



The Vitamin & Herb Stores

**Human Technology Research Synopsis**

**45th Issue Date 9 NOV 08**

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**Public release date: 25-Nov-2008**

## **Inhaled corticosteroids raise pneumonia risk for lung disease sufferers**

Call made for physicians to strongly weigh potential harm of commonly used drugs  
Lung disease experts at Johns Hopkins are calling for physicians to show much greater caution in prescribing inhaled corticosteroid drugs for people with chronic obstructive pulmonary disease after finding evidence that the widely used anti-inflammatory medications increase the risk of pneumonia by a full third.

More than 11 million Americans, the vast majority former or current smokers, are living with so-called COPD, marked by the potentially fatal, lung-diminishing conditions of emphysema and chronic bronchitis. The inhalers in question greatly relieve such symptoms as shortness of breath, wheezing, phlegm and physical exhaustion from light exercise.

The call for caution is based on the Hopkins team's review and analysis of adverse events recorded in 11 clinical studies that in total involved more than 14,000 men and women with COPD. The team's review, believed to be the largest and most comprehensive performed in the last decade among COPD sufferers, compared adverse events among those who took inhaled corticosteroids and others who did not.

In their report, set to appear in the Journal of the American Medical Association online Nov. 26, researchers found that the increased risk mostly occurred in people taking the highest possible doses, such as 500 micrograms of fluticasone twice daily for a relatively short time (less than two years), whose lung function was 40 percent or lower than expected and who also combined their steroid therapy with bronchodilators, used to keep the airways open.

Researchers say it remains unclear why the treatment increases risk of lung infection, but they suspect that the drugs suppress the immune system.

Despite the increased pneumonia risk, the team found no clear evidence that the drug therapy also pushes up rates for other steroid-related problems, such as bone fractures, nor was there an increase in deaths.

Senior study investigator and critical care specialist Eddy Fan, M.D., says the results of the analysis should not alarm patients or cause them to stop taking their medications but should spur physicians to screen and monitor their patients to find the lowest possible steroid dose that works, especially in the elderly, people with immune system problems, and people who have had multiple bouts of pneumonia and for whom repeat bacterial infection might be a life-threatening complication.

"Inhaled corticosteroids are not of equal benefit to all, and what we are seeing is that the treatment may be more harmful and pose a greater risk of harm to some," says Fan, an

instructor at the Johns Hopkins University School of Medicine.

"Physicians really need to strongly evaluate a patient's individual characteristics before prescribing these steroid medications, and patients, in turn, should weigh the risks and benefits of taking the drugs, despite their proven record in providing symptomatic relief," he says.

According to pulmonologist M. Brad Drummond, M.D., M.H.S., who led the study, "catching this bacterial infection can seriously disrupt quality of life, making it harder for COPD patients to breathe and possibly leading to hospitalization."

Drummond says the new findings should serve as a reminder to people with the severe lung disease to take steps that reduce the chance of getting pneumonia, which doubles their risk of dying when compared to people with healthy lungs. He also advises COPD sufferers, in addition to weighing the benefits and harms of steroids, to get the pneumonia vaccination every five years and an annual flu vaccination because these shots reduce the chance of getting a lung infection.

A postdoctoral clinical research fellow at Hopkins, Drummond also advises lung disease sufferers to take additional precautions, including more frequent hand washing, and vigilant monitoring for the first and earliest signs of sickness, such as increased phlegm in the throat, shortness of breath, fever or chills.

In their analysis, researchers culled their 11 key studies from more than 3,100 conducted in over 40 countries. All of the studies tracked men and women with COPD for complications from treatment, including some for pneumonia, bone cracking and death. The 11 studies were all randomized controlled trials completed between 1999 and 2007 that involved participants who had seriously diminished lung function, at less than 70 percent of expected. In addition, all were initially diagnosed with COPD at age 40 and older, which is typically the age group most affected by COPD. About half were prescribed the handheld, disposable corticosteroid inhalers, such as puffers, turbohalers, diskhalers and nebulizers, while the rest were not. And all were monitored for between six months and three years, with some participants taking steroid therapy alone or in combination with bronchodilators, which contain different drugs. Studies that included people with asthma, a related lung disease that complicates treatment of COPD, were excluded from the analysis.

The merged analysis from seven studies that kept track of infections from pneumonia revealed a 34 percent higher rate among those who underwent steroid therapy (777 infections in 5,405 people), compared to those who did not during the same time frame (561 infections in 5,371). In five studies that recorded death rates and three that counted bone fractures, no significant differences emerged between the group using steroid therapy and those who did not.

In breaking down the overall rise in risk, the researchers found that in people taking the highest possible dose of each inhaled corticosteroid, there was a 46 percent increase in

risk for pneumonia. Infection risk nearly doubled in those who had less than 40 percent normal lung function, as opposed to those whose lungs were stronger.

Drummond says the absence of an overall difference in death rates between users and non-users of corticosteroids was likely due to the short-term follow-up of three years or less across all of the studies.

Fan says further research is needed to identify precisely which groups benefit long-term and which ones do not from inhaled corticosteroids, and to see if there is a link between higher risk and death.

He notes that COPD kills more than 120,000 Americans every year and is expected to become the nation's third leading cause of death in the United States by 2020, ahead of stroke and behind heart disease and cancers.

**Public release date: 26-Nov-2008**

### **Stanford/Packard study shows no benefit from drug widely used to prevent premature births**

STANFORD, Calif. — When a pregnant woman goes into early labor, her obstetrician may give her drugs to quiet the woman's uterus and prevent premature birth.

New research shows, however, that one popular drug works no better than a placebo at maintaining pregnancy after the initial bout of preterm labor is halted, say scientists at the Stanford University School of Medicine, Lucile Packard Children's Hospital and Santa Clara Valley Medical Center. The new trial is the first-ever placebo-controlled test of nifedipine, a muscle relaxant originally developed to lower blood pressure, and its effect on premature delivery with prolonged treatment.

"Medication use should be minimized in pregnancy unless it's clearly indicated," said Deirdre Lyell, MD, assistant professor of obstetrics and gynecology at Stanford and the study's lead author. **Serious side effects of nifedipine in pregnancy are rare, Lyell said, but even a low risk isn't worthwhile if the drug has no benefit.** "We all want to prevent preterm birth, but prolonged treatment with nifedipine doesn't appear to be an answer."

The findings will appear in the December issue of the journal *Obstetrics and Gynecology*.

Preterm births, defined as deliveries before 37 weeks of pregnancy, are on the rise in the United States. Pregnancy normally lasts 40 weeks. **A report released earlier in November by the March of Dimes gives the United States a "D" grade for its rate of preterm births, which increased between 1981 and 2005 from 9.4 to 12.7 percent of**

**all births.** Smoking, lack of insurance and early intervention by physicians were cited as major contributing factors.

**"The scope of the problem is enormous,"** Lyell said.

In early life, preemies face health problems such as respiratory distress, bleeding on the brain and tissue-destroying intestinal infections. Long-term complications of prematurity include neurological disorders, chronic lung disease and vision and hearing problems. The earlier the delivery, the greater the risks. That means doctors are very motivated to help women in early labor stay pregnant as long as possible. A recent survey by the Society for Maternal-Fetal Medicine found 29 percent of obstetricians prescribed drugs to keep such patients from re-entering early labor. Of those, 79 percent said nifedipine was their first-choice therapy.

Lyell's team recruited 71 women who had been successfully treated for preterm labor between 24 and 34 weeks of pregnancy. The women were then randomly assigned to receive doses of nifedipine or placebo every six hours until 37 weeks of pregnancy or until delivery, whichever came first. The researchers hoped nifedipine would prevent preterm labor from re-starting. They evaluated whether subjects' pregnancies lasted to 37 weeks and measured how long delivery was delayed. They also noted the babies' gestational age at delivery, birth weight and complications of prematurity.

The team saw no differences between nifedipine and placebo for any measurement. About 40 percent of women in both groups reached 37 weeks of pregnancy, with delivery delayed an average of a month. Babies' average health was the same in both groups, too.

Lyell cautioned that the study was designed to detect a 50 percent improvement in delayed deliveries. If nifedipine confers a smaller advantage, it would not have been spotted in this study, she said. Lyell thinks a larger study of nifedipine is warranted. "A small benefit would be especially significant at early gestational ages, and less so later on. But overall, there's no benefit to prematurity."

Based on the current lack of data to support this drug, Lyell believes obstetricians should proceed with caution. "All medications have side effects," she said. Though nifedipine has a fairly good safety record, a few case reports link it to dangerously low blood pressure in pregnant women.

"If something has not been shown to be of benefit, it shouldn't be used," Lyell concluded. "Every now and then, there will be a patient who has an unusual side effect."

"It's important to distinguish between acute treatment, which is given to a woman in preterm labor, and maintenance treatment, which is given to a woman following an episode of preterm labor that has ended," she added. "This study addresses maintenance treatment. We still use nifedipine for acute treatment of preterm labor."

**Public release date: 26-Nov-2008**

## **Vitamin K linked to insulin resistance in older men**

BOSTON - (November 26, 2008) Vitamin K slowed the development of insulin resistance in elderly men in a study of 355 non-diabetic men and women ages 60 to 80 who completed a three-year clinical trial at the Jean Mayer Human Nutrition Research Center on Aging at Tufts University (USDA HNRCA).

"Men who received vitamin K supplementation had less progression in their insulin resistance by the end of the clinical trial," said Sarah Booth, senior author and director of the Vitamin K Laboratory at the USDA HNRCA. "Conversely, we saw progression in insulin resistance in women who received vitamin K supplementation, and in the men or women who were not given vitamin K supplements."

Among those given vitamin K, both men and women took daily multivitamins containing 500 micrograms of vitamin K, five times the Adequate Intake (AI) recommended by the Institute of Medicine's Food and Nutrition Board, with instructions to maintain normal diets without any additional supplementation. They also received a calcium and vitamin D supplement. Men and women in the control group received no vitamin K supplementation but did receive the multivitamin and the calcium and vitamin D supplement. For the present study, insulin resistance was assessed by the homeostasis model (HOMA-IR). Additionally, participants' blood glucose and blood insulin levels were measured following a minimum 10-hour fast. In addition to improved insulin resistance, the supplemented men had lower blood insulin levels compared to the unsupplemented men at the conclusion of the study.

Insulin is a hormone which plays a role in transporting sugar into cells so it can be converted into energy. A pre-cursor to diabetes, insulin resistance occurs when the body cannot use insulin properly, causing glucose to build up in the blood. People who are obese or overweight are prone to insulin resistance because excess fat can interfere with insulin function.

Writing in the November issue of *Diabetes Care*, the authors speculate that weight might explain why only the vitamin K supplemented men improved their insulin resistance. "In our study, there was a higher prevalence of obese or overweight women in the vitamin K supplementation group compared to the male supplementation group," Booth said. "Vitamin K is stored in fat tissue. If there is excess fat, vitamin K may not be readily available to cells that require it to process glucose."

Because there are few studies of vitamin K and insulin resistance, the authors encourage further investigation of their findings and alternative study designs. "The original purpose of the present study was to assess the effect of vitamin K1, or phylloquinone, supplementation on changes in bone mineral density and vascular calcification," Booth said. "For instance, there is a way to achieve a more direct measure of insulin secretion than HOMA-IR. Also, our study is limited to caucasian adults. We acknowledge our findings may not apply to the general population."

Although vitamin K supplements were used for the study, the authors say the study dosage is attainable by consuming a healthy diet. Foods considered good sources of vitamin K include brussels sprouts, broccoli, and dark, leafy greens, such as spinach and collards.

**Public release date: 26-Nov-2008**

## **Down's symptoms may be treatable in the womb**

PREGNANT woman who knows her unborn child has Down's syndrome might one day be able to prevent some symptoms before giving birth.

That at least is the hope raised by experiments in mice. When fetal mouse pups that had a syndrome similar to Down's were treated with nerve-protecting chemicals, some of the developmental delays that are part of the condition were removed.

Children with Down's have an extra copy of chromosome 21, while mice engineered to have a similar condition are given an extra copy of a segment of chromosome 16. In both species, the development of certain motor and sensory abilities is delayed. These "trisomic" individuals may also have learning difficulties and symptoms of Alzheimer's later in life.

Inhibiting the neurotransmitter GABA in trisomic mice can improve cognition and some have suggested this could be used in children. It would be even better, however, to treat Down's before a child is born and so improve cognitive potential.

Previous studies both of people with Down's and trisomic mice have also revealed malfunctions in glial cells - brain cells that regulate the development of neurons by releasing certain proteins. The aberrant cells produce less of these proteins than normal. And adding segments of some of these proteins - known as NAP and SAL - to cultured neurons from people with Down's, which would otherwise degenerate, seems to protect the neurons (Current Pharmaceutical Design, DOI: 10.2174/138161207780618957).

Armed with this knowledge, Catherine Spong and colleagues at the National Institutes of Health in Bethesda, Maryland, injected NAP and SAL into mice pregnant with trisomic pups in the middle of their pregnancy. When the pups were born, they reached developmental milestones such as grasping a rod, righting themselves and responding to tactile stimulation at the same time as normal mice (Obstetrics and Gynecology, vol 112, p 1242). "We were able to prevent a significant amount of the delay," says Spong.

## **When the pups were born, they reached developmental milestones at the same time as normal mice**

The brains of the treated mice also showed normal levels of ADNP - one of the regulatory proteins underproduced by Down's-affected glial cells - and of another

compound that is a marker for healthy glial cells. Both findings indicate that some effects of Down's had been removed.

Now Spong is watching to see if mice treated as fetuses also display less of a learning deficit as they mature. She hopes that the prenatal treatment might permanently increase the expression of the proteins in question.

What works in mice or cultured human cells doesn't always work in people, of course. Several compounds have shown promise in human cells for the treatment of Alzheimer's but disappointed when tested in people, warns Jorge Busciglio, a neurobiologist at the University of California, Irvine, who was one of the team that treated cultured human neurons with NAP and SAL. Nonetheless he is cautiously optimistic.

Charles Cantor of the company Sequenom in San Diego, California, which is developing a non-invasive prenatal blood-screening test for Down's (New Scientist, 11 October, p 10), is excited at the prospect of a prenatal treatment. "I'd love to see these early screening tests lead to therapy and not just termination," he says. "It would have a big impact, especially for families that are not willing to consider abortion as an option."

**Public release date: 28-Nov-2008**

## **Selenium may slow march of AIDS**

Increasing the production of naturally occurring proteins that contain selenium in human blood cells slows down multiplication of the AIDS virus, according to biochemists.

"We have found that increasing the expression of proteins that contain selenium negatively affects the replication of HIV," said K. Sandeep Prabhu, Penn State assistant professor of immunology and molecular toxicology. "Our results suggest a reduction in viral replication by at least 10-fold."

Selenium is a micronutrient that the body needs to maintain normal metabolism. Unlike other nutrients, which bind to certain proteins and modulate the protein's activity, selenium gets incorporated into proteins in the form of an amino acid called selenocysteine.

These proteins – selenoproteins – are especially important in reducing the stress caused by an infection, thereby slowing its spread.

Upon infecting a person, the virus quickly degrades selenoproteins so that it can replicate efficiently. It is unclear just how the virus is able to silence these proteins but Prabhu and his colleagues believe that stress inflicted on cells by the rapidly dividing virus, which produces a key protein known as Tat, is the likely culprit.

Tat is one of about 14 odd proteins produced by HIV during the first stage of infection. The job of these proteins is to trigger the expression of all the other genes that the virus

needs to sustain itself. In addition, Tat also plays a key role in helping the virus replicate.

One of the proteins that targets Tat is a selenoprotein known as TR1.

"Since HIV targets the selenoproteins, we thought that the logical way to deal with the virus is to increase the expression of such proteins in the body," explained Prabhu, whose team's findings are outlined this week (Nov. 28) in the Journal of Biological Chemistry.

Researchers first isolated blood cells from healthy human volunteers who did not have HIV, and infected those cells with the virus. Next, they added tiny amounts of a selenium compound – sodium selenite – into the cell culture to see the effect on viral replication.

**Results from the tests indicate that the addition of selenium inhibits the replication of HIV at least 10-fold, compared to cell cultures in which no selenium is added.** When the researchers selectively reduced production of the selenium containing TR1 protein, they observed a 3.5-fold increase in viral replication.

"This confirms that while increasing the expression of TR1 has a negative impact on the replication of HIV, reducing it helps the virus replicate more efficiently," explained Prabhu. He believes that TR1 works by upsetting the chemical structure of Tat, which in turn reduces the virus' ability to replicate.

"Once we fully understand the function of these selenium proteins, it will give us a handle to come up with more effective drugs," said Prabhu, whose work is partly funded by the National Institutes of Health.

**Public release date: 28-Nov-2008**

## **Fast food a potential risk factor for Alzheimer's**

**Mice that were fed a diet rich in fat, sugar and cholesterol for nine months developed a preliminary stage of the morbid irregularities that form in the brains of Alzheimer's patients.** The study results, published in a doctoral thesis from the Swedish medical university Karolinska Institutet (KI), give some indications of how this difficult to treat disease might one day be preventable.

Alzheimer's is the most common form of dementia, there being roughly 90,000 patients with the disease in Sweden today. The underlying causes of Alzheimer's disease are still something of a mystery, but there are a number of known risk factors. The most common is a variant of a certain gene that governs the production of apolipoprotein E, one of the functions of which is to transport cholesterol. The gene variant is called apoE4 and is found in 15-20 per cent of the population.

For her doctoral thesis, Susanne Akterin studied mice that had been genetically modified to mimic the effects of apoE4 in humans. The mice were then fed for nine months on a diet rich in fat, sugar and cholesterol, representing the nutritional content of most fast

food.

"On examining the brains of these mice, we found a chemical change not unlike that found in the Alzheimer brain," says Ms Akterin, postgraduate at KI Alzheimer's Disease Research Center.

The change in question was an increase in phosphate groups attached to tau, a substance that forms the neurofibrillary tangles observed in Alzheimer's patients. These tangles prevent the cells from functioning normally, which eventually leads to their death. Ms Akterin and her team also noted indications that cholesterol in food reduced levels of another brain substance, Arc, a protein involved in memory storage.

"We now suspect that a high intake of fat and cholesterol in combination with genetic factors, such as apoE4, can adversely affect several brain substances, which can be a contributory factor in the development of Alzheimer's," says Susanne Akterin.

Previous research has shown that a phenomenon known as oxidative stress in the brain and a relatively low intake of dietary antioxidants can also increase the risk of Alzheimer's. Ms Akterin has now demonstrated in her thesis that two antioxidants are dysfunctional in the brains of Alzheimer patients, which can lead to nerve cell death.

"All in all, the results give some indication of how Alzheimer's can be prevented, but more research in this field needs to be done before proper advice can be passed on to the general public," she says

**Public release date: 28-Nov-2008**

## **Despite "Apology Laws," Physicians May Not Communicate Medical Errors**

One half of the adverse medical events occurring each year in the United States are due to preventable medical errors. **These adverse events cause up to 98,000 deaths each year.** In theory, "apology laws" make it easier for physicians to disclose errors by diminishing their fear that a malpractice suit will follow. In addition, evidence suggests that full disclosure increases patient satisfaction, trust, and the likelihood of a positive emotional experience. A satisfied patient would be less likely to disrupt the physician-patient relationship. Despite the well-recognized benefits of disclosure and apology, most physicians do not communicate their errors to patients. Those opposed to apology laws say that widespread disclosure and apology may "flag" errors, and prompt more claims than are dissuaded by the apologies. The authors argue that regardless of potential drawbacks, apology laws may improve doctor-patient relationships by providing doctors with new opportunities to discuss difficult topics with patients. The authors encourage physicians to talk with their state medical associations and legal counsel about how to best comply with their own states' apology laws.

**Public release date: 1-Dec-2008**

## **Lack of vitamin D could spell heart trouble**

Vitamin D deficiency—which is traditionally associated with bone and muscle weakness—may also increase the risk of cardiovascular disease (CVD). A growing body of evidence links low 25-hydroxyvitamin D levels to common CVD risk factors such as hypertension, obesity and diabetes, as well as major cardiovascular events including stroke and congestive heart failure.

In their review article, published in the December, 9, 2008, issue of the Journal of the American College of Cardiology (JACC), the authors issue practical recommendations to screen for and treat low vitamin D levels, especially in patients with risk factors for heart disease or diabetes.

"Vitamin D deficiency is an unrecognized, emerging cardiovascular risk factor, which should be screened for and treated," said James H. O'Keefe, M.D., cardiologist and director of Preventive Cardiology at the Mid America Heart Institute, Kansas City, MO. "Vitamin D is easy to assess, and supplementation is simple, safe and inexpensive."

**It is estimated that up to half of U.S. adults and 30 percent of children and teenagers have vitamin D deficiency**, which is defined as a 25(OH)D level of <20ng/ml. Low vitamin D levels activate the renin-angiotensin-aldosterone system and, in doing so, predispose patients to hypertension and a stiffening and thickening of the heart and blood vessels. Vitamin D deficiency also alters hormone levels and immune function, which can increase the risk of diabetes, a major contributor to CVD.

Recent data from the Framingham Heart Study suggest patients with vitamin D levels below 15 ng/ml were twice as likely to experience a heart attack, stroke or other CV event within the next five years compared to those with higher levels. This risk remained even when researchers adjusted for traditional CV risk factors.

"Restoring vitamin D levels to normal is important in maintaining good musculoskeletal health, and it may also improve heart health and prognosis," said Dr. O'Keefe. "We need large randomized controlled trials to determine whether or not vitamin D supplementation can actually reduce future heart disease and deaths."

### Vitamin D Basics

Vitamin D deficiency is more prevalent than once thought, and greater attention to its treatment is warranted, according to Dr. O'Keefe. Although most of the body's vitamin D requirements can come from sun exposure, indoor lifestyles and use of sunscreen, which eliminates 99 percent of vitamin D synthesis by the skin, means many people aren't producing enough.

"We are outside less than we used to be, and older adults and people who are overweight

or obese are less efficient at making vitamin D in response to sunlight," said Dr. O'Keefe. "A little bit of sunshine is a good thing, but the use of sunscreen to guard against skin cancer is important if you plan to be outside for more than 15 to 30 of intense sunlight exposure."

Vitamin D can also be consumed through supplements and food intake. Natural food sources of vitamin D include salmon, sardines, cod liver oil, and vitamin D-fortified foods including milk and some cereals.

Major risk factors for vitamin D deficiency include: older age, darkly pigmented skin, increased distance from the equator, winter season, smoking, obesity, renal or liver disease and certain medications.

#### Treating Vitamin D Deficiency

In the absence of clinical guidelines, the authors outline specific recommendations for restoring and maintaining optimal vitamin D levels in CV patients. These patients should initially be treated with 50,000 IU of vitamin D2 or D3 once weekly for 8 to 12 weeks. Maintenance therapy should be continued using one of the following strategies:

**50,000 IU vitamin D2 or D3 every 2 weeks;**

**1,000 to 2,000 IU vitamin D3 daily;**

**Sunlight exposure for 10 minutes for Caucasian patients (longer for people with increased skin pigmentation) between the hours of 10 a.m. to 3 p.m.**

Vitamin D supplements appear to be safe. In rare cases, vitamin D toxicity (causing high calcium levels and kidney stones) is possible, but only when taking in excess of 20,000 units a day.

**Public release date: 1-Dec-2008**

#### **Persistent pollutant may promote obesity**

##### ***Compound shown to affect gene activity at extremely low concentrations***

Tributyltin, a ubiquitous pollutant that has a potent effect on gene activity, could be promoting obesity, according to an article in the December issue of BioScience. The chemical is used in antifouling paints for boats, as a wood and textile preservative, and as a pesticide on high-value food crops, among many other applications.

Tributyltin affects sensitive receptors in the cells of animals, from water fleas to humans,

at very low concentrations—a thousand times lower than pollutants that are known to interfere with sexual development of wildlife species. Tributyltin and its relatives are highly toxic to mollusks, causing female snails to develop male sexual characteristics, and it bioaccumulates in fish and shellfish.

The harmful effects of the chemical on the liver and the nervous and immune systems in mammals are well known, but its powerful effects on the cellular components known as retinoid X receptors (RXRs) in a range of species are a recent discovery. When activated, RXRs can migrate into the nuclei of cells and switch on genes that cause the growth of fat storage cells and regulate whole body metabolism; compounds that affect a related receptor often associated with RXRs are now used to treat diabetes. RXRs are normally activated by signaling molecules found throughout the body.

The BioScience article, by Taisen Iguchi and Yoshinao Katsu, of the Graduate University for Advanced Studies in Japan, describes how RXRs and related receptors are also strongly activated by tributyltin and similar chemicals. Tributyltin impairs reproduction in water fleas through its effects on a receptor similar to the RXR. In addition, tributyltin causes the growth of excess fatty tissue in newborn mice exposed to it in utero. The effects of tributyltin on RXR-like nuclear receptors might therefore be widespread throughout the animal kingdom.

**The rise in obesity in humans over the past 40 years parallels the increased use of industrial chemicals over the same period.** Iguchi and Katsu maintain that it is "plausible and provocative" to associate the obesity epidemic to chemical triggers present in the modern environment. **Several other ubiquitous pollutants with strong biological effects, including environmental estrogens such as bisphenol A and nonylphenol, have been shown to stimulate the growth of fat storage cells in mice.** The role that tributyltin and similar persistent pollutants may play in the obesity epidemic is now under scrutiny.

**Public release date: 1-Dec-2008**

**Flu vaccine linked to reduced illness, impairment of academic performance among college students (Read WHOLE article),,,**

College students who are vaccinated against influenza appear less likely to develop flu-like illnesses, require related health care visits or experience impairments in academic performance during flu season, according to a report in the December issue of Archives of Pediatrics & Adolescent Medicine, one of the JAMA/Archives journals.

An estimated 9 percent to 20 percent of college and university students develop illness related to the influenza virus each year, according to background information in the article. "Some reports of influenza outbreaks on college and university campuses have

documented even higher rates of illness among the students," the authors write. "Undoubtedly, influenza is common among college and university students, and its prevention might have an important impact on their health and well-being."

Kristin L. Nichol, M.D., M.P.H., M.B.A., and colleagues at the VA Medical Center and University of Minnesota, Minneapolis, studied 12,975 students on two campuses and over four separate flu seasons between 2002 and 2006. Participants completed an initial questionnaire about demographic and health characteristics during October, and then monthly follow-up surveys between November and April regarding influenza-like illnesses and their effects on daily life. Vaccination status was assessed at the last follow-up survey.

Overall, 30.2 percent of the students were vaccinated, and 24.1 percent experienced at least one flu-like illness during flu season. Those who were vaccinated were significantly less likely to develop such an illness than those who were not vaccinated. "Vaccination was also associated with significant reductions in influenza-like illness-associated provider visits, antibiotic use, impaired school performance and numbers of days of missed class, missed work and illness during the influenza seasons," the authors write.

**When averaged over all the seasons, flu vaccination was associated with a reduction of one-half day (½ a day) of illnesses, so that one day of illness was prevented for every two students who were vaccinated. In addition, for every 17 students vaccinated, one day of missed class was prevented; 11 vaccinations prevented one day of missed work; and six vaccinations prevented one day spent in bed.**

"Current recommendations for the prevention and control of influenza encourage vaccination for all persons 6 months and older who wish to reduce their risk of influenza illness. Our findings highlight the kinds of benefits that could accrue to the nearly 18 million college and university students in this country if they were vaccinated."

Ralph's Note - This should be the death knell for this the necessity of Flu vaccinations at this juncture. There are also to basic flaws to the study. The first being the pro-active vaccinated students may tend to have a more healthy lifestyle. In addition the time taken to get that vaccine, may cut into that ½ day pf productivity.

**Public release date: 1-Dec-2008**

## **Eating eggs when pregnant affects breast cancer in offspring**

A stunning discovery based on epigenetics (the inheritance of propensities acquired in the womb) reveals that consuming choline—a nutrient found in eggs and other foods—during pregnancy may significantly affect breast cancer outcomes for a mother's offspring. This finding by a team of biologists at Boston University is the first to link choline consumption during pregnancy to breast cancer. It also is the first to identify

possible choline-related genetic changes that affect breast cancer survival rates.

"We've known for a long time that some agents taken by pregnant women, such as diethylstilbestrol, have adverse consequences for their daughters," said Gerald Weissmann, M.D., Editor-in-Chief of The FASEB Journal. "But there's an upside. The emerging science of epigenetics has yielded a breakthrough. For the first time, we've learned that we might be able to prevent breast cancer as early as a mother's pregnancy."

The researchers made the discovery in rats by studying females whose mothers were fed varying amounts of choline during pregnancy. Different groups of pregnant rats received diets containing standard amounts of choline, no choline at all, or extra choline. Then the researchers treated the female offspring with a chemical that causes cancer of the mammary gland (breast cancer). Although animals in all groups developed mammary cancer, the daughters of mothers that had received extra choline during pregnancy had slow growing tumors while daughters of mothers that had no choline during pregnancy had fast growing tumors.

**"Our study provides additional support for the notion that choline is an important nutrient that has to be considered when dietary guidelines are developed,"** said Krzysztof Blusztajn, Ph.D., Professor of Pathology at Boston University and the study's senior researcher. "We hope it will be possible to develop nutritional guidelines for pregnant women that ensure the good health of their offspring well into old age."

The researchers also found multiple genetic and molecular changes in the rats' tumors that correlated with survival outcomes. For example, the slow growing tumors in rats had a genetic pattern similar to those seen in breast cancers of women who are considered to have a good prognosis. The fast growing tumors in mice had a pattern of genetic changes similar to those seen in women with a more aggressive disease. The researchers also found evidence that these genetic changes may result from the way that choline affects modifications of the DNA within the mammary gland of fetuses as they develop in the womb.

The National Cancer Institute estimates that there will be more than 184,000 new cases of breast cancer in 2008 and more than 40,000 deaths. Treatments for women suffering from breast cancer range from hormone therapy to surgery.

**Public release date: 1-Dec-2008**

## **Vitamin D found to fight placental infection**

In a paper available at the online site of the journal *Biology of Reproduction*, a team of UCLA researchers reports for the first time that vitamin D induces immune responses in placental tissues by stimulating production of the antimicrobial protein cathelicidin.

The study involved exposing cultured human trophoblast cells to the active form of vitamin D, leading to production of cathelicidin and an increased antibacterial response in

the trophoblast cells.

The team, headed by Dr. Martin Hewison, suspects that the ability of the placenta to synthesize cathelicidin varies widely among women. Their discovery suggests that placental innate immunity can be enhanced if pregnant women supplement their diets with vitamin D.

Induction of cathelicidin production by vitamin D may help the placenta stave off infection by a variety of pathogenic organisms, including staphylococcus, streptococcus, and E. coli bacteria. Vitamin D may also enhance and sustain this bacterial killing by protecting placental trophoblast cells from infection-associated cell death.

The significance of vitamin D in human reproduction has been recognized for the past 20 years, although its exact role has not been completely understood. This study presents a new mechanism for activation of innate immune responses in the placenta to protect it from infectious bacteria and sheds new light on the possible role of vitamin D in pregnancy and pregnancy-associated infection.

**Public release date: 1-Dec-2008**

## **US infant formula safe from melamine, says FDA**

The domestic supply of infant formula in the United States is safe for consumption, the FDA has said following an investigation into contamination with the industrial chemical melamine.

FDA's melamine update, published last week, follows its risk assessment in October that had cleared all foods except infant formula from posing a risk.

At the time, the agency had said it was impossible to establish a limit on the chemical's presence in infant formula, owing to uncertainty over the specific impacts of melamine in an infant's body. This did not necessarily suggest that any exposure to the chemical in infant formula would harm infants, but that there was too much uncertainty to outline specific guidelines for consumers, said FDA at the time.

US formula safe

Further to the first interim assessment, the agency has confirmed the safety of US-manufactured infant formula, and recommends consumers can continue to use it.

**“Levels of melamine alone or cyanuric acid alone, at or below 1 part per million (ppm) in infant formula do not raise public health concerns,”** wrote FDA in the update to its risk assessment.

This is up to 10,000 times less than the levels of melamine reported in Chinese-manufactured infant formula.

The agency said it had been collecting and analyzing samples of domestically manufactured infant formula for the presence of melamine and melamine-related compounds. So far, tests have found “extremely low” levels of melamine in one infant formula sample and “extremely low” levels of cyanuric acid in another, it said.

**“The levels were so low (well below 1 ppm) that they do not pose a health risk to infants,” it said. To view the test results, [click here](#).**

Tighter scrutiny

The focus on melamine came to light in September, after it emerged that milk powder for infants was found to have been contaminated with melamine in China.

The contamination in China led to the death of four Chinese children, and the hospitalisation of thousands more.

Melamine is a chemical that can make it appear there is more protein in a product, and has been linked to causing kidney stones and other health problems.

**The compound alone is of low toxicity, but studies with animals have suggested that combination of melamine with cyanuric acid, a potential impurity of melamine, may lead to the kidney problems observed in China.**

More research

**FDA said it is continuing to sponsor and conduct animal studies to assess the potential toxicity from co-ingestion of melamine and cyanuric acid.**

*The agency said that once this is completed, it will update its interim safety/risk assessment for melamine and its analogues.*

For the time being, the agency states: “The safety/risk assessment assumes the analogues to have equal effect. Thus, levels of melamine or one of its analogues alone below 1.0 ppm in infant formula do not raise public health concerns.”

Ralph’s Note - This is criminal for two reasons. The first being, they don’t really know. But its OK for infants to drink while we check. The second being, this allows the Chinese to water down all their contaminated infant formula and sell it to the U.S.A.. Melamine should not be there period. It is only added as a method to deceive buyers into thinking the product is of higher quality than it actually is. This is a disgraceful act of the FDA, in its short road to appeasing industrial interest.

**Public release date: 2-Dec-2008**

**Drug marketing techniques may be risking patient safety**

Analysis: What can we learn from drug marketing efficiency?

With new drugs being reviewed by regulatory agencies and then released onto the market faster than ever before, patients' safety is being compromised, warns a study published on [bmj.com](http://bmj.com) today.

Dr David Kao from the University of Colorado Health Sciences Center, argues that while drug regulatory bodies are under pressure to make new drugs available more quickly, there are concerns that the deadlines for approving drugs have shifted the focus away from safety.

Kao reviews trends in drug approval times in the United States, and suggests how drug marketing techniques could be used to improve the way new drugs are monitored.

Previous research has shown that drugs approved in the US during the two months before the mandated deadline were more likely to be withdrawn for safety reasons or to carry a warning.

Today's marketing techniques are so sophisticated, says Kao, that once a drug has been approved the products can be released on websites within 90 minutes. He cites the example of Merck's new treatment (sitagliptin) for hyperglycaemia (high blood sugar levels)—within 14 days of approval 188 million patients or 73% of the insured US population had been targeted by the marketing campaign.

The danger with so many people trying a new drug very quickly, argues Kao, is that it can expose large numbers of patients to unknown risks. When Merck's anti-inflammatory drug Vioxx (rofecoxib) was withdrawn from the market for safety reasons it had been available for five years and 20 million patients had been exposed to it.

Regulatory agencies have been criticised for their dependence on drug companies for funding. The agencies often collect fees from drug companies so that they can hire staff to review the drugs more quickly. The European Agency for the Evaluation of Medicinal Products receives 75% of its funding in this way, 43% of the US Food and Drug Administration (FDA) budget is similarly derived, and the UK's Medicines and Healthcare Products Regulatory Agency is completely funded by drug companies.

The author believes that the systems for reporting adverse drug reactions must be improved and suggests using the very same effective drug marketing techniques to do this. For example, laws in the US already compel TV adverts to instruct patients experiencing negative side effects to report their symptoms to the FDA. This could be expanded to include campaigns dedicated to drug safety monitoring.

Kao concludes by saying that the only drug monitoring system that will minimise unknown risks must involve all the key players in healthcare, including doctors, regulatory bodies, drug companies and patients.

**Public release date: 2-Dec-2008**

## **Broccoli compound targets key enzyme in late-stage cancer**

BERKELEY — An anti-cancer compound found in broccoli and cabbage works by lowering the activity of an enzyme associated with rapidly advancing breast cancer, according to a University of California, Berkeley, study appearing this week in the online early edition of the journal Proceedings of the National Academy of Sciences.

**Indole-3-carbinol**, or I3C, is a chemical compound found in broccoli and other cruciferous vegetables and which is known to stop the growth of breast cancer cells. UC Berkeley researchers' discovery of how I3C works will help them modify the compound to improve its anti-cancer effects. (Firestone & Bjeldanes labs/UC Berkeley)The compound, indole-3-carbinol, is already undergoing clinical trials in humans because it was found to stop the growth of breast and prostate cancer cells in mice.

The new findings are the first to explain how indole-3-carbinol (I3C) stops cell growth, and thus provides the basis for designing improved versions of the chemical that would be more effective as a drug and could work against a broader range of breast as well as prostate tumors.

"I think one of the real uses of this compound and its derivatives is combining it with other kinds of therapies, such as tamoxifen for breast cancer and anti-androgens for prostate cancer," said coauthor Gary Firestone, UC Berkeley professor of molecular and cell biology. "Humans have co-evolved with cruciferous vegetables like broccoli and Brussels sprouts, so this natural source has a lot fewer side effects."

"This is a major breakthrough in trying to understand what the specific targets of these natural products are," said coauthor Leonard Bjeldanes, UC Berkeley professor of toxicology. "The field is awash with different results in various cells, but no real identification of a specific molecular target for these substances. The beauty of identifying the target like this is that it suggests further studies that could augment the activity of this type of molecule and really specify uses for specific cancers."

Firestone, Bjeldanes and their colleagues showed that I3C inhibits the enzyme elastase, which at high levels in breast cancer cells heralds a poor prognosis: decreased response to chemotherapy, reduced response to endocrine treatment and reduced survival rates.

Elastase is an enzyme that shortens a cellular chemical, cyclin E, that is involved in controlling the cell cycle. The shortened version of cyclin E accelerates the cell cycle, making cancer cells proliferate faster. Firestone showed that I3C prevents the elastase

shortening of cyclin E, thereby arresting development of breast cancer cells.

For more than 15 years, Firestone, Bjeldanes and their colleagues have studied the anti-cancer benefits of vegetables in the cabbage family that are lumped together in the genus Brassica and, because of their cross-shaped flowers, are often referred to as cruciferous vegetables.

Though the anti-cancer benefits have been recognized since the 1970s, the mechanism is only now being discovered, in part through the work of Firestone, Bjeldanes and their UC Berkeley colleagues.

"We have connected the dots on one extremely important pathway" by which indole-3-carbinol works, Firestone said.

In previous work, they found that indole-3-carbinol interferes with more than cell proliferation. It also disrupts the migration and alters adhesion properties of cancer cells, as well as counteracts the survival ability of cancer cells, all of which are implicated in cancer cell growth. To have such broad downstream effects, I3C must act at the beginning of a major cellular pathway, Firestone said. The newly reported research pins this activity to elastase and its effect on cyclin E.

Bjeldanes noted that I3C is available as a supplement and is a preferred preventative treatment for recurrent respiratory papillomatosis, a condition involving non-malignant tumors of the larynx. Improved versions of the chemical could thus help treat cancers other than those of the breast and prostate.

Graduate student Ida Aronchik and recent Ph.D. recipient Hanh H. Nguyen, along with colleagues in the Firestone and Bjeldanes labs, have already chemically modified I3C and boosted its activity in cell culture by at least a factor of 100. The lab teams currently are probing the elastase structure and how I3C interacts with it to identify the best parts of the I3C molecule to modify.

I3C is only one of many plant-derived chemicals, called phytochemicals, that Firestone is investigating in his laboratory as potential anti-cancer agents. Among them is the anti-malarial drug artemisinin. Last month, the Journal of Biological Chemistry accepted a paper by Firestone and his colleagues showing that artemisinin blocks prostate cancer cell growth by interfering with the same intracellular pathway as does I3C. This pathway involves the transcription factor SP1, which latches onto other genes to boost their activity.

"SP1 could be a generalized target of phytochemicals," Firestone said. "Phytochemicals work because they interact with and inhibit enzymes that control a host of cellular processes, including migration and adhesion."

The research is supported by the National Cancer Institute. Other coauthors of the paper are Gloria A. Brar, currently a graduate student at the Massachusetts Institute of

Technology, and former UC Berkeley undergraduate David H. H. Nguyen, now a graduate student at New York University

**Public release date: 3-Dec-2008**

## **Calcium and vitamin D may not be the only protection against bone loss**

New study finds diet rich in fruits and vegetables may strengthen bones

Chevy Chase, MD—Diets that are high in protein and cereal grains produce an excess of acid in the body which may increase calcium excretion and weaken bones, according to a new study accepted for publication in The Endocrine Society's Journal of Clinical Endocrinology & Metabolism (JCEM). **The study found that increasing the alkali content of the diet, with a pill or through a diet rich in fruits and vegetables has the opposite effect and strengthens skeletal health.**

"Heredity, diet, and other lifestyle factors contribute to the problem of bone loss and fractures," said Bess Dawson-Hughes, M.D., of Tufts University in Boston, Mass. and lead author of the study. "When it comes to dietary concerns regarding bone health, calcium and vitamin D have received the most attention, but there is increasing evidence that the acid/base balance of the diet is also important."

Average older adults consume diets that, when metabolized, add acid to the body, said Dr. Dawson-Hughes. With aging, we become less able to excrete the acid. One way the body may counteract the acid from our diets is through bone resorption, a process by which bones are broken down to release minerals such as calcium, phosphates, and alkaline (basic) salts into the blood. Unfortunately, increased bone resorption leads to declines in bone mass and increases in fracture risk.

"When fruits and vegetables are metabolized they add bicarbonate, an alkaline compound, to the body," said Dr. Dawson Hughes. "Our study found that bicarbonate had a favorable effect on bone resorption and calcium excretion. This suggests that increasing the alkali content of the diet may attenuate bone loss in healthy older adults."

In this study, 171 men and women aged 50 and older were randomized to receive placebo or doses of either: potassium bicarbonate, sodium bicarbonate, or potassium chloride for three months. Researchers found that subjects taking bicarbonate had significant reductions in calcium excretion, signaling a decrease in bone resorption.

"In this study, we demonstrated that adding alkali in pill form reduced bone resorption and reduced the losses of calcium in the urine over a three month period," said Dr. Dawson-Hughes. "This intervention warrants further investigation as a safe and well tolerated supplement to reduce bone loss and fracture risk in older men and women."

**Public release date: 4-Dec-2008**

## **A little wine boosts omega-3 in the body: Researchers find a novel mechanism for a healthier heart**

Moderate alcohol intake is associated with higher levels of omega-3 fatty acids in plasma and red blood cells. This is the major finding of the European study IMMIDIET that will be published in the January issue of the American Journal of Clinical Nutrition, an official publication of the American Society for Nutrition and is already available on line ([www.ajcn.org](http://www.ajcn.org)). The study suggests that wine does better than other alcoholic drinks. This effect could be ascribed to compounds other than alcohol itself, representing a key to understand the mechanism lying behind the heart protection observed in moderate wine drinkers.

The IMMIDIET study examined 1,604 citizens from three geographical areas: south-west London in England, Limburg in Belgium and Abruzzo in Italy. Thanks to a close cooperation with General Practitioners of these areas, all participants underwent a comprehensive medical examination, including a one year recall food frequency questionnaire to assess their dietary intake, alcohol consumption included.

Omega-3 fatty acids, mainly derived from fish, are considered as protective against coronary heart disease and sudden cardiac death, thus their high blood concentration is definitely good for our health.

Now European researchers found that moderate alcohol drinking acts like a 'trigger', boosting the amount of omega-3 fatty acids in our body.

"Several studies have shown that moderate alcohol consumption, including wine, is associated with protection against coronary heart disease and ischemic stroke - says Romina di Giuseppe, lead author of the study, from the Research Laboratories at Catholic University of Campobasso - Although the mechanisms are not completely defined, there was some evidence that alcohol intake might influence the metabolism of essential polyunsaturated fatty acids, as omega-3. That is exactly what we found in our population study. People drinking moderate amounts of alcohol, one drink a day for women and two for men, had higher concentration of omega-3 fatty acids in plasma and red blood cells independently of their fish intake".

However important these results appear to be, the best is yet to come. Researchers from Catholic University of Campobasso, in Italy, and from University of Grenoble, in France, turned their attention on the variety of alcoholic beverages consumed in order to see whether the high levels of omega-3 fatty acids detected might be ascribed to alcohol itself or to other substances.

"From our previous studies we know that association between wine drinking and increased concentration of omega-3 fatty acids have been observed – says Michel de Lorgeril, from the University of Grenoble, partner of the IMMIDIET project and co-leader of the study - Nevertheless, it was not possible to separate the effects of wine from

those of beer or spirits. Our study of 3 populations with different dietary habits and different consumption of alcoholic beverages types allowed us to explore this aspect."

"Analysis carried out on different alcoholic beverages –argues Licia Iacoviello coordinator of the IMMIDIET study at Catholic University of Campobasso - showed that the association between alcohol and omega-3 fatty acids was present in both wine drinkers and beer or spirits drinkers. However, the association was stronger between wine drinking and omega-3 fatty acids levels. This suggests that components of wine other than alcohol is associated with omega-3 fatty acids concentration. We may guess this effect can be ascribed to polyphenols".

Polyphenols are naturally occurring compounds contained in a different variety of food and beverages, such as wine. Due to their strong antioxidant activity, they are able to reduce oxidation processes caused by free radicals.

"We consider these data to be a major finding - de Lorgeril concludes - opening a new window in the field of cardiovascular prevention. Beyond the alcohol issue, our results raise crucial questions regarding the effects of polyphenols on lipids (both in blood and cell membranes) and possibly of lipids on polyphenols".

**Public release date: 4-Dec-2008**

## **Interferon as long-term treatment for hepatitis C not effective, report HALT-C researchers**

DALLAS — Dec. 4, 2008 — Use of the drug interferon as a long-term maintenance strategy to slow the progression of liver disease associated with the hepatitis C virus is ineffective, UT Southwestern Medical Center researchers and their colleagues from nine other institutions have found in a multicenter study.

Results of the 3½-year study, called the HALT-C (Hepatitis C Antiviral Long-Term Treatment Against Cirrhosis) Trial, appear in today's issue of The New England Journal of Medicine. The researchers found no difference in the rate of progression of liver disease among patients who received interferon and those who did not.

"It wasn't that there was an insignificant difference; there was absolutely no difference whatsoever in the progression to cirrhosis and other disease complications," said Dr. William M. Lee, professor of internal medicine at UT Southwestern and a principal investigator for the study. "It is a negative study but an important one."

Dr. William M. Lee and other researchers have discovered in a multicenter study that using the drug interferon as a long-term maintenance strategy to slow the progression of liver disease associated with the hepatitis C virus is ineffective.

Dr. Lee said physicians should not expect any benefit from the long-term use of interferon by itself in slowing disease progression. By contrast, use of interferon with other drugs such as ribavirin can lead to viral eradication, or complete clearance of hepatitis C virus, a result that will “stop the disease in its tracks,” Dr. Lee said.

Hepatitis C is a viral infection that causes liver inflammation and can progress over many years to cirrhosis, liver cancer, liver failure and death. The disease affects more than 3 million people in the United States and 170 million people worldwide. It is the most common reason for liver transplantation in the U.S.

There is no vaccine to prevent hepatitis C virus infection. The combination of interferon and ribavirin works for about 40 percent to 50 percent of people with the virus, while the other 50 percent to 60 percent of patients will continue to progress to later states of liver disease, Dr. Lee said.

In addition to interferon and ribavirin, new drug agents such as protease and polymerase inhibitors are being used in clinical studies at UT Southwestern to improve rates of virus eradication. Food and Drug Administration approval of these agents is likely to be three years away, Dr. Lee said.

In the HALT-C Trial, conducted between August 2000 and June 2007, 1,050 people with hepatitis C who did not respond to initial antiviral treatment were assigned randomly to either a group that received treatment with a type of interferon called peginterferon or to a group that did not. About 120 patients were enrolled at UT Southwestern.

Participants were monitored every three months and underwent liver scans and biopsies at specified intervals through the study period. Researchers found that although the level of hepatitis C virus in blood and certain enzymes in the liver decreased significantly with treatment, there was not a significant difference in ultimate clinical outcome.

“Currently, we use interferon only to clear the virus,” said Dr. Lee. “If you cannot clear the virus with treatment, the idea that struggling long term through the side effects of interferon is somehow going to help you rid yourself of cirrhosis is just not plausible any longer.”

Some patients cannot tolerate the side effects of the different types of interferon medication, which can cause extreme flu-like symptoms, such as fever, chills, fatigue, depression, muscle aches, chest pain, difficulty breathing, nausea, vomiting, and weight and hair loss.

Other researchers from UT Southwestern involved in the study were Dr. Thomas Rogers, professor of pathology, and Dr. Peter Malet, professor of internal medicine.

Also involved in the study were researchers from Saint Louis University School of Medicine; Virginia Commonwealth University Medical Center; University of Colorado School of Medicine; University of Southern California; National Institute of Diabetes and

Digestive and Kidney Diseases; University of Michigan Medical Center; University of Connecticut Health Center; University of California, Irvine, and VA Long Beach Healthcare System; and University of Washington.

The study was funded by the National Institutes of Health. Pharmaceutical manufacturer Hoffman-LaRoche, through an agreement with the NIH, also provided funding.

Dr. Lee has received consulting fees from Eli Lilly, Fibrogen and Astra Zeneca, and grant support from Hoffmann-LaRoche, Schering-Plough, Vertex Pharmaceuticals, GlaxoSmithKline, Siemens, Globelimmune and Bristol-Myers Squibb.

Alzheimer's disease breakthrough

In a paper published in the latest edition of the Journal of Alzheimer's Disease, folate is shown to be beneficial in the screening system.

Lead author, CSIRO's Dr Ian Macreadie says folate is already well known to have a protective effect against Alzheimer's disease which is believed to be caused by the loss of neurons in the brain due to a process whereby toxic multimers of a small protein called A $\beta$  are formed.

"However, a team of scientists working within CSIRO's Preventative Health Flagship has discovered a rapid screening system to identify inhibitors of this process. Compounds that inhibit the formation of the toxic multimers may lead to the prevention or delay of the disease," Dr Macreadie says.

"The yeast trial we developed could lead to the discovery of new agents which may prove useful in preventing or delaying the onset of Alzheimer's disease,"

Dr Macreadie says. **Although many other research groups and drug companies around the world are trying to find compounds that act in the same way**, the advance by the Flagship team involves using live yeast with the A $\beta$  protein fused to a green fluorescent protein that comes from jellyfish.

"The significance of this development is that the yeast trial we developed could lead to the discovery of new agents which may prove useful in preventing or delaying the onset of Alzheimer's disease."

Currently Alzheimer's disease is an incurable illness and the fourth leading cause of death in people aged 65 years and over.

**Although folate is abundant in foods like leafy green vegetables, pulses and liver, CSIRO studies have shown that many Australians do not consume enough folate to benefit from its ability to prevent cell damage. Folate levels can, however, be readily restored by dietary folate supplementation**

**Public release date: 8-Dec-2008**

## **Updated standards to reduce metal contaminants in prescription drugs**

Prescription medicines in the United States could soon have lower levels of potentially harmful metals, as the organization that sets drug standards develops new limits for impurities like mercury, arsenic, and lead, according to an article scheduled for the December 8 issue of Chemical & Engineering News, ACS' weekly newsmagazine.

In the article, C&EN Associate Editor Jyllian Kemsley notes that **researchers have known for years that potentially toxic metals can wind up in pharmaceutical ingredients through raw materials, catalysts, equipment, and other sources.** But the testing method currently prescribed by the **U.S. Pharmacopeia (USP), the nonprofit organization that sets standards for the pharmaceutical industry, has not kept pace with that new knowledge.** **That method involves a 100-year-old test that is time-consuming, difficult to interpret, and generally not quantitative, according to the article.**

USP now is developing new standards and testing methods that will be finished in 2010 and implemented over a span of years. USP will require drug makers to use improved methods and instruments to detect metal contaminants.

Ralph's note - Woah, back this up a little bit. Basically there has been no real testing going on, and won't be for many years. So USP means what again?

**Public release date: 8-Dec-2008**

## **Breaking the silence after a study ends**

**While an estimated 2.3 million people in the United States take part in clinical trials every year, there currently exists no formal requirement to inform them of study results,** an oversight that leaves participants confused, frustrated, and, in some cases, lacking information that may be important to their health. In an article published today in the Archives of Neurology, researchers at the University of Rochester Medical Center have proposed a novel and effective approach to disseminate the results of clinical trials to study volunteers.

Industry, government, and academic researchers are dependent upon the willing participation of millions of individuals to fill the estimated 50,000 clinical trials conducted every year that evaluate the safety and efficacy of experimental drugs and medical devices.

Researchers are only required to inform participants in instances when new information arises that may affect their willingness to continue participation. **However, neither federal guidelines nor institutional review boards generally require disclosure of results at the conclusion of a study – even if the study is halted.** Consequently, many research participants never learn the outcome of studies in which they volunteer.

**"Individuals who volunteer to participate in clinical research frequently expose themselves to risks, both known and unknown,"** said neurologist Ray Dorsey, M.D., the report's author. "Because of their participation, they should be informed of the results of these studies in a timely and personalized manner."

In recent years, there have been several high-profile examples in which information has been either withheld from participants (and the public), participants were not directly informed of study results, or they learned about negative study results indirectly from other sources such as the media. Despite recent federal efforts to mandate communications in instances when the product is approved, researchers are still not required to disclose results in instances when the drug or device has been tested in patients but – because of unfavorable results – abandoned before it is submitted for regulatory approval.

The paper details efforts of researchers to communicate the results of a clinical trial for an experimental drug (ethyl-EPA) for Huntington's disease. The results of the study – which showed no significant difference between the group of patients who received the drug and those who received the placebo – were also published today in the Archives of Neurology. The research was sponsored by the drug's manufacturer, Amarin Neuroscience, and conducted by the Huntington Study Group, an international network of researchers based in Rochester. The 12-month study included 316 adults with Huntington's disease and was conducted at 41 sites in the U.S. and Canada.

Over the course of the trial, the scientists and the sponsor developed a communication plan to inform participants of the study results. The goal was to directly inform participants within 48 hours of the official release of study results; federal securities law requires companies to publicly disclose study results if they have a material financial impact.

The plan included a mix of electronic communication and personal outreach. Information on the results was posted to the study's website and emailed to members of the Huntington's disease community. Additionally, study coordinators called each of the participants directly. Rochester neurologist Ira Shoulson, M.D., the study's principal investigator, and the CEO of Amarin Neuroscience also held a conference call which was open to all study participants and investigators during which they summarized the study results and then fielded questions.

The researchers surveyed participants after the communication efforts and found that more than half (56%) learned of the results of the study within 48 hours of the initial public release in 2007 by the company – the vast majority (73%) via a telephone call from the study staff. Participants reported a high level of satisfaction with the way results were communicated and had developed a strong understanding of the drugs benefits and risks.

"It is critical that we treat participants as partners in research," said Shoulson. "It is our hope that the commitment that the investigators and sponsor made to communicate the results of the clinical trial in a timely and personalized manner to research participants will set the standard for future clinical trials."

**Public release date: 8-Dec-2008**

## **Vitamin B1 could reverse early-stage kidney disease in diabetes patients**

Researchers at the University of Warwick have discovered high doses of thiamine – vitamin B1 – can reverse the onset of early diabetic kidney disease.

Kidney disease, or diabetic nephropathy, develops progressively in patients with type 2 diabetes. Early development of kidney disease is assessed by a high excretion rate of the protein albumin from the body in the urine, known as microalbuminuria.

The research is led by Dr Naila Rabbani and Professor Paul J Thornalley at Warwick Medical School, University of Warwick, in collaboration with researchers at the University of Punjab and Sheik Zaid Hospital, Lahore, Pakistan.

The team has discovered taking high oral doses of thiamine can dramatically decrease the excretion of albumin and reverse early stage kidney disease in type 2 diabetes patients.

**In a paper published online in the journal *Diabetologia*, the team show 300 mg of thiamine taken orally each day for three months reduced the rate of albumin excretion in type 2 diabetes patients. The albumin excretion rate was decreased by 41% from the value at the start of the study. The results also showed 35% of patients with microalbuminuria saw a return to normal urinary albumin excretion after being treated with thiamine.**

Forty patients with type 2 diabetes aged between 35 and 65 years old took part in the

trial. They were randomly assigned a placebo or 3 x 100mg tablets of thiamine a day for three months.

The Warwick research group has already conclusively proven that type 2 diabetes patients have a thiamine deficiency. In an earlier study led by Professor Paul Thornalley at Warwick Medical School, the research team showed that thiamine deficiency could be key to a range of vascular problems for diabetes patients.

Dr Rabbani said: "This study once again highlights the importance of Vitamin B1 and we need to increase awareness. Professor Thornalley and I are planning a foundation at the University of Warwick to further education and research in thiamine deficiency

**Public release date: 9-Dec-2008**

## **Statin warning for pregnant women**

Pregnant women or those hoping to start or extend a family should avoid using the cholesterol-lowering drugs statins, say scientists.

Current clinical guidelines already recommend that women who are pregnant should stop taking statins but the advice is based on the knowledge that cholesterol is essential for normal fetal development.

Indeed, a 2007 study examining the risk of congenital anomalies in children of pregnant women using statins suggested that the detrimental effects of the drugs may be restricted to fat-soluble or 'lipophilic' statins only.

But new research from The University of Manchester has shown that even water-soluble or 'hydrophilic' statins, such as pravastatin, can affect placental development leading to worse pregnancy outcomes.

"The rapid rise in obesity and type-2 diabetes is a major health issue and affected individuals are often treated with statins to lower circulating cholesterol levels and reduce the risk of heart disease," said Dr Melissa Westwood, a Senior Lecturer in Endocrinology based at the Maternal and Fetal Health Research Centre at St Mary's Hospital, Manchester.

"Given the evolving demographic profile of these conditions, such drugs are increasingly prescribed to women of reproductive age **but the actions of statins are not limited to the regulation of cholesterol levels, as they can affect the production of other chemicals in the body too.**

**"Our study examined the effects that both lipophilic and hydrophilic statins had on a key biological system that is crucial for maintaining the normal function of the**

**placenta, which acts as the nutrient-waste exchange barrier between mother and fetus."**

The research, funded by the Biotechnology and Biological Sciences Research Council (BBSRC), used a placental-tissue model that could be maintained in a viable state outside the body for several days and tested the effects of two different statins – one water-soluble and one that dissolves in fat.

As expected, the fat-soluble statin, cerivastatin, affected the placenta resulting in reduced growth but the researchers also found that pravastatin – the water-soluble statin thought to be potentially compatible for use in pregnancy – had the same detrimental effect.

"These results clearly show that the effect of statins on the placenta is not dependent on their lipophilicity as had previously been suggested," said Dr Westwood, whose findings are published in the Journal of Cellular and Molecular Medicine.

"While hydrophilic statins have not been reported to increase the incidence of fetal malformations, our research suggests that they will have a detrimental effect on placental growth, which is likely to result in poor pregnancy outcome.

"Healthcare professionals should continue to advise women to avoid the use of any type of statin once they plan to start a family or when a pregnancy is suspected or confirmed."

**Public release date: 9-Dec-2008**

**Pine bark reduces inflammatory marker CRP in osteoarthritis**

Third osteoarthritis study this year reveals Pycnogenol® lowers inflammatory marker CRP

Osteoarthritis (OA), a type of arthritis caused by the breakdown and loss of cartilage, affects more than 20 million Americans. While the most common prescription to treat OA is non-steroidal anti-inflammatory drugs (NSAIDs), many seek alternative treatments because of the side effects associated with these drugs. Pycnogenol (pic-noj-en-all), an antioxidant plant extract from the bark of the French maritime pine tree, has been shown to reduce osteoarthritis in multiple studies. A study published in the current issue of the journal Redox Report, reveals Pycnogenol's anti-inflammatory potency further to improving OA symptoms and pain was able to significantly lower plasma levels of C-reactive protein (CRP). With disease progression of osteoarthritis, the inflammation may reach a level where it no longer is limited to the affected joint and stresses the organisms, which in turn increases the inflammatory marker CRP in the blood.

The current study, a joint effort between Italy's Chieti-Pescara University and the University of Munster, Germany, investigated a subset 55 patients from a previous osteoarthritis with 156 patients who had significantly elevated CRP levels. Treatment

consisted of two tablets daily of either 50 mg Pycnogenol or placebo. Blood specimens were drawn at baseline of the initial study and again after three-month treatment. Results showed that Pycnogenol significantly lowered CRP from average 3.9 mg/L at baseline to 1.1 mg/L, reflecting essentially healthy levels. In the placebo group a marginal lowered CRP level was detected. Other blood parameters indicative of acute inflammation likewise decreased with Pycnogenol, such as fibrinogen (lowered 37.1 %) and reactive oxygen species (lowered by 29.9 %).

"The decrease of systemic inflammatory markers, particularly CRP, suggests Pycnogenol® properties may be potent enough to arrest the spread of inflammation from osteoarthritic joints to the whole organisms" said Dr. Peter Rohdewald, a lead researcher of the study. "When inflammatory processes are allowed to reach the whole body the degenerative processes may burden overall health including increased cardiovascular risks."

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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.**