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Supplements of Acetyl-L-Carnitine Reduce Fatigue in Patients with Multiple Sclerosis

Various carnitine compounds play vital roles in transporting fats into cellular structures called mitochondria, where they are burned for energy. Studies have found that these forms of carnitine, a nutrient found in animal protein, can reduce symptoms of chronic fatigue syndrome and chemotherapy-induced fatigue in cancer patients.

In the most recent study along these lines, Carlo Pozzilli, MD, of the University of Rome, and his colleagues reported that acetyl-L-carnitine (ALCAR) reduced fatigue in patients with multiple sclerosis (MS). MS is a degenerative neurological disease characterized by a breakdown of the protective sheaths surrounding nerves.

Pozzilli and his colleagues treated 36 MS patients with fatigue. The patients included men and women with two common types of MS – relapse-remitting MS, characterized by a history of relapses and remissions; and secondary-progressive MS, a progressively degenerative form of the disease.

The subjects were given either ALCAR (1 gram, twice daily) or the drug amantadine (100 mg, twice daily) for three months. Amantadine is commonly prescribed to treat fatigue in MS patients. After a three-month treatment-free "washout period," the therapies were reversed.

"The results of this study showed that ALCAR is well tolerated by patients with MS and is more effective than amantadine in the treatment of MS-related fatigue," Pozzilli and his colleagues wrote in the *Journal of the Neurological Sciences*.

During the study, patients completed the Fatigue Severity Scale, a questionnaire that assesses the effects of fatigue on daily activities.

Pozzilli found that 29 percent of the patients benefited from a "clinically relevant" improvement while taking ALCAR, compared with only 21 percent of those taking amantadine. However, 70 percent of patients taking ALCAR had at least some improvement, compared with only 43 percent of those taking amantadine.

In addition, five patients dropped out of the study because of side effects from amantadine, whereas only one left the study because of ALCAR side effects.

According to Pozzilli's report, ALCAR might have benefits beyond that of increasing energy. The vitamin-like substance may increase the activity of neurotransmitters, such as GABA.

He wrote that the "decrease in fatigue induced by ALCAR treatment was associated with an improvement in social interaction and mood profile of patients…"

ALCAR is the acetyl ester of carnitine. As a supplement, it is more expensive than carnitine, but studies suggest that it is also more effective.

Reference: Tomassini V, Pozzilli C, Onesti E, et al. Comparison of the effects of acetyl-L-carnitine and amantadine for the treatment of fatigue in multiple sclerosis: results of a pilot, randomized, double-blind crossover trial. *Journal of the Neurological Sciences*, 2004;218:103-108. □

Herbal Remedy Reduces Respiratory Tract Infections in Children

A combination of echinacea, propolis, and vitamin C significantly reduces the risk of respiratory tract infections in children, according to a team of Israeli physicians and researchers.

Herman A. Cohen, MD, of the Schneider Children's Medical Center, and his colleagues treated 430 children, ranging from one to five years of age, with either the herbal remedy or placebos over a 12-week winter period.

Echinacea is well known for its immune-enhancing properties. Propolis, a waxy substance produced by bees, is rich in flavonoids and has antioxidant, anti-inflammatory, and anti-microbial effects. Vitamin C can reduce cold and flu symptoms, though in much higher dosages than those used in this study.

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Children ages one to three years old were given 250 mg of echinacea extract, 250 mg of propolis, and 50 mg of vitamin C in a liquid formula twice a day. Children ages four to five years old took 375 mg of echinacea extract, 375 mg of propolis, and 75 mg of vitamin C twice a day. The dosages were doubled if a child developed an acute illness.

Cohen and and his colleagues reported that children taking the herbal remedy had a 55 percent overall reduction in illnesses and a 50 percent reduction in illnesses per child. In addition, children taking the herbal remedy had 62 percent fewer days with fever.

The supplement is a propriety product sold as Chizukit in Israel.

Reference: Cohen HA, Varsano I, Kahan E, et al. Effectiveness of an herbal preparation containing echinacea, propolis, and vitamin C in preventing respiratory tract infections in children. *Archives of Pediatric and Adolescent Medicine*, 2004;158:217-221. □

Alpha-Lipoic Acid and Psychotherapy Helpful in Burning-Mouth Syndrome

Burning-mouth syndrome (BMS) is characterized by an intense burning sensation in the mouth, but without any obvious cause. It affects an estimated 1.3 million Americans, predominantly women. BMS may affect 10 to 40 percent of women seeking medical treatment for menopausal symptoms.

Although the underlying causes of BMS are unclear, research does point to a combination of nerve disease and psychological stresses. Several studies have found that alpha-lipoic acid, an antioxidant involved in maintaining nerve function, is helpful.

BMS is complicated by the fact that low self-esteem, anxiety, depression, and difficulties in interpersonal relationships are frequently among the presenting symptoms.

In the most recent study, Felice Femiano, MD, of Antimo, Italy, and colleagues treated 192 patients (104 women and 88 men, ages 24 to 67 years old) with BMS. The patients received one of four possible treatments: psychotherapy, one-hour twice weekly for two months; alpha-lipoic acid (600 mg daily for two months); both psychotherapy and alpha-lipoic acid; or daily placebos.

Patients treated with both alpha-lipoic acid and psychotherapy had the greatest reduction in symptoms. Fifty-three percent benefited from a complete elimination of symptoms, and 31 percent had significant improvement.

Patients taking alpha-lipoic acid, but not receiving psychotherapy, also improved. Thirty-one percent had a complete resolution of symptoms, and 40 percent had significant improvements.

Ten percent of patients receiving psychotherapy alone had significant improvements, but none had a complete elimination of BMS symptoms. Patients taking placebos did not improve.

"Throughout the study, an increase n BMS pain was associated with the frustration of affectional and/or dependency needs that reactivated an earlier unresolved conflict," wrote Femiano.

Reference: Femiano F, Gombos F, Scully C. Burning mouth syndrome (BMS): open trial of psychotherapy alone, medication with alpha-lipoic acid (thioctic acid), and combination therapy. *Medicina y Patologia Oral, 2004*;9:8-13. □

Researchers Identify How Vitamin E Helps Prevent Alzheimer's Disease

Alzheimer's disease is characterized by the formation of amyloid beta-protein around brain cells. As amyloid beta-protein accumulates, it interferes with normal brain cell function and leads to a decline in thinking processes and memory. Some research has suggested that free radicals accelerate the formation of amyloid beta-protein, and several clinical studies have found that vitamin E can reduce the risk of Alzheimer's disease.

In a recent study, Mark P. Mattson, PhD, of the Johns Hopkins University School of Medicine, Baltimore, investigated the details of exactly how free radicals cause Alzheimer's disease – and how vitamin E prevents it.

Mattson and his colleagues studied brain cells obtained from seven elderly people who died from Alzheimer's disease, seven elderly people who did of other causes, and mice of different ages. They looked specifically at the abnormal metabolism of cholesterol and ceramide, two fats found in brain cells. In addition, they treated some of the mice brain cells with vitamin E.

The researchers found that amyloid beta-protein caused high levels of free radical activity in the brain cells from people with Alzheimer's disease. This free-radical activity led to the abnormal metabolism of cholesterol and ceramide, which in turn triggered "a neurodegenerative cascade that leads to clinical disease." All of these changes were more significant in brain cells from people with advanced forms of Alzheimer's disease.

Meanwhile, in experiments with brain cells from older mice, Mattson and his colleagues found that amyloid beta-protein caused similar free-radical damage and abnormal cholesterol and ceramide metabolism.

Next, Mattson and his colleagues exposed some

of the mice brain cells to vitamin E. The vitamin prevented the accumulation of cholesterol and ceramid in brain cells, and it prevented amyloid beta-protein from killing the brain cells.

Reference: Cutler RG, Kelly J, Storie K, et al. Involvement of oxidative stress-induced abnormalities in ceramide and cholesterol metabolism in brain aging and Alzheimer's disease. *Proceedings of the National Academy of Sciences*, 2004;101:2070-2075.

High Blood Levels of Iron Increase Risk of Type 2 Diabetes in Women

Women with high levels of iron have a substantially increased risk of developing type 2 diabetes, according to a study by researchers at the Harvard School of Public Health.

Although iron is an essential dietary mineral, it also stimulates the production of hydroxyl radicals, the most dangerous type of free radicals. Some research suggests that hydroxyl radicals are involved in insulin resistance, the underpinning of type 2 (adult-onset) diabetes.

Rui Jiang, MD, DrPH, and colleagues took blood samples and tracked the health of 32,826 women participating in the Nurses' Health Study. Over the next 10 years, 698 women developed diabetes, and their iron levels were compared with those of 716 healthy women.

Jiang analyzed the women's blood levels of ferritin, an iron-containing protein, as a marker of iron status. The lowest risk of diabetes occurred in women with ferritin levels less than 21 nanograms per milliliter of blood. As ferritin levels increased, so did the risk of diabetes.

Women with the highest blood levels of ferritin – more than 107 nanograms per milliliter of blood – were almost three times more likely to develop type 2 diabetes, according to Jiang's article in the *Journal of the American Medical Association*.

"Overall, women who subsequently developed diabetes during follow-up were heavier, more likely to have a family history of diabetes, less likely to exercise and consume alcohol, and had high plasma [blood] concentrations of CRP [a marker of inflammation], fasting insulin, and hemoglobin A1c at baseline," Jiang reported. They also had higher intake of trans fats, red and processed meats, and calories, but lower intake of fiber and magnesium.

The risk of diabetes is also increased in hemochromatosis, an inherited disease in which the body stores excessive amounts of iron.

Reference: Jiang R, Manson JE, Meigs JB, et al. Body iron stores in relation to risk of type 2 diabetes in apparently healthy women. *JAMA*, 2004;291: 711-717.

High Intake of Antioxidants Reduces Long-Term Risk of Type 2 Diabetes.

The elevated blood glucose levels characteristic of diabetes generate large numbers of destructive free radicals. Not surprisingly, alpha-lipoic acid, vitamins E and C, and other antioxidants have been found to reduce the risk of complications from diabetes.

Antioxidants may also play a key role in preventing diabetes, according to a study by Finnish researchers. Jukka Montonen, MSc, of the National Public Health Institute, Helsinki, and his colleagues tracked the health of 2,285 men and 2,019 women over 23 years.

The subjects' diets were evaluated at the beginning of the study. At that time, none of the subjects, who ranged from 40 to 60 years old, had been diagnosed with diabetes. But during the course of the study, 383 of them developed type 2 (adult-onset) diabetes.

Overall, men and women who consumed the most antioxidants had a significantly lower risk of developing diabetes. Those who consumed the most vitamin E had a 31 percent lower risk of developing diabetes. All subfractions of vitamin E, including tocopherols and tocotrienols, were associated with a lower risk of diabetes.

High intake of carotenoids also appeared to lower the risk of diabetes. Cryptoxanthin was associated with a 42 percent lower risk, and beta-carotene and lutein/zeaxanthin were independently associated with a 26 percent lower risk of diabetes.

Montonen and the other researchers pointed out that free radials "may contribute to the pathogenesis of type 2 diabetes by increasing insulin resistance and impairing insulin secretion." Insulin resistance, and sometimes impaired insulin secretion, set the stage for elevated blood glucose levels in diabetes.

Reference: Montonen J, Knekt P, Jarvinen R, et al. Dietary antioxidant intake and risk of type 2 diabetes. *Diabetes Care*, 2004;27:362-366.

Calorie Restriction, Even Late in Life, May Offer Substantial Health Benefits

Since 1935, dozens of experiments – with insects, rodents, monkeys, and other species – have consistently found that reductions in caloric intake significantly increase longevity. In general, animals that begin consuming one-third fewer calories shortly after birth live about 30 percent longer than normally expected. The key in most of these experiments, of course, is to provide adequate levels of vitamins and minerals (usually through supplementation) to avoid nutritional deficiencies.

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Quick Reviews of Recent Research

• Pycnogenol improves glucose control in diabetics

Eighteen men and 12 women were treated with increasing dosages of Pycnogenol, a natural antioxidant complex derived from the bark of French maritime pine trees. The initial dosage was 50 mg daily for three weeks, and it was increased to 100 mg, 200 mg, and 300 mg in three-week intervals. The patients benefited from significant improvements in fasting glucose, postprandial glucose, and hemoglobin A1c with dosages of 50 to 200 mg. The higher dosage of 300 mg provided no additional benefits.

Liu X, et al. *Diabetes Care*, 2004;27:839.

• Arthritis patients low in antioxidants

Researchers analyzed blood levels of free radicals and dietary and enzymatic antioxidants in 22 men and women with rheumatoid arthritis and compared them with 20 healthy subjects. Levels of malondialdehyde were 300 percent higher in patients with rheumatoid arthritis. In addition, their levels of vitamins A, C, and E, and superoxide dismutase and glutathione peroxidase were 21 to 36 percent lower than in healthy subjects.

Karatas F, et al. *Indian Journal of Medical Research*, 2003;118:178-181.

• Antioxidants may protect against muscle loss

Sarcopenia, the loss of skeletal muscle mass, is a common characteristic of aging and results in reduced muscle strength. In a study of 669 women ages 70 to 79, researchers found that higher blood levels of carotenoids (alpha-carotene, beta-carotene, cryptoxanthin, and lutein/zeaxanthin) and vitamin E were associated with greater grip, hip, and knee strength, all signs of higher muscle mass. The high carotenoid levels may reflect the health-promoting effects of vegetables and fruit.

Semba RD, et al. *Aging Clinical and Experimental Research*, 2003;15:482-487.

• B vitamins lower homocysteine levels

Elevated blood levels of homocysteine are an established risk factor for heart attack and stroke. Fifty patients with coronary artery disease were given various combinations of B vitamins or placebos daily for 12 weeks. Patients taking low-dose vitamin B6 by itself did not have a reduction in homocysteine levels. In contrast, patients taking a combination of folic acid (5,000 mcg) and vitamin B12 (25 mcg) benefited from a 32 percent reduction in homocysteine levels.

Lee BJ, et al. *European Journal of Clinical Nutrition*, 2004;58:481-487.

Calorie Restriction...

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Calorie restriction reduces the production of destructive free radicals, most of which are produced when food is broken down for energy. With fewer free radicals, less cell damage occurs – slowing the rate of aging. In addition, calorie restriction slows age-related changes in gene activity.

A new study, using mice, has shown that many of the longevity and health benefits of caloric restriction can be obtained relatively late in life.

Stephen R. Spindler, PhD, of the University of California, Riverside, and his colleagues placed 120 mice on either normal or calorie-restricted diets. All of the mice were 19 months old, the equivalent of late middle age. The calorie-restricted diets contained 60 percent of the animal's normal caloric intake.

Spindler found that the calorie-restricted mice lived about six months longer than mice eating a normal diet, and their rate of age-related death decreased by about three times. Between the ages of 21 and 31 months of age, deaths from cancer in the calorie-restricted mice decreased by about 13 percent.

Mice that began eating calorie-restricted diets late in life developed changes in gene activity similar to those in animals eating calorie-restricted diets shortly after birth. But when the animals were again fed a normal diet, their gene activity quickly reverted back, indicating that the changes were not permanent.

Spindler wrote that calorie restriction "begun relatively late in the lifespan of mice was as effective as calorie restriction begun early in life at decelerating mortality rate, extending remaining lifespan, and delaying the onset and/or progression as a cause of death."

Reference: Dhahbi JM, Kim JH, Mote PL, et al. Temporal linkage between the phenotypic and genomic responses to calorie restriction. *Proceedings of the National Academy of Sciences*: electronic publication March 22, 2004, ahead of print. □

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