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IN THE NEWS

New Studies Confirm Lethal Effects of Elevated C-Reactive Protein

Life Extension long ago warned about the dangers of a blood marker of systemic inflammation called C-reactive protein (CRP).

Over the past decade, more than 20 human studies confirm that high CRP levels increase risk of heart attack, stroke, type 2 diabetes, and metabolic syndrome.

A newly released study measured CRP blood levels in three independent groups and followed them for an average of 7.1 years. The objective was to identify the relationship between CRP and common diseases that strike aging humans.¹ Men with a CRP greater than 3 mg/L of blood were almost twice as likely to die from any cause compared with subjects whose CRP was under 1 mg/L of blood.

Those with CRP levels greater than 3 mg/L suffered a 2.15-fold increased risk of dying from fatal heart attack and a 1.65-fold increased risk of dying from cancer. These findings occurred after adjusting for other risk factors such as obesity, diabetes, smoking, hypertension, LDL, and cholesterol. The doctors concluded:

“Our results suggest that increased circulating high-sensitivity [CRP] concentrations are associated with an increased risk of death from several widespread chronic diseases.”

In a second report, those with CRP levels greater than 5 mg/L upon hospital admission had a 50% to 330% increase in risk of death from any cause.² This led the authors of this study to characterize CRP as a unique “triage marker for future death” and suggested that this inflammatory marker be tested in all patients to identify those in need of additional close monitoring.

An editorial that discussed 13 other trials involving 63,000 healthy individuals confirmed elevated CRP as a potent predictor of both short- and long-term risk of death.³ In men in the highest quartile of CRP, there was a striking four-fold increased risk of death compared with the men in the lowest quartile.

The Male and Female Blood Test Panels include measurement of high-sensitivity CRP so that members are alerted if they have an underlying systemic inflammatory condition. The proper use of hormones, nutrients, diet modification, and drugs (if necessary) can significantly reduce elevated CRP levels.

The Male or Female Blood Test Panel can be obtained by calling 1-800-208-3444.



Reference

1. Koenig W, Khuseyinova N, Baumert J, Meisinger C. Prospective study of high-sensitivity C-reactive protein as a determinant of mortality: results from the MONICA/KORA Augsburg cohort study, 1984-1998. *Clin Chem*. 2008 Feb;54(2):335-42.
2. Marsik C, Kazemi-Sharazi L, Schickbauer T, et al. C-reactive protein and all-cause mortality in a large hospital based cohort. *Clin Chem*. 2008;54:343-9.
3. Ridker PM. High-sensitivity C-reactive protein as a predictor of all-cause mortality: implications for research and patient care. *Clin Chem*. 2008 Feb;54(2):234-7.

Low Folate Linked to Increased Dementia Risk

Low folate levels are associated with an increased risk of future dementia, according to a recently published report.* Noting that folic acid, vitamin B12, and homocysteine have been implicated in the development of dementia, the scientists set out to determine if changes in the concentrations of any of these compounds are predictive of dementia risk.

Working with more than 500 elderly, dementia-free subjects, investigators measured serum concentrations of folate, vitamin B12, and homocysteine at baseline and again at follow-up assessments. After an average of 2.4 years, the subjects were evaluated for signs of dementia or Alzheimer's disease.

A low baseline level of folate was predictive of dementia, while an exaggerated decline in folate level was strongly linked with the onset of dementia. Likewise, a weaker increase in vitamin B12 concentrations and a dramatic increase in homocysteine level were significantly associated with the onset of dementia.

—Dale Kiefer



Reference

* Kim JM, Stewart R, Kim SW, et al. Changes in folate, vitamin B12, and homocysteine associated with incident dementia. *J Neurol Neurosurg Psychiatry*. 2008 Feb 5 [Epub ahead of print].

Vitamin B6 May Sharply Reduce Incidence of Colon Cancer

A large Scottish study has shown that increased intake of vitamin B6—from dietary and supplemental sources—is associated with a significant decrease in the risk of colorectal cancer.¹ Noting that previous laboratory and population-based studies have suggested such a link,²⁻⁴ Edinburgh-based investigators enlisted nearly 5,000 subjects and assessed their dietary patterns. After adjusting for potential confounding factors, such as folate, fiber, and total energy intake, researchers found modestly strong associations between greater vitamin B6 intake and lower risk of colorectal cancer.¹

A meta-analysis of existing published data on the subject also revealed a reverse relationship between vitamin B6 intake and risk of colorectal cancer: as intake increases, cancer risk decreases. Additionally, investigators analyzed data from subgroups within their study population and found an even stronger protective effect for subjects less than or equal to 55 years of age. Subjects with the highest intakes of vitamin B6 were about 20% less likely to develop colorectal cancer.¹

—Dale Kiefer

Reference

1. Theodoratou E, Farrington SM, Tenesa A, et al. Dietary vitamin B6 intake and the risk of colorectal cancer. *Cancer Epidemiol Biomarkers Prev*. 2008 Jan;17(1):171-82.
2. Ishihara J, Otani T, Inoue M, et al. Low intake of vitamin B-6 is associated with increased risk of colorectal cancer in Japanese men. *J Nutr*. 2007 Jul;137(7):1808-14.
3. Liu Z, Choi SW, Crott JW, et al. Mild depletion of dietary folate combined with other B vitamins alters multiple components of the Wnt pathway in mouse colon. *J Nutr*. 2007 Dec;137(12):2701-8.
4. Wei EK, Giovannucci E, Selhub J, Fuchs CS, Hankinson SE, Ma J. Plasma vitamin B6 and the risk of colorectal cancer and adenoma in women. *J Natl Cancer Inst*. 2005 May 4;97(9):684-92.

Pomegranate Improves Sperm Quality

Pomegranates have traditionally been associated with fertility. Now, scientists have shown that there may be a scientific basis for this belief, in terms of improved sperm quality.*

Researchers divided male rats into four groups. Each group received either water or one of three increasing concentrations of pomegranate juice, daily for seven weeks. After seven weeks, all animals were assessed for the status of several blood enzyme antioxidants. Various parameters related to sperm quality—including motility, concentration, and spermatogenic cell density, among other measures of sperm health—were also assessed. Additionally, investigators measured malondialdehyde, which

serves as a biomarker for oxidative stress.

All of the pomegranate juice-fed animals exhibited markedly higher levels of antioxidant enzymes, including catalase and glutathione peroxidase. They also had higher levels of vitamin C and significantly decreased malondialdehyde levels, compared with control rats. Pomegranate-fed rats also showed significant improvements in sperm-health parameters.

—Dale Kiefer

Reference

* Türk G, Sönmez M, Aydın M, et al. Effects of pomegranate juice consumption on sperm quality, spermatogenic cell density, antioxidant activity and testosterone level in male rats. *Clin Nutr.* 2008 Jan 25 [Epub ahead of print].

Oatmeal Better Than Ever for Cardiovascular Protection

A decade after the US Food and Drug Administration concluded that consumption of oatmeal may reduce the risk of coronary heart disease, leading researchers in the field report that the health benefits of wholegrain oats are even better than originally believed.*

In an article published in the *American Journal of Lifestyle Medicine*, researchers note that in the intervening years since the FDA granted a “heart-healthy” claim for oats, new research has shown “consumption of oats and oat-based products significantly reduces total cholesterol and low-density lipoprotein concentrations without adverse effects on high-density lipoprotein or triglyceride concentrations.”



Furthermore, “more recent data indicate that including oats and oat-based products as part of a lifestyle-management program may confer health benefits that extend beyond total cholesterol and low-density lipoprotein reduction.” Some of those benefits may include a decreased tendency towards obesity, a reduced risk of diabetes, and the possibility that oats may favorably alter LDL subclass and particle number, favoring a reduced risk of atherosclerosis.

—Dale Kiefer

Reference

* Andon MB, Anderson JW. State of the art reviews: the oatmeal-cholesterol connection: 10-years later. *Am J Lifestyle Med.* 2008; 2(1):51-7.

Low Vitamin E Levels Associated with Physical Decline Among Older Adults

A new study published in the prestigious *Journal of the American Medical Association* concludes that low levels of vitamin E are associated with a decline in physical function among older individuals.¹

Investigators from Cornell University randomly selected 698 community-dwelling men and women aged 65 years and older from Tuscany, Italy, to participate in this study. After measuring subjects’ micronutrient intakes at baseline, investigators assessed the subjects’ physical function using standardized tests of physical performance during a three-year follow-up period.

After adjusting for potential confounding factors, statistical analysis revealed that those with the lowest blood levels of vitamin E were 60% more likely to suffer physical decline over the three-year follow-up period.

The study’s authors concluded, “These results provide empirical evidence that a low serum concentration of vitamin E is associated with subsequent decline in physical function among community-living older adults.”

Other researchers have previously speculated that higher levels of antioxidants, such as vitamin E, may prevent some of the damage caused by free radicals, which have been implicated in aging and various degenerative diseases.^{2,3}

—Dale Kiefer

Reference

1. Bartali B, Frongillo EA, Guralnik JM, et al. Serum micronutrient concentrations and decline in physical function among older persons. *JAMA*. 2008 Jan 23;299(3):308-15.
2. Janson M. Orthomolecular medicine: the therapeutic use of dietary supplements for anti-aging. *Clin Interv Aging*. 2006;1(3):261-5.
3. Rahman K. Studies on free radicals, antioxidants, and co-factors. *Clin Interv Aging*. 2007;2(2):219-36.

Lipoic Acid May Fight Atherosclerosis, Weight Gain

Lipoic acid supplementation reduces arterial lesion formation, triglycerides, blood vessel inflammation, and weight gain in an animal model of human heart disease, according to an exciting new report.* All of these factors are involved in the development of cardiovascular disease.

Mice prone to cardiovascular disease received diets containing a normal amount of fat or extra fat, with or without supplemental lipoic acid, for ten weeks. Lipoic acid supplementation was associated with a significant reduction of atherosclerotic lesion formation and less arterial inflammation. Supplemented mice had 40% less weight gain and lower triglycerides compared with those that did not receive the compound.

Study coauthor Balz Frei, PhD, noted, "From what we understand, this supplement would be most valuable as a preventive mechanism before people have advanced cardiovascular disease. However, it may help retard the process at any stage, and may also be of value in treating diabetic complications."

—Dayna Dye

Reference

- * Zhang WJ, Bird KE, McMillen TS, LeBoeuf RC, Hagen TM, Frei B. Dietary alpha-lipoic acid supplementation inhibits atherosclerotic lesion development in apolipoprotein E-deficient and apolipoprotein E/low-density lipoprotein receptor-deficient mice. *Circulation*. 2008 Jan 22;117(3):421-8.

Reduced Choline and Betaine Levels Linked with Inflammation

High dietary intake of the B vitamins choline and betaine, found in various plant and animal foods, is linked with lower blood levels of inflammatory markers, according to a recent report.¹ Inflammatory markers have been associated with cardiovascular event risk.

More than 3,000 healthy adults in Greece provided information regarding their dietary intake of choline and betaine, and fasting blood samples were tested for levels of interleukin-6, C-reactive protein (CRP), tumor necrosis factor-alpha (TNF-alpha), and homocysteine.

Subjects whose choline intake was in the top one-third of participants had CRP levels that were 22% lower, interleukin-6 levels that were 26% lower, and TNF-alpha levels that were 6% lower than those whose intake fell in the bottom one-third. Similarly, for those whose betaine levels were in the top third, homocysteine levels were 10% lower, CRP levels were 19% lower, and TNF-alpha levels were 12% lower, compared with participants in the bottom third.¹

If further studies confirm these results, “an interesting new dietary approach may be available for reducing chronic diseases associated with inflammation.”²

—Dayna Dye

Reference

1. Detopoulou P, Panagiotakos DB, Antonopoulou S, Pitsavos C, Stefanadis C. Dietary choline and betaine intakes in relation to concentrations of inflammatory markers in healthy adults: the ATTICA study. *Am J Clin Nutr.* 2008 Feb;87(2):424-30. 2. Zeisel SH. Is there a new component of the Mediterranean diet that reduces inflammation? *Am J Clin Nutr.* 2008 Feb;87(2):277-8.

Calcium Supplements Benefit Adolescent Bone

Supplementing adolescent girls with calcium significantly increases their bone mineral content over the course of 18 months, according to a new report from the American Journal of Clinical Nutrition.*

Researchers enrolled 96 girls aged 11-12 years, whose calcium intake averaged 636 mg/day. The girls received a drink containing 792 mg calcium from calcium citrate malate or a placebo for 18 months, followed by a two-year period during which they received no supplements.

At the end of the 18-month period, girls who received supplemental calcium experienced significantly greater gains in bone mineral content at all sites except the hip. Furthermore, bone mineral density also increased at all sites in the supplemented group compared with placebo; however, by the end of the study at 42 months, these differences were no longer observed.

The scientists concluded that calcium supplementation is effective in enhancing bone mineralization during growth, and suggests that calcium needs to be taken continually for its benefits to be maintained.

These findings suggest that supplementing with calcium may provide an early start to preventing osteoporosis.

—Dayna Dye

Reference

* Lambert HL, Eastell R, Karnik K, Russell JM, Barker ME. Calcium supplementation and bone mineral accretion in adolescent girls: an 18-mo randomized controlled trial with 2-y follow-up. *Am J Clin Nutr.* 2008 Feb;87(2):455-62.

DHEA Supplementation Improves Cardiovascular Markers in Men

Supplementation with dehydroepiandrosterone (DHEA) improves blood markers of cardiovascular disease risk in men, according to a recent report.* Scientists have previously proposed that DHEA may thwart atherosclerosis development by increasing nitric oxide production, which promotes relaxation of the smooth muscle cells lining blood vessels.

Twenty-four men, average age 65 years, were randomly assigned to blindly receive either 50 mg DHEA per day, or placebo, for two months.* Numerous variables were assessed at baseline and following treatment, including blood lipid levels, testosterone, and platelet cyclic guanosine-monophosphate (cGMP) concentration (a marker of nitric oxide production).

Placebo group parameters remained unchanged. But DHEA supplemented subjects experienced significant increases in testosterone and cGMP, and significant decreases in low-density lipoprotein (LDL) and a marker of inflammation. “These findings...suggest that chronic DHEA supplementation would exert antiatherogenic effects, particularly in elderly subjects who display low circulating levels of this hormone,” investigators concluded.

—Dale Kiefer



Reference

* Martina V, Benso A, Gigliardi VR, et al. Short-term dehydroepiandrosterone treatment increases platelet cGMP production in elderly male subjects. *Clin Endocrinol (Oxf)*. 2006 Mar;64(3):260-4.

Breakthrough in Bioartificial Heart Engineering

In a remarkable new report, researchers announced they have successfully reanimated dead rat hearts by introducing cells taken from newborn rat hearts.*

Hearts from euthanized rats were stripped of their cellular linings down to the underlying collagen support structures, which acted as a sort of cellular scaffolding for the “bioartificial hearts.” Heart cells taken from newborn rats were then injected into the denuded hearts. Cardiac and endothelial cells migrated to appropriate structures and established all-new tissues and blood vessels. Investigators subsequently applied a brief external shock. Within days, microscopic contractions occurred; within two weeks, the hearts were beating strongly enough to be viewed by the naked eye.

Although the hearts pumped weakly, moving a volume of fluid roughly equivalent to one-quarter of a newborn’s normal cardiac volume, the groundbreaking experiment holds profound implications for future tissue and organ regeneration and replacement research.

—Dale Kiefer



Reference

* Ott HC, Matthiesen TS, Goh SK, et al. Perfusion-decellularized matrix: using nature’s platform to engineer a bioartificial heart. *Nat Med*. 2008 Jan 13 [Epub ahead of print].

Scientists Achieve Record Extension of Life Span in Simple Organism

In a recent study, University of Southern California researchers report that the combination of dietary restriction and knocking out two genes allowed baker's yeast to live 10 times longer than its normal life span—without any adverse effects.¹

The scientists knocked out RAS2 and SCH9, genes that had been found to promote aging in yeast and cancer in humans.¹ A companion study revealed that these same genetic knockouts reversed a yeast model of Werner/Bloom syndromes, diseases characterized by accelerated aging and an increased incidence of cancer.² The research team is currently studying a human population in Ecuador with similar mutations.



Previous research has shown that mice with a similar mutation survived 30% beyond their normal life span while being protected from osteoporosis and aging-induced cardiomyopathy.³

The scientists hope that researchers will one day use the knowledge gained in these studies “to reprogram disease prevention.”

—Dayna Dye

Reference

1. Wei M, Fabrizio P, Hu J, et al. Life span extension by calorie restriction depends on Rim15 and transcription factors downstream of Ras/PKA, Tor, and Sch9. *PLoS Genet.* 2008 Jan;4(1):e13. 2. Madia F, Gattazzo C, Wei M, et al. Longevity mutation in SCH9 prevents recombination errors and premature genomic instability in a Werner/Bloom model system. *J Cell Biol.* 2008 Jan 14;180(1):67-81. 3. Yan L, Vatner DE, O'Connor JP, et al. Type 5 adenylyl cyclase disruption increases longevity and protects against stress. *Cell.* 2007 Jul 27;130(2):247-58.

Lycopene Stops BPH in its Tracks

Supplementation with the carotenoid lycopene slows the growth of benign prostatic hyperplasia (BPH) in men, according to a recent report.* Although a benign condition, BPH is considered a risk factor for the later development of prostate cancer.

Scientists enrolled 40 cancer-free men with BPH and serum prostate-specific antigen (PSA) levels of greater than 4.0 mcg/L.

The men were randomized to receive 15 mg lycopene or placebo daily for six months.

Men who received lycopene experienced decreased PSA levels, while the placebo group saw no change. Prostate enlargement occurred in the placebo group, but not in the lycopene group. Symptoms of BPH improved more in the lycopene group compared with placebo.

The research is the first controlled clinical study to report that lycopene inhibits the progression of BPH. Lycopene may work by inhibiting 5-alpha reductase and interleukin-6 signaling, and its antioxidant properties may help prevent cell proliferation and remodeling in the prostate.

—Dayna Dye

Reference

* Schwarz S, Obermüller-Jevic UC, Hellmis E, Koch W, Jacobi G, Biesalski HK. Lycopene inhibits disease progression in patients with benign prostate hyperplasia. *J Nutr.* 2008 Jan;138(1):49-53.

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