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Could Good Nutrition – and Selenium Supplements – Stop the Annual Flu Season?

Each year, outbreaks of influenza (flu) kill more than 20,000 Americans and hospitalize another 110,000 people. Worldwide, these annual waves of infection cause millions of illnesses and the deaths of hundreds of thousands of people.

New strains of the flu virus appear annually, the result of constant mutations, making it nearly impossible for the body's immune system to develop a permanent defense against flu-causing viruses. But a dramatic new animal study – directly applicable to people – has found that adequate intake of selenium, an essential dietary mineral, can prevent dangerous mutations in the flu virus.

The research boosts earlier findings showing that a deficiency of either selenium or vitamin E lead to mutations in the coxsackie virus, which causes some 20 million cold-like infections and sore throats in the United States each year.

It also underscores how deficiencies of specific nutrients can accelerate the evolution of viruses and increase the seriousness of common infections.

In the latest research, Melinda A. Beck, PhD, a virologist at the University of North Carolina, Chapel Hill, and her colleagues exposed two groups of laboratory mice to a relatively mild strain of flu virus, influenza A Bangkok. Some of the mice had been eating diets with adequate levels of selenium, while others had been given selenium-deficient diets.

As Beck had expected, the selenium-deficient mice developed more serious infections, in part because their immune systems were compromised by inadequate selenium. But ominously, the flu viruses in selenium-deficient mice mutated into a more virulent form, which exacerabated their lung infections. Even worse, these mutated viruses were capable of causing equally serious infections in healthy mice that had been eating diets with adequate levels of selenium.

Selenium is essential for the production of glutathione peroxidase, a powerful antioxidant and immune-system stimulant. Inadequate levels of selenium disable the body's antioxidant defenses, apparently allowing free radicals to mutate otherwise-stable DNA. Once the flu virus mutated, there was no turning back – it stayed far more dangerous than the original mild virus.

To the researchers' surprise, selenium deficiency in the mice resulted in 29 different mutations to the flu virus infecting them. These mutations occurred in relatively stable sections of the animals' DNA, not in less stable DNA.

The implications of this research are profound.

"Poor nutritional status in the host may contribute to the emergence of new viral strains," Beck and her colleagues wrote in the *FASEB Journal*, a leading scientific publication. She noted that ensuring people worldwide eat nutritionally adequate diets might curb virulent flu outbreaks.

In earlier studies, published in the mid-1990s, Beck and her colleagues determined that mutations in the coxsackie virus in Chinese citizens were stimulated by deficiencies in selenium. These coxsackie virus mutations attacked the heart muscle, resulting in a form of cardiomyopathy known as Keshan disease. Animal experiments confirmed the relationship and also found that deficiencies of either selenium or vitamin E led to coxsackie virus mutations.

In addition, selenium deficiency has theoretically been linked to the virulence of both the human immunodeficiency virus (HIV) and the Ebola virus, according to research by E. Will Taylor, PhD, of the University of Georgia, Athens. Both of these viruses produce selenium-dependent proteins. When these viruses infect a person, they deplete his selenium reserves, interfering with the production of glutathione peroxidase. The subsequent depletion of glutathione peroxidase disables one of the body's key virus-fighting mechanisms.

Reference: Nelson HK, Shi Q, Van Dael P, et al. Host nutritional selenium status as a driving force for influenza virus mutations. *FASEB Journal*, 2001; 15:1481-1483. □

Diets High in Fish May Reduce Risk of Developing Prostate Cancer

Eating two or three servings of coldwater fish each week may reduce the risk of prostate cancer, according to a new study by Swedish researchers.

Such fish – including salmon, mackerel, and sardines – are rich in omega-3 fats, which have been previously found to inhibit the growth of prostate cancer cells in test tubes.

In the current study, Paul Terry, PhD, and his colleagues at the Karolinska Institute, Stockholm, tracked the health and diets of 6,272 male twins, whose average age was 56 years at the beginning of the study.

Over an average of 21 years follow up, 466 of the men developed prostate cancer and 340 of them died from the disease.

Terry reported that "men who ate no fish had a two-fold to three-fold higher frequency of prostate cancer than those who ate moderate or high amounts did."

He and the other researchers suggested that the fish rich in omega-3 fats competed with arachidonic acid, which is used to make pro-inflammatory and cancer-promoting compounds in the body.

Reference: Terry P, Lichtenstein P, Feychting M, et al. Fatty fish consumption and risk of prostate cancer. *Lancet*, 2001:357:1764-1766.

Researchers Determine How Vitamin E Reduces Inflammation, Cox-2 Levels

Coronary artery disease – what most people simply refer to as heart disease – is increasingly viewed as being caused by inflammation of the arterites. Elevated levels of inflammation-causing substances increase the risk of plaque in blood vessels breaking off and blocking a major artery.

A recent study has found, however, that hazardous molecules known as free radicals can lead to higher levels of inflammation. In contrast, vitamin E can neutralize these free radicals and reduce inflammation.

The body's production of prostaglandin E2 (PGE 2), a powerful inflammation-causing substance, increases with age and likely contributes to heart disease, arthritis, and other diseases. PGE 2 boosts the body's production of cyclooxygenase-2 (Cox-2), an enzyme involved in converting some dietary fats to even more powerful inflammatory substances.

In a study with laboratory mice, Simin Nikbin Meydani, DMV, PhD, of Tufts University, found that peroxynitrite, a free radical built around an oxygen and nitrogen molecule, raised production of Cox-2.

However, in old mice, extra vitamin E quenched peroxynitrite, which in turn reduced levels of PGE 2 and Cox-2. "Vitamin E-induced inhibition of Cox activity might contribute to its effect of reducing cardiovascular disease risk," Meydani and her colleagues wrote.

Reference: Wu D, Hayek MG, Meydani SN. Vitamin E and macrophage cyclooxygenase regulation in the aged. *Journal of Nutrition*, 2001;131: 382S-388S.

Researchers Link High Intake of Trans Fatty Acids to Diabetes

A high intake of trans fatty acids, found in partially hydrogenated vegetable oils, french fries, and margarine, may increase the risk of diabetes, according to a study by researchers at Harvard University.

Frank B. Hu, MD, and other researchers tracked the health of 84,204 women who ranged in age from 34 to 59 years at the start of the 14-year study. During the duration of the study, 2,507 cases of adult-onset diabetes were diagnosed.

When Hu and his colleagues examined the types of fat consumed, they found that a 2 percent increase in trans fatty acid intake raised the risk of diabetes by 39 percent. The typical American gets about 3 percent of energy calories from trans fatty acids.

In contrast, a higher consumption of polyunsaturated fats (regardless of whether they were from the omega-6 or omega-3 families) was associated with a 37 percent reduction in diabetes.

Total fat, saturated fat, and monounsaturated fat intakes were not associated with either an increase or a decrease in diabetes risk.

Hu estimated that replacing 2 percent of energy calories of trans fatty acids with polyunsaturated fats would lower the risk of diabetes by 40 percent.

The risk of being overweight, a principal risk factor for diabetes, was not linked to any kind of fat intake. "Women with a higher intake of trans fat were more likely to smoke, were less likely to engage in regular physical activity, and had lower intakes of alcohol and folate," Hu wrote.

Reference: Salmeron J, Hu FB, Manson JE, et al. Dietary fat intake and risk of type 2 diabetes in men. *American Journal of Clinical Nutrition*, 2001;73: 1019-26.

Diets with Adequate Beta-Carotene and Selenium May Slow the Spread of AIDS

Low levels of beta-carotene and selenium may increase a person's chances of becoming infected with the human immunodeficiency virus (HIV), which causes AIDS. However, this does not mean supple-

ments of these two antioxidants can actually protect against HIV.

Researchers believe that weakened epithelial cells, which form a lining around organs, may help HIV infections to gain a foothold in the body. The integrity of epithelial cells depends in large part on adequate vitamin A, which the body can make from beta-carotene.

In a study conducted at two clinics treating sexually transmitted diseases, Sanjay M. Mehendale, MD, and his colleagues measured blood levels of antioxidants in 44 men and women diagnosed with HIV infection at a later visit. Mehendale then compared these antioxidant levels to those in 44 people who had not contracted HIV.

The patients with low levels of either beta-carotene or vitamin A were more likely to contract an HIV infection. Those with low levels of beta-carotene were 21 times more likely to become infected. No other antioxidants appeared to be associated with the risk of HIV infection.

In a separate study, Jared M. Baeten, PhD, of the University of Washington, and his colleagues measured blood selenium levels and took cervical swabs of 301 women infected with HIV in Kenya. Women with low blood levels of selenium were three times more likely to shed HIV-infected genital cells, compared with those who had normal selenium levels.

Such shedding, or breaking loose, of genital cells suggests that selenium deficiency "may increase the infectiousness of women with HIV..." Baeten wrote.

Mehendale SM, Shepherd ME, Brookmeyer RS, et al. Low carotenoid concentration and the risk of HIV seroconversion in Pune, India. *Journal of Acquired Immune Deficiency Syndromes*, 2001;26:352-359. Baeten JM, Mostad SB, Hughes MP, et al. Selenium deficiency is associated with shedding of HIV-1-infected cells in the female genital tract. *Journal of Acquired Immune Deficiency Syndromes*, 2001;26: 360-364.

Modest Dosages of Ginseng Lower Blood Sugar, May Reduce Diabetes Risk

Several recent studies have found that large supplemental dosages of American ginseng (*Panax quinquefolius L.*) can lower blood sugar levels in both diabetics and healthy subjects. Now, researchers report that the dosage may not be nearly as important as when the supplements are taken.

Vladimir Vuksan, PhD, of the University of Toronto, gave a series of supplements at different times to 12 healthy men and women. The supplements were 1, 2, or 3 grams of ginseng or placebo, given at the same time as or 10, 20, or 40 minutes before receiving a 25-gram glucose-tolerance test.

The different dosages of ginseng blunted the increase in blood sugar levels by 9-14 percent after the glucose-tolerance test. While all of the dosages of ginseng reduced blood sugar levels, the differences between them were not significant.

"The reductions were time dependent but not dose dependent," Vuksan wrote. Ginseng had a blood-sugar lowering effect only when supplements were taken 40 minutes before the glucose-tolerance test.

Vuksan V, Sievenpiper JL, Wong J, et al. American ginseng (*Panax quinquefolius L.*) attenuates postprandial glycemia in a time-dependent but not dose-dependent manner in healthy individuals. *American Journal of Clinical Nutrition*, 2001;73: 753-758.

Low Levels of B Vitamins May Increase Risk of Alzheimer's Disease

Low blood levels of either vitamin B12 or folic acid are associated with more than double the risk of developing Alzheimer's disease, researchers from Sweden's respected Karolinska Institute have reported.

The researchers, led by Hui-Xin Wang, PhD, measured blood levels of the two vitamins in a randomly selected group of 370 men and women age 75 and older. They then tracked the health of the subjects for three years.

People with low initial levels of either vitamin B12 or folic acid had twice the risk of developing Alzheimer's disease. Those with good baseline cognition scores on tests and low levels of the vitamins were three times more likely to develop Alzheimer's disease.

The researchers suspected that low levels of vitamin B12 and folic acid allowed homocysteine, which is neurotoxic, to accumulate in the blood.

In a separate study, Susan L. Mitchell, PhD, of the University of Ottawa, Canada, found that seniors taking antiulcer medications (histamine-2 blockers or proton-pump inhibitors) were two and one-half times more likely to be prescribed vitamin B12 after five years. The reason, presumably, was that the drug caused or aggravated a vitamin B12 deficiency.

"Antiulcer medications, by design, lower gastric acidity," Mitchell wrote. "While this can provide symptomatic relief, several dietary elements, including cobalamin (B12), require an acidic environment for proper absorption."

Mitchell suggested that physicians exercise caution when prescribing antiulcer medications to the elderly. "Our data suggest that antiulcer medications

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Quick Reviews of Recent Research

• Researchers find there is no placebo effect

Physicians have long believed that about 35 percent of patients respond, at least temporarily, to a placebo effect – that is, the belief that an inert treatment is actually working. Danish researchers analyzed 114 studies of 7,500 patients with 40 different disorders. They found that the placebo effect was the same as no treatment at all. The only improvement from placebos occurred among some patients experiencing pain; these patients had reported slight subjective improvement. The researchers concluded that the placebo effect was generally related to the natural ups and downs of any progressive disease.

Hrobjartsson A, Gotzsche PC. *New England Journal of Medicine*, 2001;344:1594-1602.

• Zinc supplements may help in night blindness

Night blindness is characterized by poor visual adaptation to darkness, and it is usually resolved with supplements of vitamin A or beta-carotene. In a study with pregnant women in Nepal, some of the subjects did not improve after taking these supplements. Researchers then gave 202 women 25 mg of zinc or placebo daily for three weeks. Zinc alone did not improve night blindness, but women who took a combination of zinc and vitamin A were four times more likely to have a restoration of normal vision.

Christian P, et al. *American Journal of Clinical Nutrition*, 2001;73:1045-1051.

• Low antioxidants may exacerbate varicocele

Varicocele is essentially a varicose vein in the scrotum, which may dissipate sufficient heat to cause infertility. Taiwanese researchers measured levels of vitamin C, sulfur-containing antioxidants, and free radicals in the semen of 30 young men with varicocele, 25 young men with subclinical varicocele, and 15 healthy young men. Antioxidant levels were lower and free radical levels higher in the men with varicocele, compared with the other two groups. Men with subclinical varicocele – that is, at risk of developing a more serious condition – also had below normal levels of antioxidants and higher levels of free radicals.

Chen SS, et al. *Free Radical Biology and Medicine*, 2001;30:1328-1334.

• Isoflavones curb cancer cell growth

In cell-culture studies, Australian researchers found that genistein, the principal isoflavone found in soybeans, inhibited the growth of human breast and prostate cancer cells. In addition, two isoflavone metabolites (which are formed in the body) had a more potent inhibitory effect on the cancer cells.

Xiang H, et al. *Molecular Biology of the Cell*, 2000;11 (Suppl):448A, #2327.

• N-acetylcysteine benefits blood vessels

N-acetylcysteine (NAC) is a potent immune stimulant that boosts levels of glutathione and reduces flu symptoms. A recent study found that it can also normalize blood vessel function and blood flow. In a study of 16 patients, seven of whom had heart disease, NAC reduced "endothelial dysfunction," dilating blood vessels and improving blood flow.

Andrews NP, et al. *Journal of the American College of Cardiology*, 2001; 37:117-123.

• Antioxidants may reduce breast cancer risk

Korean researchers compared blood levels of vitamin E, vitamin A, and carotenoids in 160 women with breast cancer and 229 healthy subjects. Women with the highest blood levels of vitamin E, beta-carotene, and lutein/zeaxanthin were substantially less likely to develop breast cancer. While the antioxidants may have been protective, they may have also been markers of an overall high-antioxidant diet.

Kim MK, et al. *Nutrition Research* 2001;21: 797-809.

Alzheimer's Disease...

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should be used judiciously in older people and only when there is a sound indication. In addition, monitoring serum markers of cobalamin deficiency in patients requiring long-term antiulcer therapy may be warranted."

References: Wang HX, Wahlin A, Basun H, et al. Vitamin B12 and folate in relation to the development of Alzheimer's disease. *Neurology*, 2001;56:1188-1194. Mitchell SL, Rockwood K. The association between antiulcer medication and initiation of cobalamin replacement in older persons. *Journal of Clinical Epidemiology*, 2001;54:531-534. □

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