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Vitamin and Mineral Supplements Reduce the Risk of Cataract, Other Eye Diseases

Doctors have known for years that adequate vitamin A and zinc can prevent night blindness. But several recent medical journal articles have stressed the importance of antioxidant vitamins in the prevention of cataracts and other eye diseases.

In the latest study, in the *May Ophthalmology*, researchers reported that supplements of vitamin E or a multivitamin can greatly reduce the risk of developing cataract, a leading cause of blindness.

M. Cristina Leske, MD, MPH, of the University Medical Center at Stony Brook, N.Y., and her colleagues looked at the dietary habits, vitamin supplement usage, and blood levels of vitamin E among 764 participants in the Lens Opacities Case-Control Study. Patients' lenses were photographed at the beginning of the study, and the patients had annual follow-up eye exams.

People who took multivitamin supplements had a 31 percent reduced risk of developing "nuclear cataract" – that is, a cataract located in the center of the lens. Vitamin E users fared better, with a 57 percent lower risk of developing cataract. People with high blood levels of vitamin E had a 42 percent lower risk.

VITAMINS HELP, BUT DOSE UNCLEAR

The researchers did not report the amount of supplemental vitamin E used, but subjects who had taken the vitamin for more than five years had a substantially lower risk than those who had taken it for less than five years.

Cataract is strongly associated with age, in large part because the lens accumulates damage with time. This damage is caused by free radicals generated by ambient radiation, oxygen, and hydrogen peroxide (a byproduct of metabolism). For example, when the carotenoids lutein and zeaxanthin absorb invisible ultraviolet light, they become oxidized in the process, but they prevent the light from damaging the lens and macula of the eye.

"The eye is...a unique organ because it is relatively unprotected and is constantly exposed to radiation, atmospheric oxygen, environmental chemicals, and physical abrasion," observed Richard C. Rose, PhD, of the Chicago Medical School, North Chicago, Ill. "The retina has an additional threat from conversion of radiation to neural impulses transmitted to the brain."

A number of dietary and endogenous antioxidants can quench free radicals in the eye, including vitamins E

and C, carotenoids, and glutathione peroxidase.

In a review of the protective role of vitamins and minerals, Nicholas A. Phelps Brown, MD, a London eye surgeon, wrote in the journal *Eye* that it "is likely that vitamin supplements given to populations with poor nutrition would have a significant impact in preventing the development of cataract and that vitamin supplements given to persons with good nutrition would have a minor impact in preventing the development of cataract."

VARIOUS VITAMINS MAY BE HELPFUL

Phelps Brown and his colleagues noted that vitamins E and C protect both the eye lens and retina, and some vitamins may indirectly benefit the eye by enhancing blood circulation. In addition, vitamins B1, B2, B6, and B12 are essential for normal function of the optic nerve. Also, the eye – specifically the retina and choroid – is one of the most zinc dense organs in the body.

According to Phelps Brown, gamma-linolenic acid (GLA), an essential fatty acid found in evening primrose oil supplements, has been reported of value in various types of "dry eye" syndromes, including Sjögren's syndrome and conjunctivitis sicca.

"Patients of all ages should be encouraged to maintain healthy nutrition, including the consumption of fresh fruit and vegetables, especially green vegetables, and vegetable and fish oils in place of animal fats," he wrote. "Middle-aged and elderly patients may benefit from a dietary supplement that ensures they receive an adequate daily intake of the various vitamins and minerals...For patients already affected by cataract, it is uncertain that a supplement taken at this stage will have any effect. For those with age-related macular degeneration affecting the vision in one eye there is a possible case that a vitamin and/or mineral supplement may help protect the unaffected eye."

References: Leske MC, Chylack LT Jr, He Q, et al., "Antioxidant vitamins and nuclear opacities," *Ophthalmology*, 1998;105:831-836. Rose RC, Richer SP, Bode AM, "Ocular antioxidants and antioxidant protection," *Proceedings of the Society for Experimental Biology and Medicine*, 1998;217:397-407. Phelps Brown NA, Bron AJ, Harding JJ, et al., "Nutrition supplements and the eye," *Eye*, 1998;12:127-133. □

Research summaries continue on next page

Good Diet, High Vitamin Levels Protect Against Cervical Cancer

Most physicians know that infection with the human papillomavirus (HPV) greatly increases the risk of developing cervical cancer. But diet may be the ultimate determinant of whether HPV infection leads to cervical cancer.

Cervical cancer is typically preceded by precancerous cell changes called dysplasias. So Anna Kwasniewska, MD, of the Lublin Medical Academy, Poland, compared the dietary habits of 324 women with precancerous cervical cell changes with 228 women with normal pap smears. Kwasniewska also compared women with HPV infections but normal pap smears and women with both HPV and cervical dysplasias.

She found that women with HPV and cervical dysplasias generally consumed large amounts of fatty meats, particularly pork and red meat, as well as cheeses and white bread. They ate relatively less yogurt, fruits and vegetables.

In contrast, women infected with HPV were generally spared cervical dysplasias if they ate diets rich in vitamin C, beta-carotene, and folate (the plant form of folic acid). These women also had higher consumption of milk, yogurt, cottage cheese, fruits, and vegetables.

Reference: Kwasniewska A, Charzewska J, Tukendorf A, et al., "Dietary factors in women with dysplasia colli uteri associated with human papillomavirus infection," *Nutrition and Cancer*, 1998;30:39-45. □

Silymarin Shows Promise in Prevention of Breast Cancer

The herb milk thistle (*Silybum marianum*) has a long history of use in the treatment of alcoholic liver disease and diabetes. It increases liver levels of glutathione, which helps detoxify hazardous compounds, and it lowers and stabilizes blood sugar levels. New research shows that a key component of milk thistle may also prove helpful in the treatment of breast cancer.

In a cell-culture study, Rajesh Agarwal, PhD, of the AMC Cancer Research Center, Denver, and his colleagues investigated the fundamental molecular mechanisms of how silymarin, a complex of antioxidants found in milk thistle, blocked the growth of breast cancer cells.

Agarwal and his colleagues looked specifically at defects in the cell cycle, which often lead to cancer cells. Mammalian cell growth takes place in well-defined steps, much like the cycle of a clock. The steps, also known as phases, include G₀, G₁, S, and G₂-M. Nondividing cells stay in the G₀, or resting phase. After receiving a growth signal, the cell shifts to the G₁ phase, in which DNA is synthesized. Later, the cell divides and the cycle begins in the new cell.

"One approach to controlling breast cancer is chemopreventive intervention, a means of cancer control in which the disease is prevented, slowed, or reversed by the administration of one or a combination of naturally occurring or synthetic compounds," Agarwal wrote in *Clinical Cancer Research* to explain his rationale.

He reported that silymarin inhibited the growth of breast cancer cells, in large part by stopping the G₁ phase of the cell cycle. The effect was dose dependent, meaning that higher doses of the herbal antioxidant were more effective in inhibiting breast cancer cell growth.

The results were particularly significant, Agarwal wrote, because silymarin inhibited breast cancer growth in a way independent of the p53 tumor gene, which normally suppresses the growth of cancer cells. Defects in the p53 gene are common in most human cancers, and the antiproliferative and anticarcinogenic effects of silymarin make the natural antioxidant potentially "widely useful" in the prevention of cancers.

In a separate paper, Agarwal described a cell-culture experiment in which silymarin inhibited the growth of prostate cancer cells

Reference: Zi X, Feyes DK, Agarwal R, "Anticarcinogenic effect of a flavonoid antioxidant, silymarin, in human breast cancer cells MDA-MB 468," *Cancer Research*, 1998; 58: 1920-1929. □

Arthritis Drug Blocks Folic Acid, Increases Cardiovascular Risk

The leading drug treatment for arthritis interferes with folic acid, a key B vitamin, and likely increases the risk of coronary heart disease and stroke.

The drug, methotrexate, is prescribed each year for an estimated 184,000 Americans with rheumatoid arthritis. It is also prescribed for patients with asthma, inflammatory bowel disease, psoriasis, and autoimmune diseases.

Some of the drug's side effects are strongly associated with reducing folic acid metabolism. "Because of these relationships, monitoring of blood folate...and homocysteine levels during longterm MTX [methotrexate] therapy may have important clinical implications," wrote Sarah L. Morgan, MD, in the *Journal of Rheumatology*.

High blood levels of homocysteine are a major risk factor for coronary artery disease and stroke. Its levels can be reduced with folic acid supplements (400-800 mcg/daily) or by a diet rich in folate-containing foods, such as leafy green lettuce. (Folate is the plant form of the vitamin, whereas folic acid is the better absorbed supplemental form.)

In a recent study, Morgan gave 79 patients taking methotrexate very high doses of folic acid – either 5 mg (not mcg) or 27.5 mg – or a placebo each week for a year.

She found that patients receiving either dose of folic acid were more likely to maintain normal blood levels of the vitamin and homocysteine.

In contrast, patients taking methotrexate without supplemental folic acid had lower blood levels of folic acid and higher levels of homocysteine, with a presumably higher risk of cardiovascular disease.

Morgan, of the University of Alabama, Birmingham, argued there were three justifications for giving folic acid supplements to patients taking methotrexate: to prevent methotrexate toxicity, to prevent or treat folic acid deficiency, and to prevent an elevation in homocysteine levels.

Reference: Morgan SL, Baggott, JE, Lee JY, et al., "Folic acid supplementation prevents deficient blood folate levels and hyperhomocysteinemia during longterm, low dose methotrexate therapy for rheumatoid arthritis: implications for cardiovascular disease prevention," *Journal of Rheumatology*, 1998; 25: 441-446. □

High Vitamin C Levels Help Protect Against Cardiovascular Diseases

Two new studies add to the evidence that vitamin C is good for the heart. In the first, Joel A. Simon, MD, of the San Francisco Veterans Administration Hospital investigated the relationship between blood levels of vitamin C and subsequent risk of coronary heart disease and stroke among 6,600 people in the Second National Health and Nutrition Examination Survey (NHANES II).

People with the highest blood levels of vitamin C were 27 percent less likely to develop coronary heart disease and 26 percent less likely to suffer a stroke, compared with people with low vitamin C levels.

Normal blood serum levels of vitamin C fall in the 0.5-1.0 mg/dl range. For every 0.5 mg/dl increase in vitamin C levels, subjects had a 10 percent reduction in coronary heart disease risk, explained Simon.

"Differences in nutrient antioxidant status may account for as much as 40% of the coronary heart disease risk not explained by known cardiovascular disease risk factors," he wrote. Vitamin C helps maintain normal blood vessel walls, breaks down cholesterol, and prevents free radical damage to cholesterol.

In the other study, Joseph A. Vita, MD, of the Boston University Medical Center, analyzed relationships between blood plasma levels of antioxidants and the severity of heart disease among 149 patients undergoing cardiac catheterization. Of the patients, 65 had stable angina and 84 had unstable angina or a heart attack within two weeks of the quasi-surgical procedure.

Although antioxidant levels generally did not correlate with the extent of heart disease [all of the patients had serious heart disease], lower levels of vitamin C were strongly associated with unstable angina or a recent heart

attack. The patients with the most unstable heart disease had low levels of vitamin C and sulfur-containing antioxidants (e.g., glutathione).

References: Simon JA, Hudes ES, Browner WS, "Serum ascorbic acid and cardiovascular disease prevalence in U.S. adults," *Epidemiology*, 1998;9:316-321. Vita JA, Keaney JF, Raby KE, et al., "Low plasma ascorbic acid independently predicts the presence of an unstable coronary syndrome," *Journal of the American College of Cardiology*, 1998;31:980-986. □

Grumpy? Diets High in Selenium or Fat Lead to Better Moods

Diets high in selenium and fat improve mood, whereas diets low in these nutrients lead to hostility, anxiety, and other signs of bad mood, according to two recent studies.

John W. Finley, PhD, and James G. Penland, PhD, of the USDA's Agricultural Research Service, Grand Forks, ND, placed 20 healthy male volunteers on either a high- or low-selenium diet for 105 days. At the beginning of the study and periodically throughout, they assessed the subjects' moods with the Profile of Mood States/Bi Polar form (POMS-BI), the Global Vigor Affect Scale, and a sleep behavior inventory (SBI). They also measured the subjects' blood plasma levels of selenium.

Although the low-selenium diet did not change blood levels of the nutrient, the high-selenium diet did increase its levels in the subjects after only one week.

By the end of the study, the two groups displayed significant differences in mood. The subjects eating a high-selenium diet were more clearheaded and less confused, more composed and less anxious, and more confident and less unsure. They also had a significant decrease in overall mood disturbance.

In contrast, the low-selenium group was more confused and less clearheaded and more depressed and less elated.

In the other study, Anita S. Wells, MD, of the University of Sheffield, England, placed 20 healthy men and women on a high-fat diet (41-percent of calories) for one month, then had 10 of the subjects eat a low-fat (25 percent) diet for another month. The subjects' moods were rated during the study with the POMS test.

Subjects eating the low-fat diet for a month had significant increases in anger/hostility and depression/dejection. In contrast, people eating the high-fat diets had slight improvements in these aspects of mood. In addition, tension/anxiety declined among the people eating high-fat diets, but did not change in those eating low-fat diets.

References: Finley JW and Penland JG, "Adequacy or deprivation of dietary selenium in healthy men: clinical

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Quick Reviews of Recent Research

• Vitamin K availability poor

Vitamin K is needed for normal clotting of blood and development of bone. In American diets, the vitamin is found chiefly in leafy green vegetables and four vegetable oils (soybean, cottonseed, canola, and olive). However, absorption of vitamin K from food is poor.

Booth SL and Suttie JW, *Journal of Nutrition*, 1998;128:785-788.

• Free radicals associated with varicocele

Varicocele is essentially a varicose vein in the testicles that radiates heat and kills sperm, causing infertility. Researchers compared free radical and antioxidant levels in semen from men with and without varicocele. Men with varicocele had higher levels of free radicals and lower levels of antioxidants. The researchers wrote that these "findings suggest a possible rationale for antioxidant supplementation in men with varicocele."

Kolettis PN, et al., *Journal of Urology*, 1998;159 (5) Suppl: 269 (Abst # 1032).

• Vitamin C and kidney stones

Vitamin C does not increase the risk of kidney stones, according to a review of the literature on this subject. One study cited found that people taking more than 1,500 mg of vitamin C daily had a lower risk of kidney stones than people consuming less vitamin C.

Gerster H, *Annals of Nutrition and Metabolism*, 1997; 41:269-282.

• How genistein inhibits cancer cells

Genistein, an antioxidant flavonoid found in soy, has anticancer properties. Cancer cells protect themselves against apoptosis (cell suicide) by producing stress proteins. In cell-culture experiments, genistein was found to inhibit the activation of stress proteins.

Zhou Y and Lee AS, *Journal of the National Cancer Institute*, 1998;90:381-388.

• Herbal oils have antibacterial properties

The essential oils of oregano, thyme, and rosewood can kill some species of bacteria in a process called lysis. The oils were effective in breaking down *Streptococcus pneumoniae*, a common cause of ear infections in children. The oils were also somewhat effective against *Escherichia coli* and some types of fungi but not against *Staphylococcus aureus*.

Horne D, presented at the American Society of Microbiology, April 1998.

Selenium, Fat, and Mood...

Continues from previous page and psychological findings," *Journal of Trace Elements in Experimental Medicine*, 1998;11:11-27. Wells AS, Read NW, Laugharne JDE, et al., "Alterations in mood after changing to a low-fat diet," *British Journal of Nutrition*, 1998;79:23-30. □

• Minerals, herb lower blood pressure

In a study with laboratory rats, researchers increased blood pressure with a high-sugar diet. Supplemental chromium decreased systolic blood pressure, but high levels of sugar (sucrose) overcame this benefit. Vanadium decreased sugar-induced hypertension and the effect was resistant to high levels of sugar. The herb *Gymnema sylvestre* increased blood pressure, though it significantly lowered cholesterol.

Preuss HG, et al., *Journal of the American College of Nutrition*, 1998;17:116-123.

• Veggies protect against carcinogen

Nitrosamines, formed during the cooking and metabolism of meat, are well established for their ability to induce cancerous cell changes. In a cell-culture study, extracts of broccoli, onion, carrot, and licorice protected against nitrosamine-induced cell changes. Extracts of apple, kiwi, and pineapple did not.

Martinez A, et al., *Journal of Agricultural and Food Chemistry*, 1998;46:585-589.

• Fish oils decrease colon cancers

In a study with laboratory rats, researchers found that diets supplemented with fish oil decreased colon tumors whereas corn oil increased colon tumors. Fish oil maintained a high level of apoptosis among the cancer cells.

Chang W-C, et al., *Journal of Nutrition*, 1998, 128-491-497.

• Selenium, vitamin E normalize glucose

Selenium and vitamin E deficiencies are strongly associated with the ability of the coxsackie virus to cause Keshan disease, a type of cardiomyopathy. Researchers fed laboratory rats grain (containing pathogenic factors) from Chinese regions in which Keshan disease is common. The animals developed diabetes-like increases in blood sugar and decreases in insulin. Supplemental selenium and vitamin E prevented these changes.

Tong W-M and Wang F, *Metabolism*, 1998;47:415-419.

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