



The Vitamin & Herb Stores

# #81

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**Public release date: 20-Apr-2010**

## **The sweet smell of aging**

What does the smell of a good meal mean to you? It may mean more than you **think. Specific odors that represent food or indicate danger are capable of altering an animal's lifespan and physiological profile by activating a small number of highly specialized sensory neurons**, researchers at the University of Michigan, University of Houston, and Baylor College of Medicine have shown in a study publishing next week in the online, open-access journal PLoS Biology.

Recent research in model organisms and in humans has shown that sensory experiences can impact a wide range of health-related characteristics including athletic performance, type II diabetes, and aging. Nematode worms and fruit flies that were robbed of their ability to smell or taste, for example, lived substantially longer. However, the specific odors and sensory receptors that control this effect on aging were unknown.

Using molecular genetics in combination with behavioral and environmental manipulations, a collaboration between the laboratories of Scott Pletcher and Gregg Roman has succeeded in identifying carbon dioxide (CO<sub>2</sub>) as the first well-defined odorant capable of altering physiology and affecting aging. **Flies incapable of smelling CO<sub>2</sub> live longer than flies with normal olfactory capabilities**. They are also resistant to stress and have increased body fat. To many insects, including fruit flies, CO<sub>2</sub> represents an ecologically important odor cue that indicates the presence of food (e.g. rotting fruit or animal blood) or neighbors in distress (it has been implicated as a stress pheromone). Indeed, this group of researchers **previously showed that merely sensing one's normal food source is capable of reversing the health and longevity benefits that are associated with a low calorie diet**. They now establish that CO<sub>2</sub> is responsible for this effect.

"We are working hard to understand how sensory perception affects health, and our new result really narrows the playing field. Somehow these 50 or so neurons, whose primary job it is to sense CO<sub>2</sub>, are capable of instigating changes that accelerate aging throughout the organism," says Scott Pletcher.

Sensory perception has been shown to impact aging in species that are separated by millions of years of evolution, suggesting that similar effects may be seen in humans. "For us, it may not be the smell of yeast, for example, or the sensing of CO<sub>2</sub> that affects how long we live, but it may be the perception of food or danger," says Pletcher. **If so, a clever program of controlled perceptual experience might form the basis of a simple yet powerful program of disease prevention and healthy aging.**

**Public release date: 21-Apr-2010**

## **British heroin substitute may be associated with wide-ranging sight problems (methadone)**

Ophthalmic, clinical and visual electrophysiological findings in children born to mothers prescribed substitute methadone in pregnancy

Children born to mothers prescribed the heroin substitute methadone during pregnancy may be at risk of wide-ranging sight problems, indicates a small study published ahead of print in the British Journal of Ophthalmology.

There may be as many as 350,000 children in the UK whose parents are problem drug users, say the authors.

Methadone is a synthetic opioid, which provides a longer lasting "high" than most opioids, and is much less likely to be misused.

It is usually prescribed as a substitute for heroin, and is associated with a more stable maternal lifestyle and less likelihood of stunted fetal growth or preterm birth.

But most babies born to mothers, who are prescribed it during their pregnancy, have significant withdrawal symptoms, known as neonatal abstinence syndrome or NAS. These symptoms are severe enough to warrant treatment in up to 80% of cases.

They assessed the eyesight of 20 children with vision problems, whose mothers had taken methadone during the pregnancy.

Most of the children had also been exposed to either benzodiazepines (55%) or heroin (40%) while in the womb.

**Virtually all the children (95%) had poor eyesight in addition to which seven out of 10 had involuntary eye movement (nystagmus), while in half vision had not yet developed fully (delayed visual maturation).**

Eleven out of 12 children who had been treated for NAS had nystagmus, compared with only three out of eight whose NAS had not been severe enough to warrant treatment.

One in three (35%) also had a squint (strabismus), while a similar proportion (30%) had blurred vision or long or short sightedness problems (refractive errors). And one in four had impaired brain function relating to sight.

**One in four children also had significant developmental problems, including developmental delay and cerebral palsy.**

The underlying causes of the children's visual problems are unclear, say the authors, but the developing visual system is particularly sensitive to unexpected stressors before birth, they point out.

The incidence of substance misuse during pregnancy is on the rise, say the authors, citing an anonymous screening study from one UK clinic which indicated that between 11% and 16% of expectant mothers were taking at least one illicit drug during their pregnancy.

**Public release date: 21-Apr-2010**

## **New evidence that green tea may help fight glaucoma and other eye diseases**

Scientists have confirmed that the healthful substances found in green tea — renowned for their powerful antioxidant and disease-fighting properties — do penetrate into tissues of the eye. Their new report, the

first documenting how the lens, retina, and other eye tissues absorb these substances, raises the possibility that green tea may protect against glaucoma and other common eye diseases. It appears in ACS' bi-weekly Journal of Agricultural and Food Chemistry.

Chi Pui Pang and colleagues point out that so-called green tea "catechins" have been among a number of antioxidants thought capable of protecting the eye. Those include vitamin C, vitamin E, lutein, and zeaxanthin. Until now, however, nobody knew if the catechins in green tea actually passed from the stomach and gastrointestinal tract into the tissues of the eye.

Pang and his colleagues resolved that uncertainty in experiments with laboratory rats that drank green tea. Analysis of eye tissues showed beyond a doubt that eye structures absorbed significant amounts of individual catechins. The retina, for example, absorbed the highest levels of gallic catechin, while the aqueous humor tended to absorb epigallocatechin. The effects of green tea catechins in reducing harmful oxidative stress in the eye lasted for up to 20 hours. "Our results indicate that green tea consumption could benefit the eye against oxidative stress," the report concludes.

**Public release date: 21-Apr-2010**

## **How red wine may shield brain from stroke damage**

Johns Hopkins researchers discover pathway in mice for resveratrol's apparent protective effect  
Researchers at Johns Hopkins say they have discovered the way in which red wine consumption may protect the brain from damage following a stroke.

Two hours after feeding mice a single modest dose of resveratrol, a compound found in the skins and seeds of red grapes, the scientists induced an ischemic stroke by essentially cutting off blood supply to the animals' brains. **They found that the animals that had preventively ingested the resveratrol suffered significantly less brain damage than the ones that had not been given the compound.**

Sylvain Doré, Ph.D., an associate professor of anesthesiology and critical care medicine and pharmacology and molecular sciences at the Johns Hopkins University School of Medicine, **says his study suggests that resveratrol increases levels of an enzyme (heme oxygenase) already known to shield nerve cells in the brain from damage. When the stroke hits, the brain is ready to protect itself because of elevated enzyme levels. In mice that lacked the enzyme, the study found, resveratrol had no significant protective effect and their brain cells died after a stroke.**

"Our study adds to evidence that resveratrol can potentially build brain resistance to ischemic stroke," says Doré, the leader of the study, which appears online in the journal *Experimental Neurology*.

Red wine has gotten a lot of attention lately for its purported health benefits. Along with reducing stroke, moderate wine consumption has been linked to a lowered incidence of cardiovascular disease — the so-called French paradox. Despite diets high in butter, cheese and other saturated fats, the paradox goes, the French have a relatively low incidence of cardiovascular events, which some have attributed to the regular drinking of red wine.

Doré cautions against taking resveratrol supplements, available alongside vitamins and minerals and on websites touting its benefits, because it is unclear whether such supplements could do harm or good. He has not tested resveratrol in clinical trials. And while resveratrol is found in red grapes, it's the alcohol in the wine that may be needed to concentrate the amounts of the beneficial compound. Doré also cautions that drinking alcohol carries risks along with potential benefits.

He also notes that even if further research affirms the benefits of red wine, no one yet knows how much would be optimal to protect the brain, or even what kind of red wine might be best, because not all types contain the same amount of resveratrol. More research is needed, he says.

Doré says his research suggests that the amount needed could end up being quite small because the suspected beneficial mechanism is indirect. "Resveratrol itself may not be shielding brain cells from free radical damage directly, but instead, resveratrol, and its metabolites, may be prompting the cells to defend themselves," he suggests.

"It's not likely that brain cells can have high enough local levels of resveratrol to be protective," he says. The resveratrol is needed to jump-start this protective enzymatic system that is already present within the cells. "Even a small amount may be sufficient," Doré says.

Doré says his ongoing research also suggests some therapeutic benefits to giving resveratrol to mice after a stroke to limit further neuronal damage.

**Public release date: 22-Apr-2010**

## **New strain of virulent airborne fungi, unique to Oregon, is set to spread**

DURHAM, N.C. – A newly discovered strain of an airborne fungus has caused several deaths in Oregon and seems poised to move into California and other adjacent areas, according to scientists at Duke University Medical Center.

**"This novel fungus is worrisome because it appears to be a threat to otherwise healthy people," said Edmond Byrnes III, a graduate student in the Duke Department of Molecular Genetics and Microbiology. "Typically, we see this fungal disease associated with transplant recipients and HIV-infected patients, but that is not what we are seeing." Byrnes and other Duke co-authors work in the laboratory of senior author Joseph Heitman, M.D., Ph.D., and chair of the Department of Molecular Genetics and Microbiology.**

Their new work on the emergence and virulence of the new genotypes of *Cryptococcus gattii* fungi in the United States was published online in PLoS Pathogens on April 22.

The mortality rate for recent *C. gattii* cases in the Pacific Northwest is running at approximately 25 percent out of 21 cases analyzed in the United States, compared to a mortality rate of 8.7 percent out of 218 cases in British Columbia, Canada, the researchers said. Most have a more complicated clinical course than people infected with the more common *Cryptococcus neoformans*.

Because the strain is so virulent when it infects some humans and animals, the researchers are calling for greater awareness and vigilance. Testing involves culturing the fungus and then sequencing its DNA to learn whether it is the virulent or more benign strain, which could affect treatment plans.

Some strains of *C. gattii* are not more virulent than *C. neoformans*, for example, but doctors need to know what type they are dealing with, Byrnes said. Using molecular techniques, the geneticists uncovered clues that showed the Oregon-only fungal type most likely arose recently, in addition to an outbreak of *C. gattii* that began in Canada in 1999 that has now spread into Washington and Oregon.

Symptoms can appear two to several months after exposure, and may include a cough lasting weeks, sharp chest pain, shortness of breath, headache (related to meningitis), fever, nighttime sweats and weight loss. In animals the symptoms are a runny nose, breathing problems, nervous system problems and raised bumps under the skin. While *C. gattii* can be treated, it cannot be prevented; there is no vaccine.

The new type of *Cryptococcus gattii* reproduces both sexually and asexually. The more virulent strain may have genetically recombined with related but less harmful strains. This novel genotype is highly virulent compared with similar isolates of *Cryptococcus* that are not causing disease outbreaks.

The researchers found that the novel genotype (VGIIc) is now a major source of *Cryptococcus gattii* illness in Oregon. Because *C. gattii* types had been found in tropical areas before, co-lead author Wenjun Li,

M.D., Ph.D., of Duke Molecular Genetics and Microbiology, speculates that environmental changes may be responsible for the evolution and emergence of this pathogen.

Determining the exact origin of the VGIIc type is difficult, and sampling thus far has failed to turn up isolates in Oregon soil, water or trees.

"We are trying to put together the evolutionary story of where these types come from by closely studying the genetics of all samples possible," said Yonathan Lewit, a research associate also in Duke Molecular Genetics and Microbiology. He said that cell components called mitochondria may play a role in the increased virulence of certain types.

VGIIc, the new Oregon strain, has yielded dozens of isolates in many specimens, including from domesticated animals: cats, dogs, an alpaca and a sheep. "Most of those are nonmigratory animals," Byrnes said, explaining that the animals probably didn't bring the pathogen from some other region, and most likely acquired it locally.

**Public release date: 22-Apr-2010**

## **Magnitude of overdiagnosis in cancer indicates need for strategies to address the problem**

Many cancers detected by screening tests are not destined to cause symptoms or death and therefore represent a phenomenon known as overdiagnosis. And because overdiagnosis leads to unnecessary treatment and other harms, it is important to develop clinical and research strategies to quantify, recognize, and manage it, according to a review published online April 22 in the Journal of the National Cancer Institute.

H. Gilbert Welch, M.D. and William Black, M.D., of the Dept. of Veterans Affairs Medical Center, White River Junction, Vt. and the Dartmouth-Hitchcock Medical Center used data from large randomized screening trials to estimate the extent of overdiagnosis. **They found that about 25% of breast cancers detected on mammograms and about 60% of prostate cancers detected with prostate-specific antigen (PSA) tests could represent overdiagnosis. In a lung cancer screening trial of chest x-rays and sputum tests, they estimate that 50% of the cancers detected represented overdiagnosis. They argue that this estimate will only increase with spiral CT scanning, which, in one observational study, found almost as many lung cancers in non-smokers as smokers.**

The authors also point to cancer incidence and mortality statistics as evidence of overdiagnosis in some cancers. **For five cancers—thyroid, prostate, kidney and breast cancer, and melanoma—data from the past 30 years show an increasing number of new cases but not an increase in deaths. In each of these cancers, an increase in screening or imaging tests has been associated with an increasing rate of new diagnoses.**

In addition to screening, other procedures, such as diagnostic imaging, may contribute to overdiagnosis. CT colonography (virtual colonoscopy) for instance, often detects abnormalities outside the colon that can lead to more tests and possibly overdiagnosis.

The authors suggest several strategies to address the problem. One is to educate patients about the risks and benefits involved with early detection.

**"Whereas early detection may well help some, it undoubtedly hurts others," they write. "Often the decision about whether or not to pursue early cancer detection involves a delicate balance between benefits and harms...different individuals, even in the same situation, might reasonably make**

### different choices."

Another strategy to reduce overdiagnosis is to raise the threshold at which a screening test result is labeled 'abnormal', or at which further steps are taken. For instance, investigators could test whether it was better to ignore small abnormalities detected on imaging tests, as is now the practice with lung nodules detected by CTscans.

"It is possible that new insights from genomics will ultimately allow us to more accurately predict tumor behavior at the individual level," the authors write. "However the field has not advanced to that point yet. We must explore other clinical strategies."

In an accompanying editorial, Laura Esserman, M.D., University of California, San Francisco and Ian Thompson, University of Texas Health Science Center at San Antonio, stress the critical importance of addressing the problem of overdiagnosis.

"What we need now in the field of cancer is the coming together of physicians and scientists of all disciplines to reduce the burden of cancer death AND cancer diagnosis," they write. "We must advocate for and demand innovation in diagnosis and management, fueled by science, harnessing modeling, molecular, and immunology tools to address this problem."

### Public release date: 22-Apr-2010

## **Poultry disease vaccine brings short-term results but long-term problems**

**Attenuated live vaccines that protect poultry against Newcastle Disease may be altering the genetic makeup of the wild virus strains**, which could make future outbreaks unpredictable and difficult to tackle, according to biologists.

Newcastle Disease is an economically devastating poultry disease that costs the industry millions of dollars.

"Many vaccines in the animal industry are developed by modifying a virulent live virus," said Mary Poss, professor of biology and veterinary and biomedical sciences, Penn State. "These vaccines elicit a strong protection against disease."

**However, vaccinated birds can shed the vaccine virus to infect other birds, and live virus vaccines do not always protect birds from infection from other viral strains of Newcastle disease.**

Poss and her Penn State colleagues Yee Ling Chong, graduate student in biology; Abinash Padhi, post-doctoral fellow and Peter J. Hudson, Willaman professor of biology, found that one vaccine strain recombined -- exchanged genetic material -- with at least three wild strains, creating new viruses. These viruses are found in both domestic and wild birds. The team's findings appear today (Apr. 22) in PLoS Pathogens.

**"Our findings indicate that birds can be simultaneously infected with the live virus vaccine and several other strains of this avian virus,"** said Poss. **"This raises concerns that modified live virus vaccines, though effective, may combine with circulating viruses to create unpredictable new strains."**

A modified live virus vaccine is essentially a weakened virus that does not cause disease but mimics a natural infection that in turn evokes a strong immune response from the infected host. But Poss argues that vaccination may be unwittingly increasing the diversity of Newcastle Disease viruses that are circulating in

wild birds.

**For instance, many poultry farmers typically vaccinate the flock by mixing the vaccine in the birds' drinking water or by aerosol, which means wild birds and pigeons can also become infected with the vaccine virus.**

**This sets up the opportunity for viral recombination. A bird is infected with two different viruses at the same time, one from the weakened vaccine and one naturally, and both viruses then infect the same cell.**

**In addition to the possibility of creating new viruses**, different strains of the virus that causes Newcastle disease may be evolving in different environments. Recombination among these strains could bring together genes that have multiple means to evade immunity in a host.

**Poss added that vaccine developers need to be aware of the potential for driving virus evolution using modified live viruses and should instead consider using killed or inactivated viruses.** Scientists are already using that approach against Newcastle Disease in some areas but not globally.

"We need to step up the surveillance and monitoring of viral diseases in poultry and wild birds," said Poss. "We need to be aware that management practices including the use of live virus vaccines can change viral diversity and the consequences of such changes will not be evident for several generations."

While many virus strains undergo a boom and bust cycle -- they are present for a period of time and then die out -- Poss notes that the use of live virus vaccines creates a persistent level of the vaccine strains in the global bird population.

Poultry farmers around the world vaccinate birds with vaccine made from one of two live strains of an avian virus that causes Newcastle Disease. While vaccines from the first strain are used mainly in Asia, the second strain is used in vaccines worldwide. Since the 1950s, vaccines derived from the two strains have helped poultry farmers avoid devastating economic losses.

To determine the impact of vaccination on the evolution of wild viruses, researchers analyzed the evolutionary history of 54 samples of full-length genome sequences of the avian paramyxovirus -- the virus that causes Newcastle Disease -- isolated from infected birds.

If all six genes that make up the paramyxovirus shared the same ancestor, Poss reasoned, the family trees of each gene would look the same. However, genes that are derived from a different strain would have family trees distinct from the other genes of that virus, a strong signature of recombination.

Statistical analysis of the gene sequences indicates that recombination occurred in at least five of the sampled genomes. Four of these five genomes contained gene sequences from one of the two vaccine strains.

Researchers next reconstructed the population history of the different viral strains. The strain from which the vaccine was derived showed a higher and more constant population size compared to other circulating strains.

**"When viruses don't change, it is typically a good thing," Poss explained. "But as soon as they start to change, like the flu, we don't know what the transmission and disease potential are going to be like from one year to another. So driving up viral diversity is not a good thing."**

**Public release date: 25-Apr-2010**

## **Chokeberry extract found to regulate weight gain, blood glucose, and inflammation in rats**

Chokeberry bushes have for centuries been residents of eastern deciduous forests where their bright red and dark purple fruits continue to be favorite snacks of local bird species. Native Americans have also traditionally eaten dried chokeberries and prepared teas from parts of the plant, and several domesticated varieties now grace contemporary lawns and gardens from coast to coast. However, the chokeberry (Aronia) is enjoying a new claim-to-fame as a potentially powerful antioxidant, and can now be found for sale in the dietary supplement and "health food" aisles of your local pharmacies and grocery stores.

What makes the humble chokeberry so healthful? Scientists think the answer lies in their unusually high levels of substances called anthocyanins (from the Greek anthos + kyanos meaning dark blue). There are many different anthocyanins in these colorful berries, but they all function as antioxidants – originally protecting the chokeberry seed from sunshine-induced oxidative stress. And when we eat them, they also appear to protect our bodies from a variety of damaging situations, including exposure to pollution and metabolically-derived free radicals. Indeed, a growing body of scientific literature has shown promising effects of chokeberry consumption on diseases ranging from cancer to obesity. These health-promoting effects may be due to the potent anti-inflammatory properties of anthocyanins, as uncontrolled inflammation is now universally recognized as a common thread in many of our most prevalent and deadly diseases. In addition, certain anthocyanins – including those found in chokeberry – have also been shown to improve blood sugar and the function of insulin.

To better understand how chokeberries influence health, Drs. Bolin Qin and Richard Anderson from the US Department of Agriculture in Beltsville, MD studied what happens when prediabetic rats are fed chokeberry extracts for an extended period of time. The results of their research will be presented on April 25 at the Experimental Biology 2010 meeting in Anaheim, CA. This presentation is part of the scientific program of the American Society for Nutrition, home of the world's leading nutrition researchers.

The researchers first made 18 male rats "prediabetic" or insulin insensitive by feeding them a fructose-rich diet for 6 weeks. Then they randomized the animals to continue drinking either pure water or water spiked with low or high levels of chokeberry extract (CellBerry®, Integrity Nutraceuticals International). After drinking this water for 6 weeks, the groups were compared in terms of body weight, body fat, blood glucose regulation, and molecular markers for inflammation.

Qin and Anderson found that at the end of the study the rats consuming the **chokeberry-spiked water weighed less than the controls; both levels of chokeberry had the same effect in this regard. Similar beneficial effects of chokeberry consumption were found for body fat (specifically, that of the lower abdominal region). They also discovered that animals that had been drinking chokeberry extract had lower blood glucose and reduced levels of plasma triglycerides, cholesterol, and low-density lipoprotein (LDL) cholesterol when compared to the control animals.** These alterations would theoretically lead to lower risk for diabetes and cardiovascular disease in humans. And to add even more evidence for a healthful impact of this super-berry, the researchers documented numerous alterations in expression of genes that would likely lead to reduced chronic inflammation and perhaps even lower cancer risk. For instance, drinking chokeberry extract lowered expression of the gene coding for interleukin-6 (IL-6), a protein that normally triggers inflammation following trauma or infection. Chronic overproduction of IL-6 has been documented in many diseases such as diabetes, arthritis, and atherosclerosis and is thought to be a partial cause of these conditions.

Of course, human studies will be needed before scientists can declare whether we derive the same health benefits from the chokeberry, but Qin and Anderson believe that their study "provides evidence that the chokeberry extract inhibits weight gain in insulin-resistant animals and that it modulates multiple genes associated with adipose tissue growth, blood glucose regulation, and inflammatory pathways." A final word to the wise: raw chokeberries are exceptionally bitter, so don't be tempted to harvest the shrubs in your backyard. Instead, look for this unassuming berry in fruit juice blends, jellies, and sweetened syrups.

**Public release date: 29-Apr-2010**

## **Gut bacteria offer new insights -- and hope -- for people with celiac disease**

New research published in the Journal of Leukocyte Biology suggests that striking a balance of intestinal microbiota could play a role in early stages of celiac disease-related immune responses

Dietary changes that include probiotics and/or prebiotics (found in some foods) may help alleviate the severity of celiac disease for some patients. According to a new research study appearing in the May 2010 print issue of the Journal of Leukocyte Biology (<http://www.jleukbio.org>), differing intestinal bacteria in celiac patients could influence inflammation to varying degrees. **This suggests that manipulating the intestinal microbiota with dietary strategies such as probiotics and prebiotics, could improve the quality of life for celiac patients, as well as patients with associated diseases such as type 1 diabetes and other autoimmune disorders.**

"We hope the study will ultimately add to the understanding of the mechanisms of action of the intestinal microbiota in immune-mediated diseases," said Yolanda Sanz, one of the scientists involved in the research from the National Spanish Research Council in Valencia, Spain. "This study may also help to design novel strategies, which could improve the quality of life of celiac disease patients in the future."

To make this discovery, scientists used cultures of human peripheral mononuclear cells (PBMCs) as in vitro models, as intestinal mucosa monocytes are constantly replenished by blood monocytes and accurately represent an in vivo situation. To simulate the intestinal environment of celiac disease, cell cultures were exposed to Gram-negative bacteria isolated from celiac patients and bifidobacteria, both alone and in the presence of disease triggers. The effects on surface marker expression and cytokine production by PBMCs were determined. The Gram-negative bacteria induced higher pro-inflammatory cytokines than the bifidobacteria. These bacteria also up-regulated expression of cell surface markers involved in inflammatory characteristics of the disease, while bifidobacteria up-regulated the expression of anti-inflammatory cytokines. Although human clinical trials are necessary, this evidence could be the first step toward changing how celiac disease is treated and possibly prevented.

"Just as some foods can lead to poor health," said Louis Montaner, D.V.M., M.Sc., D.Phil. Editor-in-Chief of the Journal of Leukocyte Biology, "it's no surprise that others can have positive effects. For people with celiac disease, this opens a line of research into new therapies that may be as accessible as a grocer's shelf."

According to the National Institute of Diabetes and Digestive and Kidney Diseases, U.S. National Institutes of Health, celiac disease affects more than two million people in the United States. It causes damage to the small intestine and interferes with absorption of nutrients from food. People who have celiac disease cannot tolerate gluten, a protein in wheat, rye, and barley. When people with celiac disease eat foods or use products containing gluten, their immune system responds by damaging or destroying villi—the tiny, fingerlike protrusions lining the small intestine. Without healthy villi, nutrients cannot be absorbed properly, leading to malnutrition, no matter how much food one eats.

**Public release date: 29-Apr-2010**

## **Low vitamin D levels are related to ms brain atrophy, cognitive function, studies show**

BUFFALO, N.Y. -- Low vitamin D levels may be associated with more advanced physical disability and cognitive impairment in persons with multiple sclerosis, studies conducted by neurologists at the University at Buffalo have shown.

Their results, reported at the American Academy of Neurology meeting, held earlier this month, indicated that:

- The majority of MS patients and healthy controls had insufficient vitamin D levels.**
- Clinical evaluation and magnetic resonance imaging (MRI) images show low blood levels of total vitamin D and certain active vitamin D byproducts are associated with increased disability, brain atrophy and brain lesion load in MS patients.**
- A potential association exists between cognitive impairment in MS patients and low vitamin D levels. The MRI study involved 236 MS patients -- 208 diagnosed with the relapsing-remitting type and 28 with secondary progressive, a more destructive form of MS -- and 22 persons without MS.**

All participants provided blood serum samples, which were analyzed for total vitamin D (D2 and D3) levels as well as levels of active vitamin D byproducts. MRI scans performed within three months of blood sampling were available for 163 of the MS patients.

Results showed that only seven percent of persons with secondary-progressive MS showed sufficient vitamin D, compared to 18.3 percent of patients with the less severe relapsing-remitting type.

Higher levels of vitamin D3 and vitamin D3 metabolism byproducts (analyzed as a ratio) also were associated with better scores on disability tests, results showed, and with less brain atrophy and fewer lesions on MRI scans.

Bianca Weinstock-Guttman, MD, UB associate professor of neurology/Jacobs Neurological Institute and director of the Baird Multiple Sclerosis Center, is first author on the study. Commenting on these results, Weinstock-Guttman said: "Clinical studies are necessary to assess vitamin D supplementation and the underlying mechanism that contributes to MS disease progression."

While lower-than-normal vitamin D status is known to be associated with a higher risk of developing MS, little is known about its relationship to cognitive impairment.

Sarah A. Morrow, MD, UB assistant research professor of neurology/Jacobs Neurological Institute and lead author on the cognitive-impairment study, compared vitamin D levels in blood samples of 136 MS patients with the results of their neuropsychological assessments that tested multiple types of cognition affected by MS.

"Results showed that MS patients who were impaired on tests of executive function --critical reasoning and abstract thinking -- and the ability to plan and organize, were more likely to be deficient in vitamin D," said Morrow.

"This relationship held true when controlling for the season during which vitamin D was measured, as well as depression, which is known to be associated with lower vitamin D levels." Morrow noted there also was a suggestion that verbal fluency (word generation) and visual-spatial memory (learning and memory of shapes and figures) is more likely to be affected when vitamin D levels are not sufficient.

**Public release date: 30-Apr-2010**

## **Vitamin E effective for 'silent' liver disease**

NIH-funded, NEJM study is largest ever to look at nonalcoholic steatohepatitis, an obesity-related condition

NEW YORK (April 29, 2010) -- Vitamin E has been shown effective in treating nonalcoholic steatohepatitis (NASH), an obesity-associated chronic liver disease that can lead to cirrhosis, liver cancer, and death. NASH also is related to or a part of type 2 diabetes, lipid disorders and cardiovascular disease.

The often asymptomatic condition affects 2 to 5 percent of Americans, although an additional 10 to 20 percent of the population has fat in their liver, but no inflammation or liver damage, a condition called "fatty liver" that is a precursor to NASH. There is no established treatment.

The government-funded multicenter study was organized by the Nonalcoholic Steatohepatitis Clinical Research Network of the National Institute of Diabetes and Digestive and Kidney Diseases, and is the largest ever placebo-controlled randomized trial of treatment for NASH. Results are published in the April 28 online edition of the New England Journal of Medicine.

Beginning in the late 1990s, study of vitamin E for NASH was pioneered in pilot trials by Dr. Joel Lavine, now a faculty member in the Department of Pediatrics at Columbia University College of Physicians and Surgeons and chief of gastroenterology, hepatology and nutrition at New York-Presbyterian/Morgan Stanley Children's Hospital. Researchers followed patients at nine centers, including the University of California, San Diego, where Dr. Lavine was previously on faculty.

"There is an increasing prevalence of nonalcoholic steatohepatitis in this country, something that is directly related to the obesity epidemic," says Dr. Lavine, co-chair of the Network's steering committee and a co-author of the study. **"The good news is that this study showed that cheap and readily available vitamin E can help many of those with the condition. We also looked at the drug pioglitazone, which showed some benefits, although not as dramatic as with vitamin E."**

Dr. Lavine cautions that there are risks with any therapy, even vitamin E, and all treatment should be done under medical supervision. "Individuals who are overweight or have a family history of liver disease should ask their doctor to be tested for the condition. In addition, physicians should be aware that liver enzyme levels considered normal are actually elevated. Healthy levels are <30 U/L for a man and <20 for a woman."

In the Pioglitazone or Vitamin E for NASH Study (PIVENS), investigators randomly assigned 247 nondiabetic adults with biopsy-confirmed NASH to receive vitamin E, pioglitazone or placebo. Vitamin E functions as an antioxidant while pioglitazone improves the sensitivity of cells to insulin, a hormone that controls both sugar and fat metabolism.

After 96 weeks of treatment, vitamin E improved all features of NASH with the exception of the amount of scar tissue in the liver; 43 percent of those treated with vitamin E met the primary endpoint of the trial, which was a composite of the scores for several features of NASH indicative of disease activity, compared with only 19 percent of those who received a placebo. Pioglitazone also improved many features of NASH and met the primary endpoint in 34 percent of individuals who received it but fell short of statistical significance. Pioglitazone treatment led to an average weight gain of 10 pounds over the 96-week duration of this study. Liver enzyme tests, which are commonly used to assess liver injury, also improved in those who received either pioglitazone or vitamin E. However, upon stopping the medications, the liver enzymes worsened again suggesting the need for long-term treatment.

The study was conducted in those with NASH who did not have diabetes, and the benefits of either drug for those with NASH who also have diabetes remain unknown. Also, the study lasted for two years only and the potential long-term benefits and risks of taking vitamin E or pioglitazone in these doses are uncertain.

Lead author of the study and the other NASH Clinical Research Network co-chair is Dr. Arun Sanyal, professor of medicine and chairman of the Division of Gastroenterology at Virginia Commonwealth University in Richmond.

Pioglitazone (trade name Actos) was provided by Takeda Pharmaceuticals North America, and vitamin E was provided by Pharmavite. Both also supplied placebos.

Dr. Lavine joined New York-Presbyterian/Columbia from the University of California San Diego in

February and brought his NIH grant for the study of fatty liver to NewYork-Presbyterian/Columbia. He is currently preparing a report on a multicenter study he led of vitamin E and the diabetes drug metformin for NASH in children.

**Public release date: 1-May-2010**

## **Probiotics help extremely premature infants gain weight**

VANCOUVER, BRITISH COLUMBIA – Extremely low birthweight infants (ELBW) who received feedings supplemented with probiotics had better weight gain than infants who were not given the supplements, according to a randomized, controlled, double-blind study to be presented Saturday, May 1 at the Pediatric Academic Societies (PAS) annual meeting in Vancouver, British Columbia, Canada.

Probiotics, which means "for life" in Latin, are healthy, live organism supplements that provide benefit to the host. Their effect on digestive health and immune function has been studied. However, the safety and efficacy of probiotic supplementation in ELBW infants has not been explored thoroughly.

In this study, Mohamad Al-Hosni, MD, and colleagues from three medical centers, in collaboration with Vermont Oxford Network, evaluated the effect of supplementing enteral (tube) feedings with probiotics in extremely premature infants who weighed 2 pounds, 2 ounces or less. They hypothesized that infants who received probiotic-supplemented feedings would tolerate larger volumes of feeding per day, grow faster and require fewer days of antimicrobial treatment than those in the control group.

**Fifty infants received 500 million colony-forming units (CFU) of *Lactobacillus rhamnosus* GG and 500 million CFU of *Bifidobacterium infantis* in enteral feedings once a day until discharge or 34 weeks postmenstrual age. Fifty-one infants received feedings with no probiotics.**

**Results showed superior weight gain in infants who received the probiotics even though the average daily volume of their feedings was less than infants in the control group. There were no statistically significant differences in other complications of prematurity such as sepsis or necrotizing enterocolitis. In addition, no side effects were seen as a result of probiotic supplementation, according to Dr. Al-Hosni, an assistant professor of pediatrics at Saint Louis University School of Medicine in the division of neonatal-perinatal medicine at SSM Cardinal Glennon Children's Medical Center.**

"These findings strongly suggest that probiotic supplementation to enteral feedings plays a major role in feeding tolerance and nutrient absorption," he said. "Improved tolerance of feedings and nutrient absorption lead to better weight gain in this extremely premature infant group."

Dr. Al-Hosni concluded that larger clinical trials are needed to demonstrate the safety and efficacy of probiotic supplementation to enteral feeding in this group of infants.

**Public release date: 1-May-2010**

## **Researchers recommend pregnant women take 4,000 IU vitamin D a day**

VANCOUVER, BRITISH COLUMBIA – Taking vitamin D supplements during pregnancy is not only safe for mother and baby, but also can prevent preterm labor/births and infections, according to results of a randomized controlled study to be presented at the Pediatric Academic Societies (PAS) annual meeting in Vancouver, British Columbia, Canada.

In the 1950s and '60s, people were concerned that vitamin D could cause birth defects, according to Carol L. Wagner, MD, lead author of the study and a pediatric researcher at Medical University of South

Carolina. It now is known that vitamin D is important for maternal and infant health, including bone health and immune function.

Recent studies have shown that vitamin D deficiency during pregnancy is a serious public health issue.

**"Diet doesn't provide enough vitamin D, and we don't go in the sun as much as we need," Dr. Wagner said.**

Therefore, she and her colleagues, including Bruce W. Hollis, PhD, who has worked in the field of vitamin D research for the last 30 years, set out to determine the optimal dose of vitamin D supplements for pregnant women without doing harm.

Researchers randomized 494 pregnant women at 12-16 weeks' gestation into three treatment groups. Group one received 400 International Units (IU) of vitamin D a day until delivery; group two received 2,000 IU and group three received 4,000 IU. The women were evaluated monthly to ensure safety.

**"No adverse events related to vitamin D dosing were found in any of the three arms of the study," Dr. Wagner said.**

Investigators also looked at the effects of vitamin D supplementation on complications during pregnancy, including preeclampsia, gestational diabetes, infections, and preterm labor and birth.

**"The spectacular part of the study was it showed women replete in vitamin D had lower rates of preterm labor and preterm birth, and lower rates of infection," Dr. Wagner said.**

The greatest effects were seen among women taking 4,000 IU of vitamin D per day. Therefore, the researchers recommend this daily regimen for all pregnant women.

**Public release date: 1-May-2010**

## **Olive oil could guard against developing ulcerative colitis**

Eating more olive oil could help prevent ulcerative colitis, according to a new study co-ordinated by medical researchers at the University of East Anglia (UEA).

Presented today at the Digestive Disease Week conference in New Orleans, the findings show that people with a diet rich in oleic acid – which is present in olive oil – are far less likely to develop ulcerative colitis. Oleic acid is a monounsaturated fatty acid found in olive oil, peanut oil and grapeseed oil, as well as in butter and certain margarines.

The researchers, led by Dr Andrew Hart of UEA's School of Medicine, studied more than 25,000 people aged 40-65 living in Norfolk, UK. The volunteers were recruited to the EPIC study (European Prospective Investigation into Diet and Cancer) between 1993 and 1997. The participants, none of whom had ulcerative colitis at the outset, completed detailed food diaries which were later analysed by specially trained nutritionists working in Cambridge.

**By 2004, 22 participants in the study had developed ulcerative colitis and the researchers compared their diets with those who did not develop the disease. They found that those with the highest intake of oleic acid had a 90 per cent lower risk of developing the disease.**

"Oleic acid seems to help prevent the development of ulcerative colitis by blocking chemicals in the bowel that aggravate the inflammation found in this illness," said Dr Hart.

"We estimate that around half of the cases of ulcerative colitis could be prevented if larger amounts of oleic acid were consumed. Two-to-three tablespoons of olive oil per day would have a protective effect," said Dr Hart.

Ulcerative colitis is a distressing disease affecting 120,000 people of all ages in the UK and 1 million in the US. It is characterized by inflammation of the lining of the colon or large bowel, which causes abdominal pain, diarrhoea and weight loss.

Similar work in other countries is now required to determine if these results are reproducible there, before the link can be said to be definite. If it is confirmed that oleic acid is truly protective, dietary modifications should be considered to prevent colitis. Additionally, the use of oleic acid supplements should also be assessed in the future as a possible treatment for colitis sufferers.

**Public release date: 3-May-2010**

## **Regular use of aspirin increases risk of Crohn's disease by 5 times**

People who take aspirin regularly for a year or more may be at an increased risk of developing Crohn's disease, according to a new study by the University of East Anglia (UEA).

Led by Dr Andrew Hart of UEA's School of Medicine, the research will be presented for the first time at the Digestive Disease Week conference in New Orleans today.

Crohn's disease is a serious condition affecting 60,000 people in the UK and 500,000 people in the US. It is characterized by inflammation and swelling of any part of the digestive system. This can lead to debilitating symptoms and requires patients to take life-long medication. Some patients need surgery and some sufferers have an increased risk of bowel cancer.

Though there are likely to be many causes of the disease, previous work on tissue samples has shown that aspirin can have a harmful effect on the bowel. To investigate this potential link further, the UEA team followed 200,000 volunteers aged 30-74 in the UK, Sweden, Denmark, Germany and Italy. The volunteers had been recruited for the EPIC study (European Prospective Investigation into Cancer and Nutrition) between 1993 and 1997.

The volunteers were all initially well, but by 2004 a small number had developed Crohn's disease. When looking for differences in aspirin use between those who did and did not develop the disease, the researchers discovered that those taking aspirin regularly for a year or more were around five times more likely to develop Crohn's disease.

The study also showed that aspirin use had no effect on the risk of developing ulcerative colitis – a condition similar to Crohn's disease.

"This is early work but our findings do suggest that the regular use of aspirin could be one of many factors which influences the development of this distressing disease in some patients," said Dr Hart.

"Aspirin does have many beneficial effects, however, including helping to prevent heart attacks and strokes. I would urge aspirin users to continue taking this medication since the risk of aspirin users possibly developing Crohn's disease remains very low – only one in every 2000 users, and the link is not yet finally proved."

Further work must now be done in other populations to establish whether there is a definite link and to check that aspirin use is not just a marker of another risk factor which is the real cause of Crohn's disease. The UEA team will also continue its wider research into other potential factors in the development of Crohn's disease, including diet.

**Public release date: 3-May-2010**

## **Broccoli component limits breast cancer stem cells, U-M study finds**

ANN ARBOR, Mich. — A compound derived from broccoli could help prevent or treat breast cancer by targeting cancer stem cells -- the small number of cells that fuel a tumor's growth -- according to a new study from researchers at the University of Michigan Comprehensive Cancer Center.

The study tested sulforaphane, a component of broccoli and broccoli sprouts, in both mice and cell cultures. Researchers found sulforaphane targeted and killed the cancer stem cells and prevented new tumors from growing.

“Sulforaphane has been studied previously for its effects on cancer, but this study shows that its benefit is in inhibiting the breast cancer stem cells. This new insight suggests the potential of sulforaphane or broccoli extract to prevent or treat cancer by targeting the critical cancer stem cells,” says study author Duxin Sun, Ph.D., associate professor of pharmaceutical sciences at the U-M College of Pharmacy and a researcher with the U-M Comprehensive Cancer Center.

Results of the study appear in the May 1 issue of *Clinical Cancer Research*.

Current chemotherapies do not work against cancer stem cells, which is why cancer recurs and spreads. Researchers believe that eliminating the cancer stem cells is key to controlling cancer.

In the current study, researchers took mice with breast cancer and injected varying concentrations of sulforaphane from the broccoli extract. Researchers then used several established methods to assess the number of cancer stem cells in the tumors. These measures showed a marked decrease in the cancer stem cell population after treatment with sulforaphane, with little effect on the normal cells. Further, cancer cells from mice treated with sulforaphane were unable to generate new tumors. The researchers then tested sulforaphane on human breast cancer cell cultures in the lab, finding similar decreases in the cancer stem cells.

“This research suggests a potential new treatment that could be combined with other compounds to target breast cancer stem cells. Developing treatments that effectively target the cancer stem cell population is essential for improving outcomes,” says study author Max S. Wicha, M.D., Distinguished Professor of Oncology and director of the U-M Comprehensive Cancer Center.

The concentrations of sulforaphane used in the study were higher than what can be achieved by eating broccoli or broccoli sprouts. Prior research suggests the concentrations needed to impact cancer can be absorbed by the body from the broccoli extract, but side effects are not known. While the extract is available in capsule form as a supplement, concentrations are unregulated and will vary.

This work has not been tested in patients, and patients are not encouraged to add sulforaphane supplements to their diet at this time.

Researchers are currently developing a method to extract and preserve sulforaphane and will be developing a clinical trial to test sulforaphane as a prevention and treatment for breast cancer. No clinical trial is currently available.

Breast cancer statistics: 194,280 Americans will be diagnosed with breast cancer this year and 40,610 will die from the disease, according to the American Cancer Society

Additional authors: Yanyan Li, Tao Zhang, Hasan Korkaya, Suling Liu, Hsiu-Fang Lee, Bryan Newman, Yanke Yu, Shawn G. Clouthier and Steven J. Schwartz

Funding: National Institutes of Health, National Cancer Institute

**Public release date: 3-May-2010**

## **Purple periwinkles battle inflammatory diseases**

### **Natural supplement boasts excellent safety**

A widely and safely used plant extract acts as a novel anti-inflammatory agent that may one day be used for the treatment of chronic obstructive pulmonary disease, or COPD, as well as other inflammatory conditions. There is an urgent need for new therapies for the treatment of chronic inflammatory diseases, such as COPD, otitis media (ear infection), and atherosclerosis (chronic inflammation in the walls of arteries), because the most effective and commonly used agents – steroids – often cause serious side effects, such as liver damage, which prevent long-term use.

**In a study published today in the Proceedings of the National Academy of Sciences, researchers at the University of Rochester Medical Center were the first to find that vinpocetine, a natural product derived from the periwinkle plant, acts as a potent anti-inflammatory agent when tested in a mouse model of lung inflammation, as well as several other types of human cells. Results of the study show that vinpocetine greatly reduces inflammation, and, unlike steroids, does not cause severe side effects.**

**"What is extremely exciting and promising about these findings is vinpocetine's excellent safety profile,"** said Chen Yan, Ph.D., associate professor within the Aab Cardiovascular Research Institute at the Medical Center and a senior author of the study. "Previously, most drugs tested in this area have failed, not because of a lack of efficacy, but because of safety issues. We're very encouraged by these results and believe vinpocetine has great potential for the treatment of COPD and other inflammatory diseases."

Vinpocetine is a well-known natural product that was originally discovered nearly 30 years ago and is currently used as a dietary supplement for the prevention and treatment of cognitive disorders, such as stroke and memory loss, in Europe, Japan and China. **The therapy has no evidence of toxicity or noticeable side effects in human patients. Scientists at the University of Rochester hope to reposition this compound as an anti-inflammatory agent for the treatment of COPD, and potentially other inflammatory conditions, such as asthma, otitis media, rheumatoid arthritis, atherosclerosis and psoriasis in the future.**

While steroids successfully combat inflammation, patients often pay a high price when it comes to side effects. Steroids can cause liver damage, and can also suppress the immune system, increasing the likelihood of infections. With such a high risk profile, steroids are usually only used for a short period of time, which is problematic when treating chronic diseases.

"In managing chronic conditions such as COPD, it is crucial to have a therapy that can be used safely over the long term," said Jian-Dong Li, M.D., Ph.D., professor in the Department of Microbiology and Immunology at the University of Rochester Medical Center and a senior author of the study. "There is a great need for a drug like vinpocetine, because patients currently have no good options when it comes to long-term care."

Vinpocetine decreases inflammation by targeting the activity of a specific enzyme, known as IKK. IKK is responsible for regulating inflammation, and does so through the activation of a key protein, nuclear-factor kappaB (NF-κB). By directly inhibiting IKK, vinpocetine is able to switch off NF-κB, which normally produces pro-inflammatory molecules that cause inflammation. Halting the activity of NF-κB ultimately reduces inflammation.

"Inflammation is a hallmark of a wide range of human diseases, so there is great potential for vinpocetine to be used for several indications," said Bradford C. Berk, M.D., Ph.D., CEO of the University of Rochester

Medical Center and co-author of the study. "Given vinpocetine's efficacy and solid safety profile, we believe there is great potential to bring this drug to market."

Repositioning a therapy – taking a known compound that has been used safely in humans and testing it for a new application – can be an effective way to bring new therapies to market more quickly than starting the discovery process from scratch.

Inflammatory diseases are a major cause of illness worldwide. For example, chronic obstructive pulmonary disease is the fourth leading cause of death in the United States. In people with COPD, airflow is blocked due to chronic bronchitis or emphysema, making it increasingly difficult to breathe. Most COPD is caused by long-term smoking, although genetics may play a role as well. Approximately 13.5 million people in the United States are diagnosed with COPD each year, and in 2004 the annual cost of the disease was \$37.2 billion.

**Public release date: 3-May-2010**

## **Flaxseed-fed chickens shed light on ovarian cancer**

the race to find answers about ovarian cancer, researchers now have something to cluck about. For five years, University of Illinois researchers have been using the chicken as a model to study this deadly disease and have recently discovered that a diet enriched with flaxseed decreases severity of ovarian cancer and increases survival in hens.

Flaxseed is the richest plant source of alpha-linolenic acid, one type of omega-3 fatty acid. Several studies have already shown that flaxseed inhibits the formation of colon, breast, skin and lung tumors.

For these reasons, it was logical to study how omega-3 fatty acids affect ovarian cancer as there continues to be no effective treatment at this time, said Janice Bahr, a professor emerita in the U of I Department of Animal Sciences and one of the nation's leading poultry researchers.

According to Bahr, 25,000 women are diagnosed with ovarian cancer each year and 15,000 die. The incidences of death in other cancers have dropped recently, but ovarian cancer death rates have remained the same.

"The chicken is the only animal that spontaneously develops ovarian cancer on the surface of the ovaries like humans," Bahr said. "In this study, we evaluated how a flaxseed-enriched diet affected 2-year-old laying hens (hens that have ovulated as many times as a woman entering menopause)."

The results showed that hens fed a flaxseed-enriched diet for one year experienced a significant reduction in late-stage ovarian tumors.

"Most women diagnosed with ovarian cancer have a very poor prognosis because they are not diagnosed until stage 3 or 4 when the cancer has metastasized and spread to other parts of the body," Bahr said.

Hens fed the control diet had significantly more late-stage tumors that presented with fluid and metastases as compared to the hens fed a flaxseed diet. Though hens fed the flaxseed diet did not have a decreased incidence of ovarian cancer, they did experience fewer late-stage tumors and higher survival rates.

"In hens fed flaxseed, we found that more tumors were confined to the ovary and they had less metastatic spread," she said. "This is an important finding as the metastases that accompany late-stage ovarian cancer are the main cause of death from this disease. If the cancer is found at an early stage, when the tumor is still confined to the ovary, women have a much better prognosis and more treatment options."

In addition, researchers found that hens fed the flaxseed diet had better weight control which is important because obesity increases cancer risk. Both diets had equal caloric content, however the flaxseed-fed hens

weighed less at six months than the control-fed hens. But at 12 months, the flaxseed-fed hens were the same weight and the control-fed hens had lost significant weight, which was indicative of their failing health. Ultimately, the flaxseed-enriched diet helped the birds maintain a healthy weight and resulted in less sickness and death.

"Through this research, we have proven that flaxseed supplementation for one year is able to reduce the severity of ovarian cancer in hens," she said. "These findings may provide the basis for a clinical trial that evaluates the efficacy of flaxseed as a chemopreventive of ovarian cancer in women."

The cause of ovarian cancer remains unknown, but one of the most prevalent theories is the "incessant ovulation hypothesis," proposed by MF Fathalla in 1971. He suggests that inflammation associated with continuous ovulation leaves ovarian surface epithelial cells susceptible to malignant transformation. The observation that egg-laying domestic hens frequently develop ovarian cancer supports this hypothesis.

Bahr believes this hypothesis is valid and is currently in the middle of a four-year study to determine if long-term dietary intervention with flaxseed will reduce the incidence of ovarian cancer development. The hens started the flaxseed-supplemented diet at 22 weeks of age, as soon as they commenced egg laying and before damage from ovulation had accumulated.

This research was published in *Gynecologic Oncology* and funded by a National Institutes of Health (NIH) National Center for Complementary and Alternative Medicine Grant, an American Institute for Cancer Research Grant, and an NIH Training Grant.

Researchers included principal investigator Dale Buchanan Hales of Southern Illinois University. Co-principal investigators include Janice Bahr of the University of Illinois at Urbana-Champaign; Kristine Ansenberger and Cassandra Richards of the University of Illinois at Chicago; and Yan Zhuge, Judith Luborsky and Animesh Barua of Rush University Medical Center.

**Public release date: 5-May-2010**

## **Dietary protein may reduce hip fractures in the elderly**

Hebrew SeniorLife Institute for Aging Research recommends more protein in diet to prevent fractures  
BOSTON—Seniors who consume a higher level of dietary protein are less likely to suffer hip fractures than seniors whose daily dietary protein intake is less, according to a new study by the Institute for Aging Research of Hebrew SeniorLife in Boston, an affiliate of Harvard Medical School.

**The study, which examined the daily protein intake of 946 seniors from the Framingham Osteoporosis Study, found that individuals who were in the lowest 25 percent of dietary protein intake had approximately 50 percent more hip fractures than those who consumed greater amounts of dietary protein (all within normal intakes). Those who suffered hip fractures consumed less than the 46 grams of dietary protein per day recommended for adults.**

"Study participants who consumed higher amounts of protein in their diet were significantly less likely to suffer a hip fracture," says senior study author Marian T. Hannan, D.Sc., M.P.H., co-director of the Musculoskeletal Research Program at the Institute for Aging Research.

The study, which was funded in part by the National Institute of Arthritis and Musculoskeletal and Skin Diseases, will be published this week in the online-first edition of *Osteoporosis International*. It builds on previous studies that included mostly women and reported a relationship between greater dietary protein intake and decreased risk of hip fracture.

While other studies have shown that dietary protein intake is also linked with higher bone mineral density, Dr. Hannan says dietary protein may further protect elderly people against hip fracture by building stronger muscles in the legs. Most fractures occur after a fall, which may be caused by less muscle mass and

decreased strength in the lower extremities.

Dr. Hannan, an associate professor of medicine at Harvard Medical School, recommends that older women consume at least 46 grams of protein per day, and that older men consume at least 56 grams of protein daily. This can come from both animal sources (meat, poultry, fish, eggs, milk, cheese and yogurt) and plants (legumes, grains, nuts, seeds and vegetables). The study did not examine the type of protein consumed.

In addition to increased dietary protein, Dr. Hannan says regular exercise to build stronger muscles and better balance, as well as other falls prevention strategies, such as reducing hazards in the home, can help protect seniors against falls and hip fractures.

More than 25 million Americans over the age of 50 have either osteoporosis, a disease in which bones become fragile and more likely to break, or osteopenia, a condition in which bone mineral density is lower than normal, but not low enough to be considered osteoporosis. More than 95 percent of hip fractures in people over the age of 65 are caused by falls and can lead to severe health problems, including decreased quality of life and premature death.

Scientists at the Institute for Aging Research conduct rigorous medical and social studies, leading the way in developing strategies for maximizing individuals' strength, vigor and physical well-being, as well as their cognitive and functional abilities in late life.

**Public release date: 3-May-2010**

## **Drug maker AstraZeneca to pay \$520 million**

WASHINGTON – The federal government on Tuesday reached a \$520 million settlement with pharmaceutical manufacturer AstraZeneca, resolving allegations of illegal marketing of the company's antipsychotic drug Seroquel.

At a news conference, Attorney General Eric Holder and Health and Human Services Secretary Kathleen Sebelius made the case a centerpiece of the federal government's crackdown on health care fraud.

AstraZeneca allegedly marketed Seroquel for off-label uses — those not approved by federal drug regulators — including insomnia and psychiatric conditions other than schizophrenia and bipolar disorder.

U.S. Attorney Michael Levy of Philadelphia, where the settlement was filed, said that the company had "turned patients into guinea pigs in an unsupervised drug test."

AstraZeneca, which has its U.S. headquarters in Wilmington, Del., faces more than 25,000 product liability lawsuits over Seroquel, with most alleging that the drug caused diabetes. Seroquel has been on the market since 1997.

The government said AstraZeneca paid kickbacks to doctors recruited to serve as authors of articles by Astra Zeneca and the company's agents about the unapproved uses of Seroquel.

The company also made payments to doctors to travel to resort locations to advise AstraZeneca about marketing messages for unapproved uses of the drug, the government stated.

AstraZeneca denied the allegations leveled by the government in the civil case settled Tuesday, saying it wanted to avoid the delay, uncertainty and expense of a protracted legal battle.

"The company is committed to meeting the expectations and obligations of a leading biopharmaceutical company, while continuing to provide valuable medicines to millions of patients," Glenn Engelmann, the company's U.S. general counsel, said in a statement.

Partly because of the off-label use of Seroquel, the drug brought in \$4.9 billion to AstraZeneca in 2009, making it the company's second-best seller.

The Food and Drug Administration approves drugs for specific uses, but doctors are free to prescribe as they see fit. Such off-label use is a gray area and a long-running controversy when it comes to drug regulation.

Drug companies are supposed to market medications only for uses that the FDA has approved. But salespeople can find lots of ways to get around the restriction. For example, they can let doctors know about research indicating that a given drug shows promise to treat a condition that the FDA hasn't yet cleared it for.

Doctors are eager to get the latest treatments for their patients, especially if other physicians are also prescribing the medication.

Shares of AstraZeneca fell 2 percent, or \$1.05, to \$43.86 in afternoon trading.

**Public release date: 3-May-2010**

## **Flouridation may not do much for cavities**

When it comes to fluoridating drinking water, Ontario and Quebec couldn't be further apart. Ontario has the country's highest rate of adding the tooth-enamel-strengthening chemical into municipal supplies, while Quebec has one of the lowest, with practically no one drinking fluoridated water.

But surprisingly, the two provinces have very little difference in tooth-decay rates, a finding that is likely to intensify the ongoing controversy over the practice of adding fluoride to water as a public health measure.

Quebeckers have more cavities than people in Ontario, but the difference is slight. Among children 6 to 19, considered the most decay-prone part of the population, the rate in Ontario was lower by less than half a cavity per child.

In the 6-11 age group, Ontario kids have 3.5 per cent fewer cavities than those in Quebec: 1.7 cavities compared to 1.76 in Quebec.

In the 12-19 age group, Ontario youths have 15.8 per cent fewer cavities than those in Quebec: 2.35 cavities compared to 2.79.

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Details of the cavity rates in the two provinces have been compiled by Statistics Canada in a study it conducted recently into the health status of Canadians. Experts peered into the mouths of more than 5,000 Canadians from 2007 to 2009, tallying the number of cavities and teeth with fillings, to try to get an idea of the state of oral health of the nation.

After a request from The Globe and Mail for a breakdown of the cavity rates by province, Statistics Canada tabulated the figures for Ontario and Quebec, where it said it had a sufficient number of people to be a representative sample.

Statscan said it couldn't compile meaningful data for British Columbia and Alberta, which are in a similar situation. British Columbia has practically no one drinking fluoridated water, while nearly three-quarters of Albertans rely on municipal supplies where the chemical is added.

The paper sought the information to see what light it would shed on the effectiveness of fluoridation, which has been touted by the U.S. Centers for Disease Control and Prevention as one of the top 10 great public health achievements of the 20th century, and is endorsed by all dental associations in the country and by Health Canada.

But the results showed that if fluoridation is the only major difference between the two provinces, the chemical is preventing fewer than half a cavity per child in Ontario.

Health Canada down played the significance of the findings.

“While accurate,” the data on the children are “an incomplete picture of the tooth decay situation.... [and] cannot be used to form conclusions regarding the efficacy of fluoride use in water,” Health Canada said.

The federal department said firm conclusions can't be drawn from the Statscan survey because it didn't collect assessments on individual intakes of the chemical. To make a proper assessment, Health Canada said it would need detailed information on whether people in the two provinces differ in their intake fluoride supplements, drink tap water or bottled water, and use fluoridated toothpaste.

But fluoridation is one major and obvious difference between the provinces. More than three-quarters of Ontario residents live in areas where municipal water supplies contain the chemical. In Quebec, 94 per cent have water free of the additive, according to figures

published by Health Canada in 2007.

Since then, Quebec City has voted to stop fluoridating, indicating that the difference between the two provinces is currently even more pronounced.

Some critics of fluoridation say the survey does raise questions about the practice.

“Fluoridation is no longer effective,” contends Hardy Limeback, head of the preventive dentistry program at the University of Toronto, who says adding the chemical to water is “more harmful than beneficial.”

Although fluoridation is touted as an unalloyed benefit by public health agencies, which estimate it cuts cavity rates by 20 per cent to 40 per cent, many community groups have sprung up across Canada lobbying to stop the practice, which is subject to repeal by local referendums. Some health professionals are worried fluoridation may have under-appreciated risks.

While fluoride toughens the outside of teeth to make them more resistant to bacteria-causing decay, a number of medical journal studies have linked exposure to altered thyroid function, and to reduced IQ levels in children, although the intellectual impairments were found at levels of the chemical in water well above those used for municipal supplies.

The most worrisome study, by Harvard researchers, appeared in 2006 in the journal *Cancer Causes and Control* and found that boys aged 7 exposed to high levels of fluoridated water were about four times more likely to develop childhood osteosarcoma. It's a rare bone cancer that felled Canadian icon Terry Fox and almost always leads to amputations.

There has also been a worldwide reduction in cavity rates, regardless of whether countries use the chemical, suggesting factors other than adding it to water supplies are at work.

One theory is that most people are already getting adequate exposure to fluoride through toothpastes, so the amounts in water aren't making much difference in tooth decay rates.

“The parallel reduction in caries [cavities] incidents in countries with a lot of fluoridation and countries with not much fluoridation is quite dramatic,” says Warren Bell, former head of the Canadian Association of Physicians for the Environment, a group that questions the practice.

Dr. Limeback said factors that might be preventing caries include increased exposure to vitamin D, better oral hygiene, less sugar consumption, and even antibiotics.

When fluoridation started 60 years ago, doctors thought swallowing the chemical was beneficial by strengthening teeth from the inside out. Dr. Limeback said more recent

research shows that if there is a benefit, it is from the topical application of fluoride to the surface of teeth, which suggests that brushing with a toothpaste is more effective than drinking water containing the chemical.

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**These reports are done with the appreciation of all the Doctors, Scientist, and other Medical Researchers who sacrificed their time and effort. In order to give people the ability to empower themselves. Without the base aspirations for fame, or fortune.  
Just honorable people, doing honorable things.**