

LE Magazine May 2004

IN THE NEWS

Vitamins C and E Found to Prevent Alzheimer's Disease



Taking vitamin C and E supplements together significantly lowers the risk of developing Alzheimer's disease, according to a new study published in the Archives of Neurology.*

The research began in 1995, when approximately 5,000 elderly residents of Cache County, Utah, were assessed for dementia and Alzheimer's disease. They were also questioned about their use of vitamin supplements. The researchers again assessed the participants' mental status an average of three years later.

At the beginning of the study, those participants who had already been taking vitamin C and E supplements in combination had a 78% lower risk of having Alzheimer's disease than those who were not taking the supplements. This benefit seemed to persist, as the risk factor for Alzheimer's was 64% lower for supplement users at the end of the study period.

"The results of our study suggest that taking vitamins E and C in supplement doses (greater than 400 IU of E and 500 mg of C) may reduce the risk of developing Alzheimer's disease," lead researcher Dr. Peter Zandi of the Johns Hopkins Bloomberg School of Public Health told Life Extension.

The researchers believe that the vitamins' antioxidant properties account for their protective powers against the oxidative stress-related damage that leads to Alzheimer's disease. Interestingly, no evidence of a protective effect was seen with the use of vitamin C or vitamin E supplements alone, with multivitamins alone, or with vitamin B-complex supplements. The researchers suspect that the use of vitamins C and E probably offers protection against Alzheimer's disease only when taken together in the higher doses available in individual supplements.

—Marc Ellman, MD

Reference

* Zandi PP, Anthony JC, Khachaturian AS, et al. Reduced risk of Alzheimer's disease in users of antioxidant vitamin supplements: the Cache County Study. Arch Neurol. 2004 Jan;61(1):82-8.

Vitamins C and E Boost Cognitive Function in Elderly Women



Long-term use of vitamin C and E supplements appears to improve cognitive function in older women, research suggests.*

In an effort to determine the effect of supplement use on mental agility, researchers at Brigham and Women's Hospital in Boston conducted telephone interviews of nearly 15,000 female participants in the Nurses' Health Study. At the time of the interviews, all of the women were between 70 and 79 years of age. The researchers tested cognitive function by asking the women to perform such tasks as recalling a list of 10 words and repeating a series of numbers backwards. They then compared the results to the women's self-reported use of vitamin supplements.

"We found evidence of better overall performance on our cognitive tests among long-term users of vitamins E and C combined than among women who had never taken either vitamin, and performance improved significantly with increasing duration of use," wrote the researchers in the American Journal of Clinical Nutrition.

The two antioxidants appear to work best together, as vitamin C supplementation alone had no effect on cognitive function and vitamin E supplementation alone had minimal effect when compared to taking the two antioxidants together.

—Marc Ellman, MD

Reference

* Grodstein F, Chen J, Willett WC. High-dose antioxidant supplements and cognitive function in community-dwelling elderly women. *Am J Clin Nutr.* 2003 Apr;77(4):975-84.

Fiber Slows Progression of Atherosclerosis

Consumption of dietary viscous fiber appears to decrease the progression of atherosclerosis, according to researchers at the University of Southern California in Los Angeles.*

Atherosclerosis describes the deposition of fat-laden plaques on the inside walls of the body's medium- and large-sized arteries, which is associated with the development of cardiovascular disease. To determine the effect of fiber consumption on the development of atherosclerosis, the researchers measured the thickness of the carotid arteries (major blood vessels in the neck) of more than 500 adults. They then repeated these measurements twice over the next three years, and compared their findings to the participants' reported fiber consumption and blood cholesterol levels.

The researchers found that the participants with the highest fiber consumption had the most optimal cholesterol levels. They also found that the more viscous fiber that the participants consumed, the slower their progression of carotid artery wall thickening. Viscous fibers, which were previously termed "water-soluble fibers," include pectin, gums, and mucilage. Many fruits and vegetables are rich in viscous fibers.

"Cardiovascular disease due to advanced atherosclerosis is the leading cause of death and disability in the United States," noted the researchers in the *American Journal of Clinical Nutrition*. "The present study suggests that increased dietary fiber intake has significant cardiovascular benefit and that the regulation of serum lipids by dietary fiber may be partially involved in the process of slowing the progression of atherosclerosis."

—Marc Ellman, MD

Reference

* Wu H, Dwyer KM, Fan Z, Shircore A, Fan J, Dwyer JH. Dietary fiber and progression of atherosclerosis: the Los Angeles Atherosclerosis Study. *Am J Clin Nutr.* 2003 Dec;78(6):1085-91.

Curcumin Shown to Inhibit Tumor Angiogenesis

APN, a membrane-bound enzyme (CD13/aminopeptidase N), is found in tumor and other types of blood vessels undergoing the formation and differentiation of blood vessels (angiogenesis). However, it is not found in the vessels of other normal tissues. Because of this, APN is considered critical in anticancer therapies that seek to block tumor angiogenesis and metastasis. Curcumin, a potent chemopreventive agent, is now in clinical trials because it binds to APN and blocks its activity, thereby inhibiting tumor cell invasion and angiogenesis.

In recent studies, curcumin inhibited the invasiveness of human cancer cells (melanoma and fibrosarcoma) that contained APN, indicating that APN is the direct target for curcumin anti-invasive activity. Curcumin also inhibited growth-factor-induced angiogenesis in endothelial cells.

The study authors conclude that targeted APN inhibition is a novel approach to prevent tumor angiogenesis and metastasis, and that the possible development of potent derivatives of curcumin may be considered, since APN has been defined as the functional target of the compound for antiangiogenesis.

—Carmia Borek, PhD

Reference

* Shim JS, Kim JH, Cho HY, et al. Irreversible inhibition of CD13/aminopeptidase N by the antiangiogenic agent curcumin. *Chem Biol.* 2003 Aug;10(8):695-



IN THE NEWS

Head Injury Study: Melatonin Is Neuroprotective

Researchers at Israel's Hebrew University in Jerusalem report that melatonin, a hormone with antioxidant activity that is produced in the brain's pineal gland, is neuroprotective.*

Traumatic brain injury leads to massive production of reactive oxygen species, which in turn increases brain damage. Melatonin enhances brain antioxidants, including vitamin C, and blocks nuclear factor-kappa beta (NF-kB), a gene that regulates pro-inflammatory substances.

In the study, mice subjected to closed head injury were tested one hour later for neurological damage, using the Neurological Severity Score. They were then injected with melatonin or a substance in which melatonin is administered but which lacks melatonin. The Neurological Severity Score was reevaluated 24 hours later. The response to melatonin showed a bell-shaped curve—that is, neuroprotection was achieved in animals given 5 mg/kg but not in those given 1 mg/kg or 10 mg/kg.

Melatonin facilitated recovery and caused a twofold decrease in brain lesion size.

Treatment with 5 mg/kg produced a sustained (four-day) increase in total antioxidants (yet to be identified) and a higher content of vitamin C in the brain cortex. Antioxidant levels were unaffected by the neuroprotective endocannabinoid 2AG given after injury, underscoring the specificity of melatonin-induced neuroprotection.

Melatonin blocks the AP-1 and NF-kB genes that are activated in closed head injury. NF-kB regulates numerous genes, including production of pro-inflammatory cytokines that interact with free radicals and exacerbate brain injury.

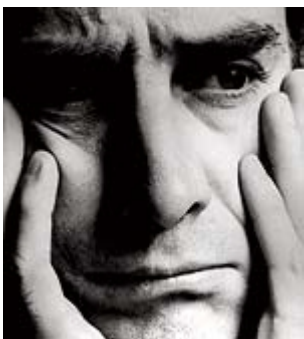
The authors suggest that the use of melatonin as a therapeutic strategy may stimulate beneficial antioxidants and inhibit destructive responses such as inflammation.

—Carmia Borek, PhD

Reference

* Beni SM, Kohen R, Reiter RJ, Tan DX, Shohami E. Melatonin-induced neuroprotection after closed head injury is associated with increased brain antioxidants and attenuated late-phase activation of NF-kappaB and AP-1. *FASEB J.* 2004 Jan;18(1):149-51. Epub 2003 Nov 03.

Study Links Depression to Omega-3 Deficiency



In recent years, scientists have discovered that chemical balances in the brain influence depression. Some antidepressant drugs, for example, modify the reuptake of the neurotransmitter serotonin, helping to improve mood. New research has shown that the composition of fatty acids in the diet can have an effect on brain-receptor function and signal transmission, suggesting that the amount and types of fat eaten can affect vitality and happiness.

A team of researchers at the Erasmus University Medical Centre in Rotterdam, Netherlands, looked at the association between depression and the fatty-acid composition of blood plasma in 264 subjects with depressive symptoms and 461 randomly selected reference subjects who screened negative for depression.* After an overnight fast, all of the participants had their blood drawn, which was then analyzed for omega-3 and omega-6 fatty acids and for C-reactive protein (an indicator of

immune response).

The Dutch scientists found a correlation between the intake of fatty acids and depressive disorders in the elderly after adjustment for demographic and biological factors. As the amount of omega-3 fatty acids (such as EPA and DHA) increased in the participants' diets relative to omega-6 acids (like linoleic acid and arachidonic acid), the incidence of depression declined.

Moreover, the strength of this association grew as C-reactive protein levels dropped. The researchers believe that this is because people with impaired immune systems are sicker and more likely to be depressed, so diet is not as big a factor in determining their mood. The healthier you are, the more your dietary choices influence your frame of mind. While it has been known for some time that eating cold-water fish and taking fish-oil capsules are good for the heart, it now appears that consuming more omega-

Reference

* Tiemeier H, van Tuijl HR, Hofman A, Kiliaan AJ, Breteler MM. Plasma fatty acid composition and depression are associated in the elderly: the Rotterdam study. *Am J Clin Nutr.* 2003 Jul;78(1):40-6.

Testosterone Supplementation Found Safe in New Report



Last November, the Institute of Medicine issued a report on testosterone and aging (see “Testosterone Attacked by the Media,” February 2004) that was cautious, and in some instances critical, of the use of testosterone supplementation in aging men. A new study challenges issues raised in that report concerning the safety of testosterone supplementation with regard to prostate cancer and heart disease.*

The Institute of Medicine report voiced concern that testosterone supplementation may cause prostate cancer, though to date no scientific study has demonstrated such a link. Likewise, because heart disease is more common in men than women, some have surmised that testosterone could be a risk factor for heart disease.

According to researchers at Boston’s Beth Israel-Deaconess Medical Center who conducted an exhaustive review of more than 70 studies on the safety of testosterone replacement therapy, testosterone supplementation is not associated with an increased risk of prostate cancer or heart disease. In their report published in the *New England Journal of Medicine*, the authors conclude: “We reviewed decades of research and found no compelling evidence that testosterone replacement therapy increases the incidence of prostate cancer or cardiovascular disease.”

—Edward R. Rosick, DO, MPH, MS

Reference

* Snyder PJ. Hypogonadism in elderly men— what to do until the evidence comes. *N Engl J Med.* 2004 Jan 29;350(5):440-2.

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