

The NUTRITION REPORTER™

THE INDEPENDENT NEWSLETTER THAT REPORTS VITAMIN AND MINERAL THERAPIES © MARCH 1999 VOL 10 NO 3 BY JACK CHALLEM

Prenatal Vitamin Supplements Reduce Risk of Brain Tumors in Children

Prenatal supplements are routinely recommended to pregnant women. A new study points to an unexpected benefit: the children of women who supplement are less likely to develop brain tumors.

The vitamins, researchers believe, may reduce the risk of cancer by blocking the hazardous effects of nitrites in cured meats, such as sausages and hot dogs.

Researchers found that the longer women took vitamin supplements while pregnant, the greater was the reduction in brain tumor risk in their children.

"The greatest risk reduction was among children diagnosed under 5 years of age whose mothers used supplements during all 3 trimesters," wrote Susan Preston-Martin, MD, of the University of Southern California, Los Angeles.

Children born to such mothers had a 40 percent reduced risk of developing brain tumors. If the mother took vitamin supplements during only two trimesters, the reduction in risk was 30 percent.

Most of the women took multivitamin supplements and some also took individual supplements. Although Preston-Martin noted that it was difficult to isolate the benefits of individual nutrients, vitamins C, E, A, and folic acid seemed to be especially protective.

The study was conducted at eight medical centers in six countries. Supplement use varied from about 3 percent of women in Israeli and French medical centers to as much as 92 percent in American medical centers.

"Brain tumors are the leading cause of cancer deaths in children in developed countries," Preston-Martin wrote.

The study included 1,051 cases of brain tumors and 1,919 controls for comparison. The reduction in risk of childhood brain tumors appeared unrelated to maternal vitamin use before pregnancy or during breast feeding.

Preston-Martin suggested that the vitamins might be protective by blocking the formation of N-nitroso compounds in the digestive track. N-nitroso compounds are formed when nitrite-containing foods, such as hot dogs and bacon, are broken down in an acidic environment, as in the stomach.

N-nitroso compounds are known to damage deoxyribonucleic acid (DNA) and to cause tumors in laboratory animals. Other studies have shown that

vitamins may protect against this damage.

Some studies have found that children have a relatively high risk of developing brain tumors if their mothers had consumed large amounts of nitrite-containing foods while pregnant.

In an analysis of related research, Greta R. Bunin, PhD, of the University of Pennsylvania School of Medicine, Philadelphia, described the consistent association between pregnant women who ate nitrite-containing foods, which also include many luncheon meats, and brain tumors in their children. Nine such studies have been published since 1982, and most showed that high intake of nitrite-containing foods doubled the risk of brain tumors in children. Studies show that fruits and vegetables may be protective.

References: Preston-Martin S, Pogoda JM, Mueller BA, et al., "Prenatal vitamin supplementation and risk of childhood brain tumors," *International Journal of Cancer*, 1998;11:17-22. Bunin GR, "Maternal diet during pregnancy and risk of brain tumors in children," *International Journal of Cancer*, 1998;11:23-25. □

High-Carotenoid Diets Associated with Lower Risk of Diabetes

People with high blood levels of carotenoids have a relatively low risk of developing diabetes.

Earl S. Ford, PhD, of the Centers for Disease Control and Prevention, analyzed the diets of 1,665 people ages 40-74. The subjects included people with normal glucose tolerance, impaired glucose tolerance (a prediabetic state), recently diagnosed diabetes, and established diabetes. In particular, Ford focused on blood levels of beta-carotene, alpha-carotene, lutein/zeaxanthin, lycopene, and cryptoxanthin.

Beta-carotene levels declined progressively among subjects with normal glucose tolerance, impaired glucose tolerance, and frank diabetes. People with impaired glucose tolerance had 13 percent less beta-carotene, and those with diabetes had 20 percent less beta-carotene in the blood. Lycopene levels followed a similar pattern, but the relationship was not as significant as that with beta-carotene.

Although the study does not show a clear cause

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and effect between low carotenoid levels and diabetes, there is indirect evidence supporting that view. According to Ford, "free radicals have been shown to disrupt insulin action and total body glucose disposal." Dietary studies have found that high-vegetable diets, which are rich in free radical-quenching antioxidants, may reduce the risk of diabetes.

Reference: Ford ES, Will JC, Bowman BA, et al., "Diabetes mellitus and serum carotenoids: findings from the third national health and nutrition examination survey," *American Journal of Epidemiology*, 1999;149:168-176. □

Tests Find Cherries To Be Potent Antiinflammatory and Antioxidant

Cherries are a traditional Cherokee Indian remedy for arthritis and gout. A new study explains why they work: the fruit is rich in antioxidant and antiinflammatory anthocyanidins and cyanidins, both subgroups of flavonoids.

In a laboratory study, Muraleedharan G. Nair, PhD, of Michigan State University, East Lansing, found that about 20 tart cherries (~100 grams) contain 12.5 to 25 mg of anthocyanidins.

Laboratory assays by Nair found that cherry anthocyanidins had antioxidant activity similar to vitamin E. In addition, assays found that the anthocyanidins were also powerful antiinflammatories. For example, cherry anthocyanidins inhibited two inflammation-promoting enzymes, cyclo-oxygenase-1 and cyclooxygenase-2 at doses more than 10 times lower than aspirin.

"The antioxidant and antiinflammatory properties of anthocyanidins and cyanidin suggest that consumption may have the potential to reduce cardiovascular or chronic diseases in humans," Nair wrote.

Reference: Wang H, Nair M, Strasburg GM, et al., "Antioxidant and antiinflammatory activities of anthocyanidins and their aglycon, cyanidin, from tart cherries," *Journal of Natural Products*, 1999;62:86-88. □

Vitamin E, Alpha-Lipoic Acid May Help Protect Against Blast Damage

Vitamin E and alpha-lipoic acid, a natural antioxidant, may bolster the body's defenses against explosions, weapons fire, and other high-energy noises, according to a recent animal study.

Blast overpressure can seriously damage hollow organs, such as the ears and lungs. Lung damage in particular can lead to the rupture of blood vessels, which in turn can cause hemorrhaging and edema. Blast overpressure has also been associated with reductions in cognition, performance, and endurance.

In the study, Major Karen L. Armstrong, DVM, of Walter Reed Army Institute of Research, Washington, D.C., gave laboratory rats vitamin E, alpha-lipoic acid, vitamin C, or inert materials for three days. On the fourth day, the animals were anesthetized and exposed to a simulated blast wave.

Blood samples indicated that the unsupplemented animals had lower levels of oxygen in blood after the blast, a possible sign of hemoglobin (the oxygen-carrying molecule in the blood) breaking down.

In contrast, animals given vitamin E and alpha-lipoic acid maintained normal oxygen levels in the blood. Vitamin C had no effect.

The findings of this study "suggest that a brief dietary loading of vitamin E or alpha-lipoic acid may offer at least partial protection from blast-induced injury which may have occupational benefits to those repeatedly at risk of exposure to high-energy impulse noise," Armstrong wrote.

Reference: Armstrong KL, Cooper MF, Williams MT, et al., "Vitamin E and lipoic acid, but not vitamin C improve blood oxygenation after high-energy IMPULSE noise (BLAST) exposure," *Biochemical and Biophysical Research Communications*, 1998;253:114-118. □

Vitamin K Helps Strengthen Bones, Reduce Fractures

Diets high in vitamin K appear to reduce the risk of hip fractures in women, according to a study of more than 72,000 nurses.

Diane Feskanich, ScD, and colleagues at the Harvard Medical School analyzed dietary data obtained in the mid-1980s from 72,000 women ages 38-63. During 10 years of follow up, 270 hips fractures were reported.

Women who consumed modest to large quantities of vitamin K-containing foods were 30 percent less likely to suffer hip fractures, compared with women who consumed very little or none of the vitamin.

Iceberg and romaine lettuce provided the greatest amounts of vitamin K in the diets of the women, and these foods were the most protective. Broccoli, cooked spinach, and cabbage also provided substantial amounts of vitamin K.

Vitamin K is widely recognized as a key nutrient that enables blood to clot. Over the past few years, several studies have shown that the vitamin also plays an important role in the formation of bone. Low levels of vitamin K has been associated with thinning bones and fractures. In addition, there is evidence that vitamin K and vitamin D work together in the formation of bone tissues.

Reference: Feskanich D, Weber P, Willett WC, et

al., "Vitamin K intake and hip fractures in women: a prospective study," *American Journal of Clinical Nutrition*, 1999;69:74-79. □

Alpha-Lipoic Acid May Reduce Risk of Cataracts

Alpha-lipoic acid may reduce the risk of cataracts, according to a recent animal study.

Researchers at the University of Michigan Medical Center, Ann Arbor, induced diabetes in a group of laboratory rats, gave some of them supplemental alpha-lipoic acid, and then compared them to normal animals. They noted a number of changes in energy metabolism within the lenses of the rats' eyes.

Diabetes induced numerous alterations in the Krebs cycle and oxidative phosphorylation, processes that govern the breakdown of glucose and the creation of energy within cells. Among these changes was an apparent inhibition of glycolysis, a key step in the burning of sugar within cells.

In animals given supplemental alpha-lipoic acid, an antioxidant that plays key roles in energy production, these diabetes-related changes to lenses were "substantially prevented." Taking alpha-lipoic acid and vitamin E, wrote the researchers, "could thus help to avoid oxidative stress to the lens and thereby possibly diabetes-associated cataract formation."

Reference: Obrosova I, Cao X, Greene DA, et al., "Diabetes-induced changes in lens antioxidant status, glucose utilization and energy metabolism: effect of DL-a-lipoic acid," *Diabetologia*, 1998;41:1442-1450. □

Vitamin E Can Reduce Oxidative Stress in Diabetics

Diabetes is often viewed as a "model" of accelerated aging. The reason is that diabetics characteristically develop age-related diseases, such as heart disease, earlier in life than do nondiabetics.

Diabetic patients tend to suffer from relatively high levels of oxidative stress – that is, a high body burden of free radicals. As one indicator, diabetics have elevated levels of isoprostane, which are byproducts of free radical reactions in fats. They also have elevated levels of thromboxane B2, which promotes platelet aggregation and blood clots.

In a recent study of 85 diabetic patients, Giovanni Davi, MD, of the University of Chieti School of Medicine, Italy, found a "highly significant" association between isoprostane and glucose levels, "suggesting that lipid peroxidation may be, at least in part, related to determinants of glycemic control."

Urinary levels of isoprostane were higher in diabetics than nondiabetics and they were strongly correlated with blood sugar and urinary levels of

thromboxane B2.

After 10 patients were given 600 IU of vitamin E daily for two weeks, they benefited from a significant 37 percent reduction in isoprostane and a 43 percent decrease in urinary thromboxane B2 levels. Vitamin E also improved the "metabolic control" of diabetes in patients taking the supplement.

"We believe that our results have potential clinical implications for the prevention of atherothrombosis in diabetic patients," Davi wrote.

Reference: Davi G, Ciabattoni G, Consoli A, et al., "In vivo formation of 8-iso-prostaglandin F2a and platelet activity in diabetes mellitus," *Circulation*, 1999;99:224-229. □

Foods Rich in Beta-Carotene May Reduce Breast Cancer Risk

Eating a diet rich in beta-carotene may reduce the risk of breast cancer in postmenopausal women. That's the finding of a study comparing the diets of 273 women with breast cancer and 371 women without the disease.

Aisha O. Jumaan, PhD, of the Centers for Disease Control and Prevention, Atlanta, found that the protective effect of beta-carotene-containing diets was strongest among women who had been eating such diets for 20-45 years. The benefits were less clear among women who had been eating such diets for less than 20 years.

Jumaan wrote that "beta-carotene may be only a marker for other protective compounds in fruits and vegetables, including other micronutrients, phytochemicals, or fiber."

Reference: Jumaan AO, Holmberg L, Zack M, et al., "Beta-carotene intake and risk of postmenopausal breast cancer," *Epidemiology*, 1999;10:49-51. □

Calcium, Vitamin D Lower Risk of Some Types of Cancer

Calcium and vitamin D are known for their roles in building strong bones. A new study has found that they may also reduce the risk of some types of cancer.

Martin Lipkin, MD, of the Strang Cancer Research Laboratory, New York City, fed laboratory mice a Western-style high-fat diet low in calcium and vitamin D for nine weeks. After eating this diet, the mice had an abnormal increase in the growth – hyper-proliferation – of pancreatic, prostatic, and breast epithelial cells.

According to Lipkin, several experimental and epidemiological studies have similarly found that high-fat intake and low calcium and vitamin D intake are associated with cancers of the pancreas,

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Quick Reviews of Recent Research

• Flavonoids may help diabetics

Ten diabetic patients were placed on a low-flavonoid diet for two weeks, followed by a diet that included flavonoid-rich foods, specifically onions (in tomato sauce) and six cups of tea daily. Flavonoid consumption was estimated at 76-110 mg daily, mostly from quercetin in the onions. Blood from the diabetics was drawn during both diets and exposed to hydrogen peroxide to generate DNA damage. The high-flavonoid diet reduced DNA damage by about 12 percent.

Lean MEJ, et al., *Diabetes*, 1999;48:176-181.

• Selenium forms have different effects

Selenium, an essential dietary mineral, has been shown to reduce the risk of cancer in people. In a study with laboratory rats, researchers tried to identify the effects of selenite, selenate, and selenomethionine. Selenite and selenate prevented precancerous cell changes in the colon, but not in the liver of the rats. Selenomethionine increased blood and liver levels of glutathione peroxidase, an antioxidant enzyme that requires selenium.

Davis CD, et al., *Journal of Nutrition*, 1999;129:63-69.

• Garlic boosts antioxidant levels

Hamsters with cancer suffer from high levels of free radical damage to fats in their livers and low levels of several glutathione antioxidant compounds. Giving the animals garlic extract reduced free radical damage and enhanced antioxidant levels.

Balasantil S and Nagini S, *Medical Science Research*, 1998;26:849-851.

• Selenium, vitamin E correct lipid problems

Obese laboratory rats were fed diets either with or without selenium and vitamin E. After 32 weeks, the rats' obesity led to an increase in blood fats (e.g. triglyceride), insulin levels, and markers of free radicals. Selenium and vitamin E corrected the elevated

triglyceride levels and reduced markers of free radicals.

Douillet C, et al., *Biological Trace Element Research*, 1998;65:221-236.

• Silymarin turns off inflammatory gene

Silymarin, an antioxidant extract from the herb milk thistle, is well established for its liver-protecting properties. Nuclear factor kappa-B (NF-kB) is a transcription factor involved in activating proinflammatory genes, such as in the liver. NF-kB can be activated by free radicals, bacteria and viruses, and radiation. In a recent experiment, researchers determined that silymarin inhibited the activation of NF-kB.

Saliou C, et al., *FEBS Letters*, 1998;440:8-12.

• Beta-glucan helps control glucose and insulin

Beta-glucan is a component of fiber that has been shown helpful in diabetes. In a study of 11 healthy men, researchers found that diets high in beta-glucan (e.g. in barley) slowed the absorption of carbohydrates and blunted increases in blood sugar and insulin.

Bourdon I, *American Journal of Clinical Nutrition*, 1999;69:55-63.

• Vitamin E linked to cognitive function

In a study of almost 1,800 middle-age and elderly men and women, researchers found that the highest cognitive test scores were associated with diets high in vitamin E.

Schmidt R, et al., *Journal of the American Geriatrics Society*, 1998;46:1407-1410.

• Pycnogenol® slows age-related changes in mice

In a study of mice bred to age prematurely, researchers noted that the animals developed declines in learning and memory, immunity, and blood cell formation. Mice given Pycnogenol® showed increases in numerous aspects of immunity, including white blood cells and antibody-forming cells, as well as in blood-forming cells.

Liu FJ, et al., *Cellular and Molecular Life Sciences*, 1998;54:1168-1172.

Calcium, Vitamin D...

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prostate, and breasts.

Adding calcium and vitamin D had a dramatic inhibitory effect on the abnormal growth of cells. "Adding dietary calcium and vitamin D markedly suppressed the Western-style diet-induced hyperproliferation of epithelial cells in those tissues," Lipkin and his colleagues wrote.

Reference: Xue L, Lipkin M, Newmark H, et al., "Influence of dietary calcium and vitamin D on diet-induced epithelial cell hyperproliferation in mice," *Journal of the National Cancer Institute*, 1999;91:176-181.□

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THE NUTRITION REPORTER™

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