of 400 mcg folic acid combined with vitamins B12 and B6 normalizes homocysteine levels in patients with coronary artery disease."

He noted that this dose of folic acid, combined with the other B vitamins, "may be equivalent to higher doses" in reducing homocysteine levels.

In a separate study of 17 healthy subjects, British researchers found that an increase in homocysteine levels led to the rapid onset on endothelial dysfunction—the inability of blood vessels to relax. Disorders of the endothelium, a layer of cells in blood vessel walls, are a risk factor for heart disease.

Continues on next page

Pretreatment with vitamin C (1 gram daily) did not alter homocysteine levels, but it did reduce the endothelial dysfunction. "Our results support the hypothesis that the adverse effects of homocysteine on vascular endothelial cells are mediated through oxidative stress mechanisms," wrote Jaspal S. Kooner, MD.

References: Lobo A, Naso A, Arheart K, "Reduction of homocysteine levels in coronary artery disease by low-dose folic acid combined with vitamin B6 and B12," *American Journal of Cardiology*, 1999;83:821-825. Chambers JC, McGregor A, Jean-Marie J, et al., "Demonstration of rapid onset vascular endothelial dysfunction after hyperhomocysteinemia. An effect reversible with vitamin C therapy," *Circulation*, 1999;99:1156-1160. □

Clue to Cancer Prevention: Green Tea Inhibits Angiogenesis

Many studies have shown that green tea can reduce a person's risk of cancer. The tea is rich in antioxidant flavonoids known to quench free radicals, which can cause cancerous cell mutations.

Now, a study has found that a key ingredient in green tea inhibits angiogenesis, the growth of new blood vessels that tumors need to flourish.

In an experiment, Yihai Cao, PhD, of the Karolinska Institute, Sweden, used "vascular endothelial growth factor (VEGF)" to stimulate the growth of new blood vessels in the eyes of laboratory mice. VEGF is a potent inducer of angiogenesis, and the growth of small blood vessels in the eyes (called corneal vascularization) is similar to what happens in tumors.

Some of the mice were given plain water to drink, and others received green tea. Cao measured blood levels of epigallocatechin-3-gallate (EGCG) in the blood of tea-drinking mice and found them to be comparable to levels in people who have consumed two to three cups of tea. The tea significantly decreased the growth of blood vessels in the eye.

In a separate experiment, Cao found that EGCG inhibited the growth of blood vessels in a dose-dependent manner. In other words, the higher the dose, the more blood-vessel growth was inhibited.

Reference: Cao Y and Cao R, "Angiogenesis inhibited by drinking tea," *Nature*, 1999;398:381-382. □

Pancreatic Cancer Linked to Low Folic Acid and Vitamin B6

Other than age and smoking, researchers have been unable to pinpoint other consistent risk factors for pancreatic cancer. The disease is the 11th most common type of cancer and the fifth leading cause of

cancer-related deaths in the United States.

But a new study suggests that low levels of folic acid and vitamin B6 may increase the risk of pancreatic cancer.

Rachel Z. Stolzenberg-Solomon, PhD, of the National Cancer Institute, analyzed data from the Alpha-Tocopherol, Beta-Carotene Cancer Prevention study, which centered around 29,000 middle-age and elderly Finnish smokers.

She found that pancreatic cancer was inversely related to blood levels of both folic acid and pyridoxal-5'-phosphate, the biologically active form of vitamin B6. Men with the highest levels of folic acid and vitamin B6 had about half the risk of developing pancreatic cancer, compared with men who had low levels of the nutrients.

In general, study subjects had low levels of these vitamins. Ninety percent of subjects had low levels of folic acid, with 25 percent being deficient. Half of the subjects also had low vitamin B6 levels.

Stolzenberg-Solomon suggested that a lack of folic acid and vitamin B6 interfere with normal methylation reactions, which are necessary for the synthesis of deoxyribonucleic acid (DNA). Imbalances in methylation can affect the stability of chromosomes and gene expression, leading to mutations and a higher risk of cancer.

The amino acid methionine, in the form of S-adenosyl methionine (SAME), plays a central role in methylation reactions. However, folic acid and other B vitamins contribute to methylation reactions.

Other studies, noted Stolzenberg-Solomon, have found that low levels of folic acid increase the risk of colon cancer.

Reference: Stolzenberg-Solomon RZ, Albanes D, Nieto FJ, et al., "Pancreatic cancer risk and nutrition-related methyl-group availability indicators in male smokers," *Journal of the National Cancer Institute*, 1999;91:535-541. □

Broccoli, Cruciferous Vegetables May Lower Bladder Cancer Risk

Men who regularly eat broccoli have a low risk of bladder cancer, compared with men who do not eat this vegetable. That's the finding of a new study by researchers at the Harvard School of Public Health.

Bladder cancer is the sixth most common cancer in the United States, and it affects three to four times more men than women.

Dominique S. Michaud, ScD, analyzed the dietary habits of almost 48,000 men in the Health Professionals Follow-Up Study. At first, Michaud noted a weak relationship between overall fruit and vegetable intake and a reduced risk of bladder cancer.

When she analyzed individual groups of vegetables, she found that cruciferous vegetables were associated with a 51 percent lower risk of bladder cancer. In contrast, yellow and green leafy vegetables were not protective against this type of cancer.

Broccoli was the most frequently eaten cruciferous vegetable, and both broccoli and cabbage were independently related to a low risk of bladder cancer. Cauliflower, Brussels sprouts, and kale were also associated with a low but statistically insignificant risk of bladder cancer.

The protective effect of cruciferous vegetables was strongest among men who had never smoked. Smoking is strongly associated with bladder cancer risk.

Neither sauerkraut nor coleslaw influenced the risk of bladder cancer.

Reference: Michaud DS, Spiegelman D, Clinton SK, et al., "Fruit and vegetable intake and incidence of bladder cancer in a male prospective cohort," *Journal of the National Cancer Institute*, 1999;91:605-613. □

Hypothesis: NAC May Be Helpful in Parkinson's Disease

N-acetylcysteine (NAC) is a potent sulfur-containing antioxidant that hospitals routinely use as an antidote for acetaminophen overdose. Studies have found that it can substantially reduce influenza symptoms and extend the life expectancy of AIDS patients.

In a recent paper in *Life Sciences*, Marcos Martinez, PhD, of the La Paz University Hospital, Madrid, Spain, built a scientific argument that NAC may be beneficial to patients with Parkinson's disease.

Parkinson's is characterized by the degeneration of neurons in a part of the brain known as the substantia nigra. Free radical damage to the substantia nigra plays a central role in Parkinson's. In addition, there is a decrease in bioenergetics and energy production in substantia nigra cells.

According to Martinez, levels of glutathione, a principal cellular antioxidant, are low in the substantia nigra of patients with Parkinson's. NAC can boost glutathione production, and this is how it counters acetaminophen poisoning. NAC also has a direct antioxidant effect against free radicals.

NAC may boost cellular energy production and protect sulfur compounds (sulfhydryl groups) involved in energy production. These effects would offset age-related declines in cellular energy production.

Because NAC is safe and easy to administer as a dietary supplement, Martinez wrote that it is potentially useful in the treatment of Parkinson's.

Reference: Martinez M, Martinez N, Hernandez

AI, et al., "Hypothesis: Can N-acetylcysteine be beneficial in Parkinson's disease?" *Life Sciences*, 1999;64:1253-1257. □

Creatine Found Helpful in Muscular Dystrophy, Related Disorders

Creatine, a nutrient that enhances the strength of body builders, can also benefit people with neuromuscular diseases, such as muscular dystrophy.

Mark Tarnopolsky, MD, of the McMaster University Medical School, Hamilton, Ontario, recently tested the effects of creatine monohydrate supplements in two groups of patients. The first consisted of 81 subjects with muscular dystrophies, mitochondrial myopathies, and other disorders that limit the production of energy in muscle cells. These people were given 10 grams of creatine monohydrate daily for five days, followed by 5 grams for an average of six days.

The second consisted of 21 patients who were given a placebo for 11 days, followed by creatine supplementation. Tarnopolsky measured all of the subjects' hand, foot, and leg strength before and after they received the creatine.

Patients taking creatine supplements averaged a "significant" 10-15 percent improvement in strength, demonstrated by an increased ability to perform high-intensity exercises. They also gained weight and muscle mass.

Reference: Tarnopolsky M and Martin J, "Creatine monohydrate increases strength in patients with neuromuscular disease," *Neurology*, 1999;52:854-7. □

Researchers Pinpoint Yet Another Way Vitamin E Lowers Heart Risk

Inflammation of blood vessel walls plays a crucial role in the development of coronary heart disease. Now, researchers report, vitamin E inhibits the release of a proinflammatory compound known to promote heart disease.

In a series of experiments, Ishwarlal Jialal, MD, PhD, and Sridevi Devaraj, PhD, of the University of Texas Southwestern Medical Center, Dallas, focused on a hormone-like proinflammatory cytokine known as interleukin-1 beta (IL-1B). IL-1B promotes the formation of blood clots and encourages monocytes (a type of white blood cell) to adhere to blood vessel walls. Both are fundamental processes that set the stage for coronary heart disease.

Free radicals stimulate the production of IL-1B. In addition, free radical oxidized low-density lipoprotein (LDL) cholesterol augments the release of IL-1B. Earlier experiments by Jialal found that

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Quick Reviews of Recent Research

• Beta-carotene supplements reduce deaths

Pregnant women in developing nations are 50-100 times more likely to die than are women in industrialized nations. Researchers gave supplements of beta-carotene or vitamin A, or placebo, to 20,000 pregnant women in rural Nepal for at least 3.5 years. Women taking beta-carotene supplements had a 49 percent lower risk of death, compared with women taking the placebo. Vitamin A supplements reduced the risk of death by 40 percent. Twenty-seven percent of the reduction was related to a decrease in obstetrical problems.

West KP Jr, et al., *BMJ*, 1999;318:570-575.

• Soy milk linked to low prostate cancer risk

A study of more than 12,000 Seventh-Day Adventist men in California found that drinking soy milk more than once a day was associated with a 70 percent reduction in the risk of prostate cancer. Soy contains estrogen-mimicking isoflavones that, in animal studies, reduce the likelihood of developing prostate cancer.

Jacobsen BK, et al., *Cancer Causes and Control*, 1998;9:553-557.

• Multivitamins improve cholesterol levels

Researchers gave 46 subjects, ages 40-75, either a multivitamin supplement or placebo for eight weeks. After a four-week washout period, during which no supplements were given, the vitamins and placebos were reversed among the study participants. In the vitamin group, the "good" high-density lipoprotein (HDL) form of cholesterol increased by an average 31 percent. Overall, cardiovascular risk factors declined by 23 percent.

Morcos NC, *Medical Science Research*, 1999;27:121-125.

Vitamin E Blocks Inflammation...

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vitamin E prevented the oxidation of LDL, which would reduce IL-1B activity.

In their current experiment, Jialal and Devaraj found that activated monocytes released large amounts of IL-1B. However, increasing amounts of vitamin E reduced the release of IL-1B by 45 to 66 percent.

Vitamin E accomplished this by blocking the activity of an enzyme, 5-lipoxygenase, which controls the release of IL-1B.

Reference: Devaraj S and Jialal I, "a-tocopherol decreases interleukin-1B release from activated human monocytes by inhibition of 5-lipoxygenase," *Arteriosclerosis, Thrombosis and Vascular Biology*; 1999;19:1125-1133. □

• Alpha-lipoic acid may reduce birth defects

Diabetic women are more likely than nondiabetics to deliver infants with birth defects. Researchers found that alpha-lipoic acid substantially reduced the risk of neural-tube defects, fetal resorption, and weight loss in pregnant diabetic laboratory rats.

Wiznitzer A, *American Journal of Obstetrics and Gynecology*, 1999;188-193.

• St. John's wort helps in fatigue

Because St. John's wort has reduced fatigue in depressed patients, researchers investigated whether the herb might be beneficial in patients whose primary complaint was fatigue. Twenty patients received extracts of St. John's wort for six weeks. Fatigue decreased after two weeks and was reduced significantly after six weeks. In addition, depression (which had affected half the subjects) and anxiety were also reduced.

Stevinson C, et al., *Phytomedicine*, 1998;5:443-447.

• Vitamin E protects smokers

Researchers gave either vitamin E supplements or placebos to 13 subjects with elevated cholesterol, 14 smokers with normal cholesterol, and 15 smokers with elevated cholesterol. Vitamin E helped maintain normal endothelial function among the smokers with high cholesterol levels. The vitamin also reduced the number of antibodies against oxidized low-density lipoprotein cholesterol, suggesting a more normal response to LDL.

Heitzer T, et al., *Journal of the American College of Cardiology*, 1999;33:499-505.

• Nutrient deficiencies tied to brittle asthma

Researchers compared the diets of 20 subjects with brittle asthma, 20 with nonbrittle asthma, and 20 without asthma. Subjects with brittle asthma generally had lower dietary intakes of vitamins A and E, compared with the other groups. Reduced antioxidant activity contributes to brittle asthma.

Baker JC, et al., *Thorax*, 1999;54:115-118.

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