

# The NUTRITION REPORTER™

THE INDEPENDENT NEWSLETTER THAT REPORTS VITAMIN AND MINERAL THERAPIES © APRIL 2000 VOL 11 No 4 BY JACK CHALLEM

## Supplemental Carnitine and Arginine Beneficial in Patients with Heart Failure

Congestive heart failure, a condition in which the heart cannot pump sufficient blood to nourish the body, affects an estimated 5 million Americans. The prognosis is generally poor with conventional drug therapies; half of the people with heart failure live only five years after diagnosis.

But new studies add to the evidence that supplements of two common nutrients, carnitine and arginine, can improve heart function in patients with heart failure. Arginine is an amino acid (protein building block), and L-carnitine is a "trimethylated" amino acid; both are obtained from food and also made by the body.

Carnitine plays key roles in the production of cellular energy, a process needed for normal function of the heart muscle. It helps transport fats into cells where they are burned for energy, and it also regulates the use of coenzyme A (built around the B vitamin pantothenic acid) in energy production.

In the first study, Ioannis Rizos, MD, of the University of Athens Medical School, Greece, studied 70 patients who took either 2 grams of carnitine or a placebo daily for three years. The patients suffered from heart failure resulting from dilated cardiomyopathy (an enlarged heart that lacks the muscular energy to pump blood).

During the study, patients taking carnitine had a significantly better rate of survival, compared with those taking the placebo. Only one person died in the carnitine group, whereas six died in the placebo group. In addition, only one patient in the carnitine group developed arrhythmias, compared with seven in the placebo group.

"Results from this trial therefore suggest that L-carnitine may improve the functional status of patients with moderate to severe heart failure attributable to dilated cardiomyopathy," Rizos wrote in the *American Heart Journal*.

In a separate study, Rainer Hambrecht, MD, and his colleagues at the Leipzig Heart Center, Germany, described how arginine and mild exercise training improved cardiovascular function in patients with chronic heart failure.

Hambrecht asked 40 patients to follow one of four regimens: take 8 grams of arginine daily, perform

daily handgrip exercises, take arginine and do handgrip exercises, and a control group.

After four weeks of L-arginine supplementation, the subjects benefited from a four-fold improvement in cardiovascular responsiveness (measured by endothelial function) and blood flow. Handgrip exercises also led to improvements in cardiovascular responsiveness, and still greater improvements occurred with a combination of arginine and handgrip exercises.

References: Rizos I. Three-year survival of patients with heart failure caused by dilated cardiomyopathy and L-carnitine administration. *American Heart Journal*, 2000;139:S120-S123. Hambrecht R, Hilbrich L, Erbs S, et al. Correction of endothelial dysfunction in chronic heart failure: additional effects of exercise training and oral L-arginine supplementation. *Journal of the American College of Cardiology*, 2000;35:706-713. □

### Commentary...

#### What Do Negative Studies Mean?

Over the past couple of months, two negative studies on vitamins E and C have grabbed headlines – and left people wondering whether they should continue taking their supplements.

It's important to look at such studies within the context of all the scientific and clinical evidence on these vitamins. The reason is that scientific research on any topic is rarely consistent. Disparate results could result from a study's organization, the unknown genetics of the subjects, and many other factors. That's the nature of scientific research.

The first report, published in the *New England Journal of Medicine*, found that a large group of patients with either cardiovascular disease or diabetes, failed to benefit from taking 400 IU of vitamin E daily for more than four years.

It's not easy to explain the lack of a positive outcome in this study. But here's my guess: medications (beta-blockers, cholesterol-lowering drugs, and anti-coagulants) taken by most of the subjects could have masked the benefits of vitamin E. At this point, no one really knows for sure.

Continues on next page

The second report, presented at a medical meeting in March and published as a one-paragraph abstract in the journal *Circulation*, found that vitamin C supplements were associated with slightly increased thickness of the carotid artery, a marker of cardiovascular disease.

In a response, Balz Frei, PhD, director of the Linus Pauling Institute at Oregon State University, noted that the finding directly contradicted a 1995 *Circulation* study, which reported that people taking vitamin C supplements had a decrease in carotid artery thickness. He also noted that more than 20 studies since 1996, most published in *Circulation*, have found vitamin C beneficial in cardiovascular diseases.

Does the thickness of the carotid artery even matter? It depends. Hugh D. Riordan, M.D., told me that a change in the carotid artery lumen (the opening) would have been far more significant, because that would have influenced blood flow. The researchers did not measure the diameter of the lumen.

When I look at the breadth of scientific research on vitamins E and C, the evidence in favor of supplements is nothing less than overwhelming. Vitamin E has been used with clinical success for more than 50 years. The disappointing results in the recent vitamin E trial should be balanced with the positive findings of a study that, several years ago, found a 77 percent reduction in heart attacks.

As for vitamin C, Frei said it best in a public statement: "People taking vitamin C supplements should continue to do so, as the known health benefits of vitamin C far outweigh alleged, unconfirmed risks. There is no scientific evidence that vitamin C supplements increase the risk of heart attacks or strokes. Vitamin C supplements of 500 mg per day have been shown to normalize vasodilation and lower blood pressure, two major cardiovascular risk factors."

— Jack Challem

## Studies Close the Gap Between Homocysteine and Heart Disease

Dozens of studies have shown that elevated blood levels of homocysteine increase the risk of coronary heart disease. Many other studies show that folic acid and vitamin B6 can lower homocysteine levels. But the "missing link" has been a well-controlled study showing that supplemental B vitamins actually reduce the risk of heart disease.

Two studies have now helped firm up the beneficial effect of B vitamins in reducing homocysteine and preventing heart disease.

Erik Vermeulen, MD, of the University Hospital Vrije Universiteit, Netherlands, and his colleagues studied 158 siblings of patients who developed heart

disease relatively early in mid-life. Many of these siblings had elevated homocysteine levels and other signs of subclinical heart disease.

Vermeulen and his colleagues asked the siblings to take either 5 mg of folic acid and 250 mg of vitamin B6 or a placebo daily for two years.

As expected, the subjects taking the vitamins had a significant decrease in blood homocysteine levels. However, they also had a significantly lower rate of abnormal exercise electrocardiography tests, a change consistent with a decreased risk of heart disease, compared with subjects taking the placebo.

"These data suggest that vitamin treatment aimed at lowering concentrations of total homocysteine can favourably influence the course of atherosclerotic disease," Vermeulen and his colleagues wrote.

In a separate study, Ton J. Rabelink, MD, PhD, of University Hospital Utrecht, Netherlands, and his colleagues fed a high-fat meal to 20 healthy young men and women. In response, their triglycerides rose, and their blood vessels became less flexible, both changes related to an increased risk of heart disease. In addition, the dietary fat increased their excretion of free radical byproducts, indicating an increase in free radical production.

Pretreatment with folic acid (10 mg daily for two weeks) did not alter the increase in triglyceride levels after eating fat. However, the folic acid supplements did normalize blood vessel flexibility and excretion of free radical byproducts.

"Because these observations were made in healthy volunteers with normal folate and homocysteine levels, it is suggested that a higher folate intake in the general population may have vasculoprotective effects," noted Rabelink and his colleagues.

Reference: Vermeulen EGJ, Stehouwer CDA, Twisk JWR, et al. Effect of homocysteine-lowering treatment with folic acid plus vitamin B6 on progression of subclinical atherosclerosis: a randomized, placebo-controlled trial. *Lancet*, 2000;355:517-522. Wilimink HW, Stroes ESG, Erkelens WD, et al. Influence of folic acid on postprandial endothelial dysfunction. *Arteriosclerosis, Thrombosis, and Vascular Biology*, 2000;20:185-188. □

## Omega-3 Fatty Acids Prevent Breakdown of Joint Cartilage

Many people take fish oil supplements to ease the pain of rheumatoid arthritis and osteoarthritis. Now, molecular biologists have determined exactly why they help: fish oils reduce inflammation and inhibit the breakdown of cartilage.

In a series of experiments, Bruce Caterson, PhD, and his colleagues at Cardiff University, Wales,

studied the effects of various omega-3 fatty acids on chondrocytes, one of the key cells that make up articular (joint) cartilage.

By exposing bovine joint cartilage chondrocytes to linolenic acid, the parent molecule of the omega-3 fatty acids, Caterson found that the cells readily absorbed the linolenic acid while displacing other polyunsaturated fatty acids.

He obtained identical results when culturing chondrocytes with two other omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA).

Perhaps most significantly, he found that omega-3 fatty acids deactivated aggrecanases, a family of enzymes that break down cartilage. Omega-3 fatty acids also inhibited genetic activity that program proinflammatory compounds, including interleukin-1 (IL-1), tumor necrosis factor alpha (TNF $\alpha$ ), and cyclooxygenase-2 (COX-2).

Caterson and his colleagues wrote that "dietary fish oil supplementation can reduce inflammatory and degradative aspects of articular joint disease and thus modulate disease progression."

Reference: Curtis CL, Hughes CE, Flannery CR, et al. n-3 fatty acids specifically modulate catabolic factors involved in articular cartilage degradation. *Journal of Biological Chemistry*, 2000;275:721-724. □

## Glucosamine and Chondroitin Found Helpful in Osteoarthritis

Glucosamine sulfate and chondroitin sulfate reduce symptoms of osteoarthritis and have fewer side effects than other treatments, according to a report in the *Journal of the American Medical Association*.

"Because of their safety, these remedies would have great utility in the treatment of osteoarthritis even if they were only modestly effective," wrote rheumatologist Timothy E. McAlindon, DM, and his colleagues at Boston University.

McAlindon and his colleagues analyzed 15 published studies on the use of glucosamine and chondroitin in osteoarthritis. They found that glucosamine had a moderate effect on arthritic symptoms and that chondroitin had greater benefits.

However, McAlindon criticized the quality of studies conducted on these supplements and suggested that they are not as effective as many people believe.

An editorial by Tanveer E. Towheed, MD, and Tassos P. Anastassiades, MD, PhD, noted that the problems with studies on glucosamine and chondroitin are probably no worse than those of studies using nonsteroidal antiinflammatory drugs (NSAIDs) in the treatment of osteoarthritis and rheumatoid arthritis.

Reference: McAlindon TE, LaValley MP, Gulin JP,

et al. Glucosamine and chondroitin for treatment of osteoarthritis: a systematic quality assessment and meta-analysis. *JAMA*, 2000;283:1469-1475. Towheed TE, Anastassiades TP. Glucosamine and chondroitin for treatment of osteoarthritis: evidence is widely touted but incomplete. *JAMA*, 2000;283:1483-1484. □

## Carotenoids May Help Protect Against Angina Pectoris

Eating a diet high in carotenoids may reduce the risk of angina pectoris, a type of heart pain associated with physical exertion.

Earl S. Ford, MD, and Wayne H. Giles, MD, of the Centers for Disease Control and Prevention, Atlanta, analyzed blood levels of nutrients and the health among 10,000 participants in the National Health and Nutrition Examination Survey III (NHANES III).

They found that people with the highest levels of three carotenoids had about half the risk of developing angina pain. People with high alpha-carotene levels were 55 percent less likely to develop angina. People with high levels of either beta-carotene or beta-cryptoxanthin were 43 percent less likely to have angina, compared with subjects with the lowest levels of these nutrients.

Vitamins A, C, E, B12, and folic acid were not associated with angina risk.

Reference: Ford ES, Giles WH. Serum vitamins, carotenoids, and angina pectoris: findings from the National Health and Nutrition Examination Survey III. *Annals of Epidemiology*, 2000;10:106-116. □

## Researchers Consider Whether Low Vitamin A Ups Breast Cancer Risk

A defect in the body's use of vitamin A may increase the risk of breast cancer, according to a recent study.

Vitamin A is necessary for the differentiation of normal cells. The uptake and metabolism of vitamin A depends on cellular retinol-binding protein (CRBP), and low CRBP activity would reduce vitamin A activity.

Recognizing the crucial role of CRBP, Rafael Mira-y-Lopez, MD, of the Mount Sinai School of Medicine, N.Y., and his colleagues found CRBP to be present in all 15 normal breast tissue specimens, as well as in 33 of 35 samples of normal breast tissue that were adjacent to tumors.

However, no CRBP could be detected in 12 (24 percent) of the 49 samples of cancerous breast tissue. The authors suggested that the lack of CRBP could sometimes enhance the growth of cancer cells.

Reference: Kuppumbatti YS, Bleiweiss IJ, Mandeli JP, et al. Cellular retinol-binding protein expression and breast cancer. *Journal of the National Cancer Association*, 2000, 92:475-480. □

## Quick Reviews of Recent Research

### • Vitamin E helps destroy cancer cells

Radiation and chemotherapy generate cancer-destroying free radicals. However, some researchers have questioned whether antioxidants may in fact protect cancer cells against such therapies. Researchers exposed irradiated normal cells and cervical, ovarian, and lung cancer cells to natural vitamin E succinate. Vitamin E stopped the growth of all three types of cancer cells, but not normal cells. It also halted the growth of cervical cancer cells.

Jha MN, et al., *Nutrition and Cancer*, 2000;35:189-194.

### • Carotenoids and vitamin E protect skin

Free radicals are generated when skin is exposed to ultraviolet rays in sunlight. In a 12-week study, researchers gave 26 men and women either 25 mg of natural mixed carotenoids (principally beta- and alpha-carotene), 500 mg (745 IU) vitamin E, or both. Subjects taking the carotenoids became more resistant to sunburn after eight weeks of supplementation. However, subjects taking both carotenoids and vitamin E had better protection against sunburn after just four weeks.

Stahl W, et al., *American Journal of Clinical Nutrition*, 2000;71:795-798.

### • Vitamin E prevents blood clots

Researchers investigated the effect of vitamin E on platelet aggregation in human and cell experiments. After taking 600 mg of vitamin E daily for two weeks, subjects has less platelet aggregation and lower levels of free radicals. The cell studies indicated that vitamin E lowered levels of thromboxane, which promotes clotting.

Pignatelli P, et al., *Artherosclerosis, Thombosis and Vascular Biology*, 1999;2542-2547.

### • Zinc effective treatment of Wilson's disease

Wilson's disease, caused by a genetic mutation, results in the toxic accumulation of copper, leading to liver disease and neurological disorders. Zinc acetate and two drugs are the FDA-approved treatments of Wilson's disease, but the drugs have side effects and may damage fetuses. In a study of 19 pregnant women with Wilson's disease, zinc acetate was an effective treatment and safe for mothers and fetuses. Zinc works by inducing intestinal metallothionein, which binds copper and prevents it from entering the blood.

Brewer GJ, et al., *Hepatology*, 2000;31:364-370.

### • Refined grains may boost stomach cancer risk

Researchers studied the eating habits and risk of disease among 12,000 middle-age men from seven countries. Men who ate a lot of refined grains generally consumed relatively little fruit. High fruit consumption

was associated with a lower risk of stomach cancer, whereas high refined-grain consumption increased the risk of cancer.

Jansen MCJF, et al., *Nutrition and Cancer*, 1999;34:49-55.

### • Many people take supplements

Researchers analyzed data from the third National Health and Nutrition Examination Survey (NHANES III), which included almost 34,000 people representative of the total U.S. population. Overall, about four of ten people reported taking vitamin and mineral supplements.

Balluz LS, et al., *Archives of Family Medicine*, 2000;9:258-262.

### • Low selenium may aggravate Crohn's disease

Researchers compared 26 patients with Crohn's disease and 15 healthy subjects. They found low selenium levels in the Crohn's patients. Selenium is an essential part of glutathione peroxidase, which has antiinflammatory properties.

Reimund JM, et al., *Clinical Nutrition*, 2000;19:43-48.

### • Elevated homocysteine doubles heart attack risk

In a study of 3,173 subjects, researchers found that blood levels of vitamin B12 and folic acid were low in people with high homocysteine levels. Elevated homocysteine is a risk factor for heart disease, and people with blood levels greater than 15 micromoles per liter of blood had almost a two-fold increased risk of heart attack.

Giles WH, et al., *American Heart Journal*, 2000;139:446-453.

### • Fish oils improve cardiovascular health

After taking 4 grams of omega-3 fatty acids daily for four months, subjects with high cholesterol benefited from an improvement in endothelial function, an indicator of cardiovascular health.

Goodfellow J, et al., *Journal of the American College of Cardiology*, 2000;35:265-270.

THE NUTRITION REPORTER™ (ISSN 1079-8609) is published monthly except for August and December. This issue, Vol 11 No 4, © April 2000 by Jack ChalleM. All rights reserved. Reproduction without written permission is prohibited. Phone: (520) 529-6801. Fax: (520) 529-6840. Email addresses: Nutreport@aol.com or JchalleM@aol.com. This newsletter is strictly educational and not intended as medical advice. For diagnosis and treatment, consult your physician. Subscriptions are \$25 per year in the U.S.; either \$32 U.S. or \$48 CDN for Canada; and \$38 for other countries, payable in U.S. funds through a U.S. bank. The Nutrition Reporter is a trademark(TM) of Jack ChalleM.

#### THE NUTRITION REPORTER™

Post Office Box 30246  
Tucson AZ 85751-0246 USA

Editor and Publisher: **Jack ChalleM**

#### Medical Advisors:

London H. Smith, MD Portland, Oregon • Richard P. Huemer, MD Lancaster, California  
Ralph K. Campbell, MD Polson, Montana • Peter Langsjoen, MD Tyler, Texas  
G. Edward Desaulniers, MD The Shute Institute Medical Clinic London, Ontario  
Marcus Laux, ND Pacific Palisades, California

