



The Vitamin & Herb Stores

Human Technology Research Synopsis

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Public release date: 13-Oct-2009

Don't block folic acid in early pregnancy

Medications that block folic acid are associated with increased abnormalities

Using medication that reduces or blocks the actions of folic acid during the first trimester of pregnancy (weeks 1-12), increases the risk that the growing baby will develop abnormalities. This conclusion was reached by a team of Epidemiologists, Paediatricians, Clinical Pharmacologists, Obstetricians and Gynaecologists who examined birth and abortion data collected in Israel between 1998 and 2007.

The study drew information from 84,832 babies born at Soroka Medical Center, in Beer-Sheva, Israel. It was carried out as part of the PhD dissertation of Mgr. Ilan Matok, supervised by principal investigators Dr. Amalia Levy and Prof. Rafael Gorodischer from Ben-Gurion University of the Negev in Israel, in collaboration with the Division of Clinical Pharmacology, Hospital for Sick Children in Toronto, Canada (the BeMORE collaboration).

"After studying the data we concluded that first trimester exposure to folic acid antagonists is associated with increased risk for neural tube, cardiovascular and urinary tract defects," says paediatrician and clinical pharmacologist Rafael Gorodischer.

Healthcare professionals now encourage women to take folic acid supplements or eat food fortified with folic acid if they are planning to get pregnant as well as during early pregnancy, because there is clear evidence that this reduces the risk of any resulting baby having neural tube defects and possibly other birth defects (congenital malformations).

The team considered the effects of two groups of medications on pregnancy. Each group consists of drugs that prevent folic acid working in the body. One group (dihydrofolate reductase inhibitors), prevents folate being converted into its active metabolites and includes trimethoprim, sulfasalazine and methotrexate. The other medications are known to lower serum and tissue concentrations of folate by various mechanisms, and include antiepileptics (carbamazepine, phenytoin, lamotrigine, primidone, valproic acid and phenobarbital), and cholestyramine.

"The study shows that exposure to folic acid antagonists in the first trimester of pregnancy, more than doubled the risk of congenital malformations in the fetus, and that neural tube defects, such as spina bifida and malformations of the brain, are increased by more than six fold after exposure to these antagonists," said epidemiologist Dr. Amalia Levy.

"Clinicians should try to avoid the use of these drugs whenever possible in women contemplating pregnancy," concluded Gorodischer.

Public release date: 13-Oct-2009

Comfort food: Chocolate, water reduce pain response to heat

People often eat food to feel better, but researchers have found that eating chocolate or drinking water can blunt pain, reducing a rat's response to a hot stimulus. This natural form of pain relief may help animals in the wild avoid distraction while eating scarce food, but in modern humans with readily available food, the effect may contribute to overeating and obesity.

The study, published Wednesday in the Journal of Neuroscience by authors Peggy Mason, PhD, professor

of neurobiology, and Hayley Foo, PhD, research associate professor of neurobiology at the University of Chicago, is the first to demonstrate that this powerful painkilling effect occurs while the animals are ingesting food or liquid even in the absence of appetite.

"It's a strong, strong effect, but it's not about hunger or appetite," Mason said. "If you have all this food in front of you that's easily available to reach out and get, you're not going to stop eating, for basically almost any reason."

In the experiments, rats were given either a chocolate chip to eat or had sugar water or regular water infused directly into their mouth. As the rat swallowed the chocolate or fluid, a light-bulb beneath the cage was switched on, providing a heat stimulus that normally caused the animal to lift its paw off the floor. Mason and Foo found that rats were much slower to raise their paw while eating or drinking, compared to tests conducted while they were awake, but not eating.

Surprisingly, the researchers found no difference in the delayed paw-lift response between when the rat was eating chocolate and when it was drinking water, despite previous research indicating that only sugary substances were protective against pain.

"This really shows it has nothing to do with calories," Mason said. "Water has no calories, saccharine has no sugar, but both have the same effect as a chocolate chip. It's really shocking."

Mason and Foo then repeated the heat test as the rats were given quinine, a bitter drink that causes rats to make an expression called a gape that's akin to a child's expression of "yuck." During quinine administration, the rats reacted to heat as quickly as when not eating, suggesting that a non-pleasurable food or drink fails to trigger pain relief.

The context of ingesting was also important to whether eating or drinking blunted pain, the researchers found. When rats were made ill by a drug treatment, eating chocolate no longer delayed their response. However, drinking water still caused a reduced pain response, indicating that drinking water was considered a positive experience while ill.

By selectively inactivating a region in the brainstem called the raphe nucleus – an area previously shown to blunt pain during sleep and urination – Mason and Foo were able to remove the effect of drinking water on the rat's pain response. The brainstem controls subconscious responses such as breathing and perspiration during exercise.

"You're essentially at the mercy of your brainstem, and the raphe nucleus is part of that," Mason said. "It tells you, 'you're going to finish eating this, whether you like it or not,' just like you sweat while running whether you like it or not."

In the wild, Mason said, rats and other animals would not want to be distracted during the rare but important times that they were able to eat or drink. Therefore, the activation of the raphe nucleus during eating or drinking would allow the rat to filter out distractions until their meal was completed. For obvious reasons, this natural pain relief would be activated when an animal is eating or drinking something pleasurable, but not when it tastes something that could be toxic or harmful.

Don Katz, an associate professor of psychology and neuroscience at Brandeis University who studies taste, said that Mason and Foo's paper brings together two systems – taste and pain – that are usually studied separately.

"They're saying the purpose of the taste system is to give the animal a cue that helps it decide what stimulus they should or shouldn't pay attention to," Katz said. "This shows there is a whole region there to enable the animal to keep eating."

Mason believes that this effect is also present in humans (studies by other labs have observed similar pain reduction in infants receiving sugar water during a booster shot), but that it has detrimental effects in

modern society given our ready access to large quantities of pleasurable and fattening foods. Opening up a bag of chips could activate the brainstem such that you don't stop eating until the bag is empty, even while realizing that such behavior is bad for you.

"We've gotten a lot more overweight in last 100 to 150 years," Mason said. "We're not more hungry; the fact of the matter is that we eat more because food is readily available and we are biologically destined to eat what's readily available."

But the painkilling effect can be turned to our advantage, Mason said, perhaps as a replacement for the practice of using candy to calm children – or even adults – in the doctor's office.

"Ingestion is a painkiller but we don't need the sugar," Mason said. "So replace the doctor's lollipop with a drink of water."

Public release date: 14-Oct-2009

Popular antidepressant associated with a dramatic increase in suicidal thoughts amongst men

Nortriptyline has been found to cause a ten-fold increase in suicidal thoughts in men when compared to its competitor escitalopram. These findings are published in the open access journal BMC Medicine.

The research was carried out by Dr. Nader Perroud from the Institute of Psychiatry, Kings College London, who headed up GENDEP, an international team. Dr Perroud said "Suicidal thoughts and behaviours during antidepressant treatment have prompted warnings by regulatory bodies". He continued "the aim of our study was to investigate the emergence and worsening of suicidal thoughts during treatment with two different types of antidepressant."

Both escitalopram and nortriptyline have their effect through the mood modulating neurotransmitter systems. The former is a selective serotonin reuptake inhibitor (SSRI), preventing serotonin from re-entering the cell and thereby prolonging its effect on nerve synapses. The latter is a tricyclic antidepressant that inhibits the reuptake of noradrenaline, and to a lesser extent, that of serotonin.

The study was carried out on 811 individuals with moderate to severe unipolar depression. Whilst an overall trend in reduction of suicidal thoughts was observed, men who took nortriptyline were found to have a 9.8-fold increase in emerging suicidal thoughts and a 2.4-fold increase in worsening suicidal thoughts compared to those who took escitalopram.

Perroud concludes, "Our findings that treatment-emerging and worsening suicidal thoughts may also be associated with psychomotor activation triggered by antidepressants needs to be investigated in future studies. The study also refutes the idea that newer antidepressants such as the SSRIs are worse than older medications in terms of increasing suicidal thoughts."

Ralphs Note: Also known as **Sensoval, Aventyl, Pamelor, Norpress, Allegron** and

Nortrilen

Public release date: 16-Oct-2009

Promising novel treatment for human cancer -- Chrysanthemum indicum extract

A series of studies have demonstrated that Chrysanthemum indicum possesses antimicrobial, antiinflammatory, immunomodulatory, and neuroprotective effects. Recently, much attention has been devoted to the anticancer activity of Chrysanthemum indicum, especially in hepatocellular carcinoma (HCC). However, its anticancer mechanism of action is still not clear and needs further investigation.

A research article to be published on September 28, 2009 in the World Journal of Gastroenterology addresses this question. The research team, led by Prof. Zong-fang Li from the Second Affiliated Hospital, School of Medicine, Xi'an Jiaotong University, investigated the effects of Chrysanthemum indicum extract (CIE) on inhibition of proliferation and on apoptosis, and the underlying mechanisms, in a human HCC MHCC97H cell line.

They examined viable rat hepatocytes and human endothelial ECV304 cells by trypan blue exclusion and MTT assay, respectively, as normal controls. The proliferation of MHCC97H cells was determined by MTT assay. The cellular morphology of MHCC97H cells was observed by phase contrast microscopy. Flow cytometry was performed to analyze cell apoptosis with annexin V/propidium iodide (PI), mitochondrial membrane potential with rhodamine 123 and cell cycle with PI in MHCC97H cells. Apoptotic proteins such as cytochrome C, caspase-9, caspase-3 and cell cycle proteins, including P21 and CDK4, were measured by Western blotting.

The results showed CIE inhibited proliferation of MHCC97H cells in a time- and dose-dependent manner without cytotoxicity in rat hepatocytes and human endothelial cells. CIE induced apoptosis of MHCC97H cells in a concentration-dependent manner, as determined by flow cytometry. The apoptosis was accompanied by a decrease in mitochondrial membrane potential, release of cytochrome C and activation of caspase-9 and caspase-3. CIE arrested the cell cycle in the S phase by increasing P21 and decreasing CDK4 protein expression.

The researchers drew a conclusion that CIE exerted a significant apoptotic effect through a mitochondrial pathway and arrested the cell cycle by regulation of cell cycle-related proteins in MHCC97H cells without an effect on normal cells. The cancer-specific selectivity shown in their study suggests that the plant extract could be a promising novel treatment for human cancer.

Public release date: 19-Oct-2009

Mangosteen juice could protect health in the obese

Mangosteen juice has anti-inflammatory properties which could prove to be valuable in preventing the development of heart disease and diabetes in obese patients. A study, published in BioMed Central's open access Nutrition Journal, describes how the juice of the exotic 'superfruit' lowered levels of C-reactive protein.

Dr. Jay Udani, M.D. from Medicus Research, California, worked with a team of researchers to carry out a randomized, double-blind placebo controlled trial. He said, "For people drinking over half a liter of mangosteen juice a day, the degree of reduction in CRP levels was statistically significant – a reduction of 1.33mg/L compared to an increase of 0.9mg/L in the placebo group".

Inflammation, as measured here by CRP, is a predictor of cardiovascular disease and a precursor of metabolic syndrome. Reducing inflammation in obese people is a treatment goal, and a natural treatment may be preferable to other treatments which may carry the risk of side effect. According to Udani, "Further studies with a larger population are required to confirm and further define the benefits of this juice, which was safe at all dosages tested".

Public release date: 19-Oct-2009

Herbal tonic for radiotherapy

Radioprotection and extracts of Ginkgo biloba

Antioxidant extracts of the leaves of the Ginkgo biloba tree may protect cells from radiation damage, according to a study published in the International Journal of Low Radiation. The discovery may one day be used to help reduce side effects in cancer patients undergoing radiotherapy.

Chang-Mo Kang of the Korea Institute of Radiological and Medical Sciences in Taegu and colleagues are interested in the protective effects of well-known herbal remedies of which Ginkgo biloba is one. G. biloba is a unique tree species with no close living relatives and extracts of its leaves contain antioxidant compounds including glycosides and terpenoids known as ginkgolides and bilobalides.

These compounds are thought to protect cells from damage by free radicals and other reactive oxidizing species found in the body. These are generated continuously by the body's normal metabolism, and in excess in some diseases or after exposure to pollution or radiation. They damage proteins, DNA and other biomolecules and left unchecked can kill cells.

As such, extracts of certain plants that contain antioxidants, including G. biloba, have attracted interest for their pharmacological activity. G. biloba is currently sold as a herbal supplement and there are numerous claims for health benefits, including the possibility of preventing the onset of dementia or Alzheimer's disease.

Kang and colleagues have now collected human white blood cells, lymphocytes, from healthy donors aged 18 to 50 years. They treated half of these cells with commercially available *G. biloba* extract in the laboratory and doused the other half with salt solution as an experimental control. They then compared the effects of gamma radiation from radioactive cesium on the white blood cells compared to the untreated control samples.

The team uses a light microscope to look for lymphocytes undergoing programmed cell death, or apoptosis, as a result of radiation exposure. They found that there was a significant increase in apoptosis in the untreated cells compared with those treated with *G. biloba* extract. Almost a third of the untreated cells underwent apoptosis compared with approximately one in twenty of the treated cells. Parallel studies with laboratory mice also demonstrated a similar protective effect against radiation poisoning.

The results suggest that the extracts can neutralize the free-radicals and oxidizing agents produced in the cells by the radiation and so prevent them from undergoing apoptosis.

Public release date: 20-Oct-2009

Drinking coffee slows progression of liver disease in chronic hepatitis C sufferers

Patients with chronic hepatitis C and advanced liver disease who drink three or more cups of coffee per day have a 53% lower risk of liver disease progression than non-coffee drinkers according to a new study led by Neal Freedman, Ph.D., MPH, from the National Cancer Institute (NCI). The study found that patients with hepatitis C-related bridging fibrosis or cirrhosis who did not respond to standard disease treatment benefited from increased coffee intake. An effect on liver disease was not observed in patients who drank black or green tea. Findings of the study appear in the November issue of *Hepatology*, a journal published by Wiley-Blackwell on behalf of the American Association for the Study of Liver Diseases.

Hepatitis C virus (HCV) infects approximately 2.2% of the world's population with more than 3 million Americans infected. The Centers for Disease Control and Prevention (CDC) cites HCV as the leading cause of liver transplantation in the U.S. and accounts for 8,000 to 10,000 deaths in the country annually. Globally, the World Health Organization (WHO) estimates 3 to 4 million persons contract HCV each year with 70% becoming chronic cases that can lead to cirrhosis of the liver and liver cancer.

This study included 766 participants enrolled in the Hepatitis C Antiviral Long-Term Treatment against Cirrhosis (HALT-C) trial who had hepatitis C-related bridging fibrosis or cirrhosis and failed to respond to standard treatment of the anti-viral drugs peginterferon and ribavirin. At the onset of the study, HALT-C patients were asked to report their typical frequency of coffee intake and portion size over the past year, using 9 frequency categories ranging from 'never' to 'every day' and 4 categories of portion size (1 cup, 2 cups, 3-4 cups, and 5+ cups). A similar question was asked for black and green tea intake. "This study is the first to address the association between liver disease progression related to hepatitis C and coffee intake," stated Dr. Freedman.

Participants were seen every 3 months during the 3.8-year study period to assess clinical outcomes which included: ascites (abnormal accumulation of fluid in the abdomen), prognosis of chronic liver disease, death related to liver disease, hepatic encephalopathy (brain and nervous system damage), hepatocellular carcinoma (liver cancer), spontaneous bacterial peritonitis, variceal hemorrhage, or increase in fibrosis. Liver biopsies were also taken at 1.5 and 3.5 five years to determine the progression of liver disease.

Results showed that participants who drank 3 or more cups of coffee per day had a relative risk of .47 for reaching one of the clinical outcomes. Researchers did not observe any association between tea intake and liver disease progression, though tea consumption was low in the study. "Given the large number of people affected by HCV it is important to identify modifiable risk factors associated with the progression of liver disease," said Dr. Freedman. "Although we cannot rule out a possible role for other factors that go along with drinking coffee, results from our study suggest that patients with high coffee intake had a lower risk of disease progression." Results from this study should not be generalized to healthier populations cautioned the authors.

Release Date: October 14, 2009

GAO: FDA fails to follow up on unproven drugs

By MATTHEW PERRONE, AP Business Writer Matthew Perrone, Ap Business Writer

WASHINGTON – The Food and Drug Administration has allowed drugs for cancer and other diseases to stay on the market even when follow-up studies showed they didn't extend patients' lives, say congressional investigators.

A report due out Monday from the Government Accountability Office also shows that the FDA has never pulled a drug off the market due to a lack of required follow-up about its actual benefits — even when such information is more than a decade overdue.

When pressed about that policy, agency officials said they have no plans to get more aggressive.

The GAO says the FDA should do more to track whether drugs approved based on preliminary results actually have lived up to their promise.

The FDA responded that the report paints an overly negative picture of its so-called "accelerated approval" program, which is only used to approve drugs for the most serious diseases.

"Millions of patients with serious or life-threatening illnesses have had earlier access to new safe and effective treatments," thanks to the program, the FDA said in its response to the report.

In 1992, the FDA began speeding up the approval of novel drugs based on so-called surrogate endpoints, or laboratory measures that suggest the drug will make real improvements in patient health. HIV drugs, for example, are cleared based on their virus-lowering power, a predictor of increased survival.

Drugmakers favor the program because it helps them get products to market sooner, without conducting long-term patient studies that can take years and cost hundreds of millions of dollars. A condition of quicker approvals is that drugmakers conduct follow-up studies to show the drug's benefits actually panned out.

But the GAO report, a copy of which was obtained by The Associated Press, identified several drugs still on the market that never lived up to their initial promise. And in the 16 years that the FDA has used accelerated approval, it has never once pulled a drug off the market due to missing or unimpressive follow-up data.

"FDA has fallen far short of where it should be for patient safety," said Sen. Charles Grassley, R-Iowa, who requested the investigation.

Of the 144 studies the FDA has required under the program since 1992, 64 percent have been completed and more than one-third are still pending, according to the GAO. Investigators said the FDA does not rigorously track whether companies are making progress on their required studies, although the agency is improving.

FDA officials say they have overhauled their tracking system since the GAO completed its report. And an outside analysis by contractor Booz Allen Hamilton concluded last month that most companies are meeting their study requirements on time.

But in the case of Shire Laboratories' low blood pressure treatment ProAmatine, the required study has gone incomplete for more than 13 years. The GAO found that ProAmatine has generated more than \$257 million in sales, even though "the clinical benefit of the drug has never been established."

Shire did not respond to a request for comment Friday.

In other cases, the FDA has failed to act even when company studies show drugs did not improve patient outcomes.

The FDA approved AstraZeneca's lung cancer drug Iressa in 2003 based on early results showing it reduced the size of tumors. But later studies showed the drug did not significantly extend patient lives.

The FDA has left the drug on the market, despite hundreds of reports of a sometimes fatal pneumonia.

FDA officials explain that access to Iressa has been restricted to a small number of patients who have shown benefit. The agency recommends all other patients try two alternative drugs.

Iressa "is not available to new patients," AstraZeneca confirmed in a statement.

The GAO concluded that the FDA has no policy for pulling drugs off the market that were approved using surrogate endpoints. When GAO investigators confronted FDA officials about this lack of enforcement, they reportedly said it would be "difficult, if not impossible," to draft a standard policy for withdrawals, given the unique circumstances of individual drugs.

In certain cases, FDA officials say withdrawing a drug would mean eliminating the only available treatment for a condition.

"FDA should explain the principles it uses to make decisions such as drug withdrawals," said Principal Deputy Commissioner Dr. Joshua Sharfstein, in an interview with the AP. "But we don't want to lock ourselves into a specific set of criteria that takes away the flexibility to do what's right for the public health."

Sharfstein added that the agency has a task force assigned to look at policies like drug withdrawals.

Some consumers advocates say that's not good enough.

"The FDA has talked a lot about doing more enforcement, but this is an area where they're basically defending not enforcing the law," said Dr. Sidney Wolf, of the consumer advocacy group Public Citizen.

Wolfe said the lax policy sends a message to companies that there is no penalty for failing to complete studies.

The GAO recommends the FDA clarify when it will pull drugs off the market.

"As the scientific experts charged with overseeing the use of drugs it approves, FDA should be in a position to implement this recommendation," the report states

Public release date: 21-Oct-2009

Amphetamine use in adolescence may impair adult working memory

(Ritalin ?)

CHAMPAIGN, Ill. — Rats exposed to high doses of amphetamines at an age that corresponds to the later years of human adolescence display significant memory deficits as adults – long after the exposure ends, researchers report.

The declines in short-term or "working" memory are most pronounced when the rats are exposed during adolescence, rather than as adults, the researchers found.

"Animals that were given the amphetamine during the adolescent time period were worse at tasks requiring working memory than adult animals that were given the same amount of amphetamine as adults," said psychology professor Joshua Gulley, who led the study with graduate student Jessica Stanis. "This tells us that their working memory capacity has been significantly altered by that pre-exposure to amphetamine."

Gulley and his colleagues will present their findings Wednesday (Oct. 21) at the annual meeting of the Society for Neuroscience in Chicago.

The researchers tested two types of amphetamine exposure: intermittent (a steady dose every other day) and "binge-escalation," in which increasing amounts of the drug were given over a period of four days, followed by a simulated binge – a high dose every two hours for eight hours on the fifth day.

The findings reveal some of the potential long-term consequences of amphetamine abuse by adolescents and also may be relevant to those taking amphetamines for therapeutic purposes, such as for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). Gulley cautions that the doses given to the rats are on the high end of what an older, larger adolescent might receive as a therapeutic dose, and that further study is needed to tease out the implications for human health.

The concerns are most robust for adolescents who abuse amphetamines, Gulley said, as they may use much higher doses than those who are prescribed drugs that contain amphetamines.

"Adolescence is a time when the brain is continuing to develop into its mature form, so drug exposure during this critical period could have long-lasting, negative consequences," he said. "Our findings reveal that adolescents are particularly sensitive to the adverse effects of amphetamine on cognitive function and that these effects can persist well after drug use is discontinued."

Public release date: 22-Oct-2009

Pesticides exposure linked to suicidal thoughts

A new study in China has found that people with higher levels of pesticide exposure are more likely to have suicidal thoughts. The study was carried out by Dr Robert Stewart from the Institute of Psychiatry at King's College London together with scientists from Tongde Hospital Zhejiang Province.

The agricultural pesticides commonly used in China are organophosphates which are in wide use in many lower income countries but have been banned in many Western nations. It is well known that they are very dangerous if ingested as an overdose but there is also biological evidence that **chronic low-grade exposure to these chemicals, which are very easily absorbed into the body through the skin and lungs, may have adverse effects on mental health. This study is the first epidemiological evidence to suggest possible effects on suicidal thoughts.**

The study was carried out in central/coastal China, a relatively wealthy area with a rapidly developing

economy. In a very large survey of mental health in rural community residents, participants were also asked about how they stored pesticides. The study found that people who stored pesticides at home, i.e. those with more exposure, were more likely to report recent suicidal thoughts. Supporting this, the survey also found suicidal thoughts to be associated with how easily accessible these pesticides were in the home and that the geographic areas with highest home storage of pesticides also had highest levels of suicidal thoughts in their populations.

Given the high level of pesticide exposure and the high suicide risk in rural China, clarification of the causal mechanisms underlying this association and the development of appropriate interventions should be priorities for public health and health policy.

Dr Robert Stewart comments: 'Organophosphate pesticides are widely used around the world although are banned in many countries because of their risk to health. **They are particularly lethal chemicals when taken in overdose and are a cause of many suicides worldwide.** Our research findings that suggest that higher exposure to these chemicals might actually increase the risk of suicidal thoughts provides further support for calls for tighter international restrictions on agricultural pesticide availability and use.'

Dr Jianmin Zhang, Associate Chief Psychiatrist, Tongde Hospital of Zhejiang Province, and Vice Director, Zhejiang Office of Mental Health, China added: 'The findings of this study suggested potential causal links and might partially account for the much higher incidence of suicide in rural than urban areas of China. However, further studies particularly with more precisely defined and assessed exposure are critically needed, as awareness of safer access to pesticides is important both to policy-makers and pesticide users.'

Ralph's Note - Uhhh, well one more reason to eat organic....

Public release date: 22-Oct-2009

Long-term treatment with proton pump inhibitor (Antacids) can increase weight

Gastroesophageal reflux disease (GERD) is the most common esophageal disorder, and frequently encountered in the primary care setting. Accumulating evidence has confirmed the excellent efficacy and safety of proton pump inhibitor (PPI) therapy in patients with all grades of GERD, making these agents the mainstay of treatment. However, the possible impact of changes in body weight (BW) or body mass index (BMI) in reflux patients while on long-term PPI therapy has not been examined.

A clinical research team from Japan elucidated the effect on nutritional parameters such as body weight and BMI in patients receiving long-term PPI therapy. Their study will be published on October 14, 2009 in the World Journal of Gastroenterology.

The subjects were 52 patients with GERD and 58 sex- and age-matched healthy controls. GERD patients were treated with PPI for a mean of 2.2 years (range, 0.8-5.7 years), and also advised on lifestyle modifications (e.g. selective diet, weight management). BW, BMI and other parameters were measured at baseline and end of study.

Their results showed there were no differences in BW and BMI between reflux patients and controls at baseline. Patients with GERD showed increases in BW, but no such changes were noted in the control group. **Mean BW increased by 3.5 kg (6.2% of**

baseline) in 37 (71%) reflux patients but decreased in only 6 (12%) patients during treatment.

They concluded that reflux patients treated with a daily maintenance therapy of PPI should be strongly encouraged to manage their body weight through lifestyle modifications such as proper diet and avoidance of overeating. This measure may reduce the overall medical costs associated with obesity-related illness as well as GERD. Lifestyle modification must therefore remain the backbone of treatment for all patients with GERD, even in the PPI era.

Public release date: 23-Oct-2009

Why antidepressants don't work for so many

Northwestern research finds drugs aim at wrong target

CHICAGO --- More than half the people who take antidepressants for depression never get relief.

Why? Because the cause of depression has been oversimplified and drugs designed to treat it aim at the wrong target, according to new research from the Northwestern University Feinberg School of Medicine. The medications are like arrows shot at the outer rings of a bull's eye instead of the center.

A study from the laboratory of long-time depression researcher Eva Redei, presented at the Neuroscience 2009 conference in Chicago this week, appears to topple two strongly held beliefs about depression. One is that stressful life events are a major cause of depression. The other is that an imbalance in neurotransmitters in the brain triggers depressive symptoms.

Both findings are significant because these beliefs were the basis for developing drugs currently used to treat depression.

Redei, the David Lawrence Stein Professor of Psychiatry at Northwestern's Feinberg School, found powerful molecular evidence that quashes the long-held dogma that stress is generally a major cause of depression. Her new research reveals that there is almost no overlap between stress-related genes and depression-related genes.

"This is a huge study and statistically powerful," Redei said. "This research opens up new routes to develop new antidepressants that may be more effective. There hasn't been an antidepressant based on a novel concept in 20 years."

Her findings are based on extensive studies with a model of severely depressed rats that mirror many behavioral and physiological abnormalities found in patients with major depression. The rats, after decades of development, are believed to be the most depressed in the world.

Little Overlap Between Stress and Depression Genes

Redei used microarray technology to isolate and identify the specific genes related to depression in these animals. She examined the genes in the brain regions -- the hippocampus and amygdala -- commonly associated with depression in rats and humans.

Then she took four genetically different strains of rats and exposed them to chronic stress for two weeks. Afterwards, she identified the genes that had consistently increased or decreased in response to the stress in all four strains in the same brain regions.

Redei now had one set of depression-related genes that came out of an animal model of depression and one set of stress-related genes that came out of her chronic stress study.

Next she compared the two sets of genes to see if there were any similarities. "If the 'stress causes depression theory' was correct, there should have been a significant overlap between these two sets of genes," she said. "There weren't."

Out of a total of over 30,000 genes on the microarray, she discovered approximately 254 genes related to stress and 1275 genes related to depression, with an overlap of only five genes between the two.

"This overlap is insignificant, a very small percentage," Redei said. "This finding is clear evidence that at least in an animal model, chronic stress does not cause the same molecular changes as depression does."

Antidepressants Treat Stress Not Depression

Most animal models that are used by scientists to test antidepressants are based on the hypothesis that stress causes depression. "They stress the animals and look at their behavior," she said. "Then they manipulate the animals' behavior with drugs and say, 'OK, these are going to be good anti-depressants.' But they are not treating depression; they are treating stress."

That is one key reason why current antidepressants aren't doing a great job, Redei noted. She is now looking at the genes that differ in the depressed rat to narrow down targets for drug development.

She said another reason current antidepressants are often ineffective is that they aim to boost neurotransmitters based on the popular molecular explanation of depression, which is that it's the result of decreased levels of the neurotransmitters serotonin, norepinephrine and dopamine. But that's wrong, Redei said.

Drugs Aim at Wrong Molecular Target

In the second part of the study, Redei found strong indications that depression actually

begins further up in the chain of events in the brain. The biochemical events that ultimately result in depression actually start in the development and functioning of neurons.

"The medications have been focusing on the effect, not the cause," she said. "That's why it takes so long for them to work and why they aren't effective for so many people."

Her animal model of depression did not show dramatic differences in the levels of genes controlling neurotransmitters functions. "If depression was related to neurotransmitter activity, we would have seen that," she said.

Similarities Between Human and Rodent Brains

Her findings in depressed rats, she said, are very likely applicable to humans.

"The similarities between these regions of the human and rodent brain are remarkable," Redei explained. "The hippocampus and amygdala are part of the so-called ancient lizard brain that controls survival and are the same in even primitive organisms."

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Neurologists Investigate Possible New Underlying Cause of MS (43 FOLD Increase)

UB neurologist Robert Zivadinov is principal investigator on a new study that could change understanding of MS.

BUFFALO, NY – Neurologists at the University at Buffalo are beginning a research study that could overturn the prevailing wisdom on the cause of multiple sclerosis (MS).

The researchers will test the possibility that the symptoms of MS result from narrowing of the primary veins outside the skull, a condition called "chronic cerebrospinal venous insufficiency," or CCSVI.

CCSVI is a complex vascular condition discovered and described by Paolo Zamboni, M.D., from Italy's University of Ferrara. In the original Italian patients, **CCSVI was found to be strongly associated with MS, increasing the risk of developing MS by 43 fold.**

This narrowing restricts the normal outflow of blood from the brain, causing alterations in the blood flow patterns within the brain that eventually causes injury to brain tissue and degeneration of neurons.

"If we can prove our hypothesis, that cerebrospinal venous insufficiency is the underlying cause of MS," said Robert Zivadinov, M.D., Ph.D., UB associate professor of neurology,

director of the Buffalo Neuroimaging Analysis Center (BNAC) and principal investigator on the study, "it is going to change the face of how we understand MS."

Michael Cain, M.D., professor and dean of the UB School of Medicine and Biomedical Sciences, said a positive outcome from this trial would have enormous implications for the treatment of MS. "Being able to identify those at risk of developing MS before symptoms take their toll could change the lives of millions of persons who now face inevitable lifestyle restrictions."

Margaret Paroski, M.D., executive vice president and chief medical officer of Kaleida Health, parent of Buffalo General Hospital where the BNAC is located, commented: "Will Rogers once said, 'It isn't what we don't know that gives us trouble, it's what we do know that ain't so'. Challenging basic assumptions about diseases has led to some very important discoveries.

"When I was in medical school, we thought peptic ulcer disease was due to stress. We now know that 80 percent of cases are due to a bacterial infection. Dr. Zivadinov's work may lead to a whole different way of thinking about multiple sclerosis."

The preliminary findings were based on a pilot study at the BNAC headed by Zivadinov, and at the Universities of Ferrara and Bologna, Italy, directed by Zamboni and Fabrizio Salvi, M.D, respectively. The study showed that several abnormalities affecting the predominant pathways that return venous blood from the brain to the heart occurred more frequently in MS patients than in controls.

This research, supported by the Hilarescere Foundation of Italy and the BNAC, was conducted to replicate the findings of the Italian investigators.

"Results of this preliminary study, which involved 16 relapsing-remitting MS patients and eight age-and-sex-matched healthy controls, showed that all the MS patients, but none of the controls, had chronic insufficient blood flow out of the brain," said Zivadinov.

Bianca Weinstock-Guttman, M.D., UB associate professor of neurology and a co-principal investigator on the pilot study, added: "The images from this study were acquired using a method called Doppler ultrasound. The method identified anomalies in the venous blood flow associated with strictures, malformed valves and peculiar webs within the large veins of the neck and brain"

Weinstock-Guttman directs the Baird Multiple Sclerosis Center at the Jacobs Neurological Institute (JNI), UB's Department of Neurology. The JNI and BNAC are located in Buffalo General Hospital of Kaleida Health.

Advanced magnetic resonance imaging scanning (MRI) of the MS study patients conducted at the BNAC also identified distinct areas of iron deposits in the brain, and showed that those deposits may be associated with the location of MS lesions and sites of

impaired drainage. The scans also revealed increased brain atrophy and changes in the flow of cerebrospinal fluid in the MS patients.

These results, which form the basis of the current larger investigation, were presented at the 25th Congress of the European Committee for Treatment and Research in Multiple Sclerosis held in September in Dusseldorf, Germany

The new study will involve 1,600 adults and 100 children. The cohort will be comprised of 1,100 patients who were diagnosed with possible or definite MS, 300 age-and-sex matched normal controls, and 300 patients with other autoimmune and neurodegenerative diseases. Enrollment in the study has begun and will continue for two years. MS patients from across the U.S. are eligible to participate in the study.

"The prevailing wisdom that central nervous system damage in MS is predominantly the result of abnormal immune responses against the patient's nervous tissue has been challenged by research findings, which have demonstrated a significant neurodegenerative component in MS and the progressive loss of neurons" said Zivadinov.

However, these inflammatory and neurodegenerative processes occur concurrently in MS and vary considerably among patients, making it difficult to identify the cause, or causes of the disease. Consequently, the origin and development of MS remains poorly understood, and its cause remains elusive."

To determine if these preliminary findings can be repeated, Zivadinov and Weinstock-Guttman organized the present study, which will evaluate both the velocity of blood flow through both the brain's blood vessels and the extracranial veins, using Doppler ultrasound.

The technical name of the study is "combined transcranial and extracranial venous Doppler (CTEVD) evaluation in MS and related diseases".

All study subjects will undergo a general clinical examination and a Doppler scan of the head and neck to acquire images of the direction of venous blood flow in different body postures. Participants also will provide blood samples, and complete an extensive environmental questionnaire to identify potential MS risk factors.

All MS patients will undergo MRI of the brain to measure iron deposits in lesions and surrounding areas of the brain using a method called susceptibility-weighted imaging. Iron findings on these images will be related to neuropsychological symptoms. The neuropsychological part of the study will be conducted by Ralph Benedict, Ph.D., professor of neurology and psychiatry at the JNI, UB's Department of Neurology.

A sub-cohort of 250 consecutive patients and controls will undergo MRI of the veins of the neck to confirm diagnosis of CCSVI.

Murali Ramanathan, Ph.D., associate professor in the Department of Pharmaceutical Sciences, UB School of Pharmacy and Pharmaceutical Sciences, will analyze blood samples for proteins and soluble factors associated with central nervous system injury. He also will be looking for other factors of interest in MS research, such as vitamin D metabolites and cigarette smoking, which have been linked to increased risk for developing MS as well as MS disease progression.

The data will be unblinded at three predetermined time-points, with the initial unblinding scheduled for November 2009. For more details on the study, send an email to ctevd@bnac.net.

Zivadinov said results of the study may lead to a larger multicenter North-American trial that will evaluate the occurrence of CCSVI in MS.

Public release date: 26-Oct-2009

Latest analysis confirms suboptimal vitamin D levels in millions of US children

National data suggest non-whites are especially at risk

Boston, Mass. -- Millions of children in the United States between the ages of 1 and 11 may suffer from suboptimal levels of vitamin D, according to a large nationally representative study published in the November issue of *Pediatrics*, accompanied by an editorial.

The study, led by Jonathan Mansbach, MD, at Children's Hospital Boston, is the most up-to-date analysis of vitamin D levels in U.S. children. It builds on the growing evidence that levels have fallen below what's considered healthy, and that black and Hispanic children are at particularly high risk.

Both the optimal amount of vitamin D supplementation and the healthy blood level of vitamin D are under heated debate in the medical community. **Currently, the American Academy of Pediatrics recommends children should have vitamin D levels of at least 50 nmol/L (20 ng/ml). However, other studies in adults suggest that vitamin D levels should be at least 75 nmol/L (30 ng/ml), and possibly 100 nmol/L (40 ng/ml), to lower the risk of heart disease and specific cancers.**

Mansbach and collaborators from the University of Colorado Denver and Massachusetts General Hospital used data from the National Health and Nutrition Examination Survey (NHANES) to look at vitamin D levels in a nationally representative sample of roughly 5,000 children from 2001-2006. **Extrapolating to the entire U.S. population, their analysis suggests that roughly 20 percent of all children fell below the recommended 50 nmol/L. Moreover, more than two-thirds of all children had levels below 75 nmol/L, including 80 percent of Hispanic children and 92 percent of non-Hispanic black children.**

"If 75 nmol/L or higher is eventually demonstrated to be the healthy normal level of vitamin D, **then there is much more vitamin D deficiency in the U.S. than people realize**," Mansbach says.

Mansbach and his co-authors suggest that all children take vitamin D supplements, because of the generally low levels that they found and the potential health benefits of boosting vitamin D to normal levels. Vitamin D improves bone health and prevents rickets in children, and recent studies suggest that it also may prevent a host of common childhood illnesses, including respiratory infections, childhood wheezing, and winter-related eczema.

Although sun exposure generates healthy doses of vitamin D, it can also cause skin cancer. Dermatologists and the AAP recommend wearing sunblock, but this actually blocks our skin's ability to make vitamin D. Furthermore, children with more highly pigmented skin require much more sun exposure than fair-skinned children to obtain healthy levels of vitamin D. Vitamin D can also be obtained from certain foods, like liver and fatty fish, but almost all children in the U.S. don't consume these foods in high enough quantities to match the vitamin D that could be provided by summer sunshine or vitamin D supplements.

In the study, children taking multi-vitamins that included vitamin D had higher levels overall, but this accounted for less than half of all children. **Mansbach recommends that all children take vitamin D supplements, especially those living in high latitudes, where the sun is scarce in the wintertime.**

"We need to perform randomized controlled trials to understand if vitamin D actually improves these wide-ranging health outcomes," Mansbach says. "At present, however, there are a lot of studies demonstrating associations between low levels of vitamin D and poor health. Therefore, we believe many U.S. children would likely benefit from more vitamin D."

Ralph's Note - To all those who say vitamins are just a waste of money, despite volumes of science. I hope you sleep well knowing your irrational vigilance against facts has harmed untold numbers of people.

Public release date: 26-Oct-2009

Weekly and biweekly vitamin D2 prevents vitamin D deficiency

(Boston) – Boston University School of Medicine researchers (BUSM) have found that 50,000 International Units (IU) of vitamin D2, given weekly for eight weeks, effectively treats vitamin D deficiency. Vitamin D2 is a mainstay for the prevention and treatment of vitamin D deficiency in children and adults. Continued treatment with the same dose of vitamin D2 every other week for up to six years after the initial eight-week period prevents vitamin D deficiency from recurring with no toxicity. The BUSM study appears

online in the journal Archives of Internal Medicine.

Vitamin D is essential for strong bones because it helps the body absorb calcium and phosphorus from the food we eat. Vitamin D deficiency can lead to rickets in children and the painful bone disease osteomalacia in adults. Vitamin D deficiency can also cause osteoporosis and has been linked to increased risk of cancer, heart disease, diabetes, autoimmune diseases and infectious diseases including influenza, according to senior author Michael F. Holick, PhD, MD, director of the Bone Healthcare Clinic and the Vitamin D, Skin and Bone Research Laboratory at Boston University School of Medicine.

Of the 86 patients researchers studied, 41 patients who were vitamin D deficient received eight weeks of 50,000 IU of vitamin D2 weekly prior to starting maintenance therapy. For those patients, the mean pre-treatment 25-hydroxyvitamin D status (25(OH)D) level was 19 ng/ml, which increased to 37 ng/ml after eight weeks of weekly therapy. These patients were then treated with 50,000 IU of vitamin D2 every other week and had a mean final 25(OH)D level of 47 ng/ml.

For the 45 patients who received only maintenance therapy of 50,000 IU of vitamin D2 every two weeks, the mean pre-treatment 25(OH)D level was 27 ng/ml and the mean final level was 47 ng/ml.

"Vitamin D2 is effective in raising 25(OH)D levels when given in physiologic and pharmacologic doses and is a simple method to treat and prevent vitamin D deficiency," said Holick, who is also director of the General Clinical Research Unit and professor of medicine, physiology and biophysics at BUSM. "While treating and preventing vitamin D deficiency, these large doses of vitamin D2 do not lead to vitamin D toxicity."

According to Holick, this is the first study demonstrating the efficacy of a prescription therapy to prevent vitamin D deficiency longterm in routine clinical practice.

Public release date: 26-Oct-2009

Music makes you smarter

Regularly playing a musical instrument changes the anatomy and function of the brain and may be used in therapy to improve cognitive skills.

There is growing evidence that musicians have structurally and functionally different brains compared with non-musicians. In particular, the areas of the brain used to process music are larger or more active in musicians. Even just starting to learn a musical instrument can change the neurophysiology of the brain.

Lutz Jäncke, a member of Faculty of 1000 Medicine, proposes using music in neuropsychological therapy, for example to improve language skills, memory, or mood. In a review for Faculty of 1000 Biology Reports, an online publication in which leading

researchers highlight advances in their field, Jäncke summarizes recent studies of professional musicians.

The brain regions involved in music processing are also required for other tasks, such as memory or language skills. "If music has such a strong influence on brain plasticity," writes Jäncke, "this raises the question of whether this effect can be used to enhance cognitive performance."

Several studies indeed show that musical practice increases memory and language skills, and Jäncke suggests expanding this field: "Hopefully, the current trend in the use of musicians as a model for brain plasticity will continue ... and extend to the field of neuropsychological rehabilitation

Ralph's Note - Wow, major reason not to cut music programs in school.

Public release date: 27-Oct-2009

Medical food reduces medical costs and use of anti-convulsant medication

HealthCore study shows Metanx also reduces health plan costs
Paris—Oct. 27, 2009—Diabetic patients diagnosed with peripheral neuropathy had lower medical costs and reduced use of anticonvulsant medications when treated with a folate-enriched prescription medical food, according to data presented today at the International Society for Pharmacoeconomics and Outcomes Research 12th Annual European Congress.

The results of the HealthCore, Inc. study, funded by PamLab, L.L.C., which manufactures the medical food Metanx®, showed that patients' health plan costs to treat diabetes-related peripheral neuropathy were reduced by about \$400 a year.

"In this study, health care savings were driven by lower costs related to hospitalization and outpatient services," said Ron Wade, lead researcher and research operations director for HealthCore, the outcomes research subsidiary for WellPoint, Inc. "Overall, this was more than a 30 percent reduction in costs for medical care related to diabetic peripheral neuropathy."

The study, "Administrative Claims Analysis of an L-Methylfolate Combination Product in Patients with Diabetic Peripheral Neuropathy," was co-authored by Wade and Qian Cai of HealthCore and Dr. Tina Thethi, assistant professor of endocrinology, Tulane School of Medicine. The abstract for this study was published in the Sept. 15 online edition of Value in Health.

Diabetic peripheral neuropathy is a disorder of the peripheral nerves usually affecting the hands and feet, causing weakness, numbness, tingling and pain. Anticonvulsant medication is commonly used to control these symptoms.

The HealthCore study found that the group of patients **prescribed Metanx tablets reduced their use of anticonvulsants by 31 percent one year after treatment**, compared with the control group that reduced their use by 10 percent.

Metanx contains **L-methylfolate, pyridoxyl-5-phosphate, and methylcobalmin** and has been shown in pilot studies to increase epidermal nerve fiber density in humans, restore sensation and reduce neuropathic pain by increasing nitric oxide levels, which improves endothelial function and increases blood flow to the nerves in the hands and feet.

"From clinical trials, we are seeing what Metanx can do clinically, but it is also reassuring to know that in this time of soaring health care costs that Metanx may help reduce costs related to patients with diabetic peripheral neuropathy," said Chet Busby, head of PamLab's scientific affairs.

Ralph's Note - Biologically active Folic acid, B-6 and B-12

Release Date: October 14, 2009

Vegetables can protect unborn child against diabetes

New evidence is emerging for how important it is for pregnant women to eat good, nutritious food. Expecting mothers who eat vegetables every day seem to have children who are less likely to develop type 1 diabetes, a new study from the Sahlgrenska Academy has revealed.

The study was performed in collaboration with Linköping University, which is conducting a population study called ABIS (All Babies in Southeast Sweden). The results have been published in the journal *Pediatric Diabetes*.

"This is the first study to show a link between vegetable intake during pregnancy and the risk of the child subsequently developing type 1 diabetes, but more studies of various kinds will be needed before we can say anything definitive," says researcher and clinical nutritionist Hilde Brekke from the Sahlgrenska Academy.

Blood samples from almost 6,000 five year-olds were analysed in the study. In type 1 diabetes, certain cells in the pancreas gradually get worse at producing insulin, leading to insulin deficiency. Children at risk of developing type 1 diabetes have antibodies in their blood which attack these insulin-producing cells.

Of the 6,000 children tested, three per cent had either elevated levels of these antibodies or fully developed type 1 diabetes at the age of five. These risk markers were up to twice as common in children whose mothers rarely ate vegetables during pregnancy. The risk was lowest among children whose mothers stated that they ate vegetables every day.

"We cannot say with certainty on the basis of this study that it's the vegetables

themselves that have this protective effect, but other factors related to vegetable intake, such as the mother's standard of education, do not seem to explain the link," says Brekke. "Nor can this protection be explained by other measured dietary factors or other known risk factors."

The term "Vegetables "in this study included all vegetables except for root vegetables

**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.**