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In Experiments, Supplements Boost Energy Levels, Reverse Some Age-Related Changes

Two little known supplements can partially reverse the aging process, according to recently published animal studies. In a series of experiments, researchers found that acetyl-L-carnitine and alpha-lipoic acid increased energy levels, physical activity, and mental funtion in laboratory rats – and the findings have clear relevance to people.

Both acetyl-L-carnitine and alpha-lipoic acid play crucial roles in mitochondria, microscopic structures found in every cell. Mitochondria are widely considered the energy factories of the body because they break down sugars and fats and oxidize (or burn) them for energy. Many researchers believe that accumulated damage to the mitochondria, caused by the inevitable production of free radicals, underscores the aging process.

Acetyl-L-carnitine and alpha-lipoic acid were selected for the study because both nutrients are known to enhance the activity of mitochondria. However, acetyl-L-carnitine can increase free radical levels. That led Tory M. Hagen, PhD, of Oregon State University, Corvallis, and his colleagues, to combine it with alpha-lipoic acid, a powerful antioxidant.

In experiments, Hagen fed either acetyl-L-carnitine or alpha-lipoic acid, or a combination of them, to groups of young and old laboratory rats. Typically, old rats are lethargic and exhibit only about one-third of the physical activity of young rats.

After receiving the supplements for two to four weeks, the physical activity of the old rats doubled – a clear rejuvenative and energy-boosting effect. Furthermore, energy levels in the young rats increased by about one-third. These improvements paralleled increases in the rats' mitochondrial activity.

Hagen also reported that the energy levels in old rats taking the supplements approached that of young rats not taking any supplements. Both supplements worked better in combination than either did by itself.

Another positive improvement was that both young and old supplemented rats maintained higher levels of vitamin C. That's likely because the alpha-lipoic acid enhanced the vitamin's production or recycling. In addition, supplemented rats had lower levels of free radicals.

In general, the improvements were comparable to giving a 75-year-old person the vigor of someone 30-40 years younger.

In a related study, Jiankang Liu, PhD, and Bruce N. Ames, PhD, of the University of California, Berkeley, measured the effect of acetyl-L-carnitine and alpha-lipoic acid on the activity of carnitine acetyltransferase (CAT), a key enzyme involved in burning fats for energy in the mitochondria. CAT activity declines with age.

When the researchers fed either alpha-lipoic acid or a combination of alpha-lipoic acid and acetyl-L-carnitine to old rats, CAT activity in their brains increased and was similar to that in young rats.

References: Hagen TM, Liu J, Lukkesfeldt J, et al. Feeding acetyl-L-carnitine and lipoic acid to old rats significantly improves metabolic function while decreasing oxidative stress. *Proceedings of the National Academy of Sciences of the USA*, 2002;99:1870-1875. Liu J, Killilea DW, Ames BN. Age-associated mitochondrial oxidative decay: improvement of carnitine acetyltransferase substrate-binding affinity and activity in brain by feeding old rats acetyl-L-carnitine and/or R-a-lipoic acid. *Proceedings of the National Academy of Sciences of the USA*, 2002;99:1876-1881. □

High Levels of Antioxidants May Offer Some Protection Against Breast Cancer

Maintaining high levels of antioxidant nutrients may help reduce the risk of breast cancer, according to a study conducted at the University of Western Australia.

Enrico Rossi, PhD, and his colleagues compared blood levels of numerous antioxidants in the blood of 153 women recently diagnosed with breast cancer and 151 healthy subjects.

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Women with the highest overall blood levels of antioxidants, as well as specifically beta-carotene, were 53 percent less likely to be diagnosed with breast cancer. High levels of vitamin A and bilirubin appeared to be almost as protective.

It is important to note that the study showed an association between high levels of antioxidants and a low risk of breast cancer, but not a direct benefit from antioxidants. The high levels of antioxidants may have reflected an overall healthy diet.

Ching S, Ingram D, Hahnel R, et al. Serum levels of micronutrients, antioxidants and total antioxidant status predict risk of breast cancer in a case control study. *Journal of Nutrition*, 2002;132:303-306. □

Adequate Intake of Folic Acid May Protect Against Parkinson's Disease

Elevated blood levels of homocysteine, a byproduct of protein metabolism, increase the risk of heart disease and stroke. Conversely, the B-vitamin folic acid lowers homocysteine levels and reduces the risk of these disorders.

Now, researchers have clearly shown that the absence of folic acid and increases in homocysteine can increase susceptibility to Parkinson's disease, which is characterized by tremors in the face and hands. The physical changes in Parkinson's disease are related, in part, to reduced production of the neurotransmitter dopamine.

Mark P. Mattson, PhD, of the Johns Hopkins University School of Medicine, and his colleagues fed laboratory mice diets with and without folic acid. Mice receiving the diet deficient in folic acid developed an eight-fold increase in homocysteine levels.

Both groups of mice were subsequently exposed to a chemical (MPTP, or 1-methyl-4-phenyl-1,2,3,6-tetrahydropyridine) known to cause Parkinson's-like symptoms. The animals lacking folic acid exhibited significant deteriorations in physical activity and balance, whereas those consuming folic acid did not suffer any adverse effects from MPTP.

A lack of folic acid by itself did not cause any Parkinson's-like symptoms, and mice consuming the vitamin maintained normal levels of dopamine-producing brain cells. However, deficient mice exposed to MPTP suffered a 50-60 percent decrease in dopamine-producing brain cells. That finding is consistent with other research showing that exposures to toxic chemicals may be a cause of Parkinson's disease.

In related experiments, the researchers infused homocysteine directly into the brains of some of the mice treated with MPTP. These mice had a significant increase in Parkinson's-like symptoms, indicating that homocysteine is directly toxic to brain cells.

According to Mattson and his colleagues, the study "provides direct evidence that a single dietary nutrient can modify the pathogenic cascade thought to occur in Parkinson's disease."

Reference: Duan W, Ladenheim B, Cutler RG, et al. Dietary folate deficiency and elevated homocysteine levels endanger dopaminergic neurons in models of Parkinson's disease. *Journal of Neurochemistry*, 2002;80:101-110. □

Vitamins Benefit Patients Undergoing Heart-Transplant Surgery

New research on patients undergoing heart-transplant operations strongly supports the benefits of vitamin supplements in preventing the recurrence of heart disease and death.

James C. Fang, MD, of Brigham and Women's Hospital, Boston, led a team of researchers there and at Oregon State University, Corvallis, in studying the effects of supplemental vitamins E and C or placebos on 40 patients who had undergone heart-transplant surgery within the previous two years.

Nineteen of the patients received 400 IU of natural vitamin E and 500 mg of vitamin C twice daily for one year. Twenty-one patients received placebos, and all of the patients also received a cholesterol-lowering statin drug (pravastatin).

The differences were significant. Using sophisticated ultrasound techniques to measure changes in the thickness of blood vessel walls, Fang and his colleagues found that patients taking the vitamin combination had less than a 1 percent increase in plaque formation on artery walls. In contrast, patients taking placebos experienced an 8 percent increase in plaque formation after one year.

Post-transplant heart disease occurs in 70 percent of patients within three years of surgery. More than tissue rejection, the development of further heart disease is the major factor affecting long-term survival of heart-transplant patients.

Fang wrote that "vitamins C and E had an inhibitory effect on plaque growth over and above that of statins, shown previously to retard the progression of transplant-associated arteriosclerosis." Because free radicals are involved in heart disease, the beneficial effect of antioxidants "suggests a potentially useful therapy for this disease."

A separate study, by Killian Robinson, MD, of Wake Forest University, Winston-Salem, N.C., found that low blood levels of vitamin B6 predicted cardiovascular complications and overall risk of death among heart-transplant patients.

Robinson and his colleagues tracked the

progress of 160 heart-transplant patients for an average of six years. Elevated homocysteine levels, common in transplant patients, did not predict the further risk of disease; nor did the patients' blood levels of folic acid and vitamin B12.

However, patients with low blood levels of vitamin B6 were almost three time more likely to die of cardiovascular complications and mortality from all causes.

References: Fang JC, Kinlay S, Beltrame J, et al. Effect of vitamins C and E on progression of transplant-associated arteriosclerosis: a randomised trial. *Lancet*, 2002;359:1108-1113.Nahlawi M, Seshadri N, Boparai N, et al. Usefulness of plasma vitamins B6, B12, folate, homocysteine, and creatinine in predicting outcomes in heart transplant recipients. *American Journal of Cardiology*, 2002;89:834-837.

Eating Fish or Taking Fish-Oil Capsules Lowers Risk of Sudden Cardiac Death

Two groups of researchers have reported that either consuming large amounts of fish or taking fish oil capsules can significantly reduce the risk of sudden cardiac death. The condition results in the death of 250,000 Americans each year, and preventing it is important because half of the people who die from sudden cardiac death had no previous symptoms of cardiovascular disease.

In the first study, Christine M. Albert, MD, and her colleagues at the Harvard University School of Public Health focused on 94 men participating in the Physicians' Health Study. Albert compared their blood levels of various fats and other cardiovascular risk factors to 184 comparable men.

She found that the more fish men consumed, the lower their risk of sudden cardiac death. Men who consumed the most fish, regardless of their age or smoking habits, were 81 percent less likely to die from sudden cardiac death, compared with men who ate little or no fish. Men who consumed modest amounts of fish had a 72 percent lower risk of sudden cardiac death.

Earlier studies have found that the omega-3 fatty acids in fish reduce the risk of irregular heartbeats and blood clots, both of which may help prevent sudden cardiac death.

In the second study, Roberto Marchioli, MD, of Consorzio Mario Negri Sud, Italy, and his colleagues tracked the health of more than 11,000 patients who had recently suffered a heart attack. All of the patients were encouraged to follow a Mediterranean-style diet, including fish, olive oil, fruits, and vegetables. Some of the patients were also given 1 gram of fish oil supplements daily.

Over the next three and one-half years, Marchioli found that patients taking the fish oil capsules were significantly less likely to die from any cause, with the benefits emerging after just three months of supplementation. After four months, patients taking the fish oil capsules had a 53 percent lower overall risk of death, mostly related to a reduction in sudden cardiac death.

Currently, the American Heart Association recommends that people consume at least two servings per week of fatty fish, such as salmon or mackerel.

References: Albert CM, Campos H, Stampfer MJ, et al. Blood levels of long-chain n-3 fatty acids and the risk of sudden death. *New England Journal of Medicine*, 2002;346:1113-1118. Marchioli R, Barzi F, Bomba E, et al. Early protection against sudden death by n-3 polyunsaturated fatty acids after myocardial infarction. Time-course analysis of the results of the Gruppo Italiano per lo studio della sopravvivenza nell'infarto miocardico (GISSI)-prevenzione. *Circulation*, 2002;105:1897-1903.

Use of Probiotics Significantly Reduces Length of Infectious Diarrhea Episodes

Treatment with "good" *Lactobacillus* bacteria can significantly shorten a bout of infectious diarrhea in infants and children, according to an analysis of nine controlled studies.

Cornelius W. Van Niel, MD, of the University of Washington, Seattle, and his colleagues analyzed nine studies that used *Lactobacillus* in capsules or rehydration drinks to treat diarrhea. They found that the infants and toddlers recovered almost a day earlier after consuming the *Lactobacillus*, compared with untreated children. According to Van Niel, $10 of *Lactobacillus* would save about 17 hours of care.

"The results of this meta-analysis suggest that *Lactobacillus* is safe and effective as a treatment for children with acute infectious diarrhea," Van Niel and his colleagues wrote in *Pediatrics*.

An estimated 21-37 million cases of diarrhea occur among 16.5 million children under the age of five each year in the United States. These cases account for three million annual physician visits and 163,000 hospitalizations.

"For at least a century, researchers have hypothesized that live bacterial cultures, such as those found in yogurt, may help treat and prevent diarrhea... Despite these reports, health professionals in the United States do not routinely recommend *Lactobacillus*, perhaps believing that its effectiveness has not yet been proved," Van Niel wrote.

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Quick Reviews of Recent Research

• Vitamin E succinate shows anti-cancer effects

Researchers tested the effect of the natural d-alpha tocopheryl succinate form of vitamin E on human stomach cancer cells. Vitamin E blocked the synthesis of DNA in the cancer cells, leading to their destruction. The researchers wrote that vitamin E succinate "can function as a potent chemotherapeutic agent against human gastric carcinogenesis."

Wu K, et al. *World Journal of Gastroenterology*, 2002;8:26-30.

• High-glycemic foods linked to breast cancer risk

High-glycemic foods, which are typically refined carbohydrates, rapidly boost blood sugar and insulin levels and are known to increase the risk of diabetes and heart disease. Elevated insulin levels may in turn boost levels of insulin-like growth factors, which have been linked to cancer risk. Researchers analyzed the amounts of high-glycemic foods in the diets of 2,569 women with breast cancer and 2,588 without the disease. High-glycemic foods, such as white bread, were associated with about a one-third increase in breast cancer risk.

Augustin LSA, et al. *Annals of Oncology*, 2001;12:1533-1538.

• Green tea may slow muscle disease

Duchenne muscular dystrophy (MD) is the most common type of MD in childhood. Researchers tested the effects of an antioxidant extract of green tea on laboratory mice bred to develop symptoms similar to Duchenne MD. They found that the antioxidant extract reduced the deterioration of muscle in the mice, suggesting that the course of MD may be influenced by antioxidants.

Buetler TM, et al. *American Journal of Clinical Nutrition*, 2002;75:749-753.

• Low B vitamins result in mixed-mood disorder

Psychiatrists from Greece reported the case of a 42-year-old woman who was admitted to the hospital in a depressed state and with suicidal thoughts. Diagnosed with bipolar disorder, she was treated with pharmaceuticals, but was unresponsive to the therapy. Additional symptoms included irritability, distractibility, pressure to keep talking, insomnia, and feelings of worthlessness. Blood tests indicated very low levels of vitamin B12 and folic acid. After regular injections of both vitamins, the woman's mood improved. Two years later, still receiving monthly vitamin B12 injections, the woman's mental status was regarded as normal.

Fafouti M, et al. *General Hospital Psychiatry*, 2002;24:106-109.

• Fruits and veggies boost vitamin C levels

Researchers investigated blood levels of nutrients most likely influenced by fruit and vegetable consumption. In this study of 116 men, researchers found that diets rich in fruits and vegetables were associated with relatively high blood levels of vitamin C and carotenoids. However, vitamin C levels were more closely associated with fruit and vegetable intake. The researchers wrote that "it is possible that raising ascorbic acid [vitamin C] levels may be an important mechanism by which fruit and vegetable consumption confers protective benefits."

Block G, et al. *American Journal of Epidemiology*, 2001;154:1113-1118.

• Lack of folic acid may contribute to Alzheimer's

Alzheimer's disease is characterized by amyloid-beta protein damage to brain cells, and some research indicates that elevated levels of homocysteine may be a risk factor for Alzheimer's disease. In a study of laboratory mice, researchers found that a deficiency of folic acid led to an increase in homocysteine, which impaired normal DNA repair processes in brain cells. The reduction in DNA repair activities appeared to leave brain cells susceptible to free radical damage caused by amyloid-beta protein.

Kurman II, et al. *Journal of Neuroscience*, 2002; 22:1752-1762.

Probiotics and Diarrhea...

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The same type of beneficial bacteria is commonly found in live-culture yogurt. However, infants under 12 months of age should not be given yogurt sweetened with honey. The reason is that the immature immune systems of infants cannot protect against microorganisms normally found in honey.

Van Niel CW, Feudtner C, Garrison MM, et al. Lactobacillus therapy for acute infectious diarrhea in children: a meta-analysis. *Pediatrics*, 2002;109: 678-684. □

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