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IN THE NEWS**Supplements Boost Cardioprotective Nitric Oxide**

Antioxidants, L-arginine, and exercise reduce the risk of atherosclerosis in mice bred to have elevated cholesterol levels, according to research conducted by Nobel Laureate Louis J. Ignarro and his colleagues at the University of California, Los Angeles.

The researchers administered a high-cholesterol diet, the same diet with vitamins C and E, or the diet with the vitamins and the amino acid L-arginine to hypercholesterolemic mice for 18 weeks. Two weeks into their various diets, some of the mice in each group were also put on a moderate exercise regimen.*

All of the mice that exercised experienced weight loss and decreased total cholesterol compared to mice that did not exercise or receive supplements. While the mice that exercised and did not receive supplements experienced a 35% reduction in atherosclerotic lesions, those that did not exercise but received supplements experienced a 40% reduction. Dr Ignarro noted this shows that

“the supplements work well even in the absence of exercise.”

The effect was magnified in mice that exercised and received antioxidants combined with L-arginine; these mice experienced a significant regression of their atherosclerotic lesions compared to the other groups. The researchers attributed this to the increased nitric oxide produced by exercise and arginine. Nitric oxide lowers blood pressure, prevents excessive clotting and inflammation associated with coronary artery disease, and protects against heart attack and stroke.

By removing oxidants from the blood, vitamins C and E stabilize the nitric oxide, which allows it to rise to higher levels, producing greater benefits. “This is the first study that shows that if you exercise in addition to taking dietary supplements, you have a markedly enhanced production of nitric oxide,” said Dr. Ignarro. He recommends moderate exercise and a low-fat diet enhanced with dietary supplements: “I would say just do it. It works in mice, it’ll work in humans.”

—Dayna Dye

Reference

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Glucosamine Relieves Osteoarthritis Symptoms

Glucosamine, an amino derivative of glucose, has been shown for the first time to slow and even stop the progression of debilitating osteoarthritis, according to newly published research.

Osteoarthritis, the most common form of joint disease, affects 85% of American adults over the age of 65 and more than 50 million Americans altogether. While not a normal consequence of aging, osteoarthritis is a frequent accompaniment of aging.

Osteoarthritis chiefly affects weight-bearing joints in areas such as the ankles, knees, hips, and spine, as well as the hands. The goal of treatment is generally the relief of pain and restoration of physical activity, most often achieved with non-steroidal anti-inflammatory drugs (NSAIDs), including aspirin. Joint replacement has been the treatment of last resort.

Glucosamine is a building block for glycosaminoglycans and proteoglycans, which are constituents of articular cartilage along with water, cellular elements, and proteins such as collagen, elastin, and fibronectin. Although its mechanism of action is not precisely known, glucosamine is known to be an anti-inflammatory agent. In a systematic review and meta-analysis of randomized clinical trials, glucosamine was found to be effective in ameliorating painful symptoms associated with



osteoarthritis.¹

Newly published research has shown for the first time that glucosamine slows and even stops the progression of osteoarthritis.² Study participants received 1500 mg per day of glucosamine sulfate (as has long been recommended by Life Extension) for three years and were permitted to use NSAIDs as well. While the group that received placebo experienced a worsening of clinical symptoms, those who received glucosamine reported a significant improvement in symptoms.

—Dean S. Cunningham, MD, PhD

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US Faces “Tidal Wave of Chronic Ocular Disease”

More than 28 million Americans over the age of 40 have eye ailments that put them at risk for vision loss and blindness, a number that is expected to rise rapidly as the population ages, according to research published in the *Archives of Ophthalmology*.

An estimated 20.5 million American adults have cataracts, a figure expected to climb to 30.1 million in the next 20 years.¹ Cataracts are the leading cause of blindness worldwide and of poor vision in the US. Like other major causes of blindness and vision loss such as macular degeneration, glaucoma, and diabetic retinopathy, cataracts are strongly linked with aging.

Macular degeneration affects about 1.8 million adults. Another 2.2 million US adults suffer from glaucoma, while 4 million are afflicted with diabetic retinopathy.

The numbers are alarming in part “because of the substantial increases in health care costs they spell,” said Dr. Nathan Congdon, an associate professor of ophthalmology at Johns Hopkins University. The US spends more than \$3 billion yearly on cataract treatment alone, Congdon noted.

In the absence of a significant investment in prevention and treatment to reverse this trend, the US faces a “tidal wave of chronic ocular disease over the next few decades,” fellow Johns Hopkins University researcher James Tielsch wrote in an accompanying editorial.



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Meat Consumption Tied to Risk of Gout

Newly published research has found that diets high in meat raise one's risk of contracting gout.

Gout is an inflammatory arthritis that affects several million men and women in the US. Gout develops when elevated serum levels of uric acid lead to the deposition of urate crystals in the joints and tissues. The clinical manifestations of gout include recurrent attacks of arthritis, joint deformation, the formation of kidney stones, and kidney damage. The incidence of gout is increasing in the US and has reached epidemic proportions in some groups, such as the Maori of New Zealand.¹

Obesity, alcohol consumption, and the use of diuretics generally are considered the dominant predisposing factors for gout. While genetic differences underlie the magnitude of uric acid levels to some degree, diet appears to correlate most strongly with the risk of developing gout.

A recent study clearly demonstrated that diets high in meats (more than 1.92 servings per day compared with less than 0.81 servings per day) led to an increase in the risk of gout.² In fact, the relative risk increased by as much as 21% with each additional portion of meat consumed daily. In like manner, increased seafood consumption (of greater than 0.56 servings per day compared with less than 0.15 servings per day) also increased the risk for gout, and even more so in men with a body mass index (BMI) of less than 25. No relationship was found to exist between total protein intake and the risk of gout, or between consumption of purine-rich vegetables and the risk of gout.

—Dean S. Cunningham, MD, PhD

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IN THE NEWS

Homocysteine Raises Risk of Osteoporosis

Although preventable, osteoporosis or “brittle bones” afflicts one of every two American women and one of every four American men over the age of 50. A new study suggests a clear link between osteoporosis and high blood levels of the amino acid homocysteine.

The complications of osteoporosis take the form of noticeable height loss and fractures of the hip, spine, and wrist. Osteoporosis is implicated in more than 300,000 hip fractures in the US each year; of those affected, approximately 25% will die within one year and another 25% will no longer be able to walk without assistance.

Homocysteine is involved in methionine metabolism, and normally is recycled into methionine or converted into cysteine. An excessive accumulation of homocysteine in the body, however, entails a heightened risk for heart disease and stroke, among other diseases.

In the study, 2,406 men and women over the age of 55 were followed prospectively. Those with homocysteine levels in the highest quartile had twice the risk of osteoporotic fracture compared to those in the other three quartiles.¹ This increased risk is comparable to that of acquiring cardiovascular disease or dementia for those with high levels of homocysteine.

In a second study of 1,999 men and women recruited as part of the Framingham Study, men whose homocysteine levels placed them in the highest quartile were nearly four times more likely to sustain an osteoporotic fracture compared to other subjects.² Women whose homocysteine placed them in the highest quartile were twice as likely to sustain a fracture as other female subjects.

Dietary supplementation with folate and vitamins B6 and B12, even in the absence of measurable deficiencies of these nutrients, helps lower homocysteine levels and may help protect against osteoporosis.

—Dean S. Cunningham, MD, PhD



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Curcumin Corrects Cystic Fibrosis Defects



The spice pigment curcumin, a powerful antioxidant and anticarcinogenic agent, has properties that correct for a defective protein implicated in cystic fibrosis, according to newly published research.

Cystic fibrosis is a genetic disease affecting approximately 30,000 children and adults in the US. A defective gene causes the body to produce an abnormally thick, sticky mucus that clogs the lungs, leads to life-threatening lung infections, and obstructs the pancreas, preventing digestive enzymes from reaching the intestines to help break down and absorb food. Cystic fibrosis is uniformly fatal, with a median survival time of 30 years.

The molecular basis of cystic fibrosis involves a defective protein called CFTR, which is required for energy transport. The defective CFTR protein is not delivered to the cell membrane, its site of action. When human cells with the cystic fibrosis mutation are treated in the laboratory with calcium-pump inhibitors, normal movement of CFTR to the cell membrane results.¹

Curcumin is a calcium-pump inhibitor, albeit a weak one. Recently, researchers at Yale University demonstrated that administering curcumin orally to mice homozygous for the defective CFTR protein resulted in the expression of normal CFTR activity in both the respiratory and gastrointestinal tracts.²

Mice that are homozygous for the defective CFTR protein have a 60% mortality rate within 10 weeks, with death caused by intestinal obstruction and characterized by progressive weight loss. When such mice were administered curcumin, the mortality rate dropped to 10% and the surviving mice gained weight, as did their normal littermates.²

—Dean S. Cunningham, MD, PhD

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Acetyl-L-Carnitine Improves Andropause Symptoms

New research suggests that the supplement acetyl-L-carnitine relieves the depression, fatigue, and sexual dysfunction that often accompany andropause, or male aging.

Multiple studies have shown that levels of bioavailable carnitine decrease with age in both men and women.¹ Carnitine, and its more bioavailable forms such as acetyl-L-carnitine, are essential cofactors for transporting fatty acids into the mitochondria, the cellular engines that produce energy for the body.

Italian researchers conducted a randomized study to determine whether supplemental acetyl-L-carnitine could improve these symptoms in aging men. Over a six-month period, 120 men aged 60-74 received either 160 mg per day of testosterone undecanoate,² grams per day of acetyl-L-carnitine and propionyl-L-carnitine, or placebo.² The men treated with testosterone reported significant improvements in erectile capability and sexual desire, and a decrease in fatigue and depression; no improvement was noted in orgasm or general sexual well-being. Men who received the carnitine supplements saw significant improvements in erectile capability, sexual desire, orgasm, and general sexual well-being, along with fewer complaints of fatigue and depression.

These impressive findings led the study authors to conclude: "Testosterone and, especially, carnitine proved to be active drugs for the therapy of symptoms associated with male aging."

—Edward R. Rosick, DO, MPH, MS

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Green Tea Inhibits Esophageal Cancer



Green tea contains a mechanism that inhibits esophageal cancer associated with Barrett's esophagus, according to a study presented at the Digestive Disease Week convention held in New Orleans last May.

Barrett's esophagus is a precancerous condition resulting from chronic irritation of the esophagus that occurs with gastroesophageal reflux disorder. Drinking tea has been linked with a lower risk of several cancers of the gastrointestinal tract. Consuming green tea is believed to expose the esophagus to high levels of green tea polyphenols such as epigallocatechin gallate (EGCG).

Howard Y. Chang, MD, and colleagues at Harvard Medical School and the Veterans Administration Boston Healthcare System administered varying concentrations of EGCG to cultured human Barrett's esophagus-associated adenocarcinoma cells and compared them to untreated cells. They found that cell growth was inhibited in a dose-dependent

manner within 72 hours of exposure to EGCG.

The team concluded that EGCG induces the programmed cell death known as apoptosis, which occurred in as little as 24 hours in the cells exposed to the compound. Further research found an elevation of caspase 3 (an enzyme involved in apoptosis) in the treated cells compared to the untreated cells, as well as increased cleaved PARP protein levels, another indicator of apoptosis.

According to Dr Chang, “Research suggests that drinking green tea may be both a valuable chemopreventive therapy as well as a treatment for esophageal adenocarcinoma. Our results suggest that extracts in green tea may help to lower the prevalence of esophageal adenocarcinoma, one of the fastest growing cancers in Western countries.”

—Dayna Dye

IN THE NEWS

Obesity, Blood Pressure Rising in the Young



More than 15% of children and adolescents are now considered overweight, and these statistics are amplified in minority and socioeconomically disadvantaged youth.^{1,2} Now researchers report that blood pressure among the young is also on the rise, a trend they attribute to growing rates of obesity.

Overweight children often become overweight adults at increased risk of degenerative diseases such as heart disease, high blood pressure, and diabetes. These “diseases of aging” result in premature death, and new evidence suggests they are having a premature onset as well—in other words, children not only have high blood pressure, but their blood pressure is on the rise. Indeed, high blood pressure is nine times more common in overweight children than in those of normal

weight.

Researchers compared the blood pressure measurements of children and adolescents aged 8-17 from the NHANES III study of 1988-1994 with those of the NHANES study of 1999-2000.³ They found a small yet significant increase in blood pressures between the two groups. Systolic blood pressure was 1.4 mm Hg higher in the 1999-2000 participants than in the earlier group, while diastolic blood pressure was 3.3 mm Hg higher than in the 1988-1994 group.

According to the researchers, an increase in body mass index (BMI) among children and adolescents over the time period between the two NHANES studies accounts for some of the observed blood pressure elevations. By implementing weight maintenance and weight loss strategies such as dietary modification and increased physical activity, the blood pressure crisis in children and adolescents may yet be averted.

—Dean S. Cunningham, MD, PhD

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The Medicare Debacle Hurts Patients

Editorial by Dr. Jonathan Wright



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It would almost be entertaining to watch the Medicare prescription drug fiasco—if it did not affect millions of people so negatively. First, the act, officially known as the Medicare Prescription Drug Improvement and Modernization Act of 2003, is passed under duress. It barely makes it through the House, and it only escapes the Senate under the threat of filibuster. Lawmakers on both sides of the fence have issues with it. While it is nice to see our lawmakers can occasionally unite in their assessment of a stinker, the resounding dislike for the bill still did not keep it from being passed. Then, early this year, tales of withheld budget and actuarial information started to surface. A number-cruncher named Richard Foster gets caught up in a maelstrom of allegations. It seems that lawmakers were told the bill would cost \$400 billion; Foster put it at closer to \$551 billion—but he was not allowed to tell anyone.

Months after the bill was passed, a mysterious fax surfaces that reveals Foster's figures (I am telling you, this stuff is right out of *All the President's Men*). When questioned, Foster claims his boss threatened to fire him if he released those numbers to lawmakers. Earlier this month, a relatively quick and painless inquiry into the ethics of this whole situation reveals that, yes, the

boss gagged the employee, but, no, he will not be prosecuted any time soon due to some technicality in the law. In fact, none of the employees involved even had to appear to testify on the matter.

The boss in question, Thomas A. Scully, is now a private consultant, and apparently had too busy of a travel schedule to even respond to inquiries into the matter for 10 days. Quietly enough, the President revised the estimated cost of the overhaul to \$534 billion. I wish I could say it gets better, but it does not. In fact, it gets worse. Another inquiry was launched into \$20 million that went into ads and marketing materials for the new program. Finally, an element of the new program was rolled out last month: Medicare drug-discount cards. By all accounts to date, these are so confusing that they border on being completely useless.

In a Kaiser Health Poll Report Survey done last month, six in 10 seniors did not even know about the discount card or did not think they were eligible. This mess is so wide and so deep, it is hard to know where to start. The saddest part is that, once again, Medicare recipients—and, of course, taxpayers—will be the ones to pay the price for such shenanigans. If there is any consolation here, it may be that we are in an election year—one of the few times that lawmakers might actually listen to us.

Make your voice heard. Contact your congressman, join an advocacy or watchdog group that is active on this issue, and pay attention to the press. When these kinds of dramas can get swept under the rug so easily, despite all the red flags flying all along the way, I am afraid we are in deep, deep trouble. And if you would like to learn more about the bill or the discount drug program, go to: www.medicare.gov or call 1-800-MEDICARE. Please let us know your experiences with Medicare under the new plan as they roll it out. We would like to know how this legislation is affecting our readers, for better or worse.*

Life Extension's comments: It is interesting that executives from dozens of corporations are facing possible life terms in prison for accounting fraud, whereas the \$151 billion accounting fraud perpetrated by government employees, and the accompanying perjury committed before Congress, is not even considered a crime. This \$151 billion cover-up may exceed the aggregate amount of dollars recently pillaged from public companies.

Reference

* Compiled by Amanda Ross, managing editor of Agora Publishing, from Dr. Wright's monthly newsletter, "Nutrition & Healing."

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