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Human Technology Research Synopsis

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Compiled By Ralph Turchiano

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Public release date: 24-Jun-2009

Irritability should be considered when diagnosing bipolar disorder in children

EAST PROVIDENCE, RI – A new study from Bradley Hospital and The Warren Alpert Medical School of Brown University, as well as two other institutions, adds to mounting evidence that clinicians consider irritability as a symptom when diagnosing pediatric bipolar disorder.

Reporting in the July issue of the Journal of the American Academy of Child and Adolescent Psychiatry, researchers say a small percentage of children with bipolar disorder experience manic episodes without extreme elation – one of the hallmarks of the disorder – and are diagnosed based on irritable mood alone.

"Diagnosing children with bipolar disorder is challenging. One of the chief controversies is whether irritability should be included among the criteria for this diagnosis because it can also overlap with a number of other psychiatric disorders, such as attention deficit hyperactivity disorder," says lead author Jeffrey Hunt, MD, a child psychiatrist and training director at Bradley Hospital. "Our findings confirm that while irritable-only mania is uncommon, it does exist – particularly in younger children – and should be considered in a bipolar diagnosis."

Bipolar disorder is characterized by dramatic mood swings from euphoria, elation and irritability – the manic phase of the disorder – to severe depression. Bipolar disorder often begins in late adolescence or early adulthood, although it can develop as early as the preschool years. Recent studies have shown that the number of children and teens being treated for bipolar disorder has grown dramatically in the last decade. Although it is unclear what has caused this increase, experts believe it may be due in part to more aggressive diagnoses by physicians and a greater awareness of pediatric bipolar disorder in the medical community.

Hunt and colleagues studied 361 children between the ages of 7 and 17 with bipolar disorder participating in the multi-site Course and Outcome of Bipolar Illness in Youth (COBY) study at Bradley Hospital and Alpert Medical School, the University of Pittsburgh and the University of California-Los Angeles. COBY is the largest and most comprehensive study of children and adolescents with bipolar disorder to date.

Researchers quantified the frequency and severity of manic symptoms of each participant, including whether irritability and elation were present. Based on this data, the group was then reclassified into three subgroups: elation-only, irritable-only and both elated and irritable.

Approximately 10 percent of children fell into the irritable-only category, while elated-only constituted about 15 percent. Nearly three-quarters experienced both elation and irritability. The irritable-only participants were significantly younger in age than the other two groups; however, there were no other sociodemographic differences between the groups. There were also no significant differences in terms of bipolar subtype, rate of psychiatric comorbidities, severity and duration of illness, and family history of mania and other psychiatric disorders. However, depression and alcohol abuse in second-degree relatives occurred more frequently in the irritable-only subgroup.

"The fact that the irritable-only and elation-only subgroup had similar clinical characteristics and family histories of bipolar disorder provides support for continuing to consider episodic irritability in the diagnosis of pediatric bipolar disorder," says Hunt, who is an assistant professor of psychiatry and human behavior at Alpert Medical School. Hunt is also training director of the child and adolescent fellowship and triple board residency programs.

The authors say continual, long-term follow-up of this study sample will help clarify whether the presence or predominance of elation or irritability at baseline will predict future clinical outcomes.

Public Release: 25-Jun-2009

Kidney damage from medical imaging procedures can cause long-term health problems

Most patients are told that injury is only temporary

Kidney injury that can arise after undergoing certain medical imaging procedures increases a patient's risk of having a stroke or heart attack over the next year or two, according to a study appearing in an upcoming issue of the Clinical Journal of the American Society Nephrology (CJASN). The findings indicate that seemingly minor and reversible kidney damage from these common clinical procedures is a serious health threat.

Medical imaging often uses contrast agents, substances such as iodine and barium that enhance the contrast of structures or fluids within the body. For example, contrast agents may be used during cardiac angiography and computed tomography procedures to visualize blood vessels and changes in tissues. Exposure to contrast agents can injure the kidneys, but patients are often told that this is only a temporary side effect. Recent research has suggested that such contrast-induced kidney damage may actually be more serious, although no thorough studies have looked into the hypothesis.

To investigate the issue, Richard Solomon, MD (University of Vermont), and his colleagues studied 294 patients with kidney disease who were exposed to contrast agents during cardiac angiography. Patients in the CARE (Cardiac Angiography in RENally Impaired Patients) trial were randomly divided to receive one of two contrast agents: iopamidol or iodixanol. **After following patients for at least one year, the researchers found that 92 (31%) of the patients experienced negative health effects. Thirty-eight (13%) of the patients experienced a major event, such as death, stroke, heart attack, or end-stage renal disease. Individuals who developed contrast-induced kidney injuries had twice as many long-term negative health effects compared with patients whose kidneys were not damaged.** In the absence of contrast-induced kidney injury, there was no difference in the incidence of long-term negative health effects between patients taking iopamidol or iodixanol. However, the investigators found that patients taking iopamidol had reduced incidences of both kidney damage and long-term negative effects. These parallel decreased incidences support the theory that contrast-induced kidney injury causes long-term negative effects.

The CARE trial findings should prompt investigators to design additional studies on the long-term negative health effects of contrast-induced kidney damage.

Public release date: 25-Jun-2009

Chemicals in common consumer products may play a role in pre-term births

Cincinnati, OH, June 25, 2009 -- Many parents worry about their child's exposure to phthalates, the chemical compounds used as plasticizers in a wide variety of personal care products, children's toys, and medical devices. Phthalate exposure can begin in the womb and has been associated with negative changes in endocrine function. A new study soon to be published in the *Journal of Pediatrics* examines the possibility that in utero phthalate exposure contributes to low birth weight in infants. Low birth weight is the leading cause of death in children under 5 years of age and increases the risk of cardiovascular and metabolic disease in adulthood.

To investigate the associations between in utero phthalate exposure and low birth weight, Dr. Renshan Ge of the Population Council and colleagues from Fudan University and Second Military Medical University in Shanghai studied 201 pairs of newborns and their mothers between 2005 and 2006. Of the 201 infants studied, 88 were born with low birth weight. The researchers analyzed samples of the infants' meconium, the first bowel movement that occurs after birth, and cord blood to determine phthalate levels.

They found quantifiable levels of phthalate and phthalate metabolites in more than 70% of the samples. Infants with low birth weight had consistently higher levels of phthalates. According to Dr. Ge, "The results showed that phthalate exposure was ubiquitous in these newborns, and that prenatal phthalate exposure might be an environmental risk factor for low birth weight in infants." Although these associations are not conclusive, this study supports the accelerating efforts to minimize phthalate exposure

Public release date: 25-Jun-2009

Vitamin A derivative provides clues to better breast cancer drugs

Retinoic acid, a derivative of vitamin A, could lead researchers to a new set of drug targets for treating breast cancer, researchers from the University of Chicago report in the June 25, 2009, issue of the journal *Cell*.

The most common forms of breast cancer are fueled by the female hormone estrogen. By comparing the effects of estrogen and retinoic acid on the entire genome, the researchers found that they have a "yin-yang" effect. They alter the expression of many of the same genes, with estrogen tipping the scales towards cell proliferation and retinoic acid restoring the balance by inhibiting cellular growth.

This balanced control of gene expression regulates fundamental cellular processes, say the authors. When it is dysregulated, it can lead to cancer.

"Understanding all the components of this process could be used against breast cancer care in three ways," said study leader, Kevin White, PhD, professor of human genetics and director of the Institute for Genomics and System Biology at the University of Chicago. "It suggests new ways to think about preventing the disease in those at high risk. It offers molecular tools that could provide a more precise diagnosis and predict outcomes. It could also be used to enhance current therapies, making existing drugs, such as tamoxifen, that selectively block estrogen's effects even more powerful, or even to develop new anti-cancer drugs."

White's team studies the effects of nuclear receptors, a class of proteins found within cells that control the response to various hormones. When a hormone enters a cell and connects with its receptor, that receptor alters the pattern of expression of specific genes--often hundreds or more.

For this study, White and colleagues Sujun Hua and Ralf Kittler focused on the retinoic acid receptors. Retinoic acid, known for its anticancer effects and already in use to treat a rare form of leukemia, has also been associated with anti-proliferative changes in breast cancer cells.

So the team combined two laboratory techniques--a process known as "ChIP-chip analysis" that blends chromatin immunoprecipitation (ChIP), to see where the retinoic acid receptors bound to the genome, with micro-array gene-chip analysis, to measure expression levels of specific genes.

The combination enabled them to map out all the genetic effects of retinoic acid and its receptors in a cell line derived from patients with breast cancers that were fueled by estrogen.

They found that 39 percent of the genomic regions bound by estrogen receptor alpha overlapped with those bound by retinoic acid. They also found that the binding of estrogen and retinoic acids receptors to target sites were often mutually exclusive. This means the two hormones compete to activate or repress many of the same genes.

The two signaling pathways were mainly antagonistic. Estrogen increased expression of 139 genes that retinoic repressed. Retinoic acid activated 185 genes that retinoic acid repressed. For about 140 genes, estrogen and retinoic acid had the same effect.

"Collectively, note the authors, "these findings indicate an extensive crosstalk" between the effects of estrogen and retinoic acid. Despite their opposing effects, certain versions of the estrogen and retinoic acid receptors actually activate each other. This provides "an additional level of control," say the authors, "for achieving a balanced regulation of gene expression."

This competition between the two signals also provides a new tool to predict outcomes. **The researchers compared the effects of retinoic acid on tissues from 295 breast cancer**

patients against the results from their initial study using a typical breast cancer cell line. They found that the more responsive a tumor was to retinoic acid, the better the odds of long-term relapse-free survival.

Some of the genes that respond to retinoic acid were expressed even in difficult-to-treat tumors, such as those that do not have estrogen receptors or the molecule targeted by the drug Herceptin, the so-called double- or triple-negative breast cancers. "Some of these genes may provide new drug targets," White said.

Although retinoic acid is approved for treatment of leukemia, it can be quite toxic and patients can develop resistance to the drug. This study suggests a long series of downstream targets that are activated by the RA receptor.

"The goal would be to develop drugs that could activate these cancer-inhibiting targets," said White. "Retinoic acid itself is probably not the solution because of its side effects and metabolic byproducts," He cautioned, "but our results provide a molecular justification for finding ways to overcome its limitations in the clinic."

"This work reveals important insights on the interplay between vitamin A and estrogen action," said Myles Brown, MD, professor of medicine at Harvard Medical School and the Dana Farber Cancer Institute. "These insights will hopefully lead to new approaches for the prevention and treatment of the most common form of breast cancer."

Public release date: 25-Jun-2009

Your Arteries on Wonder Bread

Landmark study from TAU shows how high carb foods cause heart attacks

Doctors have known for decades that foods like white bread and corn flakes aren't good for cardiac health. In a landmark study, new research from Tel Aviv University now shows exactly how these high carb foods increase the risk for heart problems.

"Looking inside" the arteries of students eating a variety of foods, Dr. Michael Shechter of Tel Aviv University's Sackler School of Medicine and the Heart Institute of Sheba Medical Center — with collaboration of the Endocrinology Institute — visualized exactly what happens inside the body when the wrong foods for a healthy heart are eaten. He found that foods with a high glycemic index distended brachial arteries for several hours.

Elasticity of arteries anywhere in the body can be a measure of heart health. But when aggravated over time, a sudden expansion of the artery wall can cause a number of negative health effects, including reduced elasticity, which can cause heart disease or sudden death.

Using a clinical and research technique pioneered by his laboratory in Israel, Dr. Shechter was able to visualize what happens inside our arteries before, during and after eating high carb foods. It is a first in medical history. The results were published in the Journal of the American College of Cardiology.

Time to skip the wedding cake?

Dr. Michael Shechter

"It's very hard to predict heart disease," says Dr. Shechter, a fellow of the American College of Cardiology and the American Heart Association. "But doctors know that high glycemic foods rapidly increase blood sugar. Those who binge on these foods have a greater chance of sudden death from heart attack. Our research connects the dots, showing the link between diet and what's happening in real time in the arteries."

Like the uncomfortable medical warnings on packets of cigarettes, this new research could lead to a whole new way to show patients the effects of a poor diet on our body.

Using 56 healthy volunteers, the researchers looked at four groups. One group ate a cornflake mush mixed with milk, a second a pure sugar mixture, the third bran flakes, while the last group was given a placebo (water). Over four weeks, Dr. Shechter applied his method of "brachial reactive testing" to each group. The test uses a cuff on the arm, like those used to measure blood pressure, which can visualize arterial function in real time.

The results were dramatic. Before any of the patients ate, arterial function was essentially the same. After eating, except for the placebo group, all had reduced functioning.

All roads lead to the endothelium

Enormous peaks indicating arterial stress were found in the high glycemic index groups: the cornflakes and sugar group. "We knew high glycemic foods were bad for the heart. Now we have a mechanism that shows how," says Dr. Shechter. "Foods like cornflakes, white bread, french fries, and sweetened soda all put undue stress on our arteries. We've explained for the first time how high glycemic carbs can affect the progression of heart disease." During the consumption of foods high in sugar, there appears to be a temporary and sudden dysfunction in the endothelial walls of the arteries.

Endothelial health can be traced back to almost every disorder and disease in the body. It is "the riskiest of the risk factors," says Dr. Shechter, who practices at the Chaim Sheba Medical Center — Tel Hashomer Hospital. There he offers a treatment that can show patients — in real time — if they have a high risk for heart attacks. "Medical tourists" from America regularly visit to take the heart test.

The take-away message? Dr. Shechter says to stick to foods like oatmeal, fruits and vegetables, legumes and nuts, which have a low glycemic index. Exercising every day for

at least 30 minutes, he adds, is an extra heart-smart action to take.

Public release date: 26-Jun-2009

Tryptophan deficiency may underlie quinine side effects

Researchers have found that the anti-malarial drug quinine can block a cell's ability to take up the essential amino acid tryptophan, a discovery that may explain many of the adverse side-effects associated with quinine. Once confirmed, these findings would suggest that dietary tryptophan supplements could be a simple and inexpensive way to improve the performance of this important drug.

Quinine is a very commonly used anti-malarial drug, yet to this day the principal mode of quinine action against the malaria parasite is still largely unclear, as is the basis for adverse reactions like nausea, headaches, and blurred vision. To address these gaps, Simon Avery and colleagues at the University of Nottingham took advantage of yeast genetics, examining the effects of quinine on a collection of 6000 yeast mutants, each one lacking exactly one of the yeast's 6000 genes. While quite different from humans, yeast is comparable on a cellular level and yeast is frequently, and successfully, used as front-line agents in testing chemicals and small molecule drugs.

Their screen revealed that strains unable to make tryptophan were extremely susceptible to quinine poisoning, which led them to identify a tryptophan transporter as a key quinine target (yeast that cannot make their own tryptophan have to rely exclusively on external sources, and thus die if tryptophan transport is blocked).

This discovery fits in well with evidence that quinine reactions are more severe in malnourished individuals. Unlike yeast, humans cannot make their own tryptophan and thus require dietary tryptophan, which is abundant in meat but limited in yams, a staple food crop in the tropics where malaria is prevalent. If quinine severely reduces tryptophan uptake, then it follows that people with preexisting tryptophan deficiencies would be especially at risk to this drug.

The authors also note that tryptophan is important as a precursor for the brain chemical serotonin, so the enhanced tryptophan deficiency induced by quinine could explain why many of quinine's side effects are localized to the head region. They also note that side-effects could be averted simply by taking dietary tryptophan supplements in conjunction with quinine treatments, though it is not yet known if tryptophan may affect quinine action against the malaria parasite.

Public release date: 29-Jun-2009

Mice run faster on high-grade oil

Between the 1932 and 2008 Olympic Games, world record times of the men's 100m sprint improved by 0.6 seconds due to improved training techniques and technological

advances. Imagine if this improvement could be achieved by a simple change in diet. Scientists at the Research Institute of Wildlife Ecology in Austria have managed to achieve an equivalent feat in mice fed on a diet high in polyunsaturated fatty acids.

Polyunsaturated fatty acids are important dietary components which mammals cannot synthesize de novo. The research, to be presented on 29th June 2009 at the Society for Experimental Biology Annual Meeting, has shown that mice fed for two weeks on a diet high in sunflower oil, which contains n-6 polyunsaturated fatty acids, ran on average 0.19m/s faster than mice fed a diet rich in linseed oil, which is high in n-3 fatty acids.

This means that, over a 2 second sprint, a mouse fed on a high n-6 fatty acid diet would have a 0.4m advantage. This represents a 6.3% improvement which equals that achieved in the 100m world records

over more than 75 years. For a mouse, or other small mammal, this would be significant in evolutionary terms when escaping from a predator or catching prey. "The results of the current study on mice suggest that moderate differences in dietary n-6/n-3 polyunsaturated fatty acid intake can have a biologically meaningful effect on maximum running speed", says Dr Christopher Turbill who will be presenting the research.

A previous study by the group, which looked at a range of mammal species, found that those with a relatively high n-6 fatty acid content in their skeletal muscles had a greater maximum running speed. Combined, these two studies suggest that diets enriched in these fatty acids "could also affect the maximum (or burst) running speed of other vertebrates, including humans" says Dr Turbill. "The application of this research to the performance of elite athletes (specifically those in sports that involve short distance sprints, including cycling) is uncertain, but in my opinion certainly deserves some further attention" he says.

Public release date: 29-Jun-2009

Report: Prostate cancer screening has yet to prove its worth

ATLANTA—June 29, 2009—The recent release of two large randomized trials suggests that if there is a benefit of screening, it is, at best, small, says a new report in *CA: A Cancer Journal for Clinicians*. Authored by Otis W. Brawley, M.D. of the American Cancer Society and Donna Ankerst, Ph.D. and Ian M. Thompson, M.D. of the University of Texas Health Science Center at San Antonio, the review says because prostate cancer is virtually ubiquitous in men as they age, it is clear that a goal of "finding more cancers" is not acceptable. Instead, public health principles demand that screening must reduce the risk of death from prostate cancer, reduce the suffering from prostate cancer, or reduce health care costs when compared with a non-screening scenario. The authors suggest prostate cancer screening has yet to reach one of these standards to date.

No major medical group, including the American Cancer Society, currently recommends routine prostate cancer screening for men at average risk. In the United States, prostate cancer will affect one man in six men during his lifetime. Since the mid-1980s, screening

with the prostate-specific antigen (PSA) blood test has more than doubled the risk of a prostate cancer diagnosis. The review says a decrease in prostate cancer death rates has been observed since that time, but the relative contribution of PSA testing as opposed to other factors, such as improved treatment, has been uncertain.

The report says a computer modeling study using National Cancer Institute's Surveillance, Epidemiology, and End Results (SEER) registries estimated that more than one in four cancers detected in whites (29 percent) and nearly half of cancers detected in blacks (44 percent) were overdiagnosed cancers. A similar model using data from Europe estimated a 50 percent overdiagnosis rate. The authors say patients who are diagnosed with clinically insignificant tumors are subject to unnecessary diagnostic tests and unneeded treatment and suffer psychosocial harms. They are also labeled "a cancer patient," which can have negative economic consequences. Also, say the authors, overdiagnosis significantly affects 5-year survival statistics, making them uninformative in demonstrating progress in cancer control.

The report says the future of prostate cancer will include better screening tests, better methods to assess a man's risk of prostate cancer, and prevention strategies, including the use of finasteride, a drug currently used for the treatment of urinary symptoms related to prostate enlargement.

In a separate but related editorial, Peter Boyle, Ph.D., D.Sc., of the International Prevention Research Institute, Lyon, France and report co-author Dr. Brawley say "the real impact and tragedy of prostate cancer screening is the doubling of the lifetime risk of a diagnosis of prostate cancer with little if any decrease in the risk of dying from this disease." They say in 1985, before PSA screening was available, an American man had an 8.7 percent lifetime risk of being diagnosed with prostate cancer and a 2.5 percent lifetime risk of dying from the disease. Twenty years later, in 2005, an American man had a 17 percent lifetime risk of being diagnosed with prostate cancer and a 3 percent risk of dying from the disease. They add that even in the best case scenario, applying the findings of a European trial that found PSA led to a 20 percent reduction in the risk of death, the average **man who chooses screening decreases his risk of prostate cancer death from a lifetime risk of 3 percent to a lifetime risk of 2.4 percent. *In exchange, he doubles the chances of becoming a prostate cancer patient, his risk of diagnosis rising from about nine percent to at least 17 percent.**

They conclude that "men should discuss the now quantifiable risks and benefits of having a PSA test with their physician and then share in making an informed decision," and that "the weight of the decision should not be thrown into the patient's lap."

Ralph's Note - **If I read this right. Prostate screening increases your risk of death.**

Public release date: 29-Jun-2009

Magic ingredient in breast milk protects babies' intestines

Scientists at Queen Mary, University of London have discovered that an ingredient in human breast milk protects and repairs the delicate intestines of newborn babies.

The ingredient called pancreatic secretory trypsin inhibitor, or PSTI, is found at its highest levels in colostrum - the milk produced in the first few days after birth.

The lining of a newborn's gut is particularly vulnerable to damage as it has never been exposed to food or drink. The new study* highlights the importance of breastfeeding in the first few days after the birth.

The researchers found small amounts of PSTI in all the samples of breast milk they tested but it was seven times more concentrated in colostrum samples. The ingredient was not found in formula milk.

The researchers examined the effects of PSTI on human intestinal cells in the lab. When they inflicted damage to the cells they found that PSTI stimulated the cells to move across the damaged area forming a natural protective 'plaster'. They also found that PSTI could prevent further damage by stopping the cells of the intestine from self-destructing. Additional research suggests that PSTI could reduce damage by 75 per cent.

PSTI is a molecule which is normally found in the pancreas where it protects the organ from being damaged by the digestive enzymes it produces. Research suggests that it plays a similar protective role in the gut.

The team at Queen Mary have also found that PSTI is produced in the breast but until now they did not know exactly why.

Professor Ray Playford of Barts and the London School of Medicine and Dentistry, part of Queen Mary, University of London led the study.

He said: "We know that breast milk is made up of a host of different ingredients and we also know that there are a number of health benefits for babies who are breast-fed.

"This study is important because it shows that a component of breast milk protects and repairs the babies delicate intestines in readiness for the onslaught of all the food and drink that are to come.

"It reinforces the benefits of breast feeding, especially in the first few days after birth."

Public release date: 29-Jun-2009

**K-STATE RESEARCHER STUDIES THE ANTI-CANCER
CAPABILITIES OF A SPECIAL PURPLE SWEET POTATO**

MANHATTAN -- A Kansas State University researcher is studying the potential health benefits of a specially bred purple sweet potato because its dominant purple color results in an increased amount of anti-cancer components.

K-State's Soyoung Lim, doctoral student in human nutrition, Manhattan, is working with George Wang, associate professor of human nutrition at K-State, to understand the pigment effects of a Kansas-bred purple sweet potato on cancer prevention.

Lim said purple sweet potatoes have high contents of anthocyanin, which is a pigment that presents the purple color in the vegetable. The pigment can produce red, blue and purple colors depending on the source's chemical structure, such as in foods like blueberries, red grapes and red cabbage.

She said anthocyanins have been epidemiologically associated with a reduced cancer risk, but the anti-cancer ability of the purple sweet potato has not been well investigated.

Lim used a sweet potato with pronounced purple flesh and skin that was developed by K-State's Ted Carey, professor of horticulture, at K-State's John C. Pair Horticultural Center in Haysville.

"Sometimes we can find purple sweet potatoes in the grocery store, but they don't have this purple color on the skin and inside," Lim said.

Three different purple sweet potatoes were used that had varying amounts of anthocyanin for the project. To quantify the amount in each potato, Lim extracted pigments from the vegetables and injected them into an HPLC-MS Analysis, which she said is a method that separates components.

The potatoes were segregated by multiple traits based on flesh pigmentation and fiber contents. The analysis determined that the Kansas-bred potato had significantly higher anthocyanin contents compared to the other potatoes. The analysis also found two derivatives of anthocyanin that were dominant: cyanidin and peonidin, Lim said.

Lim also measured the potatoes' total phenolic content. Lim said phenols are chemical compounds that have been found to have anti-aging and antioxidant components. The specially bred purple sweet potato had a much higher total phenolic content and antioxidant capacity than the other regularly occurring purple sweet potatoes, she said.

The K-State researchers also wanted to see the specific effects of cyanidin and peonidin. Lim treated human colon cancer cells with low concentrations of the pigment derivatives and also studied the effects on the cell cycles.

Cyanidin and peonidin showed significant cell growth inhibition for the cancer cells, but there were no significant changes in the cell cycle. Lim said a better understanding of the underlying mechanisms in the Kansas-bred potato could provide scientific evidence of its health benefits.

Lim presented the research at the Experimental Biology Meeting in New Orleans in April. She is doing a follow-up study this summer that will involve treating animal cancer cells with the pigments.

Other contributors to the project include Takeo Iwamoto, research assistant professor of biochemistry at K-State; and K-State students Genna Gehrt, Alma, and Kacey Provenzano, Derby, both May 2009 bachelor's graduates in nutritional sciences.

Public release date: 1-Jul-2009

Triggering muscle development -- a therapeutic cure for muscle wastage?

Scientists in the UK and Denmark have shown that if elderly men were given growth hormone and exercised their legs showed an appreciable muscle mass increase. Dr. Geoff Goldspink (Royal Free and University College Medical School, UK) says: "This raises the question: Can age-related loss of muscle strength and increased fragility be ameliorated by the therapeutic application of mechano growth factor (MGF)?" There is hope that MGF can also help sufferers of diseases such as muscular dystrophy, ALS, renal disease or cancer, for whom intensive exercise is not an option. It may even prove useful to ameliorate muscle loss resulting from long periods in zero-gravity conditions during space travel. Dr. Mark Lewis (University College London, UK) will present their latest results on how MGF exerts its effects during his talk at the Society of Experimental Biology Annual Meeting in Glasgow on Wednesday 1st July 2009.

When muscles are stretched during exercise, they produce a specific substance known as mechano growth factor (MGF) that activates stem cells already present in the tissue. Once activated, these progenitor cells begin to divide, creating additional muscle fibres and increasing the size and strength of the muscle. In addition to intensive exercise, muscles need to be stimulated by growth hormone (GH) in order to release MGF. Since there is a natural decrease in the levels of this hormone as we age, this may combine with the lack of intensive physical activity to cause muscle wasting in elderly people. "The downside", warns Dr. Goldspink, "is that MGF has great potential for doping in sports. A synthetic version is already available over the internet, and although it is still very expensive, it is expected that new technologies will bring down the price to make it comparable to that of human insulin".

Public release date: 1-Jul-2009

Acid-reducing medicines may lead to dependency

Data suggests proton pump inhibitors can induce acid-related symptoms in healthy adults Bethesda, MD (July 1, 2009) – Treatment with proton pump inhibitors (PPIs) for eight weeks induces acid-related symptoms like heartburn, acid regurgitation and dyspepsia

once treatment is withdrawn in healthy individuals, according to a new study in *Gastroenterology*, the official journal of the American Gastroenterological Association (AGA) Institute.

"The observation that more than 40 percent of healthy volunteers, who have never been bothered by heartburn, acid regurgitation or dyspepsia, develop such symptoms in the weeks after cessation of PPIs is remarkable and has potentially important clinical and economic implications," said Christina Reimer, MD, of Copenhagen University and lead author of the study. "This study indicates unrecognized aspects of PPI withdrawal and is a very strong indication of a clinically significant acid rebound phenomenon that needs to be investigated in proper patient populations."

The use of PPIs for acid-related symptoms and disorders is extensive and rapidly escalating. While the incidence of new patients being treated with PPIs remains stable, the prevalence of long-term treatment is rising, the reasons for which are not fully known. Studies have shown that up to 33 percent of patients who initiate PPI treatment continue to refill their prescriptions without an obvious indication for maintenance therapy. Rebound acid hypersecretion, defined as an increase in gastric acid secretion above pre-treatment levels following antisecretory therapy, is observed within two weeks after withdrawal of treatment and could theoretically lead to acid-related symptoms such as heartburn, acid regurgitation or dyspepsia that might result in resumption of therapy.

In a randomized double-blind placebo-controlled trial, researchers aimed to determine the clinical relevance of rebound acid hypersecretion in order to establish if long-term treatment with a PPI creates a need for continuous treatment. A total of 120 healthy participants were randomized to 12 weeks of placebo or eight weeks of esomeprazole (40 mg per day) followed by four weeks with placebo. The Gastrointestinal Symptom Rating Scale (GSRS) was filled out weekly.

The symptoms observed in this trial caused mild to moderate discomfort and appeared for the majority of subjects in the first two weeks after withdrawal of therapy. While there were no significant differences between the groups in GSRS scores at baseline, GSRS scores for acid-related symptoms were significantly higher in the PPI group in weeks 10, 11 and 12. Of those randomized to PPIs, 44 percent reported at least one relevant acid-related symptom in weeks nine through 12 compared to 15 percent in the placebo group. The proportion reporting dyspepsia, heartburn or acid regurgitation in the PPI group was 22 percent in week 10, 22 percent in week 11 and 21 percent in week 12. Corresponding figures in the placebo group were 7 percent, 5 percent and 2 percent.

"We find it highly likely that the symptoms observed in this trial are caused by rebound acid hypersecretion and that this phenomenon is equally relevant in patients treated long term with PPIs. If rebound acid hypersecretion induces acid-related symptoms, this might lead to PPI dependency. Our results justify the speculation that PPI dependency could be one of the explanations for the rapidly and continuously increasing use of PPIs," Dr. Reimer added.

Public release date: 2-Jul-2009

Doubts cast on credibility of some published clinical trials

Randomised Controlled Trials (RCTs) are considered the 'gold standard' research method for assessing new medical treatments. But research published in BioMed Central's open access journal **Trials shows that the design of a remarkable 93 percent of 2235 so-called RCTs published in some Chinese medical journals during 1994 to 2005 was flawed**, casting doubt on the reliability of research that is likely to influence medical decision-makers.

Researchers led by Taixiang Wu of the Chinese Cochrane Centre at Sichuan University, China and Ottawa Hospital Research Institute investigated clinical trials published in China between 1994 and 2005, searching the China National Knowledge Infrastructure (CNKI) electronic database for RCTs on 20 common diseases. To determine how many of these met recognised standards for randomly allocating participants to treatment groups, trained investigators interviewed the first or co-authors of 2235 trial reports by phone.

Less than seven percent of self-described RCTs published in some Chinese medical journals meet criteria for authentic randomisation. The researchers looked at both conventional and traditional Chinese medicine trials, but there was no difference between these in terms of study authenticity rates. However, all RCTs of pre-market drug clinical trial were authentic, and RCTs conducted at hospitals affiliated with medical universities were more likely to be authentic than trials conducted at lower tier level three and level two hospitals. More than half of the trials at university-affiliated hospitals met RCT criteria, which means lower-tier hospital research is the least rigorous in design terms.

"The fact that so many non-RCTs were published as RCTs reflected that peer-review needs to be improved and a Good Practice of Peer Review, including how to identify the authenticity of the study, urgently needs to be developed," says Wu.

Misleading reporting of medical research is not unique to China. Studies labelled as RCTs are more likely to influence health policy-makers meaning falsely reported RCTs have the potential to mislead health care providers, consumers and policy-makers. The results of this study suggest authors of systematic reviews – articles that combine the results of multiple RCTs – need to be aware that RCTs in some Chinese journals may not be RCTs at all.

The approximately 1100 medical journals now active in China are rapidly increasing their output of research reports, including many identified by their authors as RCTs. But these trials present mostly positive results (they favour the treatment being investigated), which can be influenced by inadequate randomisation of patients when designing the study.

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Caffeine reverses memory impairment in Alzheimer's mice

New studies show caffeine markedly reduced the hallmark protein for Alzheimer's disease in the brains and blood of the mice

Tampa, FL (July 5, 2009) – Coffee drinkers may have another reason to pour that extra cup. When aged mice bred to develop symptoms of Alzheimer's disease were given caffeine – the equivalent of five cups of coffee a day – their memory impairment was reversed, report University of South Florida researchers at the Florida Alzheimer's Disease Research Center.

Back-to-back studies published online today in the *Journal of Alzheimer's Disease*, show caffeine significantly decreased abnormal levels of the protein linked to Alzheimer's disease, both in the brains and in the blood of mice exhibiting symptoms of the disease. Both studies build upon previous research by the Florida ADRC group showing that caffeine in early adulthood prevented the onset of memory problems in mice bred to develop Alzheimer's symptoms in old age.

"The new findings provide evidence that caffeine could be a viable 'treatment' for established Alzheimer's disease, and not simply a protective strategy," said lead author Gary Arendash, PhD, a USF neuroscientist with the Florida ADRC. "That's important because caffeine is a safe drug for most people, it easily enters the brain, and it appears to directly affect the disease process."

Based on these promising findings in mice, researchers at the Florida ADRC and Byrd Alzheimer's Center at USF hope to begin human trials to evaluate whether caffeine can benefit people with mild cognitive impairment or early Alzheimer's disease, said Huntington Potter, PhD, director of the Florida ADRC and an investigator for the caffeine studies. The research group has already determined that caffeine administered to elderly non-demented humans quickly affects their blood levels of β -amyloid, just as it did in the Alzheimer's mice.

"These are some of the most promising Alzheimer's mouse experiments ever done showing that caffeine rapidly reduces beta amyloid protein in the blood, an effect that is mirrored in the brain, and this reduction is linked to cognitive benefit," Potter said. "Our goal is to obtain the funding needed to translate the therapeutic discoveries in mice into well-designed clinical trials."

Arendash and his colleagues became interested in caffeine's potential for treating Alzheimer's several years ago, after a Portuguese study reported that people with Alzheimer's had consumed less caffeine over the last 20 years than people without the neurodegenerative disease. Since then, several uncontrolled clinical studies have reported moderate caffeine consumption may protect against memory decline during normal aging. The highly controlled studies using Alzheimer's mice allowed researchers to

isolate the effects of caffeine on memory from other lifestyle factors such as diet and exercise, Arendash said.

The just-published Florida ADRC study included 55 mice genetically altered to develop memory problems mimicking Alzheimer's disease as they aged. After behavioral tests confirmed the mice were exhibiting signs of memory impairment at age 18 to 19 months – about age 70 in human years – the researchers gave half the mice caffeine in their drinking water. The other half got plain water. The Alzheimer's mice received the equivalent of five 8-oz. cups of regular coffee a day. That's the same amount of caffeine – 500 milligrams -- as contained in two cups of specialty coffees like Starbucks, or 14 cups of tea, or 20 soft drinks.

At the end of the two-month study, the caffeinated mice performed much better on tests measuring their memory and thinking skills. In fact, their memories were identical to normal aged mice without dementia. The Alzheimer's mice drinking plain water continued to do poorly on the tests.

In addition, the brains of the caffeinated mice showed nearly a 50-percent reduction in levels of beta amyloid, a substance forming the sticky clumps of plaques that are a hallmark of Alzheimer's disease. Other experiments by the same investigators indicate that caffeine appears to restore memory by reducing both enzymes needed to produce beta amyloid. The researchers also suggest that caffeine suppresses inflammatory changes in the brain that lead to an overabundance of beta amyloid.

Since caffeine improved the memory of mice with pre-existing Alzheimer's, the researchers were curious to know if it might further boost the memory of non-demented (normal) mice administered caffeine from young adulthood through old age. It did not. Control mice given regular drinking water throughout their lives performed as well on behavioral tests in old age as normal mice who received long-term caffeine treatment, Arendash said. "This suggests that caffeine will not increase memory performance above normal levels. Rather, it appears to benefit those destined to develop Alzheimer's disease."

The researchers do not know if an amount lower than the 500 mg. daily caffeine intake received by the Alzheimer's mice would be effective, Arendash said. For most individuals, however, this moderate level of caffeine intake poses no adverse health effects, according to both the National Research Council and the National Academy of Sciences. Nonetheless, Arendash said, individuals with high blood pressure or those who are pregnant should limit their daily caffeine intake.

If larger, more rigorous clinical studies confirm that caffeine staves off Alzheimer's in humans, as it does in mice, this benefit would be substantial, Arendash said. Alzheimer's disease attacks nearly half of Americans age 85 and older, and Alzheimer's and other dementias triple healthcare costs for those age 65 and older, according to the Alzheimer's Association.

In addition to the Florida ADRC, Byrd Alzheimer's Center and Eric Pfeiffer Suncoast

Alzheimer's and Gerontology Center at USF, researchers from the Bay Pines VA Healthcare System; Saitama Medical University, Saitama, Japan; and Washington University School of Medicine, St. Louis, collaborated on the research. The studies were supported by grants to investigators in the Florida ADRC, a statewide project sponsored by the National Institute on Aging and housed at the University of South Florida's Byrd Alzheimer's Center.

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Researchers find possible environmental causes for Alzheimer's, diabetes

Call for reducing nitrate levels in fertilizer and water, detoxifying food and water
Providence, RI – A new study by researchers at Rhode Island Hospital have found a substantial link between increased levels of nitrates in our environment and food with increased deaths from diseases, including Alzheimer's, diabetes mellitus and Parkinson's. The study was published in the Journal of Alzheimer's Disease (Volume 17:3 July 2009).

Led by Suzanne de la Monte, MD, MPH, of Rhode Island Hospital, researchers studied the trends in mortality rates due to diseases that are associated with aging, such as diabetes, Alzheimer's, Parkinson's, diabetes and cerebrovascular disease, as well as HIV. They found strong parallels between age adjusted increases in death rate from Alzheimer's, Parkinson's, and diabetes and the progressive increases in human exposure to nitrates, nitrites and nitrosamines through processed and preserved foods as well as fertilizers. Other diseases including HIV-AIDS, cerebrovascular disease, and leukemia did not exhibit those trends. De la Monte and the authors propose that the increase in exposure plays a critical role in the cause, development and effects of the pandemic of these insulin-resistant diseases.

De la Monte, who is also a professor of pathology and lab medicine at The Warren Alpert Medical School of Brown University, says, "We have become a 'nitrosamine generation.' In essence, we have moved to a diet that is rich in amines and nitrates, which lead to

increased nitrosamine production. We receive increased exposure through the abundant use of nitrate-containing fertilizers for agriculture." She continues, "Not only do we consume them in processed foods, but they get into our food supply by leeching from the soil and contaminating water supplies used for crop irrigation, food processing and drinking."

Nitrites and nitrates belong to a class of chemical compounds that have been found to be harmful to humans and animals. More than 90 percent of these compounds that have been tested have been determined to be carcinogenic in various organs. They are found in many food products, including fried bacon, cured meats and cheese products as well as beer and water. Exposure also occurs through manufacturing and processing of rubber and latex products, as well as fertilizers, pesticides and cosmetics.

Nitrosamines are formed by a chemical reaction between nitrites or other proteins. Sodium nitrite is deliberately added to meat and fish to prevent toxin production; it is also used to preserve, color and flavor meats. Ground beef, cured meats and bacon in particular contain abundant amounts of amines due to their high protein content. Because of the significant levels of added nitrates and nitrites, nitrosamines are nearly always detectable in these foods. Nitrosamines are also easily generated under strong acid conditions, such as in the stomach, or at high temperatures associated with frying or flame broiling. Reducing sodium nitrite content reduces nitrosamine formation in foods.

Nitrosamines basically become highly reactive at the cellular level, which then alters gene expression and causes DNA damage. The researchers note that the role of nitrosamines has been well-studied, and their role as a carcinogen has been fully documented. The investigators propose that the cellular alterations that occur as a result of nitrosamine exposure are fundamentally similar to those that occur with aging, as well as Alzheimer's, Parkinson's and Type 2 diabetes mellitus.

De la Monte comments, "All of these diseases are associated with increased insulin resistance and DNA damage. Their prevalence rates have all increased radically over the past several decades and show no sign of plateau. Because there has been a relatively short time interval associated with the dramatic shift in disease incidence and prevalence rates, we believe this is due to exposure-related rather than genetic etiologies."

The researchers recognize that an increase in death rates is anticipated in higher age groups. Yet when the researchers compared mortality from Parkinson's and Alzheimer's disease among 75 to 84 year olds from 1968 to 2005, the death rates increased much more dramatically than for cerebrovascular and cardiovascular disease, which are also aging-associated. For example, in Alzheimer's patients, the death rate increased 150-fold, from 0 deaths to more than 150 deaths per 100,000. Parkinson's disease death rates also increased across all age groups. However, mortality rates from cerebrovascular disease in the same age group declined, even though this is a disease associated with aging as well.

De la Monte notes, "Because of the similar trending in nearly all age groups within each disease category, this indicates that these overall trends are not due to an aging

population. This relatively short time interval for such dramatic increases in death rates associated with these diseases is more consistent with exposure-related causes rather than genetic changes." She also comments, "Moreover, the strikingly higher and climbing mortality rates in older age brackets suggest that aging and/or longer durations of exposure have greater impacts on progression and severity of these diseases."

The researchers graphed and analyzed mortality rates, and compared them with increasing age for each disease. They then studied United States population growth, annual use and consumption of nitrite-containing fertilizers, annual sales at popular fast food chains, and sales for a major meat processing company, as well as consumption of grain and consumption of watermelon and cantaloupe (the melons were used as a control since they are not typically associated with nitrate or nitrite exposure).

The findings indicate that while nitrogen-containing fertilizer consumption increased by 230 percent between 1955 and 2005, its usage doubled between 1960 and 1980, which just precedes the insulin-resistant epidemics the researchers found. They also found that sales from the fast food chain and the meat processing company increased more than 8-fold from 1970 to 2005, and grain consumption increased 5-fold.

The authors state that the time course of the increased prevalence rates of Alzheimer's, Parkinson's and diabetes cannot be explained on the basis of gene mutations. They instead mirror the classical trends of exposure-related disease. Because nitrosamines produce biochemical changes within cells and tissues, it is conceivable that chronic exposure to low levels of nitrites and nitrosamines through processed foods, water and fertilizers is responsible for the current epidemics of these diseases and the increasing mortality rates associated with them.

De la Monte states, "If this hypothesis is correct, potential solutions include eliminating the use of nitrites and nitrates in food processing, preservation and agriculture; taking steps to prevent the formation of nitrosamines and employing safe and effective measures to detoxify food and water before human consumption."

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Muscle damage may be present in some patients taking statins

Structural muscle damage may be present in patients who have statin-associated muscle complaints, found a new study in CMAJ (Canadian Medical Association Journal) <http://www.cmaj.ca/press/cmaj-181-E11.pdf> (www.cmaj.ca).

Statins are one of the most widely prescribed medications in the world, given their importance in reducing the risk of cardiovascular disease. Many patients on statins develop muscle weakness and pain. In some cases, muscle biopsies show underlying structural injury, even in patients without elevated levels of circulating creatine phosphokinase.

The study, by researchers from the University of Bern, Switzerland and the Tufts-New England Medical Center in Boston, Massachusetts, looked at muscle biopsies from 83 patients, 20 of whom had never taken statins. **They found significant muscle injury in patients who had taken statins, including several who had discontinued medication before the biopsy.**

"Although in clinical practice, the majority of patients with muscle symptoms improve rapidly after cessation of therapy, our findings support that a subgroup of patients appears to **be more susceptible to statin-associated myotoxicity, suffering persistent structural injury,**" write Dr. Annette Draeger from the University of Bern and coauthors.

They note there is a need to evaluate alternative treatment strategies for patients with significant muscle symptoms.

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Health food supplement may curb compulsive hair pulling

Patients with the disorder, known as trichotillomania, reported feeling much improved after taking the supplement

MINNEAPOLIS/ ST. PAUL (July 6, 2009) – University of Minnesota Medical School researchers have discovered that a common anti-oxidant, widely available as a health food supplement, may help stop the urges of those with trichotillomania, a disorder characterized by compulsive hair-pulling.

Fifty people enrolled in a double-blind 12 week study; half were given N-Acetylcysteine, an amino acid commonly found in health food supplements. The average age of patients who enrolled was about 34, and most started pulling hair compulsively by the age of 12. Patients were given 1,200 mg of N-Acetylcysteine every day for six weeks. For the following six weeks, the dosage was increased to 2,400 mg per day. **After nine weeks, those on supplement had significantly reduced hair-pulling. By the end of the 12 week study, 56 percent reported feeling much or very much improved, while only 16 percent on the placebo reported less pulling.**

The study is published in the July, 2009 issue of the Archives of General Psychiatry.

"Trichotillomania is compulsive in the sense that people can't control it. People feel unable to stop the behavior even though they know it is causing negative consequences," said Jon Grant, M.D., J.D., a University of Minnesota associate professor of psychiatry and principal investigator of the study. "Some people don't even know they are doing it."

Those who have trichotillomania compulsively or habitually pull their hair to the point of noticeable loss. It is most commonly associated with women, but men can also be affected, and pulling can occur anywhere on the body. Grant believes 2 to 4 percent of the general population is impacted by trichotillomania on some level.

"These are people who have tried all kinds of things that have never worked," Grant said. "The reality is that if you pull hair and it is on a noticeable part of the body, people are really disabled by this. It's not easy to go out in public if people are noticing your bald spots. Self esteem is a huge problem. This supplement may offer hope."

The study is significant on another level because it's one of the first studies of compulsive behaviors to look at lowering levels of glutamate – a chemical that triggers excitement – in the brain to curb harmful behavior rather than serotonin, a naturally occurring chemical most commonly linked to compulsive behavior. This supplement affects levels of glutamate in a specific area of the brain, making it easier for patients to put the breaks on their harmful behavior.

For that reason, Grant believes glutamate modulators such as N-Acetylcysteine may be applicable to other disorders, addictions, and compulsive behaviors.

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Sugar substitute appears to prevent early childhood cavities

Children given an oral syrup containing the naturally occurring sweetener xylitol may be less likely to develop decay in their baby teeth, according to a report in the July issue of Archives of Pediatrics & Adolescent Medicine, one of the JAMA/Archives journals.

Early childhood caries (cavities), also called baby bottle tooth decay or nursing caries, continue to increase in prevalence, according to background information in the article. "Poor children experience rates twice as high as those of their more affluent peers, and their disease is more likely to be untreated," the authors write. "Poor oral health affects diet and nutrition and significantly diminishes quality of life. However, tooth decay is a disease that is largely preventable."

Xylitol, approved in the United States for use in food since 1963, has been shown to effectively prevent tooth decay by acting as an antibacterial agent against organisms that cause cavities. These previous investigations have primarily involved chewing gum or lozenges used in school-age children with permanent teeth. Peter Milgrom, D.D.S., of the University of Washington, Seattle, and colleagues evaluated the effectiveness of applying oral syrup containing xylitol among 94 children age 9 to 15 months in the Republic of the Marshall Islands, where early childhood tooth decay is a serious health care problem.

Two active treatment groups received 8 grams per day of xylitol syrup divided into two (33 children) or three (32 children) doses per day. A third, control group of 29 children received a small amount (a single 2.67-gram dose) of xylitol syrup per day because the internal review committee appointed by the secretary of health of the Republic of the Marshall Islands did not permit the use of a placebo.

After an average of 10.5 months, eight of 33 children (24.2 percent) receiving two doses

of xylitol per day and 13 of the 32 children (40.6 percent) receiving three doses of xylitol per day had tooth decay, compared with 15 of the 29 children (51.7 percent) in the control group. The average numbers of decayed teeth were 0.6 in the two-dose xylitol group, one in the three-dose xylitol group and 1.9 in the control group.

"Our results suggest that exposure to xylitol (8 grams per day) in a twice-daily topical oral syrup during primary tooth eruption could prevent up to 70 percent of decayed teeth," the authors write. "Dividing the 8 grams into three doses did not increase the effectiveness of the treatment. These results provide evidence for the first time (to our knowledge) that xylitol is effective for the prevention of decay in primary teeth of toddlers." More research is needed to develop vehicles and strategies for optimal public health, but in populations with high rates of tooth decay, xylitol is likely to be a cost-effective preventive measure, they conclude.

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.