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IN THE  
NEWS**Deficient Vitamin D Levels Associated With Increased Heart Attack Risk**

Men who have deficient vitamin D levels have a greater risk of myocardial infarction (heart attack) than men whose blood levels of the vitamin are sufficient, Harvard researchers reported in the *Archives of Internal Medicine*.\*

Scientists examined data from men aged 40 to 75 who participated in the Health Professionals Follow-up Study. Blood samples collected from 1993 to 1995 were analyzed for plasma 25-hydroxy-vitamin D as well as lipoprotein and triglyceride levels, and diet and lifestyle factors were ascertained via questionnaires.

During 10 years of follow-up, 454 men suffered fatal coronary heart disease or non-fatal heart attack. These subjects were matched for age, smoking status, and time of blood collection with 900 men without heart disease.

Adjusted analysis found that subjects with plasma vitamin D levels of  $\leq 15$  ng/mL (37 nmol/L) had a 2.42 times greater risk of heart attack compared with those whose levels were sufficient at  $\geq 30$  ng/mL (75 nmol/L). Men with intermediate vitamin D levels had a 43-60% greater risk of heart attack compared with men who had sufficient levels. Men with low levels of vitamin D were more likely to live in northern states, and less likely to be white or to use a multivitamin supplement.

The authors cited vitamin D's effect on smooth muscle cell proliferation, inflammation, vascular calcification, and blood pressure as possible protective mechanisms against myocardial infarction.

"These results further support an important role for vitamin D in myocardial infarction risk," the authors wrote. "The present findings add further support that the current dietary requirements of vitamin D need to be increased to have an effect on circulating 25-hydroxyvitamin D levels substantially large enough for potential health benefits."

—Dayna Dye



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**Reference**

\* Giovannucci E, Liu Y, Hollis BW, Rimm EB. 25-hydroxyvitamin D and risk of myocardial infarction in men: a prospective study. *Arch Intern Med*. 2008 Jun 9;168(11):1174-80.

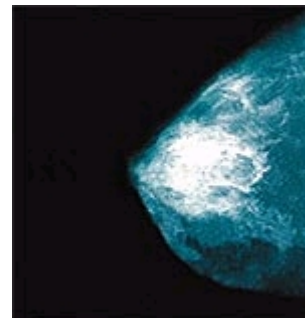
**Vitamin D Prolongs Breast Cancer Survival**

Breast cancer patients with inadequate vitamin D blood levels may have poorer survival and prognosis than those with adequate levels of the "sunshine vitamin."\*

In a study presented at a recent meeting of the American Society of Clinical Oncology, scientists from the University of Toronto measured vitamin D blood levels in 512 women with an average age of 50 years who had been newly diagnosed with breast cancer and tracked their progress for a median of 12 years.

At the onset of the study, only 24% of women had adequate vitamin D blood levels ( $>29$  ng/mL or 72 nmol/L) while nearly 38% had deficient levels ( $<20$  ng/mL or 50 nmol/L). By the end of the study,

vitamin D-deficient women at study entry had nearly double the risk of their disease progressing and a 73% greater risk of death compared with women who had adequate levels.



The study authors noted this is “the first time that vitamin D has been linked to breast cancer progression.” They added that “vitamin D deficiency is common at breast cancer diagnosis” and emphasized blood tests to ensure adequate levels of the vitamin, especially in women with breast cancer.

—Bina Singh

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## Reference

\* Available at: [http://www.asco.org/ASCO/Abstracts+%26+Virtual+Meeting/Abstracts?&vmview=abst\\_detail\\_view&confID=55&abstractID=31397](http://www.asco.org/ASCO/Abstracts+%26+Virtual+Meeting/Abstracts?&vmview=abst_detail_view&confID=55&abstractID=31397). Accessed June 12, 2008.

## Inhaled Insulin Increases Lung Cancer Risk

A groundbreaking report by Dr. T.R. Shantha in the September 2007 issue of *Life Extension* warned that inhaled insulin could increase cancer risk.<sup>1</sup> Two months later, Pfizer Pharmaceuticals, the largest maker of inhaled insulin, abruptly halted sales of its product Exubera®.<sup>2</sup>

A new study may reveal why. A review of clinical trial data shows a dramatic increase in lung cancer incidence among users of inhaled insulin.<sup>3</sup>

Insulin is a weak growth factor that may promote aberrant cell growth.<sup>1</sup> The amount of insulin used in inhaled products is three to ten times greater than the amount diabetics use for subcutaneous injection, since little more than 10% of inhaled insulin reaches the lungs' alveoli for systemic absorption.<sup>4,5</sup>

Dr. Shantha has long believed that inhaled insulin can act as a growth-promoting agent to encourage cancer growth in the linings of the mouth, throat, tongue, cheeks, gums, tonsils, trachea, bronchial tree, vocal cords, larynx, nose and nasal air sinuses, olfactory mucosa, and lungs. Further, Dr. Shantha believes that inhaled insulin enhances the carcinogenic effects of tobacco products and that its widespread use will dramatically increase cancer incidence.

*Life Extension* extends its compliments to Dr. Shantha, who has warned about the potential dangers of inhaled insulin ever since it has been under development by various pharmaceutical companies. When the FDA approved the use of inhaled insulin, Dr. Shantha wrote an article reporting his suspicions of the drug's dangers to put the product's developer and the FDA on notice. He had no power, however, to stop the drug's approval by the FDA and its sale to the public.

Dr. Shantha personally thanked *Life Extension* for having the courage to publish his findings at a time when the FDA and major pharmaceutical companies assured that inhaled insulin was safe. “For three years I warned about these cancer risks and nobody listened to me except the *Life Extension* Foundation,” he stated.

Inhaled insulin can thus be added to the long list of drugs the FDA approves as “safe,” but are then removed from the marketplace because of side-effect risks.

—Alan Rosen

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## Reference

1. Shantha TR. Unknown health risks of inhaled insulin. *Life Extension*. 2007 Sept;13(9):79-82.
2. Mack GS. Pfizer dumps Exubera. *Nat Biotechnol*. 2007 Dec;25(12):1331-2.
3. Available at: <http://www.medscape.com/viewarticle/572779>. Accessed June 27, 2008.
4. Agu RU, Ugwoke MI, Armand M, Kinget R, Verbeke N. The lung as a route for systemic delivery of therapeutic proteins and peptides. *Respir Res*. 2001;2(4):198-209.
5. Available at: <http://formularyjournal.mediwire.com/main/Default.aspx?P=Content&ArticleID=282691>. Accessed July 2, 2008.

## Apple Extracts Prevent Stomach Damage Due to Aspirin



Apple polyphenol extracts protected rats from stomach damage due to aspirin in an Italian study.\* Aspirin, a nonsteroidal anti-inflammatory drug (NSAID), can cause gastrointestinal problems such as bleeding and ulcers, even at the low doses given for cardiovascular health.



In this study, 45 rats underwent pretreatment with apple polyphenol extracts or no pretreatment, followed by administration of aspirin to produce stomach injury. Apple polyphenol pretreatment reduced microscopic and macroscopic stomach injury by 40-45% compared with untreated rats and prevented increases in cyclo-oxygenase-2 and other damaging substances. Protection was observed after both acute and chronic aspirin injury. Apple polyphenols did not interfere with gastric acid secretion or therapeutic blood levels of aspirin.

The apple polyphenol extract dosage given to the rats was equivalent to about two apples per day for a human. Using a natural food product with antioxidant effects may prove safer and cheaper than medications that inhibit gastric acid secretion, such as proton pump inhibitors.

—Laura J. Ninger, ELS

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## Reference

\* D'Argenio G, Mazzone G, Tuccillo C, et al. Apple polyphenol extracts prevent aspirin-induced damage to the rat gastric mucosa. *Br J Nutr.* 2008 May 16:1-9.

## Anti-Aging Research Foundation Receives Charitable Status

The gap between anti-aging research and its medical applications moved closer recently by the granting of a new charitable status for the Biogerontology Research Foundation (BGRF) in the UK.\*

The foundation, which was started with the help of some of the world's most prominent scientists and businessmen, actively pursues research projects that target the causes of age-related disease rather than just its symptoms. By developing biotechnological interventions to prevent or remediate the molecular and cellular deficits that accumulate with aging, the foundation addresses aging damage at its most fundamental level.

Using the entire scope of modern biotechnology, the foundation represents a valuable opportunity to produce effective and lasting treatments for the diseases and disabilities of aging. For more information on the BGRF and how you can donate to the foundation, please contact Dr. Alex Zhavoronkov at [alex.zhavoronkov@bg-rf.org.uk](mailto:alex.zhavoronkov@bg-rf.org.uk).

—Bina Singh

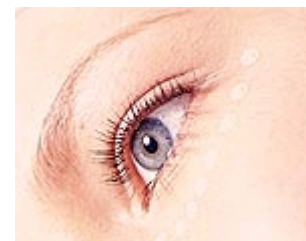
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\* Available at: <http://www.prlog.org/10078538-biogerontology-research-foundation-receives-charitable-status-from-the-charity-commission.html>. Accessed June 12, 2008.

## Lutein, DHA May Prevent Age-Related Macular Degeneration

Supplementation with lutein, an antioxidant, and docosahexaenoic acid (DHA), an omega-3 fatty acid, promotes beneficial changes in the eye that may help prevent age-related macular degeneration.\* Lutein and DHA are important components of the macular pigment and retina, respectively.



Participants were 49 women aged 60 to 80 years who were randomly assigned to take DHA (800 mg/day), lutein (12 mg/day), DHA + lutein, or placebo. The scientists chose this population because the risk of macular degeneration increases with age. The study outcome was macular pigment optical density measured in the eye after four months of supplementation.

Lutein supplementation increased macular pigment density in most subjects. DHA also enhanced macular pigment density, although in other regions of the eye. DHA may exert its effects in part by boosting blood levels of beneficial high-density

lipoprotein (HDL), which facilitates uptake of lutein in the eye.

—Laura J. Ninger, ELS

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#### Reference

\* Johnson EJ, Chung HY, Caldarella SM, Snodderly DM. The influence of supplemental lutein and docosahexaenoic acid on serum, lipoproteins, and macular pigmentation. *Am J Clin Nutr.* 2008 May;87(5):1521-9.

## Pygeum Africanum Extract Prevents Prostate Cancer

New research adds further credence to the notion that it may be possible to prevent the occurrence of prostate cancer through the regular use of botanical extracts.\*

Scientists at the University of Missouri-Columbia showed that an extract of *Pygeum africanum* is capable of inhibiting growth and inducing cellular suicide in two standard human prostate cancer cell lines in tissue culture. Furthermore, the extract was shown to sharply reduce the incidence of prostate cancer in laboratory mice genetically engineered to develop the disease.



Extracts of the bark of the *Pygeum africanum*, or African plum, tree have been used for the control of benign prostatic hyperplasia (BPH) in Europe for a number of years, and more recently, for promotion of general prostate health and prostate cancer prevention in the United States.

“*Pygeum africanum*...has a significant role in regulation of prostate cancer...and therefore may be a useful supplement for people at high risk for developing prostate cancer,” researchers concluded.

—Dale Kiefer

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#### Reference

\* Shenouda NS, Sakla MS, Newton LG, et al. Phytosterol *Pygeum africanum* regulates prostate cancer in vitro and in vivo. *Endocrine.* 2007 Feb;31(1):72-81.

## LEF Board Member Addresses European Stem Cell Congress

Life Extension Foundation board member, Michael West, PhD, unveiled promising new avenues of stem cell research at the European Stem Cells & Regenerative Medicine Congress earlier this year in London, England.\*

In his talk, "Mapping the human embryome: multiplex strategies for the purification and characterization of human embryonic progenitor cells," Dr. West focused on pioneering plans to create the first systematic map of all the cell types derived from human embryonic stem cells as was done with human DNA or genome mapping in the 1990s.

He hopes that this map will speed the day when stem cells will be used as immune-compatible cell therapies for degenerative diseases associated with aging.

Dr. West is CEO of BioTime, Inc, a California-based manufacturer of medical and surgical supplies, including artificial blood replacement products. BioTime's wholly owned subsidiary, Embryome Sciences, Inc, is leading the company's foray into the promising field of regenerative medicine with plans to develop new medical and research products using embryonic stem cell technology. The Life Extension Foundation helps to financially support Dr. West's stem cell research.

—Dale Kiefer

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### Reference

\* Available at: <http://www.biotimeinc.com/news.htm>. Accessed July 1, 2008.

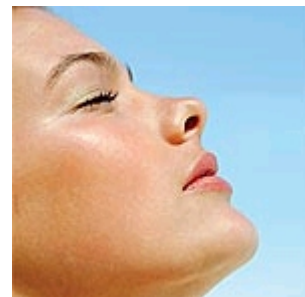
## Beta Carotene Protects Against Sunburn

Supplementation with beta carotene markedly reduces the likelihood of sunburn, according to a recent review of the literature.\* Beta carotene is a well-known antioxidant that may have anti-aging effects in the skin.

German researchers conducted a meta-analysis and identified seven relevant studies of the association between beta carotene supplementation and sunburn risk. The pooled data showed a beneficial effect of beta carotene. Protection became significant only after at least 10 weeks of supplementation and increased with each additional month of beta carotene use.

Although beta carotene achieves a sun protection factor (SPF) of about four, much lower than sunscreens, supplementation achieves a chronic rather than acute type of protection that is uniform over the skin surface. The authors conclude that "topical application of sunscreens and systemic photoprotection with beta carotene are not competing strategies which are intended to replace each other, but instead they are complementary in nature and should be combined."

—Laura J. Ninger, ELS



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### Reference

\* Köpcke W, Krutmann J. Protection from sunburn with beta carotene—a meta-analysis. *Photochem Photobiol.* 2008 Mar-Apr;84(2):284-8.

## Nutrient Combination is Protective Against Ischemic Stroke Damage

A nutritional supplement consisting of blueberry, green tea, vitamin D3, and carnosine provides animals with significant protection against the damage induced by an ischemic stroke, according to a report in *Rejuvenation Research*.\*

Rats received the nutrient blend or a placebo for two weeks. They then underwent standardized tests of behavioral performance prior to an artificially induced ischemic stroke.

Rats that had received the supplement blend prior to stroke induction fared 24% better on tests of neurological dysfunction than controls. Supplement-fed rats also experienced a significant 75% reduction in a measure of cerebral infarction damage compared with control animals. Additionally, supplement-fed rats showed significantly greater signs of neurogenesis (generation of new nerve cells), signaling better recovery from stroke-induced injury.

“These data demonstrate the remarkable neuroprotective effects of [the supplement blend] when given prior to stroke, possibly acting via its neurogenic potential,” concluded researchers.

—Dale Kiefer

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#### Reference

\* Yasuhara T, Hara K, Maki M, et al. Dietary supplementation exerts neuroprotective effects in ischemic stroke model. *Rejuvenation Res.* 2008 Feb;11(1):201-14.

## Calcium and Magnesium Reduce Chemotherapy Side Effects

A presentation from the 44th annual meeting of the American Society of Clinical Oncology revealed that calcium and magnesium administered intravenously to patients undergoing chemotherapy results in a significant reduction in neurotoxicity, a common side effect of chemotherapeutic drugs.\* Neurotoxicity is characterized by pain in the extremities that can be severe enough to prevent cancer patients from continuing their treatment.

Researchers with the North Central Cancer Treatment Group administered intravenous calcium and magnesium before and after treatment with the chemotherapeutic drug oxaliplatin to 50 of 102 patients with advanced colon cancer. The remaining 52 patients received oxaliplatin with an intravenous placebo.

The research team found a significant reduction in neurotoxicity incidence, severity, and time to onset associated with the use of calcium and magnesium compared with the placebo group. Importantly, calcium and magnesium did not reduce the activity of oxaliplatin-based chemotherapy.

“Now that we have shown the effectiveness of calcium and magnesium in reducing oxaliplatin-induced neurotoxicity, a further step may be to evaluate the benefit of calcium and magnesium in reducing neurotoxicity caused by other medications,” the study co-chair noted.

—Dayna Dye



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#### Reference

\* Available at: <http://www.newswise.com/articles/view/540875/>. Accessed June 30, 2008.

## Low-Dose Resveratrol Gets to the Heart of Longevity

Resveratrol produces cardioprotective benefits, even at relatively low doses, according to a new report.\* Previous research demonstrates that resveratrol, which is found in grapes, pomegranates, and other foods, favorably modulates the genetic changes that occur with aging.

Researchers fed middle-aged (14-month-old) rats a control diet, a diet containing a small amount of resveratrol, or a calorie-restricted diet until the animals were 30 months of age.

Calorie restriction and resveratrol produced similar genetic effects in the heart, skeletal muscle, and brain. While aging altered the expression of 1,029 heart genes in the control animals, calorie restriction reduced 90% of these age-related alterations in gene expression, and resveratrol mitigated 92% of such changes.

“Thus, resveratrol at doses that can be readily achieved through dietary supplementation in humans is as effective as calorie restriction in opposing the majority of age-related transcriptional alterations in the aging heart,” the authors wrote.

—Dayna Dye



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## Reference

\* Available at: <http://www.plosone.org/article/info:doi%2F10.1371%2Fjournal.pone.0002264>. Accessed June 30, 2008.

## Melatonin Improves Sleep in Critically Ill Patients

Melatonin supplementation improves both the quantity and quality of sleep in critically ill patients compared with placebo, according to a British study.\* Melatonin is a hormone that regulates the sleep-wake cycle.

The researchers studied 24 patients hospitalized in an intensive care unit who were being taken off mechanical ventilation. Participants were randomly assigned to take melatonin 10 mg, given as a liquid, or placebo each night for four nights and then monitored for sleep quality. On average, the placebo group achieved only 2.5 hours of sleep per night, but melatonin use was associated with 3.5 hours of sleep, for an increase of 47%. The quality of sleep was also markedly better in the treated group.

No important adverse effects were noted. Use of melatonin in critically ill patients therefore holds promise, although the authors note that a lower dose of 1-2 mg would probably be sufficient.

—Laura J. Ninger, ELS



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## Reference

\* Bourne RS, Mills GH, Minelli C. Melatonin therapy to improve nocturnal sleep in critically ill patients: encouraging results from a small randomised controlled trial. *Crit Care*. 2008 Apr 18;12(2):R52.

## Luteolin Tames the Flames

The flavonoid luteolin may help reduce inflammation in the brain, according to a recent report from the *Proceedings of the National Academy of Sciences*.\*

Researchers studied luteolin's effects in microglia—brain cells involved in immune defense. Although inflammatory cytokines produced by these cells help fight invading microorganisms, the resulting neuroinflammation can destroy neurons, which may contribute to cognitive impairment or neurodegenerative diseases.

Scientists pretreated microglia with varying concentrations of luteolin, and exposed the cells to lipopolysaccharide to initiate inflammation. Luteolin inhibited the production of the proinflammatory cytokine interleukin-6 (IL-6) by as much as 90% compared with untreated cells.

In another experiment, researchers gave varying concentrations of luteolin to mice 21 days before injecting them with lipopolysaccharide. Luteolin helped decrease IL-6 levels; mice that received the highest concentration experienced particular protection in the brain's hippo-campus, which is involved with memory and learning.

These findings suggest that luteolin may help mitigate brain inflammation and its consequences, which can include cognitive deficits.

—Dayna Dye

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#### Reference

\* Jang S, Kelley KW, Johnson RW. Luteolin reduces IL-6 production in microglia by inhibiting JNK phosphorylation and activation of AP-1. *Proc Natl Acad Sci USA*. 2008 May 27;105(21):7534-9.

## Calcium Reduces Fracture Risk

Calcium supplementation may reduce the risk of bone fractures by an impressive 72% in generally healthy adults, according to a recent study published in the *American Journal of Clinical Nutrition*.<sup>1</sup>

Using a controlled study design, the researchers administered 1,200 mg elemental calcium or placebo to study participants with an average age of 61 years. The supplemented individuals experienced significantly fewer fractures over a four-year period. Interestingly, the protective benefits of calcium ceased once supplementation was stopped.<sup>1</sup> The results of this study remind both patients and doctors of the critical importance of calcium supplementation as one ages.

While an earlier meta-analysis published by the same group failed to find that calcium supplementation reduced fracture risk,<sup>2</sup> other scientists have proposed that calcium supplementation is optimally successful when accompanied with vitamin D supplementation, as calcium does not function in isolation in optimizing bone health.<sup>3</sup>

—Jonathan Ozner

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#### Reference

1. Bischoff-Ferrari HA, Rees JR, Grau MV, Barry E, Gui J, Baron JA. Effect of calcium supplementation on fracture risk: a double-blind randomized clinical trial. *Am J Clin Nutr*. 2008 Jun;87(6):1945-51.
2. Bischoff-Ferrari HA, Dawson-Hughes B, Baron JA, et al. Calcium intake and hip fracture risk in men and women: a meta-analysis of prospective cohort studies and randomized controlled trials. *Am J Clin Nutr*. 2007 Dec;86(6):1780-90.
3. Nieves JW, Lindsay R. Calcium and fracture risk. *Am J Clin Nutr*. 2007 Dec;86(6):1579-80.

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