



The Vitamin & Herb Stores

**Human Technology Research Synopsis**

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**Public release date: 11-Nov-2009**

**Workplace BPA exposure increases risk of male sexual dysfunction**

First human study to measure effects of BPA on male reproductive system

November 11, 2009 (Oakland, Calif.) – High levels of workplace exposure to Bisphenol-A may increase the risk of reduced sexual function in men, according to a Kaiser Permanente study appearing in the journal Human Reproduction, published by Oxford Journals. [1]

The five-year study examined 634 workers in factories in China, comparing workers in BPA manufacturing facilities with a control group of workers in factories where no BPA was present. The study found that the workers in the BPA facilities had quadruple the risk of erectile dysfunction, and seven times more risk of ejaculation difficulty.

This is the first research study to look at the effect of BPA on the male reproductive system in humans. Previous animal studies have shown that BPA has a detrimental effect on male reproductive system in mice and rats.

Funded by the U.S. National Institute of Occupational Safety and Health, this study adds to the body of evidence questioning the safety of BPA, a chemical made in the production of polycarbonated plastics and epoxy resins found in baby bottles, plastic containers, the lining of cans used for food and beverages, and in dental sealants.

The BPA levels experienced by the exposed factory workers in the study were 50 times higher than what the average American male faces in the United States, the researchers said.

"Because the BPA levels in this study were very high, more research needs to be done to see how low a level of BPA exposure may have effects on our reproductive system," said the study's lead author, De-Kun Li, MD, Ph.D., a reproductive and perinatal epidemiologist at Kaiser Permanente's Division of Research in Oakland, Calif. "This study raises the question: Is there a safe level for BPA exposure, and what is that level? More studies like this, which examine the effect of BPA on humans, are critically needed to help establish prevention strategies and regulatory policies."

The researchers explained that BPA is believed by some to be a highly suspect human endocrine disrupter, likely affecting both male and female reproductive systems. This first epidemiological study of BPA effects on the male reproductive system provides evidence that has been lacking as the U.S. Food and Drug Administration, and various U.S. government panels have explored this controversial topic.

This study is the first of series of studies that examine the BPA effect in humans and are to be published by Dr. Li and his colleagues.

The study finding, Dr. Li also points out, may have implications of adverse BPA effects beyond male sexual dysfunction. Male sexual dysfunction could be a more sensitive early indicator for adverse BPA effects than other disease endpoints that are more difficult to study, such as cancer or metabolic diseases.

For this study, researchers compared 230 workers exposed to high levels of BPA in their jobs as packagers, technical supervisors, laboratory technicians and maintenance workers in one BPA manufacturing facility and three facilities using BPA to manufacture epoxy resin, in several regions near Shanghai, to a control group of 404 workers in the same city from factories where no BPA exposure in the workplace was recorded. The factories with no BPA exposure produced construction materials, water supplies, machinery,

garments, textiles, and electronics. The workers from the two groups were matched by age, education, gender, and employment history.

Researchers gauged BPA levels by conducting spot air sampling, personal air sample monitoring and walk-through evaluations, by reviewing factory records and interviewing factory leaders and workers about personal hygiene habits, use of protective equipment, and exposures to other chemicals. A subset of workers also provided urine samples for assaying urine BPA level to confirm the higher BPA exposure level among the workers with occupational BPA exposure.

Researchers measured sexual function based on in-person interviews using a standard male sexual function inventory that measures four categories of male sexual function including erectile function, ejaculation capability, sexual desire, and overall satisfaction with sex life.

After adjusting for age, education, marital status, current smoking status, a history of chronic diseases and exposure to other chemicals, and employment history, the researchers found the BPA-exposed workers had a significantly higher risk of sexual dysfunction compared to the unexposed workers.

The BPA-exposed workers had a nearly four-fold increased risk of reduced sexual desire and overall satisfaction with their sex life, greater than four-fold increased risk of erection difficulty, and more than seven-fold increased risk of ejaculation difficulty.

A dose-response relationship was observed with an increasing level of cumulative BPA exposure associated with a higher risk of sexual dysfunction. Furthermore, compared to the unexposed workers, BPA-exposed workers reported significantly higher frequencies of reduced sexual function within one year of employment in the BPA-exposed factories.

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## **Faulty body clock may make kids bipolar**

Malfunctioning circadian clock genes may be responsible for bipolar disorder in children. Researchers writing in the open access journal BMC Psychiatry found four versions of the regulatory gene RORB that were associated with pediatric bipolar disorder.

Alexander Niculescu from Indiana University School of Medicine, Indianapolis, US, worked with a team of researchers at Harvard, UC San Diego, Massachusetts General Hospital and SUNY Upstate Medical University to study the RORA and RORB genes of 152 children with the condition and 140 control children. They found four alterations to the RORB gene that were positively associated with being bipolar. Niculescu said, "Our findings suggest that clock genes in general and RORB in particular may be important candidates for further investigation in the search for the molecular basis of bipolar disorder".

RORB is mainly expressed in the eye, pineal gland and brain. Its expression is known to change as a function of circadian rhythm in some tissues, and mice without the gene exhibit circadian rhythm abnormalities. According to Niculescu, "Bipolar disorder is often characterized by circadian rhythm abnormalities, and this is particularly true among pediatric bipolar patients. Decreased sleep has even been noted as one of the earliest symptoms discriminating children with bipolar disorder from those with attention deficit hyperactivity disorder (ADHD). It will be necessary to verify our association results in other independent samples, and to continue to study the relationship between RORB, other clock genes, and bipolar disorder".

Pediatric bipolar disorder is a controversial diagnosis characterized by alternating bouts of depression and mania in children, although it does not affect all young people in the same way and the duration and severity of the disorder can vary enormously.

**Public release date: 11-Nov-2009**

## **New evidence that dark chocolate helps ease emotional stress**

The "chocolate cure" for emotional stress is getting new support from a clinical trial published online in ACS' Journal of Proteome Research. It found that eating about an ounce and a half of dark chocolate a day for two weeks reduced levels of stress hormones in the bodies of people feeling highly stressed. Everyone's favorite treat also partially corrected other stress-related biochemical imbalances.

Sunil Kochhar and colleagues note growing scientific evidence that antioxidants and other beneficial substances in dark chocolate may reduce risk factors for heart disease and other physical conditions. Studies also suggest that chocolate may ease emotional stress. Until now, however, there was little evidence from research in humans on exactly how chocolate might have those stress-busting effects.

In the study, scientists identified reductions in stress hormones and other stress-related biochemical changes in volunteers who rated themselves as highly stressed and ate dark chocolate for two weeks. "The study provides strong evidence that a daily consumption of 40 grams [1.4 ounces] during a period of 2 weeks is sufficient to modify the metabolism of healthy human volunteers," the scientists say.

**Public release date: 12-Nov-2009**

## **Despite some benefit, drug ads can be harmful to your health**

As Congress revisits drug ad regulation, researchers make recommendations for minimizing harm and maximizing benefits of drug ads

WASHINGTON, D.C. —While the debate over prescription drug advertising persists, a new study released online in the American Journal of Public Health offers guidelines for improving drug ads in order to minimize potential harm and maximize benefits. The study reveals that while there are some benefits from prescription drug direct-to-consumer advertising (DTCA), there are significant risks that are magnified by the prominence of DTCA.

"American television viewers see as many as 16 hours of prescription drug advertisements each year, and the reality is that these ads are not doing a good job of helping consumers make better decisions about their health," said Dominick L. Frosch, Ph.D., assistant professor of medicine at the University of California, Los Angeles and lead author of the study. "If the pharmaceutical industry isn't willing to change the ads to make them more useful to consumers, Congress should consider passing legislation that will regulate the ads to improve the information provided in order to help patients make more informed choices."

Several members of Congress, including Rep. Henry Waxman, D-Calif., are calling for changes to FDA regulations of DTCA. Advocates for prescription drug ads claim that these ads educate consumers, improve the quality of care and contribute to better patient adherence. Opponents argue that they lead to inappropriate prescribing and portray nonmedical problems as treatable medical illnesses.

In a review of the evidence for and against DTCA, Frosch and his colleagues confirm that there are some benefits to drug ads, but they are limited and can be improved. The evidence clearly shows that there is significant risk and potential harm associated with the current format of prescription drug ads. The majority of ads fail to provide enough information to allow consumers to clearly identify whether the advertised drug is right for them. The over dramatization and emotional portrayal of a drug's benefits can also be misleading to consumers, while the message about its risks are often diluted by contradicting imagery.

In light of these findings, the authors of the study propose new guidelines to improve prescription drug ads so that they better serve the health choices of consumers:

- Ads should help consumers identify whether treatment is right for them by explaining how prevalent the relevant conditions are. They should also describe who may be at risk for conditions that don't present obvious symptoms. For conditions that do present obvious symptoms, they should describe what those symptoms are.

- Ads should provide accurate and specific information about the potential benefits of advertised drugs, and should help consumers realistically judge those benefits by providing precise quantitative information. The ads should state how this drug compared to placebo or other available treatments, including generic drugs.

- Ads should provide specific quantitative information about the potential risks associated with drugs without other visual or audio distractions, so consumers can better understand the risks associated with the prescription drugs.

**Public release date: 12-Nov-2009**

## **Consumption of certain fish during pregnancy associated with poorer cognitive performance (Mercury)**

Children who eat fish more than 3 times per week show a worse performance in the general cognitive, executive and perceptual-manipulative areas. Those with higher levels of exposure to mercury show a generalised delay in cognitive, memory and verbal areas. Mercury is a contaminant found especially in oily fish and canned fish and to a lesser extent in white fish.

This conclusion emerges from research conducted at the University of Granada, which warns of the need to assess children's health risk according to fish consumption, distinguishing between varieties or species they consume, especially in those areas where fish is part of the staple diet of the population.

The work entitled "Children's exposure to environmental contaminants in Granada and potential effects on health" was carried out by Carmen Freire Warden, from the Department of Radiology and Physical Medicine of the UGR, and led by professors Nicolás Olea and Marieta Fernández Serrano Cabrera.

For this study, scientists analyzed the exposure to environmental contaminants through water, air and diet, in a sample of 220 children in the geographic health care area of San Cecilio University Hospital in Granada. This study has described for the first time the extent of childhood exposure to environmental pollutants of special concern, such as trihalomethanes, NO<sub>2</sub>, polycyclic aromatic hydrocarbons and mercury. Following the hypotheses posed, this research assessed the combination of exposure to air pollution, on the one hand, and mercury, on the other, with child neurodevelopment at 4 years of age.

### Mercury concentrations

Thus, total mercury concentrations found in the hair of 4 year-old-children from Granada were between 0.04 and 6.67 g / g. Concentrations were higher than those found in other paediatric populations with a lower consumption of fish, but lower than levels found in high consuming areas.

Important factors in this exposure were the place of residence, maternal age, passive exposure to tobacco smoke and consumption of oily fish. The results suggest that fish consumption is the main source of exposure to mercury in the sample population studied.

The work carried out at the University of Granada also suggests that in Granada, children's health risk from exposure to trihalomethanes via drinking water can be considered to be significantly lower than in other areas of the country, and that air pollutant NO<sub>2</sub> concentrations (measured in the external environment of the study area) were also lower than those described in other Spanish cities. Traffic of motor vehicles is the

main source of emission of these pollutants in the study area.

Moreover, the research also revealed that there is a direct relationship between children's passive exposure to tobacco smoke and the use of gas stoves inside houses, and the presence of 1-hydroxypyrene, an indicator of exposure to damaging health air pollutants.

Researchers warn that although environmental exposure levels found in children are low enough not to cause any obvious concern, they could have an impact on child development in the long-term, only appearing as symptoms many years after first exposure. Consequently, they explain, "whatever the extent of involvement of environmental exposures in the etiology of the disease, the simple fact of acting very early in life opens the door to a transcendental field in public health: the possibility of applying early prevention measures to minimize problems."

**Public release date: 15-Nov-2009**

## **Heart and bone damage from low vitamin D tied to declines in sex hormones**

### **Effects of vitamin D deficiency amplified by shortage of estrogen**

Researchers at Johns Hopkins are reporting what is believed to be the first conclusive evidence in men that the long-term ill effects of vitamin D deficiency are amplified by lower levels of the key sex hormone estrogen, but not testosterone.

In a national study in 1010 men, to be presented Nov. 15 at the American Heart Association's (AHA) annual Scientific Sessions in Orlando, researchers say the new findings build on previous studies showing that deficiencies in vitamin D and low levels of estrogen, found naturally in differing amounts in men and women, were independent risk factors for hardened and narrowed arteries and weakened bones. Vitamin D is an essential part of keeping the body healthy, and can be obtained from fortified foods, such as milk and cereals, and by exposure to sunlight.

"Our results confirm a long-suspected link and suggest that vitamin D supplements, which are already prescribed to treat osteoporosis, may also be useful in preventing heart disease," says lead study investigator and cardiologist Erin Michos, M.D., M.H.S.

"All three steroid hormones – vitamin D, estrogen and testosterone – are produced from cholesterol, whose blood levels are known to influence arterial and bone health," says Michos, an assistant professor at the Johns Hopkins University School of Medicine and its Heart and Vascular Institute. "Our study gives us a much better understanding of how the three work in concert to affect cardiovascular and bone health."

Michos says the overall biological relationship continues to puzzle scientists because studies of the long-term effects of adding estrogen in the form of hormone replacement therapy in women failed to show fewer deaths from heart disease. Indeed, results showed that in some women, an actual increase in heart disease and stroke rates occurred, although, bone fractures declined.

The Hopkins team's latest data were provided by analyzing blood samples from a subset of men participating in a study on cancer. That study was part of a larger, ongoing national health survey involving both men and women and was designed to compare the risk of diseases between those with the lowest blood levels of vitamin D to those with higher amounts. An unhealthy deficiency, experts say, is considered blood levels of 20 nanograms per milliliter or lower.

The men in the study had their hormone levels measured for both chemical forms of testosterone and estrogen found in blood, when each is either unattached or circulating freely, and when each is attached to a separate protein, known as sex hormone binding globulin, or SHBG for short.

Initial results showed no link between vitamin D deficiency and depressed blood levels of either hormone. And despite finding a harmful relationship between depressed testosterone levels and rates of heart disease, stroke, and high blood pressure, as well as osteopenia in men, researchers found that it was independent of deficiencies in vitamin D.

However, when researchers compared ratios of estrogen to SHBG levels, they found that rates of both diseases, especially osteopenia, the early stage of osteoporosis, were higher when both estrogen and vitamin D levels were depressed.

For every single unit decrease in ratios of estrogen to SHBG (both in nanomoles per liter), men low in vitamin D showed an 89 percent increase in osteopenia, but men with sufficient vitamin D levels had a less worrisome 64 percent jump.

Using the same measure of estrogen levels, men low in vitamin D were also at heightened risk of cardiovascular diseases, at 12 percent, compared to men with adequate levels of the vitamin, at 1 percent, numbers that researchers say are still statistically significant.

"These results reinforce the message of how important proper quantities of vitamin D are to good bone health, and that a man's risk of developing osteoporosis and heart disease is heavily weighted on the complex and combined interaction of how any such vitamin deficits interact with both their sex hormones, in particular, estrogen," Michos says.

Michos and her team next plan to analyze blood samples from women to see if the same results from men hold true.

Michos recommends that men and women boost their vitamin D levels by eating diets rich in fatty fish, such as cod, sardines and mackerel, consuming fortified dairy products, taking vitamin supplements, and in warmer weather briefly exposing skin to the sun's vitamin-D producing ultraviolet light.

She points out that clinical trials are under way to determine whether or not vitamin D supplements can prevent incidents of or deaths from heart attack, stroke and other signs of cardiovascular disease.

The U.S. Institute of Medicine suggests that an adequate daily intake of vitamin D is between 200 and 400 international units, but Michos feels this is inadequate to achieve optimal nutrient blood levels (above 30 nanograms per milliliter). Previous results from the same nationwide survey showed that 41 percent of men and 53 percent of women are technically deficient in the nutrient, with vitamin D levels below 28 nanograms per milliliter.

**Public release date: 15-Nov-2009**

## **Penn Study Finds that Antioxidant Found in Vegetables has Implications for Treating Cystic Fibrosis**

Thiocyanate Reduces Damage by Inflammatory Molecules in Lung, Nerve, Pancreas, and Vessel-Lining Cells

PHILADELPHIA – Scientists at the University of Pennsylvania School of Medicine discovered that a dietary antioxidant found in such vegetables as broccoli and cauliflower protects cells from damage caused by chemicals generated during the body's inflammatory response to infection and injury. The finding has

implications for such inflammation-based disorders as cystic fibrosis (CF), diabetes, heart disease, and neurodegeneration.

Through cell-culture studies and a synthesis of known antioxidant biochemistry, Zhe Lu, MD, PhD, Professor of Physiology, Yanping Xu, MD, PhD, Senior Research Investigator, and Szilvia Szép, PhD, postdoctoral researcher, showed that the antioxidant thiocyanate normally existing in the body protects lung cells from injuries caused by accumulations of hydrogen peroxide and hypochlorite, the active ingredient in household bleach. These potentially harmful chemicals are made by the body as a reaction to infection and injury. In addition, thiocyanate also protects cells from hypochlorite produced in reactions involving MPO, an enzyme released from germ-fighting white blood cells during inflammation. They published their finding this week in the Proceedings of the National Academy of Sciences. Lu is also an Investigator of the Howard Hughes Medical Institute.

“Dr. Lu’s work throws new light on how the genetic defect underlying CF leads to the lung illnesses that are the leading cause of death,” said Bert Shapiro, Ph.D., who oversees membrane structure grants at the National Institutes of Health’s National Institute of General Medical Sciences (NIGMS). “His team’s findings suggest that the lungs of people with the disease are more susceptible to the damaging effects of cellular oxidants. While the idea is tantalizing and creative, further testing is needed to confirm it.”

The research team demonstrated that in three additional cell types used to extend their ideas to other inflammation-related conditions – cardiovascular disease, neurodegeneration, and diabetes – thiocyanate at blood concentrations of at least 100 micromolar (micromoles per liter) greatly reduces the toxicity of MPO in cells, including those lining blood vessels. Humans naturally derive thiocyanate from some vegetables and blood levels of thiocyanate in the general population vary from 10 to 140 micromolar.

This comparison raises the possibility, the authors point out, that without an adequate dietary supply of thiocyanate, hypochlorite produced by the body during inflammation would cause additional collateral damage to cells, thus worsening inflammatory diseases, and predisposing humans to diseases linked to MPO activity, including atherosclerosis.

#### Connection to CF

For over a decade Lu and colleagues have been exploring the inner workings of ion channels and how this knowledge relates to the pathology of such diseases as CF. The CF disease originates from mutations in the CF transmembrane conductance regulator (CFTR) protein, an ion channel protein in the cell membrane commonly thought to transport mainly chloride ions. It has, however, remained a mystery why a defect in a chloride-transporting channel leads to cystic fibrosis, a disease with exaggerated inflammation in both the lungs and the digestive system.

Lung injuries inflicted by excessive inflammation and recurring infection cause about ninety percent of CF patients’ symptoms and mortality. Although known as a chloride channel, CFTR also conducts thiocyanate ions, important because, in several ways, they can limit potentially harmful accumulations of hydrogen peroxide and hypochlorite, chemicals produced by the body to fight germs.

In CF patients, there is also a high incidence of diabetes, partly caused by damage to the pancreas. Type 2 diabetes is also associated with higher levels of MPO in the blood. The researchers found that the MPO-caused injuries to pancreas cells and endothelial cells used in their experiments can be greatly reduced by as little as 100 micromolar thiocyanate. Their finding raises the possibility that MPO, in the absence of adequate thiocyanate, contributes to diabetes.

In the cell-based experiments, thiocyanate at concentrations below 100 micromolar did not eliminate hypochlorite accumulation and did not fully protect against MPO toxicity. Conceivably, inadequate thiocyanate levels would aggravate MPO-produced injuries in patients suffering from inflammatory diseases, surmise the authors.

#### Links to Other Diseases

In other studies, MPO activity has been linked to lung cancers among smokers and also implicated in neurodegenerative diseases. Intriguingly, people with congenital MPO deficiency are less likely to develop cardiovascular diseases. The research team found that MPO-caused injuries to nerve cells, as well as to blood vessel-lining endothelial cells, can be greatly reduced by 100 micromolar thiocyanate.

Genetic defects in the CFTR predispose CF patients' lungs to excessive inflammation entangled with recurring lung infection. Defective CFTR channels would be expected to result in lower thiocyanate concentrations in the affected regions within the respiratory, as well as the digestive systems, leaving tissues inadequately protected from accumulated hydrogen peroxide and overproduced hypochlorite.

Conceptually, delivering thiocyanate directly to the digestive and respiratory systems might be a therapy for CF disease, propose the researchers. As for the general population, individuals with low blood levels of thiocyanate may be at risk for chronic injuries by MPO, predisposing them to inflammatory or inflammation-mediated diseases. Many investigators have proposed developing drugs that specifically inhibit MPO-catalyzed hypochlorite production to combat these diseases, but natural thiocyanate not only decreases MPO-catalyzed formation of hypochlorite but also rapidly, once it is made, neutralizes it.

"In light of the obvious implications of this protective action of thiocyanate against the cell-damaging effect of MPO activity with regard to both CF disease and general population health, my colleagues and I will vigorously investigate the potential health benefit of thiocyanate," says Lu. He emphasizes though, "until the research community acquires a better understanding of both positive and negative impacts of thiocyanate on human health, it would be unwise for anyone to self-administer thiocyanate because like many other chemicals, thiocyanate has adverse side effects at improper doses and/or under inappropriate conditions."

The research was funded by NIGMS and the Howard Hughes Medical Institute.

**Public release date: 17-Nov-2009**

## **US gets a 'D' for preterm birth rate**

States take action to reduce risk factors

WHITE PLAINS, N.Y., NOV. 17, 2009 – For the second consecutive year, the United States earned only a "D" on the March of Dimes Premature Birth Report Card, demonstrating that more than half a million of our nation's newborns didn't get the healthy start they deserved.

In the 2009 Premature Birth Report card, seven states improved their performance by one letter grade and two fared worse. Criteria that affect preterm birth improved in many states:

- 33 states and the District of Columbia reduced the percentage of women of childbearing age who smoke;
- 21 states and the District of Columbia reduced the percent of uninsured women of childbearing age;
- 27 states, the District of Columbia, and Puerto Rico lowered the late preterm birth rate.

As in 2008, no state earned an "A," and only Vermont received a "B." The grades were determined by comparing preterm birth rates to the national Healthy People 2010 preterm birth objective, which is 7.6 percent of all live births. The U.S. preliminary preterm birth rate was 12.7 percent in 2007.

"Although we don't yet understand all the factors that contribute to premature birth, we do know some interventions that can help prevent it, and we must consistently make use of all of these," said Dr. Jennifer L. Howse, President of the March of Dimes. She cited smoking cessation programs; health care before and during pregnancy; progesterone supplementation; and improved adherence to professional guidelines on fertility treatment and early Cesarean-sections and inductions.

According to the March of Dimes, quality improvement programs also are key to lowering preterm birth rates. For example, the Intermountain Health Program in Utah reduced its elective C-sections to less than 5 percent from more than 30 percent. At Geisinger Health System in Pennsylvania, pregnant women are screened for chronic conditions and risks factors that can be treated proactively to lower the risk of preterm birth.

A program run by the Hospital Corporation of America based in Tennessee, which delivers about 5 percent of all U.S. births in the 21 states it serves, reduced the primary C-section rate, lowered maternal and fetal injuries and reduced the cost of obstetric malpractice claims by 500 percent. Also, Parkland Memorial Hospital in Texas reduced its preterm birth rate to 4.9 percent in 2006 from 10.4 percent in 1988 by establishing a comprehensive, community-based public health care system of prenatal care that targets minority pregnant women.

In the United States, more than 540,000 babies are born too soon each year. Preterm birth is a serious health problem that costs the United States more than \$26 billion annually, according to the Institute of Medicine. It is the leading cause of newborn death, and babies who survive an early birth often face the risk of lifetime health challenges, such as breathing problems, cerebral palsy, mental retardation and others.

A March of Dimes report released in October found that 13 million babies worldwide were born preterm, and more than one million die each year.

The March of Dimes released its second annual report card today, the 7th Annual Prematurity Awareness Day®, when the March of Dimes focuses the nation's attention on the growing problem of premature birth (birth before 37 weeks gestation). A special Web site – [marchofdimes.com/fightforpreemies](http://marchofdimes.com/fightforpreemies) – includes state profiles on prematurity and ways for volunteers to help reduce the premature rate.

How fish is cooked affects heart-health benefits of omega-3 fatty acids  
Abstract 1404/Poster 2071

Study highlights:

Baked or boiled fish is associated with more benefit from heart-healthy omega-3 fatty acids than fried, salted or dried fish.  
Caucasian, Japanese-American and Latino men may be more likely to get the health benefits of fish than African-American or Hawaiian men, perhaps because of how their fish is prepared or genetic predisposition.

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## **Omega-3s from plant sources such as soy may do more to improve women's heart health than fish sources.**

ORLANDO, FLA., Nov. 17, 2009 — If you eat fish to gain the heart-health benefits of its omega-3 fatty acids, baked or boiled fish is better than fried, salted or dried, according to research presented at the American Heart Association's Scientific Sessions 2009.

And, researchers said, adding low-sodium soy sauce or tofu will enhance the benefits.

“It appears that boiling or baking fish with low-sodium soy sauce (shoyu) and tofu is beneficial, while eating fried, salted or dried fish is not,” said Lixin Meng, M.S., lead researcher of the study and Ph.D. candidate at the University of Hawaii at Manoa. “In fact, these methods of preparation may contribute to

your risk. We did not directly compare boiled or baked fish vs. fried fish, but one can tell from the (risk) ratios, boiled or baked fish is in the protective direction but not fried fish.”

The findings also suggest that the cardioprotective benefits vary by gender and ethnicity — perhaps because of the preparation methods, genetic susceptibility or hormonal factors.

Many studies have suggested that eating omega-3 fatty acids reduces the risk of heart disease; however, little is known about which source is most beneficial.

In this study, researchers examined the source, type, amount and frequency of dietary omega-3 ingestion among gender and ethnic groups. Participants were part of the Multiethnic Cohort living in Hawaii and Los Angeles County when they were recruited between 1993 and 1996. The group consisted of 82,243 men and 103,884 women of African-American, Caucasian, Japanese, Native Hawaiian and Latino descent ages 45 to 75 years old with no history of heart disease.

Researchers divided their intake of canned tuna, other canned fish, fish excluding shell fish, or soy products that contain plant omega-3s (soy, tofu and shoyu) into quintiles, quartiles, or tertiles when applicable. They also surveyed the preparation methods: raw, baked, boiled; fried; salted or dried. The initial study did not consider grilled fish.

Those in the highest quintile consumed a median 3.3 grams of omega-3 fatty acids a day. The lowest quintile consumed a median of 0.8 grams a day.

Omega-3 intake was inversely associated with overall risk of death due to heart disease in men — a trend mainly observed in Caucasians, Japanese Americans and Latinos. However, there weren't many blacks or Hawaiians in the study, so the results should be interpreted cautiously, Meng said.

Overall, men who ate about 3.3 grams per day of omega-3 fatty acids had a 23 percent lower risk of cardiac death compared to those who ate 0.8 grams daily.

“Clearly, we are seeing that the higher the dietary omega-3 intake, the lower the risk of dying from heart disease among men,” Meng said.

Japanese and Hawaiians eat fish more often compared to whites, blacks and Latinos, and they prepare fish in a variety of methods, Meng noted.

For women, the omega-3 effect was cardioprotective at each level of consumption but not consistently significant, Meng said. Salted and dried fish was a risk factor in women.

In contrast, adding less than 1.1 gram/day shoyu and teriyaki sauce at the dinner table was protective for men but not for greater than 1.1 gram/day. For women, shoyu use showed a clear inverse relationship to death from heart disease. She noted that shoyu that is high in sodium can raise blood pressure, so she stressed low-sodium products. Eating tofu also had a cardioprotective effect in all ethnic groups.

“My guess is that, for women, eating omega-3s from shoyu and tofu that contain other active ingredients such as phytoestrogens, might have a stronger cardioprotective effect than eating just omega-3s,” said Meng, noting that further studies are needed to confirm the hypothesis.

During the average 11.9 years of follow-up, 4,516 heart-related deaths occurred in the group, according to state and national death records, which were cross-referenced through the end of 2005.

The study didn't consider possible dietary changes over time; subjects who were diagnosed with heart disease after their baseline food intake surveys might have modified their eating habits. Further, the study didn't account for the possible effects of fish-oil supplementation.

In light of these limitations, the researchers plan to include subjects' dietary patterns over time and a cross-

validation of their omega-3 levels through blood analysis.

“Our findings can help educate people on how much fish to eat and how to cook it to prevent heart disease,” Meng said. “Alternately, if it is verified that the interactions between fish consumption, risk factors and ethnicity are due to genetic susceptibility, the heart-disease prevention message can be personalized to ethnic groups, and future study could identify susceptibility at the genetic level.”

Co-authors are Lynne Wilkens, Dr.P.H., and Laurence Kolonel, M.D., Ph.D.

Author disclosures are on the abstract. An American Heart Association Pacific Mountain Pre-doctoral Fellowship grant funded the study. The data for this research is based on Multiethnic Cohort Study of Diet and Cancer under the NIH grant R37 CA054281.

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## **Some prescription meds can harm fetus**

University of Montreal study reveals danger of certain drugs

Montreal, November 17, 2009 – More than six percent of expectant mothers in Quebec consume prescription drugs that are known to be harmful to their fetuses, according to a Université de Montréal investigation published in the British Journal of Obstetrics and Gynaecology. Half these women will voluntarily terminate their pregnancy fearing congenital malformations, which means the abortion rate among these women is 11 percent higher than in the rest of the population.

"I never expected such results and I was extremely surprised," says senior author Anick Bérard, a professor at the Université de Montréal's Faculty of Pharmacy and director of the Research Unit on Medications and Pregnancy of the Sainte-Justine University Hospital Center.

Dr. Bérard examined data from the Quebec Pregnancy Registry on 109,344 women, aged 15 to 45, who were pregnant between 1998 and 2002. Her research team found that 6,871 pregnant women consumed one of 11 prescription drugs that are known to be harmful to fetuses through the first, second or third trimester. Of those women, 3,229 aborted; 6 percent had a miscarriage; and 8.2 percent gave birth to a child with major congenital malformations.

By comparison, the rate of fetal malformations in the general population in the province of Quebec is approximately seven percent. "If there are 80,000 births in Quebec per year, a one percent difference translates into an additional 800 children born with serious malformations," says Bérard, who is currently a visiting professor at the Université Claude Bernard in Lyon, France. "At the very best, those babies will die. In the worst case, they'll live with serious physical or psychological health problems their entire lives."

The study also examined the use of prescription drugs that are known to be fetotoxic or increase in-utero problems or premature births. The researchers found that 11,400 prescriptions – for dangerous medicines such as isotretinoin (for the treatment of acne and rosacea), anxiolytic benzodiazepines (anti-anxiety treatment) and antiepileptics (epileptic seizure treatment) – were used by pregnant women. Other drugs that were harmful to fetuses – for hypertension, anticoagulation and infection – were also widely used.

Bérard was shocked to discover that one particular acne treatment is still available on the market in Canada without proper risk management programs, since the product increases the risk of malformations by 30 percent (baseline risk is estimated at 3 percent). Of the 73 pregnant women who used isotretinoin in Quebec, she found, 78 percent got an abortion.

Dr. Bérard believes some drugs are overused, such as benzodiazepine to treat symptoms of anxiety, and should be avoided to reduce the odds of fetal malformations.

Other drugs are necessary however, such as antiepileptics. "In those cases, the pregnancy must be carefully planned and medication use must be at a strict minimum during the first trimester," she stresses. "And the expectant mother must meet with her physician regularly."

**Public release date: 17-Nov-2009**

## **When East meets West: Why consumers turn to alternative medicine**

Alternative health remedies are increasingly important in the health care marketplace. A new study in the *Journal of Consumer Research* explores how consumers choose among the many available remedies.

"Examples of the wide array of health remedy options available to consumers include drugs, supplements, acupuncture, massage therapy, Ayurveda, and Traditional Chinese Medicine (to name a few). Such medical pluralism is common in both developed and developing countries and raises the questions: How do consumers choose among health remedies, and what are the consequences for a healthy lifestyle?" write authors Wenbo Wang (New York University), Hean Tat Keh (Beijing University), and Lisa E. Bolton (Pennsylvania State University).

The authors use "lay theories of medicine" to explain how consumers choose between Western medicine and its Eastern counterparts, Traditional Chinese Medicine (TCM) and Ayurvedic medicine.

"Western Medicine is primarily concerned with the material aspect of the body and views all medical phenomena as cause-effect sequences, relying on rigorous scientific studies and research that seeks empirical proof to all phenomena," write the authors. "On the other hand, TCM and Ayurvedic Medicine favor a holistic approach, view the mind and body as a whole system, and rely upon inductive tools and methods for treatment."

Based on a series of experiments and surveys in the United States, China, and India, the authors found that consumers prefer TCM (over Western medicine) when uncertain about the cause of an illness (i.e., diagnosis uncertainty)—because a holistic medicine tolerates uncertainty better than Western Medicine. Similarly, consumers prefer TCM (over Western medicine) because of lay beliefs that TCM offers an underlying cure (versus symptom alleviation by Western Medicine).

"These findings add to the growing debate over the regulation of health marketing and the delivery of health care, the role of direct-to-consumer advertising, and marketing efforts to promote a healthy lifestyle," the authors conclude.

**Public release date: 17-Nov-2009**

## **Cancer patients and doctors report drug side effects differently**

In clinical trials for cancer, it is standard for clinicians rather than patients to report adverse symptom side effects from treatments, such as nausea and fatigue. At present, patient self-reporting, although important, is not a well studied source of this information. A new longitudinal study from researchers at Memorial Sloan-Kettering Cancer Center finds that while clinicians' and patients' reporting of treatment side effects are very different from each other, together they provide a more complete, clinically meaningful picture of the treatment experience.

The research was published online November 17 in the *Journal of the National Cancer Institute*. Ethan Basch, MD, a medical oncologist and member of the Health Outcomes Group at Memorial Sloan-Kettering, and colleagues, led an analysis of data gathered from more than 160 advanced lung cancer patients and their clinicians. All of the patients were treated at Memorial Sloan-Kettering.

The patients, both men and women with a median age of 63, were followed from 2005 to 2006 through an average of 12 office visits. All received chemotherapy during this time. Researchers tracked six common symptoms--fatigue, pain, nausea, vomiting, diarrhea, and constipation--and compared the side effects reported by the clinicians to those reported by the patients. The clinicians reported symptoms using the standard adverse event reporting tool for oncology trials, the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE.) Patients reported symptoms using a simplified version of the same reporting tool via a computer-based system.

**Patients generally reported adverse symptoms earlier, more frequently, and with greater severity than their clinicians, and their responses appeared to better reflect real-time suffering. Patient-reported symptoms were more closely related to day-to-day health status, while clinicians' reports were more predictive of significant medical events.** "The perspectives of both clinicians and patients provide a more complete picture of the negative impact of treatments compared with either perspective alone," said Dr. Basch. "Clinicians bring professional training and experience to their evaluations, whereas patients are in a better position to communicate their own subjective experiences," he adds.

The findings demonstrate the value of an approach that incorporates patient self-reporting of symptoms in cancer treatment trials. Such information has the potential to help both prospective prescribers and patients in understanding the anticipated side effects of treatment.

On the basis of this research Dr. Basch said, "We need to design models in which we can capitalize on what the patient is reporting in order to understand how toxic these drugs are. Our patients add tremendous value in their reporting; and by collecting this information we can actually enhance our understanding of toxicities in a way that will aid the FDA, aid clinicians, aid researchers, and aid patients themselves when they are trying to decide whether they want to start a treatment." **He added that, "patient-reported adverse symptoms should be collected in clinical trials and reported in drug labels."**

**Ralph's Note - I had thought that the patients reported the side effects, and the Doctors recorded it...I did not realize that the Doctors, did not have to listen to the patient reports...That changes a lot on clinical trial results.**

**Public release date: 17-Nov-2009**

## **Common herbal medicine may prevent acetaminophen-related liver damage, says Stanford researcher**

STANFORD, Calif. — A well-known Eastern medicine supplement may help avoid the most common cause of liver transplantation, according to a study by researchers at the Stanford University School of Medicine. The finding came as a surprise to the scientists, who used a number of advanced genetic and genomic techniques in mice to identify a molecular pathway that counters acetaminophen toxicity, which leads to liver failure.

"I didn't know anything about the substance that was necessary for the pathway's function, so I had to look it up," said Gary Peltz, MD, PhD, professor of anesthesiology. "My postdoctoral fellow, whose parents and other family members in Asia were taking this compound in their supplements, started laughing. He recognized it immediately."

The molecule was S-methylmethionine, which had been marketed as an herbal medicine

known as Vitamin U for treatment of the digestive system. It is highly abundant in many plants, including cabbage and wheat, and is routinely ingested by people. Coincidentally, Garnett Cheney, MD, at Stanford University performed a series of studies in the 1950s in which he used the compound to treat peptic ulcers.

Peltz is the senior author of the research, which will be published online Nov. 18 in *Genome Research*. The experiments were conducted in Peltz's laboratory at Roche Palo Alto in Palo Alto, Calif., where Peltz worked before coming to Stanford in July 2008. He is continuing the research at Stanford. The first author of the paper, Hong-Hsing Liu, MD, PhD, is now a postdoctoral scholar in Peltz's Stanford lab.

Acetaminophen is a pain reliever present in many over-the-counter cold and flu medicines. It is broken down, or metabolized, in the body into byproducts — one of which can be very toxic to the liver. At normal, therapeutic levels, this byproduct is easily deactivated when it binds to a naturally occurring, protective molecule called glutathione. But the body's glutathione stores are finite, and are quickly depleted when the recommended doses of acetaminophen are exceeded.

Unfortunately, the prevalence of acetaminophen makes it easy to accidentally exceed the recommended levels, which can occur by dosing more frequently than indicated or by combining two or more acetaminophen-containing products. However, severe liver damage can occur at even two to three times the recommended dose (the maximum adult dose is 4 grams per day; toxic daily levels range from 7 to 10 grams).

"It's a huge public health problem," said Peltz. "It's particularly difficult for parents, who may not realize that acetaminophen is in so many pediatric medicines." Acetaminophen overdose is the most common cause of liver transplantation in this country. The only effective antidote is an unpalatable compound called NAC that can induce nausea and vomiting, and must be administered as soon as possible after the overdose.

Peltz and his colleagues used 16 inbred strains of laboratory mice for their investigations. Most strains are susceptible to acetaminophen toxicity, but one is resistant. They compared how the drug is metabolized by the different strains and looked for variations in gene expression and changes in endogenous metabolites in response to acetaminophen administration. They identified 224 candidate genes that might explain the resistant strain's ability to ward off liver damage, and then plumbed computer databases to identify those involved in metabolizing acetaminophen's dangerous byproducts.

One, an enzyme called *Bhmt2*, fit the bill: It helped generate more glutathione, and its sequence varied between the resistant and non-resistant strains of mice. *Bhmt2* works by converting the diet-derived molecule S-methylmethionine, or SMM, into methionine, which is subsequently converted in a series of steps into glutathione. The researchers confirmed the importance of the pathway by showing that SMM conferred protection against acetaminophen-induced liver toxicity only in strains of mice in which the *Bhmt2* pathway was functional.

"By administering SMM, which is found in every flowering plant and vegetable, we were able to prevent a lot of the drug's toxic effect," said Peltz. He and his colleagues are now working to set up clinical trials at Stanford to see whether it will have a similar effect in humans. In the meantime, though, he cautions against assuming that dosing oneself with SMM will protect against acetaminophen overdose.

"There are many pathways involved in the metabolism of this drug, and individuals' genetic backgrounds are tremendously variable. This is just one piece of the puzzle; we don't have the full answer," he said. However, if subsequent studies are promising, Peltz envisions possibly a co-formulated drug containing both acetaminophen and SMM or using SMM as a routine dietary supplement.

**Public release date: 18-Nov-2009**

## **Women at risk from vitamin A deficiency**

**Almost half of UK women could be suffering from a lack of vitamin A due to a previously undiscovered genetic variation, scientists at Newcastle University have found.**

The team, led by Dr Georg Lietz, has shown that almost 50 per cent of women have a genetic variation which reduces their ability to produce sufficient amounts of vitamin A from beta-carotene.

Vitamin A – also known as retinol – plays a vital role in strengthening our immune system, protecting us against common infections such as flu and winter vomiting.

Vitamin A also helps to maintain healthy skin and mucus linings such as inside the nose and the lungs.

In 1987, an American study found that excessive use of vitamin A during pregnancy was associated with certain birth defects. Beta-carotene, however, was deemed to be safe and this led to the general advice that we should eat more of this nutrient, allowing the body to convert what it needs into vitamin A.

However, Dr Lietz' latest research – published in the FASEB Journal and presented this month at the 2nd Hohenheim Nutrition Conference in Stuttgart – **shows that for many women, beta-carotene is not an effective substitute for vitamin A.**

Dr Lietz explained: "Vitamin A is incredibly important – particularly at this time of year when we are all trying to fight off the winter colds and flu.

"It boosts our immune system and reduces the risk of inflammation such as that associated with chest infections.

"What our research shows is that many women are simply not getting enough of this vital

nutrient because their bodies are not able to convert the beta-carotene."

From a volunteer group of 62 women, the team found that 29 of them – 47 per cent – carried the genetic variation which prevented them from being able to effectively convert beta-carotene into vitamin A.

The study also showed that all volunteers consumed only about a third of their recommended intake from 'preformed' vitamin A – the form found in dairy products such as eggs and milk – indicating that those volunteers carrying the genetic variation were not eating enough vitamin A-rich foods to reach the optimum level their body required to function.

"Worryingly, younger women are at particular risk," explained Dr Lietz, who is based in the School of Agriculture, Food and Rural Development at Newcastle University.

"The older generations tend to eat more eggs, milk and liver which are naturally rich in vitamin A whereas the health-conscious youngsters on low-fat diets are relying heavily on the beta-carotene form of the nutrient."

The next step in the study is to assess whether the effect of the genetic variation can also be observed in men and whether our body composition will influence our ability to absorb and convert beta-carotene into vitamin

**Public release date: 18-Nov-2009**

## **Antifibrotic effects of green tea**

Several studies have shown that lipid peroxidation stimulates collagen production in fibroblasts and hepatic stellate cells (HSC), and plays an important role in the development of liver fibrosis. Hepatoprotective effects of green tea against carbon tetrachloride, cholestasis and alcohol induced liver fibrosis were reported in many studies. However, the hepatoprotective effect of green tea in dimethylnitrosamine (DMN)-induced models has not been studied.

A research article published on November 7, 2009 in the World Journal of Gastroenterology addresses this question. The research team, led by Prof. Hong-Yon Cho from Korea University examined the protective effect of green tea extract (GT) on hepatic fibrosis in a rat HSC line and in a rat model of DMN-induced hepatic fibrosis.

The results showed GT administration prevented the development of hepatic fibrosis in the rat model of DMN-induced liver fibrosis. These results were confirmed both by liver histology and by quantitative measurement of hepatic hydroxyproline content, a marker of liver collagen deposition. Accordingly, inhibition of proliferation, reduced collagen deposition, and type 1 collagen expression were observed in activated HSC-T6 cells following GT treatment. These results imply that GT reduced the proliferation of activated HSC and down regulated the collagen content and expression of collagen type 1, thereby ameliorating hepatic fibrosis.

The researchers drew a conclusion that green tea may protect liver cells and reduce the deposition of collagen fibers in the liver. Green tea provides a safe and effective strategy for improving hepatic fibrosis.

**Public release date: 19-Nov-2009**

## **Common plastics chemicals linked to ADHD symptoms**

### **Are phthalates really safe for children?**

Philadelphia, PA, 19 November 2009 - Phthalates are important components of many consumer products, including toys, cleaning materials, plastics, and personal care items. Studies to date on phthalates have been inconsistent, with some linking exposure to these chemicals to hormone disruptions, birth defects, asthma, and reproductive problems, while others have found no significant association between exposure and adverse effects.

A new report by Korean scientists, published by Elsevier in the November 15th issue of Biological Psychiatry, adds to the potentially alarming findings about phthalates. They measured urine phthalate concentrations and evaluated symptoms of attention-deficit/hyperactivity disorder (ADHD) using teacher-reported symptoms and computerized tests that measured attention and impulsivity.

### **They found a significant positive association between phthalate exposure and ADHD, meaning that the higher the concentration of phthalate metabolites in the urine, the worse the ADHD symptoms and/or test scores.**

Senior author Yun-Chul Hong, MD, PhD, explained that "these data represent the first documented association between phthalate exposure and ADHD symptoms in school-aged children." John Krystal, MD, the Editor of Biological Psychiatry, also commented: "This emerging link between phthalates and symptoms of ADHD raises the concern that accidental environmental exposure to phthalates may be contributing to behavioral and cognitive problems in children. This concern calls for more definitive research."

The U.S. Centers for Disease Control and Prevention, in the Summary of their 2005 Third National Report on Human Exposure to Environmental Chemicals, state that "very limited scientific information is available on potential human health effects of phthalates at levels" found in the U.S. population. Although this study was performed in a Korean population, their levels of exposure are likely comparable to a U.S. population.

The current findings do not prove that phthalate exposure caused ADHD symptoms. However, these initial findings provide a rationale for further research on this association.

### **Public Release: 19-Nov-2009**

## **Reflux esophagitis due to immune reaction, not acute acid burn, UT Southwestern researchers report**

DALLAS – Nov. 19, 2009 – Contrary to current thinking, a condition called gastroesophageal reflux disease (GERD) might not develop as a direct result of acidic digestive juices burning the esophagus, UT Southwestern Medical Center researchers have found in an animal study.

Rather, gastroesophageal reflux spurs the esophageal cells to release chemicals called cytokines, which attract inflammatory cells to the esophagus. It is those inflammatory cells, drawn to the esophagus by cytokines, that cause the esophageal damage that is characteristic of GERD. The condition is manifested by symptoms such as heartburn and chest pain.

"Currently, we treat GERD by giving medications to prevent the stomach from making acid," said Dr. Rhonda Souza, associate professor of internal medicine at UT Southwestern and lead author of the study appearing the November issue of Gastroenterology. "But if GERD is really an immune-mediated injury,

maybe we should create medications that would prevent these cytokines from attracting inflammatory cells to the esophagus and starting the injury in the first place.”

In the study, researchers created GERD in rats by connecting the duodenum to the esophagus. This operation allows stomach acid and bile to enter the esophagus. Researchers were surprised to learn that esophagitis didn't develop for a number of weeks after the operation.

**“That doesn't make sense if GERD is really the result of an acid burn, as we all were taught in medical school,”** said Dr. Stuart Spechler, professor of internal medicine at UT Southwestern and senior author of the study. “Chemical injuries develop immediately. If you spill battery acid on your hand, you don't have to wait a month to see the damage.”

About 40 percent of Americans suffer symptoms of GERD at some point, and 20 percent on a weekly basis, Dr. Souza said. Over the long term, GERD could eventually lead to esophageal cancer.

Previous studies had shown that if an animal esophagus is perfused with highly concentrated acid, esophageal damage develops quickly. In humans, however, the large majority of reflux episodes do not contain such highly concentrated acid, Dr. Souza said.

“In animal models of reflux esophagitis designed to mimic the human disease, researchers hadn't looked at the early events in the development of esophageal injury,” Dr. Souza noted. “Most of those investigators have been interested in the long-term consequences of GERD, and we found virtually no published data about what happens later that induces gastroesophageal reflux.”

Dr. Souza, who is also a staff physician at the Dallas Veterans Affairs Medical Center and part of the Harold C. Simmons Comprehensive Cancer Center at UT Southwestern, and Dr. Spechler, chief of gastroenterology at the Dallas VA, said the method they used to produce GERD in rats is a reasonable representation of how GERD develops in humans – acidic digestive juices from the stomach surge into the esophagus.

Soon after the operation, they expected to see the death of surface cells of the esophagus, and they expected to see the injury progress later to the deeper layers. Instead, they found the opposite. Three days after the surgery, there was no damage to surface cells, but the researchers did find inflammatory cells in the deeper layers of the esophagus. Those inflammatory cells didn't rise to the surface layer until three weeks after the initial acid exposure.

The next step for researchers is to conduct additional studies in humans.

Other UT Southwestern researchers involved in the study included Dr. Xiaofang Huo, postdoctoral researcher in internal medicine; Dr. Vivek Mittal, postgraduate trainee in internal medicine; Dr. Susanne Carmack, postgraduate trainee in pathology; Dr. Huiying Zhang, instructor of internal medicine; Dr. Robert Genta, clinical professor of pathology and internal medicine; Dr. Kathy Hormi-Carver, assistant professor of internal medicine; and Dr. Xi Zhang and Dr. Chunhua Yu, both research associates in internal medicine.

The study was supported by the Dallas VA Medical Center and the National Institutes of Health.

Visit <http://www.utsouthwestern.org/digestive> to learn about UT Southwestern's clinical services for digestive disorders.

**Public release date: 23-Nov-2009**

**Flaxseed oil and osteoporosis**

Animal studies suggest that adding flaxseed oil to the diet could reduce the risk of osteoporosis in post-menopausal women and women with diabetes, according to a report to be published in the International Journal of Food Safety, Nutrition and Public Health.

Mer Harvi and colleagues at the National Research Center, in Cairo, Egypt, have studied the effect of diabetes on bone health and evaluated how flaxseed oil in the diet might delay the onset of osteoporosis. The researchers studied 70 female albino rats of which 30 had their ovaries removed (ovx) to simulate the post-menopausal state and experimental diabetes was present in one group of rodents.

The researchers then classified the rats as control, sham, diabetic, diabetic received flaxseed oil in the diet, ovx, ovx-diabetic and ovx-diabetic received flaxseed oil in the diet.

After two months, the team collected urine and blood samples from the rats and measured serum insulin-like growth factor 1 (IGF-1) and the bone-creating protein osteocalcin. They found that these two compounds were present at higher levels in the ovx and the diabetic ovx groups, but much lower in the non-ovx diabetic group. The concentrations of IGF-1 and osteocalcin could be raised to normal levels by adding flaxseed oil to the diet.

The team also found that the levels of deoxypyridinoline in the urine were raised in the diabetic group. Deoxypyridinoline is normally present in healthy bone and its presence in urine is a specific marker for bone resorption associated with osteoporosis. Levels of this marker compound fell when the rats were given flaxseed oil.

The team concludes that diabetes has a more pronounced effect on bone health than ovariectomy and so may suggest that diabetes in post-menopausal women may also be a greater risk factor for osteoporosis than the decline in sex hormones associated with the menopause. However, their results suggest that flaxseed oil has a beneficial effect on bone mineral density and reduces markers associated with osteoporosis, suggesting that this dietary supplement could be beneficial to women with diabetes in reducing their risk of osteoporosis.

The team explains that the presence of so-called "n-3 fatty acids" in flaxseed oil may play a role in protecting the processes of matrix formation and bone mineralization, which are apparently compromised by diabetes and the menopause. "We recommend further investigations using animals and humans to confirm the effect of using dietary flaxseed oil to improve bone health and to prevent osteoporosis," Harvi and colleagues conclude.

**Public release date: 24-Nov-2009**

## **Polyphenols and polyunsaturated fatty acids boost the birth of new neurons**

New study in mice by UAB researchers confirm

**Universitat Autònoma de Barcelona (UAB) researchers have confirmed that a diet rich in polyphenols and polyunsaturated fatty acids, patented as an LMN diet, helps boost the production of the brain's stem cells -neurogenesis- and strengthens their differentiation in different types of neuron cells.** The research revealed that mice fed an LMN diet, when compared to those fed a control diet, have more cell proliferation in the two areas of the brain where neurogenesis is produced, the olfactory bulb and the hippocampus, both of which are greatly damaged in patients with Alzheimer's disease. These results give support to the hypothesis that a diet made up of foods rich in these antioxidant substances could delay the onset of this disease or even slow down its evolution.

The study will be published in the December issue of the Journal of Alzheimer's Disease and was directed

by Mercedes Unzeta, professor of the UAB Department of Biochemistry and Molecular Biology. Participating in the study were researchers from this department and from the departments of Cell Biology, Physiology and Immunology, and of Psychiatry and Legal Medicine, all of which are affiliated centres of the Institute of Neuroscience of Universitat Autònoma de Barcelona. The company La Morella Nuts from Reus and the ACE Foundation of the Catalan Institute of Applied Neurosciences also collaborated in the study.

Polyphenols can be found in tea, beer, grapes, wine, olive oil, cocoa, nuts and other fruits and vegetables. Polyunsaturated fatty acids can be found in blue fish and vegetables such as corn, soya beans, sunflowers and pumpkins. The LMN cream used in this study was composed of a mixture of natural products: dried fruits and nuts, coconut, vegetable oils rich in polyunsaturated fat and flour rich in soluble fiber. These creams were created and patented by the company La Morella Nuts, located in Reus near Tarragona. Previous studies had verified their effects on regulating cholesterol levels and hypertension, two risk factors commonly associated with heart disease and Alzheimer's disease.

During the development of the brain, stem cells generate different neural cells (neurons, astrocytes and oligodendrocytes) which end up forming the adult brain. Until the 1960s it was thought that the amount of neurons in adult mammals decreased with age and that the body was not able to renew these cells. Now it is known that new neurons are formed in the adult brain. This generative capacity of the cells however is limited to two areas of the brain: the olfactory bulb and the hippocampus (area related to the memory and to cognitive processes). Although the rhythm of cell proliferation decreases with age and with neurodegenerative diseases, it is known that exercise and personal well being can combat this process.

The main objective of this research was to study the effect of an LMN cream-enriched diet on the neurogenesis of the brain of an adult mouse. Scientists used two groups of mice for the study. One group was given a normal diet and the other was given the same diet enriched with LMN cream. Both groups were fed during 40 days (approximately five years in humans). The analyses carried out in different brain regions demonstrated that those fed with LMN cream had a significantly higher amount of stem cells, as well as new differentiated cells, in the olfactory bulb and hippocampus.

The second objective was to verify if the LMN cream could prevent damage caused by oxidation or neural death in cell cultures. Cultures of the hippocampal and cortical cells were pretreated with LMN cream. After causing oxidative damage with hydrogen peroxide, which killed 40% of the cells, scientists observed that a pretreatment with LMN cream was capable of diminishing, and in some cases completely preventing, oxidative damage. The hippocampal and cortical cells were also damaged using amyloid beta (anomalous deposits of this protein are related to Alzheimer's disease). The results obtained were similar to those obtained using hydrogen peroxide.

These results demonstrate that an LMN diet is capable of inducing the generation of new cells in the adult brain, and of strengthening the neural networks which become affected with age and in neurogenerative processes such as Alzheimer's disease, as well as protecting neurons from oxidative and neural damage, two phenomena which occur at the origin of many diseases affecting the central nervous system.

In this study researchers have used different biochemical and molecular analysis techniques, with the help of specific antibodies, to detect different neuronal markers implied in the process of differentiation.

The group of researchers led by Dr Unzeta has spent years studying the effects oxidases have on oxidative stress as a factor implied in neurodegenerative disorders such as Parkinson and Alzheimer's disease, and the effects of different natural products with anti-inflammatory and antioxidant properties in different experimental models of Alzheimer's disease.

The study forms part of the CENIT project, which was awarded to La Morella Nuts in 2006 under the auspices of the INGENIO 2010 programme, with the objective of establishing methodologies for the design, evaluation and verification of functional foods which may protect against cardiovascular diseases and Alzheimer's disease. With 21.15m euros in funding and a duration of four years, the project has included the participation of 50 doctors and technicians from nine different companies, four universities (7

departments) and 2 research centres.

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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.**