

The Nutrition Reporter™

© Jack Challem February 2003 Vol 14 No 2

The independent newsletter that reports vitamin, mineral, and food therapies

Another Study Confirms that Glucosamine Sulfate Can Slow, Reverse Osteoarthritis

European researchers have for the second time shown that supplements of glucosamine sulfate can do what no drug can – that is, reverse the progression of osteoarthritis.

The condition is characterized by a decrease in articular cartilage, which cushions bones in the knees and other joints. When the cartilage completely wears away, bone shear can create inflammation and pain and limit mobility.

Karel Pavelka, MD, of the Institute of Rheumatology, Prague, Czech Republic, and his colleagues treated 202 men and women, ages 45 to 70 years, who had mild to moderate knee osteoarthritis for at least 10 years. Half of the subjects were given 1,500 mg of glucosamine sulfate daily, and the other half were given placebos for three years.

Pavelka's team took x-rays of the subjects' knees at the start of the study and then once a year. Researchers carefully measured the size of knee cartilage in the x-rays. In addition, they used two standard tests to assess the patients' pain, stiffness, and physical function.

Overall, patients taking glucosamine sulfate supplements had increases in cartilage during the study. In contrast, those taking placebos had decreases in joint cartilage – that is, a clear progression in osteoarthritis.

Those taking placebos had an average loss of 0.09 to 0.29 mm cartilage. In contrast, patients taking glucosamine sulfate experienced a range from an insignificant 0.06 mm loss to 0.14 mm gain in cartilage.

Pavelka wrote that "this study demonstrates that glucosamine sulfate is the first pharmacological intervention that retards the progression of osteoarthritis during long-term treatment."

Pain also decreased significantly – by as much as 20 to 25 percent – among patients taking glucosamine sulfate. Only a small number of patients taking placebos had reductions in pain.

Glucosamine sulfate, derived from bovine

tracheas, provides some of the building blocks for cartilage production. It also functions as a mild Cox-2 inhibitor, which likely accounts for its rapid pain reduction effect.

A previous study, published two years ago in the journal *Lancet*, found that a combination of glucosamine sulfate and chondroitin sulfate supplements increased cartilage in the knees of people with osteoarthritis.

Several studies have found that common nonsteroidal anti-inflammatory drugs (NSAIDs) – including popular Cox-2 inhibiting drugs – actually accelerate the breakdown of cartilage and progression of osteoarthritis.

Reference: Pavelka K, Gatterova J, Olejarova M, et al. Glucosamine sulfate use and delay of progression of knee osteoarthritis. *Archives of Internal Medicine*, 2002;162:2113-2123.□

Eating One Seafood Meal a Month Reduces the Risk of Stroke in Men

Men who eat a seafood meal at least once a month appear to slash their risk of ischemic stroke by more than 40 percent. That's the finding of a new study by researchers at Harvard University's School of Public Health.

Ka He, MD, and his colleagues analyzed data from the ongoing Health Professional Follow-up Study, which includes more than 43,000 male health professionals. During a 12-year period, 608 men experienced strokes. Of these, 377 were ischemic strokes – the most common type – characterized by a narrowing of, or clots, in blood vessels in the brain.

The subjects periodically completed questionnaires asking for information about diet and health, beginning in 1986. Included were questions about their consumption of four groups of seafood: cold-water fish, such as salmon; canned tuna; white fish, such as flounder or cod; and shellfish, such as lobster, shrimp, and scallops.

Continues on next page

Men who consumed any type of seafood at least once a month were 44 percent less likely to have an ischemic stroke. Eating fish five or more times weekly (20 times monthly) was only slightly more protective, reducing the stroke risk by 46 percent. Even men who occasionally ate shrimp suffered fewer strokes.

The researchers reported no significant associations between fish consumption and the risk of hemorrhagic (bleeding) stroke.

Reference: He K, Rimm EB, Merchant A, et al. Fish consumption and risk of stroke in men. *JAMA*, 2002;288:3130-3136. □

Lycopene Supplements Reduce Size of Prostate Cancer Tumors

Many studies have found that diets high in lycopene – the red antioxidant carotenoid found in tomatoes – are associated with a lower risk of prostate cancer. Now, a small clinical trial has found that lycopene supplements can actually reduce the size of prostate cancers.

Omer Kucuk, MD, of Wayne State University, and his colleagues asked 15 men with recently diagnosed prostate cancers to take a tomato oleoresin extract containing 30 mg of lycopene daily for three weeks before surgery to remove their prostates. The prostates from these men were compared with those from 11 men who did not receive supplements before surgery.

The high-dose lycopene supplements reduced the size of the men's tumors and significantly inhibited their tendency toward invasive metastasis of other tissues. The findings are significant, given the fact that lycopene supplements were taken for only three weeks.

After supplementation, four-fifths of the men taking the lycopene supplements had relatively small tumors (less than 4 mm in size), compared with fewer than half of the men not receiving the supplements. Similarly, 73 percent of men taking lycopene had tumors confined to the prostate, compared with only 18 percent of the nonsupplemented group.

In addition, the average levels of prostate-specific antigen (PSA), a marker of prostate cancer risk, were lower after men supplemented with lycopene.

"This pilot study suggests that lycopene may have beneficial effects in prostate cancer," Kucuk wrote. "Larger clinical trials are warranted to investigate the potential preventive and/or therapeutic role of lycopene in prostate cancer."

Reference: Kucuk O, Sarker FH, Djuric Z, et al. Effects of lycopene supplementation in patients with localized prostate cancer. *Experimental Biology and Medicine*, 2002;227:881-885. □

Supplemental Glycine, an Amino Acid in Protein, Helps Control Blood Sugar

The amino acid glycine may have a beneficial role in diabetes, according to a study by researchers at the University of Minnesota and the VA Medical Center, Minneapolis.

Mary C. Gannon, PhD, and her colleagues tested the effects of glycine (found in protein) and glucose on blood sugar and insulin levels in nine healthy men and women.

"Our laboratory is interested in the metabolic response to ingested proteins, particularly in persons with type 2 diabetes," she wrote. "The reason for this interest is that ingested protein results in no increase in peripheral blood glucose concentrations or increases them only modestly. However, ingested protein stimulates both insulin and glucagon secretion."

Each of the subjects received supplemental glycine, ranging from 3.6 to 5.4 grams (depending on lean body mass), 25 grams of oral glucose, a combination of the glycine and oral glucose, or water.

The combination of glycine and glucose reduced the rise in blood sugar levels by 15 percent, compared with when the subjects were given only glucose. Gannon and her colleagues wrote that "the ingested glycine effect on the postprandial glucose concentration may be important therapeutically if a similar effect can be shown in persons with type 2 diabetes."

The researchers noted that the glycine appears to accelerate the burning of blood sugar, and that other research has suggested that glycine and glucose compete for absorption. Research dating back to 1932 found that large supplemental dosages of glycine could reduce blood sugar levels in both healthy and diabetic subjects.

Reference: Gannon MC, Nuttall JA, Nuttall FQ. The metabolic response to ingested glycine. *American Journal of Clinical Nutrition*, 2002;76:1302-1307. □

Vitamin E Supplements May Help with Some Allergy-Related Skin Disorders

Years ago, vitamin E was often dismissed as a "panacea" because it seemed to resolve so many disorders. But studies continue to confirm its diverse health benefits.

In one recent study, Italian researchers found that supplements of natural vitamin E improved a variety of skin disorders grouped as atopic dermatitis. The term is used to describe skin inflammation and itching in people with a personal or family history of asthma or allergies.

Evridiki Tsourelis-Nikita, MD, and colleagues

from the universities of Siena and Florence, asked 96 men and women with atopic dermatitis to take 400 IU of natural vitamin E or placebos daily for eight months. The patients' symptoms included facial redness, thickening of the skin, eczema, and itching.

Overall, patients taking vitamin E improved, whereas those taking placebos deteriorated.

Seven of the patients taking vitamin E had nearly complete remissions, compared with none of those taking placebos. In addition, 23 of those taking vitamin E had a "great improvement" in symptoms, compared with only one of those taking placebos. Ten in the vitamin E group had slight improvements, while only four in the placebo group did.

Only four patients in the vitamin E group worsened, compared with 36 in the placebo group. In addition, people taking vitamin E had an average 62 percent decrease in IgE (immunoglobulin E) levels, an immune factor that is typically elevated in allergies. In contrast, the patients in the placebo group had an 34 percent decrease in IgE levels.

Reference: Tsourelis-Nikita E, Hercogova J, Lotti T, et al. Evaluation of dietary intake of vitamin E in the treatment of atopic dermatitis: a study of the clinical course and evaluation of the immunoglobulin E serum levels. *International Journal of Dermatology*, 2002;41:146-150. □

Elevated Homocysteine Levels Strongly Linked to Cardiovascular Diseases

An analysis of 92 studies has found compelling evidence that elevated homocysteine levels increase the risk of cardiovascular diseases. Conversely, the researchers conclude, folic acid supplements can lower homocysteine levels and significantly reduce the risk of disease.

David S. Wald, MRCP, of Southampton Hospital, England, and his colleagues examined 72 clinical studies that focused on a genetic defect reducing the activity of a key folic acid enzyme and 20 studies of homocysteine and disease risk.

The inherited genetic defect affects the functioning of methylenetetrahydrofolate reductase, reducing its activity and consequently folic acid utilization. About 10 percent of people are severely affected and 43 percent are partially affected by it, resulting in 20 percent increases in homocysteine levels.

The analysis by Wald and his colleagues found that a 5 mmole/liter increase in homocysteine levels increased the risk of ischemic heart disease by 42 percent in people with the genetic defect and 32 percent in the general population. Similarly, the risk for deep vein thrombosis, with or without pulmonary embolism, increased by 60 percent in people with the defect. (No studies examined the risk of deep vein

thrombosis in other groups of people.) And finally, elevated homocysteine levels increased the risk of stroke by 65 percent in people with the genetic defect and 59 percent in other studies.

"Our results strengthen the evidence that a raised serum homocysteine concentration is a cause of cardiovascular disease," the researchers wrote.

They noted that a 3 mmole/liter reduction of homocysteine – achievable with daily supplementation of 800 mcg of folic acid – should reduce the risk of ischemic heart disease by 16 percent, deep-vein thrombosis by 25 percent, and stroke by 24 percent.

Reference: Wald DS, Law M, Morris JK. Homocysteine and cardiovascular disease: evidence on causality from a meta-analysis. *BMJ*, 2002;325:1202. □

Researchers Compare the Food Pyramid to More Specific Recommendations

The "food pyramid," created in 1992 by the U.S. Department of Agriculture, has often been treated as the dietary standard people love to hate.

Although well-meaning, the pyramid's dietary recommendations have been criticized for lacking specifics. For example, it recommends eating five to 11 daily servings of grains – a hefty number of calories – without differentiating between whole and refined grains. Likewise, the pyramid recommends that people reduce their consumption of fats, without making a distinction between good and bad fats.

In the December 2002 *American Journal of Clinical Nutrition*, Marjorie L. McCullough, ScD, and her colleagues at Harvard University, compared the health of people eating according to the USDA food pyramid to those eating a "better" diet.

To do this, McCullough studied people eating along the lines of the Healthy Eating Index (HEI), on which the food pyramid was based. She then tracked the health of people eating according to the Alternative Healthy Eating Index (AHEI). The AHEI includes more specific recommendations for whole grains, good fats (over bad fats), white meats (over red meats), and multivitamin supplements.

"In an attempt to improve the original HEI, we created a 9-component AHEI...designed to target food choices and macronutrient sources associated with reduced chronic disease risk," McCullough and her colleagues wrote.

The study's subjects included 38,615 men and 67,271 women in long-term Harvard health studies.

It turned out that men and women eating according to the HEI (USDA food pyramid) had an 11 and 3 percent lower overall risk of chronic disease, respectively, compared with most people in the study. In other words, the benefits were not that impressive.

Continues on next page

Quick Reviews of Recent Research

• Vitamin E succinate shows anti-cancer properties

Although vitamin E succinate has not been used in human cancer trials, cell studies continue to demonstrate its anti-cancer effects. In this study, researchers grew two different types of human prostate cancer cells. Some cells of each type were grown with vitamin E succinate, a common form of the vitamin in supplements. Vitamin E succinate reduced the growth of the two types of prostate cancer cells by 95 and 69 percent. The vitamin also increased cellular activity of p27, an anti-cancer protein, by three times. In men, low p27 activity is associated with poor survival of prostate cancer.

Venkateswaran V, et al. *Journal of Urology*, 2002;168:178-182.

• Ginkgo and ginseng supplements improve memory

Twenty young men and women took 360 mg of ginkgo, 400 mg of ginseng, a combination of both herbs, or a placebo. Consumption of each supplement was followed by memory tests for assessing cognition. All three supplements led to improvements in memory, compared with baseline measurements, including word and picture recognition, immediate word recall, and delayed word recall. Subjects subjectively reported that ginkgo supplements led to improvements in mood.

Kennedy DO, et al. *Physiology & Behavior*, 2002;75:739-751.

• Ginseng berries found helpful in diabetes

Recent studies have found that ginseng root supplements can lower blood sugar levels and improve diabetes. In this study, researchers injected an extract from ginseng berries into diabetic and overweight mice. Blood sugar levels in the mice

Food Pyramid...

Continues from previous page

But when the researchers looked at people who made more careful food choices, along the lines of the AHEI, the reduced risk of disease was significant. Men eating according to the AHEI had a 20 percent lower risk and women had an 11 percent lower risk of serious chronic diseases. Most of this improvement was the result of a 39 percent lower risk of cardiovascular disease in men and a 28 percent lower risk in women. Also, multivitamins were associated with a lower risk of both cardiovascular diseases and cancer.

Reference: McCullough ML, Feskanich D, Stampfer MJ, et al. Diet quality and major chronic disease risk in men and women: moving toward improved dietary guidance. *American Journal of Clinical Nutrition*, 2002;76:1261-1271. □

normalized, and cholesterol levels declined by 30 percent. The mice also lost about 10 percent of their body weight.

Attele AS, et al. *Diabetes*, 2002;51:1851-1858.

• Ribose supplements increase muscle strength

Ribose is one of the building blocks for adenosine triphosphate, the chemical form of stored energy in cells. Researchers asked 12 male body builders, ages 18-35 years, to take either 10 grams of ribose or placebos daily for four weeks. Men taking ribose supplements had substantial increases in muscular strength. However, they had no significant changes in body composition.

Van Gammeren D, et al. *Current Therapeutic Research – Clinical and Experimental*, 2002;63:486-495.

• Curcumin has anti-cancer effect

Curcumin, a yellow compound found in the spice turmeric, is established as an antioxidant. In this experiment, researchers grew human pancreatic cancer cells with different amounts of curcumin. The spice extract inhibited the growth of pancreatic cancer cells and reduced the activity of “nuclear factor kappa B,” a molecule involved in inflammation and free radical production. Reduction of nuclear factor kappa B also inhibited activity of the gene responsible for interleukin-8, a cell-communication molecule involved in inflammation.

Hidaka H, et al. *Cancer*, 2002;95:1206-1214.

• High vitamin intake lowers esophageal cancer risk

Ninety-nine German men with esophageal cancer were compared with 50 men without the disease. Men with higher intakes of vitamin E (greater than 13 mg daily) and vitamin C (greater than 100 mg daily) had significantly lower risks of developing either squamous cell carcinoma or adenocarcinoma of the esophagus.

Bollschweiler E, et al. *Journal of Cancer Research and Clinical Oncology*, 2002;128:575-580.

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THE NUTRITION REPORTER™

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