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IN THE
NEWS**SAMe Deficiency Linked to Development of Alzheimer's Disease**

Scientists at the University of Massachusetts, Lowell, have reported a possible link between deficiency in the naturally occurring chemical, S-adenosyl-methionine (SAMe) and the development of Alzheimer's disease. Working with mice bred to possess genetic risk factors for the development of dementia, investigators noted that these mice developed oxidative damage leading to cognitive impairment when deprived of the B-vitamin, folic acid.

The mice were found to be deficient in SAMe, which acts as a methyl donor throughout the body, facilitating countless biochemical reactions. When the animals were supplemented with SAMe, neurodegeneration was alleviated. SAMe deficiency promotes overexpression of a protein, presenilin-1, which in turn increases production of amyloid-beta, an aberrant protein directly implicated in the development of Alzheimer's disease. "These findings directly link nutritional deficiency and genetic risk factors, and support supplementation with [SAMe] for Alzheimer's therapy," investigators concluded.¹ Subsequent research by the same team confirmed and supported these conclusions.²

—Dale Kiefer

Reference

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2. Chan A, Shea TB. Folate deprivation increases presenilin expression, gamma-secretase activity, and Abeta levels in murine brain: potentiation by ApoE deficiency and alleviation by dietary S-adenosyl-methionine. *J Neurochem*. 2007 Aug;102(3):753-60.

Is Vitamin D Deficiency to Blame for Autism?

A new theory may explain the dramatic rise in autism cases seen in recent decades, while offering a simple "cure" for the alarming epidemic. Dr. John Cannell, a physician who has previously proposed a link between seasonally dwindling vitamin D levels and susceptibility to influenza, has published a novel hypothesis regarding vitamin D's implications for the developmental brain disorder, autism. Published in *Medical Hypotheses*, he proposes that physician-encouraged sunlight avoidance has contributed to widespread vitamin D deficiency.¹

"Animal data has repeatedly shown that severe vitamin D deficiency during gestation [adversely affects] dozens of proteins involved in brain development," writes Dr. Cannell. Vitamin D-deficient rats are born with "increased brain size and enlarged ventricles, abnormalities similar to those found in autistic children." What's more, he notes, "Children with vitamin D-deficient rickets have several autistic markers that apparently disappear with high-dose vitamin D treatment." Autism is also more common at higher latitudes, where vitamin D production is known to be problematic, especially during winter.²

—Dale Kiefer

Reference

1. Cannell JJ. Autism and vitamin D. *Med Hypotheses*. 2007 Oct 4; [Epub ahead of print].

Pomegranate Juice Shows Promise as Erectile Dysfunction Treatment



A recent well-controlled trial of pomegranate juice for the treatment of mild-to-moderate erectile dysfunction in men concluded, “subjects were more likely to have improved scores when pomegranate juice was consumed.”¹ The randomized, placebo-controlled, double-blind, crossover trial, conducted at a Beverly Hills men’s clinic, enrolled 53 men with mild-to-moderate impotence. Subjects blindly consumed pomegranate juice, or placebo, for four weeks. After a two-week washout period, they switched treatments.

Efficacy was assessed using two standardized scoring systems for quantification of erectile function—the International Index of Erectile Function and the Global Assessment Questionnaires. Although results did not achieve overall statistical significance, the small pilot study was considered encouraging. Investigators hope that longer studies using larger cohorts may achieve statistically significant results. The present findings support the conclusions of an earlier trial using an animal model, in which pomegranate juice reversed erectile dysfunction symptoms.² Improvements were

attributed to pomegranate’s potent antioxidant activity.

—Dale Kiefer

Reference

1. Forest CP, Padma-Nathan H, Liker HR. Efficacy and safety of pomegranate juice on improvement of erectile dysfunction in male patients with mild to moderate erectile dysfunction: a randomized, placebo-controlled, double-blind, crossover study. *Int J Impot Res.* 2007 Nov-Dec;19(6):564-7.
2. Azadzo KM, Schulman RN, Aviram M, Siroky MB. Oxidative stress in arteriogenic erectile dysfunction: prophylactic role of antioxidants. *J Urol.* 2005 Jul;174(1):386-93.

Fish Oil Alters Lipid Metabolism, Reduces Weight Gain

Japanese researchers have discovered that dietary fish oils promote weight loss by increasing lipid metabolism in the intestine.* Scientists have known for some time that the omega-3 fatty acids, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), lower blood lipid levels and reduce the tendency for obesity.

In the present study, Japanese researchers divided special obesity-prone mice into two high-fat diet groups, with and without fish oil, for five months. They found that body weight gain was significantly reduced among the fish oil-fed group, compared with the other high-fat group. Then, in a separate experiment to measure lipid metabolism at the genetic level, researchers found that ingestion of fish oil for two weeks increased intestinal lipid metabolism-related genes to levels found in the liver, one of the main sites of lipid metabolism. They concluded that “upregulation of intestinal lipid metabolism is associated with the anti-obesity effect of fish oil.”

—Dale Kiefer

Reference

- * Mori T, Kondo H, Hase T, Tokimitsu I, Murase T. Dietary fish oil upregulates intestinal lipid metabolism and reduces body weight gain in C57BL/6J mice. *J Nutr.* 2007 Dec;137(12):2629-34.

Resveratrol Suppresses Prostate Cancer Development

Researchers from the University of Alabama at Birmingham have shown that prostate cancer-prone mice fed resveratrol experience significant protection against development of the disease.¹ Found in red wine and some fruits and vegetables, resveratrol is a polyphenol antioxidant that has previously been shown to extend life span in various organisms.^{2,3} Investigators wondered if its reputed anticancer activities would extend to prostate cancer prevention.

Special mice bred to develop prostate tumors were fed either resveratrol in ordinary chow, beginning at five weeks of age, or a control diet lacking the phytochemical.¹ The animals were examined at 12 or 28 weeks old. Among mice that had received resveratrol in the diet, the incidence of prostate adenocarcinoma was reduced by 7.7-fold. Various biochemical and histological findings indicated that resveratrol suppresses prostate cancer development through a variety of mechanisms.

—Dale Kiefer

Reference

1. Harper CE, Patel BB, Wang J, Arabshahi A, Eltoun IA, Lamartiniere CA. Resveratrol suppresses prostate cancer progression in transgenic mice. *Carcinogenesis*. 2007 Sep;28(9):1946-53.
2. Valenzano DR, Cellierino A. Resveratrol and the pharmacology of aging: a new vertebrate model to validate an old molecule. *Cell Cycle*. 2006 May;5(10):1027-32.
3. Valenzano DR, Terzibasi E, Genade T, Cattaneo A, Domenici L, Cellierino CA. Resveratrol prolongs lifespan and retards the onset of age-related markers in a short-lived vertebrate. *Curr Biol*. 2006 Feb 7;16(3):296-300.

Milk Thistle Extract Suppresses Liver Cancer

Silibinin, a flavonoid derived from milk thistle, demonstrates potent activity against human liver cancer in the laboratory, according to a recent report from scientists at the University of California, Irvine.¹ Milk thistle (*Silybum marianum*) contains silibinin and silymarin—highly bioactive compounds credited with protecting the liver against a variety of insults, such as drug or alcohol-related damage. Silibinin also protects against a variety of other cancers, including prostate, breast, ovary, colon, lung, and bladder carcinomas.^{2, 3}

The present study may be the first, however, to demonstrate silibinin's potent chemopreventive activity against a variety of liver cancer cell lines. Its anticancer effects included reducing cancer cell proliferation and suppressing cell cycle progression, increasing apoptosis (programmed death of cancer cells), and altering the chromatin structure of cancer cells. Liver cancer is on the rise in the United States;⁴ silibinin may offer protection against this insidious threat.

—Dale Kiefer

Reference

1. Lah JJ, Cui W, Hu KQ. Effects and mechanisms of silibinin on human hepatoma cell lines. *World J Gastroenterol*. 2007 Oct 28;13(40):5299-305.
2. Gazák R, Walterová D, Kren V. Silybin and silymarin--new and emerging applications in medicine. *Curr Med Chem*. 2007;14(3):315-38.
3. Agarwal R, Agarwal C, Ichikawa H, Singh RP, Aggarwal BB. Anticancer potential of silymarin: from bench to bed side. *Anticancer Res*. 2006 Nov-Dec;26(6B):4457-98.
4. El-Serag HB, Mason AC. Rising incidence of hepatocellular carcinoma in the United States. *N Engl J Med*. 1999 Mar 11;340(10):745-50.

Long-Term Beta Carotene Keeps Mind Sharp



Long-term use of beta carotene helps prevent mental decline, such as dementia.* Since cognitive decline is thought to be related to oxidative stress, beta carotene's antioxidant properties may be responsible for its protective benefit.

In this study, Harvard researchers followed more than 4,000 men who were given either 50 mg of beta carotene every other day or a placebo pill. After an average of 18 years, the men who took beta carotene demonstrated significantly higher scores on several cognitive tests compared with the placebo group.

This study also included a short-term group that was followed for an average of one year. The researchers found no difference in cognitive test results for both groups after this shorter time period, highlighting the importance of continuing beta carotene use for cognitive protection. "Long-term supplementation [with beta carotene] may provide cognitive benefits," investigators concluded.

—Marc Ellman, MD

Reference

* Grodstein F, Kang JH, Glynn RJ, Cook NR, Gaziano JM. A randomized trial of beta carotene supplementation and cognitive function in men: the Physicians' Health Study II. *Arch Intern Med.* 2007 Nov 12;167(20):2184-90.

Low Male Hormone Levels Increase Risk of Early Death in Older Men



Age-associated decline in anabolic hormones, such as insulin-like growth factor-1 (IGF-1), dehydro-epiandrosterone sulfate (DHEA-S), and bioavailable testosterone, may be a strong independent predictor of early mortality in older men.*

Researchers assessed hormone levels in 410 men aged 65 years and older. Levels of the various hormones were assigned to one of four quartiles. Men increased their 6-year risk of death by 47%, 85%, and 129% if they had lower-than-threshold values of one, two, and three hormones, respectively, compared with men in the higher quartiles.

“Having multiple hormonal deficiencies rather than a deficiency in a single anabolic hormone is a robust biomarker of health status in older persons,” investigators concluded.

—Dale Kiefer

Reference

* Maggio M, Lauretani F, Ceda GP, et al. Relationship between low levels of anabolic hormones and 6-year mortality in older men: the aging in the chianti area (InCHIANTI) study. *Arch Intern Med.* 2007 Nov 12;167(20): 2249-54.

New Cancer Ablation Technique Introduced

Biomedical engineers have developed an innovative technique for the “minimally invasive” destruction, or ablation, of cancerous tumors. Known as irreversible electroporation, the technique uses carefully applied electrodes to deliver a brief, high-voltage current, which destabilizes the polarity of tumor cell membranes, without generating substantial heat.^{1,2} Healthy tissues are thus spared.

Cell membranes are normally non-porous or selectively porous; porosity is normally dependent upon subtle changes in membrane polarities. But the new technique is presumed to force membranes to develop nanoscale cracks, causing permanent permeability and the demise of affected cells.

The technique does not rely on a healthy immune system to work, which may be of additional benefit in the treatment of immunocompromised cancer patients.³ The novel technique, which involves “shocking” targeted tissue for a fraction of a second with carefully modulated electrical fields, has been successfully tested in lab animals, and human clinical trials are underway.⁴

—Dale Kiefer

Reference

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2. Rubinsky B. Irreversible electroporation in medicine. *Technol Cancer Res Treat.* 2007 Aug;6(4):255-60.
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Long-Term Supplement Users are Healthier

According to a new report published in *Nutrition Journal*,¹ long-term multiple dietary supplement users were less likely to have elevated blood pressure and diabetes compared with both non-users and those who supplemented with a multivitamin/mineral alone.

Researchers obtained information from 278 individuals regarding long-term multiple supplement use patterns, health, and nutrition through questionnaires and physical examination. Using a cross-sectional study design, and adjusting for potential confounding factors, they compared this information with data obtained from nearly 800 non-users and single multivitamin/mineral supplement users.

Consumers of multiple supplements were less likely to have hypertension and diabetes and more likely to have low levels of chronic disease-related biomarkers, such as C-reactive protein, which is associated with chronic inflammation, and homocysteine, which has been associated with elevated risk of cardiovascular disease and stroke.² Multiple supplement users were also more likely to have optimal levels of triglycerides and beneficial high-density lipoprotein (HDL).

—Dale Kiefer

Reference

1. Block G, Jensen CD, Norkus EP, et al. Usage patterns, health, and nutritional status of long-term multiple dietary supplement users: a cross-sectional study. *Nutr J*. 2007 Oct 24;6(1):30 [Epub ahead of print].
2. Wierzbicki AS. Homocysteine and cardiovascular disease: a review of the evidence. *Diab Vasc Dis Res*. 2007 Jun;4(2):143-50.

Nutritional Deficiencies Associated with Vegan Diet

Scientists caution that vegans may be deficient in essential nutrients, such as adequate complete protein, vitamin B12, which is found only in animal foods and supplements, vitamin A, calcium, zinc, and the essential omega-3 fatty acid, docosahexaenoic acid, or DHA.¹⁻⁸

Vitamin B12 deficiency may lead to elevated homocysteine levels among some vegans and vegetarians.^{1,4} Elevated homocysteine is implicated as a potential risk factor for cardiovascular disease and several diseases of the central nervous system.⁷ Breast-fed infants of vegan mothers are at risk of severe vitamin B12 deficiency, which may result in growth retardation and brain atrophy.^{2,3,5}

Docosahexaenoic acid is especially problematic for vegans, who do not consume any animal or animal-derived products, including dairy and eggs. Studies have shown, for instance, that breast-fed infants of vegan mothers obtain inadequate amounts of vitamin B12 and DHA, nutrients needed for optimal nervous system growth.^{2,3,8}

—Dale Kiefer

Reference

1. Herrmann W, Schorr H, Purschwitz K, Rassoul F, Richter V. Total homocysteine, vitamin B(12), and total antioxidant status in vegetarians. *Clin Chem*. 2001 Jun;47(6):1094-101.
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3. Kühne T, Bubl R, Baumgartner R. Maternal vegan diet causing a serious infantile neurological disorder due to vitamin B12 deficiency. *Eur J Pediatr*. 1991 Jan;150(3):205-8.
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8. Sanders TA, Reddy S. The influence of a vegetarian diet on the fatty acid composition of human milk and the essential fatty acid status of the infant. *J Pediatr*. 1992 Apr;120(4 Pt 2):S71-7.

Reduced Insulin Signaling in the Brain May Yield Longer Life

Harvard Medical School scientists have shown that a reduction in insulin-like signaling in the brains of certain mice extends the animals' life span by up to 18%. This boost in life span occurred in mice genetically engineered to lack a gene for insulin receptor substrate-2, which is involved in insulin signaling. Not only did the rodents live longer, they were also more active than control mice.¹ Researchers have previously shown that reduced insulin-like signaling extends life span in animals such as the worm and the fruit fly.

The finding may represent another piece of the puzzle of why caloric restriction increases life span in virtually all animals in which it has been studied.^{2,3} In related news, Japanese researchers demonstrated recently that reduced insulin-like growth factor signaling in rats evidently contributes to the effect of caloric restriction, which results in increased longevity.⁴

—Dale Kiefer

Reference

1. Taguchi A, Wartschow LM, White MF. Brain IRS2 signaling coordinates life span and nutrient homeostasis. *Science*. 2007 Jul 20;317(5836):369-72.
2. Simpson SJ, Raubenheimer D. Caloric restriction and aging revisited: the need for a geometric analysis of the nutritional bases of aging. *J Gerontol A Biol Sci Med Sci*. 2007 Jul;62(7):707-13.
3. Holloszy JO, Fontana L. Caloric restriction in humans. *Exp Gerontol*. 2007 Aug;42(8):709-12.
4. Yamaza H, Komatsu T, To K, et al. Involvement of insulin-like growth factor-1 in the effect of caloric restriction: regulation of plasma adiponectin and leptin. *J Gerontol A Biol Sci Med Sci*. 2007 Jan;62(1):27-33.

Zinc Helps Protect Against Pneumonia



Maintaining adequate levels of zinc may help protect nursing home-bound individuals from pneumonia and its complications, according to a report published in the *American Journal of Clinical Nutrition*.*

In this study, 617 men and women aged 65 and older received half of the recommended daily allowance of vitamins and minerals, including zinc, for one year. Scientists from the Jean Mayer USDA Human Nutrition Research Center on Aging at Tufts University measured serum zinc levels in the blood samples collected at the beginning and end of the trial.

According to the investigators, “The study participants with normal serum zinc concentrations in their blood reduced their risk of developing pneumonia by about 50%. Additionally, deaths from all causes were 39% lower in this group. Based on our data, it appears that daily zinc intake can help nursing home residents who are susceptible to pneumonia, especially those with low serum zinc concentrations in their blood.”

—Dayna Dye

Reference

- * Meydani SN, Barnett JB, Dallal GE, et al. Serum zinc and pneumonia in nursing home elderly. *Am J Clin Nutr*. 2007 Oct;86(4):1167-73.

The Life Extension Inaugural Cruise

“LEARNING AND FUN ABOARD THE SUN”

As a long-time member of the Life Extension Foundation and writer for its magazine, one thing I have always appreciated is the creativity of the Foundation when it comes to looking after its members. A great example of this is the exciting new Life Extension cruise, which set sail for the Caribbean in October, 2007. By combining a conference with a great vacation destination as a single package, this inaugural cruise was a smashing success for the Life Extension members lucky enough to attend.

ALL ABOARD THE SUN

The cruise ship was the Norwegian Sun run by Norwegian Cruise Lines, a beautiful ship by all accounts. Between sunny destinations such as Roatan (an island off Honduras), Cozumel (an island off Mexico), Belize, and Key West, Florida, Life

Extension delivered a range of informative lectures for the members on a wide variety of topics relating to health, disease prevention, and fitness, to name a few, as well as presenting the latest in integrative therapies and anti-aging research. This was also a unique opportunity for members to interact directly with medical doctors, researchers, advisors, and other Life Extension members.

UP-TO-THE-MINUTE PRESENTATIONS

The conference began with a talk by Life Extension's Vice President of Scientific Affairs and Medical Development, Dr. Steven Joyal. His opening presentation was a general "welcome to the conference," followed by an extensive look at the state of the Life Extension Foundation and the many areas of research it has both funded and focused on. His opening talk covered a wide range of topics, such as the latest research on anti-aging and disease prevention, new supplements and drugs, and strategies such as calorie restriction (CR) for preventing diseases associated with aging and extending life span.



OPTIMAL HORMONE LEVELS

Later that day, Scott Fogle, ND, Life Extension's Director of Clinical Information, gave a presentation entitled "Hormones and Optimal Health," which covered many issues surrounding the importance of optimizing various hormones. He explained in easy-to-follow terms how the many hormones in our bodies function, how they need to be properly balanced and monitored, and, a key area that is often ignored, the importance of regular blood work for accomplishing those goals.

Life Extension stresses constantly the importance of regular blood work, as do I, and I was surprised by the number of people on board who did not get regular blood work and did not know what their hormone levels were. For example, many men I spoke with did not know what their testosterone levels were and many women were unaware of their DHEA or estradiol (an estrogen) levels.

Suboptimal hormone levels are a fast way to lose muscle mass, bone mass, and general functionality as we age, which highlights the importance of regular blood work.

A number of talks also focused on the specific needs of aging men and women. Health advisor Alex Benitez gave a detailed presentation called "Prostate Cancer and Prostate Health," which covered an important topic of concern to all aging men—maintaining a healthy prostate and avoiding prostate cancer. Specific to the concerns of many women, health advisor Dr. Sevda Akhundova gave a talk entitled "Breast Cancer/Breast Health," which covered a variety of issues essential for avoiding a disease that kills thousands of women each year.



More notable lectures were given on the "Importance of Regular Blood Work" (presented by Dr. Akhundova), "Nutrition and Fitness for Life" and "Medication and Supplement Interactions" (both presented by Alex Benitez).

METABOLIC SYNDROME

Dr. Joyal then delivered an in-depth presentation on a topic important to all aging adults, "Metabolic Syndrome and Weight Loss."

Metabolic syndrome (also known as Syndrome X) is a cluster of conditions that often occur together as a result of a dysregulation in blood sugar metabolism via a decrease in insulin sensitivity. Metabolic syndrome has been estimated to affect approximately 25% of the US population. The condition often occurs as a cluster of abnormalities in one person, such as elevated levels of cholesterol, blood pressure, triglycerides, uric acid, and insulin, and excess body fat around the waist. Coupled together as metabolic syndrome, these factors greatly increase a person's risk for heart disease, stroke, and diabetes. Dr. Joyal covered the issues surrounding metabolic syndrome, how to treat it with nutrition, supplements, exercise, weight loss, and pharmaceuticals, as well as ways to prevent it.

ONE-ON-ONE MEETINGS

This is just a sample of the many lectures that were given on the first-ever Life Extension cruise. They were enjoyed by the members in attendance and provided hot topics of discussion at the group dinners we shared. Members were also able to meet one on one with the team of advisors, made up of Dr. Fogle, Dr. Akhundova, Alex Benitez, and myself.

I was tasked with the role of fitness advisor, which is one of my specialties, and I met one on one with the members to discuss their needs and concerns regarding all things fitness and health related, such as supplement intakes and altering their diets to suit their needs. Topics ranged from how to maintain one's strength and functionality with aging using resistance training to what supplements are best for different goals, such as endurance, strength, or fat loss.



I met with all manner of people of different ages and backgrounds. For example, one couple was Robert and Rose. Robert is 92 and a retired physicist, and Rose might kill me for divulging her age in the magazine, so I will not do so! They were both clearly dedicated

Life Extension members and unlike so many people in their age bracket, they were sharp and quick-witted, which I found both inspirational and hopeful for those of us in early middle age. I went over their supplement regimen with them, discussed some changes in their exercise programs, and suggested that Rose needed to increase her protein intake (protein malnutrition is very common in older Americans).

—Will Brink

Reference

Will Brink is a regular writer for a wide variety of fitness, longevity, and sports nutrition publications. He can be reached at Will@BrinkZone.com or through his website www.BrinkZone.com.

Join us for the Life Extension Fountain of Life Cruise to Alaska August 29 to September 5, 2008, leaving from Seattle, WA Join us on the second Fountain of Life Cruise and learn about the latest nutritional therapies to keep you in optimal health, presented by Life Extension staff among the backdrop of Alaska's pristine landscape on the prestigious Celebrity Infinity. Concierge class balcony suites start at \$1972.23 per person (inclusive of all fees, prices subject to change without notice; other cabin types available). Book now to reserve your cabin as space is limited. Call LE Vacations toll-free at 1-800-791-4457.

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