

Gadget may offer migraine relief

A new hand-held device that delivers a magnetic pulse to the back of the head could become an alternative to drug treatment for people with migraines. A trial found that 40% of patients were pain free two hours after using the device. Research showed there were no serious side-effects and patients found the device easy to use at home. However, doctors say more research is needed to work out the timing of the doses.

Experts from the Albert Einstein College of Medicine in New York carried out the trial to assess the safety and effectiveness of the device. Previous trials have only involved large, expensive devices which have to be used in a clinic.



The hand-held device tested in the trial can be used at home

Electrical events

The hand-held device emits a single-pulse transcranial magnetic stimulation (sTMS), thought to disrupt the electrical events in the brain which cause the preliminary symptoms of migraines with aura. Auras are sensory or visual disturbances that occur before a migraine headache sets in. These include visual symptoms such as spots of light and zigzag lines. Other symptoms include tingling, numbness and difficulties with speaking.

Two hundred patients were asked to use the device to treat migraines with aura over three months. Half of those patients were given placebo treatment. The findings, to be published in *The Lancet Neurology*, showed that the real magnetic pulse from the device was significantly more effective than placebo treatment. More patients were pain free two, 24 and 48 hours afterwards.

Dr Hans-Christoph Diener, from University Hospital Essen in Germany, said: "The use of sTMS could be a major step forward in the treatment of migraine with aura, particularly in patients in whom presently available drug treatment is ineffective."

Wendy Thomas, chief executive of the Migraine Trust, welcomed the new trials but stressed that more research into migraines would be needed before patients could access the treatment. "We look forward to hearing the results of further sTMS trials in the future.

"Migraine and headache are the least publicly funded of all neurological conditions in the UK, particularly relative to their economic impact," she said.

Obesity as protection against metabolic syndrome, not its cause

The collection of symptoms that is the metabolic syndrome - insulin resistance, high cholesterol, fatty liver, and a greater risk for diabetes, heart disease, and stroke - are all related to obesity, but, according to a review in the March 9th issue of the Cell Press publication *Trends in Endocrinology and Metabolism*, not in the way you probably think they are.

In fact, says Roger Unger of the University of Texas Southwestern at Dallas, obesity is the body's way of storing lipids where they belong, in fat tissue, in an effort to protect our other organs from lipids' toxic effects. It's when the surplus of calories coming in gets to be too much for our fat tissue to handle that those lipids wind up in other places they shouldn't be, and the cascade of symptoms known as metabolic syndrome sets in.

It comes down to simple facts that all of us know on some level or another: Americans since the 1950s eat too much high-calorie food loaded with carbs and fat (what Unger calls "potent adipogenic nutrient mixtures") and, thanks to modern technology, we move far too little. Until that changes, Unger doesn't see any end to the growing epidemic of metabolic syndrome. Still, our metabolisms aren't broken; the pathways that squirrel fat away as an energy source for use in lean times are just completely overwhelmed. "We are pushing our homeostatic capability to the maximum," says Unger, who coined the term "lipotoxicity" in 1994. "Overnutrition used to be rare - reserved for those in the castle. Today, it's just the opposite. Bad calories are so cheap that anyone can afford to get overweight."

Unger cites plenty of evidence in support of a protective role for obesity. Genetic manipulations in mice that increase or decrease fat formation have provided evidence that adipogenesis, meaning the generation of fat cells, delays other metabolic consequences of overeating. The reverse is also true, he writes. Obesity-resistant mice have in some cases been found to develop severe diabetes upon eating too much, as a result of lipid accumulation in tissues other than fat.

There is some disagreement in the field about whether insulin resistance is a primary cause of metabolic syndrome or just one of its features, Unger notes. But on this, too, he has a clear view. Insulin resistance is not the cause of metabolic syndrome, he says, it is a "passive byproduct" of fat deposition in the liver and muscle once storage in fat cells begins to fail.

MIGRAINES

They affect about 18% of women and 6% of men in the USA and Western Europe

There are two major forms of migraine – with aura and without aura.

Migraine with aura affects about 20-30% of patients

Migraine with aura is characterised by symptoms which usually precede the onset of a headache

It also makes sense in Unger's estimation that cells that have already taken on too much fat would begin to exclude glucose, causing its levels in blood and urine to rise. Once in cells, glucose becomes a substrate for the production of more fat. "The body is doing what we should have done - keep excess calories out - and it may be protective," Unger says.

At the center of the transition from protective obesity to metabolic syndrome is resistance to the fat hormone leptin, well known for its appetite-suppressing effects, Unger says. The hormone is also responsible for partitioning fat in the body. The rise of leptin as fat stores grow is therefore an adaptive response, but that can only go so far before resistance sets in.

Based on the genes they carry, some people will be better able to sustain lipid storage in fat and can get away with being overweight, even obese, without the other symptoms. Eventually, though, the need to cut calories is something all of us will face.

"Once you reach a certain age, almost everybody is leptin resistant," he says. "Nature stops protecting you once you pass the reproductive years," requiring all of us to watch our diets and do exercise.

Unger's perspective comes from the research he does at UT Southwestern's Touchstone Center for Diabetes Research and a thorough understanding of the scientific literature, but it also stems from his own memories in childhood when one only saw fat ladies at the circus. "That's how unusual it was," he says. "The younger you are, the more skewed your perception is of an epidemic that surrounds you."

Unger concludes his review article this way: "Based on evidence reviewed here, it seems that prevalent forms of metabolic syndrome and T2DM [type 2 diabetes mellitus] result from unremitting caloric surplus complicated by failure of adipocytes to maintain protection against lipotoxicity. If one imagines the USA population to be unwitting volunteers in the largest (300 million subjects) and longest (50 years) clinical research project in history, the specific aim of which was to determine if the deleterious effects of sustained caloric surplus in rodents also can occur in humans, the outcome of the project becomes clear - after 50 years of exposure to an inexpensive calorie-dense diet high in fat and carbohydrates, 200 million subjects are overweight and >50 million have metabolic syndrome. The failure of healthcare providers and pharmaceutical industries to contain the pandemic suggests that elimination of 'bargain basement' calories will be required to 'price obesity out of the market.' Unfortunately, this would have profound socioeconomic implications: How do we tax excessive calories while at the same time guaranteeing sufficient access to high-quality foods for the underprivileged?" *Scherer et al.: "Gluttony, sloth and the metabolic syndrome: a roadmap to lipotoxicity."*

Archaeologists Find Earliest Known Domestic Horses: Harnessed and Milked

An international team of archaeologists has uncovered the earliest known evidence of horses being domesticated by humans. The discovery suggests that horses were both ridden and milked. The findings could point to the very beginnings of horse domestication and the origins of the horse breeds we know today. Led by the Universities of Exeter and Bristol (UK), the research is published on Friday 6 March 2009 in journal *Science*.

The researchers have traced the origins of horse domestication back to the Botai Culture of Kazakhstan circa 5,500 years ago. This is about 1,000 years earlier than thought and about 2,000 years earlier than domestic horses are known to have been in Europe. Their findings strongly suggest that horses were originally domesticated, not just for riding, but also to provide food, including milk.



Evidence of thong bridle use suggests horses may have been ridden as early as 5,500 years ago. Credit: Illustration by Sandra Olsen, Carnegie Museum of Natural History

Through extensive archaeological fieldwork and subsequent analysis, using new techniques, the team developed three independent lines of evidence for early horse domestication. Their findings show that in the fourth millennium BC horses in Kazakhstan were being selectively bred for domestic use. They also show horses were being harnessed, possibly for riding, and that people were consuming horse milk.

Analysis of ancient bone remains showed that the horses were similar in shape to Bronze Age domestic horses and different from wild horses from the same region. This suggests that people were selecting wild horses for their physical attributes, which were then exaggerated through breeding.

The team used a new technique to search for 'bit damage' caused by horses being harnessed or bridled. The results showed that horses had indeed been harnessed, suggesting they could have been ridden.

Using a novel method of lipid residue analysis, the researchers also analysed Botai pottery and found traces of fats from horse milk. Mare's milk is still drunk in Kazakhstan, a country in which horse traditions run deep,

and is usually fermented into a slightly alcoholic drink called 'koumiss'. While it was known that koumiss had been produced for centuries, this study shows the practice dates back to the very earliest horse herders. Lead author Dr Alan Outram of the University of Exeter said: "The domestication of horses is known to have had immense social and economic significance, advancing communications, transport, food production and warfare. Our findings indicate that horses were being domesticated about 1,000 years earlier than previously thought. This is significant because it changes our understanding of how these early societies developed."

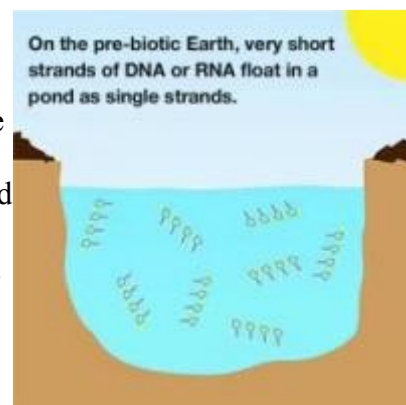
The steppe zones, east of the Ural Mountains in Northern Kazakhstan, are known to have been a prime habitat for wild horses thousands of years ago. They were a commonly hunted animal. This may have set the stage for horse domestication by providing indigenous cultures with access to plentiful wild herds and the opportunity to gain an intimate knowledge of equine behaviour. Horses appear to have been domesticated in preference to adopting a herding economy based upon domestic cattle, sheep and goats. Horses have the advantage of being adapted to severe winters and they are able to graze year round, even through snow. Cattle, sheep and goats need to be provided with winter fodder, and were a later addition to the prehistoric economies of the region.

This study was carried out by the Universities of Exeter, Bristol and Winchester (UK), Carnegie Museum of Natural History (Pittsburgh, USA), and Kokshetau University (Kazakhstan) and was supported by the Natural Environment Research Council, British Academy and National Science Foundation of America.

Unselfish molecules may have helped give birth to the genetic material of life

One of the biggest questions facing scientists today is how life began. How did non-living molecules come together in that primordial ooze to form the polymers of life? Scientists at the Georgia Institute of Technology have discovered that small molecules could have acted as "molecular midwives" in helping the building blocks of life's genetic material form long chains and may have assisted in selecting the base pairs of the DNA double helix. The research appears in the online early edition of the Proceedings of the National Academy of Sciences beginning March 8, 2010.

"Our hypothesis is that before there were protein enzymes to make DNA and RNA, there were small molecules present on the pre-biotic Earth that helped make these polymers by promoting molecular self-assembly," said Nicholas V. Hud, professor in the School of Chemistry and Biochemistry at the Georgia Institute of Technology. "We've found that the molecule ethidium can assist short oligonucleotides in forming long polymers and can also select the structure of the base pairs that hold together two strands of DNA."



[VIDEO: Unselfish molecules may have helped give birth to the genetic material of life.](#)

One of the biggest problems in getting a polymer to form is that, as it grows, its two ends often react with each other instead of forming longer chains. The problem is known as strand cyclization, but Hud and his team discovered that using a molecule that binds between neighboring base pairs of DNA, known as an intercalator, can bring short pieces of DNA and RNA together in a manner that helps them create much longer molecules.

"If you have the intercalator present, you can get polymers. With no intercalator, it doesn't work, it's that simple," said Hud.

Hud and his team also tested how much influence a midwife molecule might have had on creating DNA's Watson-Crick base pairs (A pairs with T, and G pairs with C). They found that the midwife used could determine the base pairing structure of the polymers that formed. Ethidium was most helpful for forming polymers with Watson-Crick base pairs. Another molecule that they call aza3 made polymers in which each A base is paired with another A.

"In our experiment, we found that the midwife molecules present had a direct effect on the kind of base pairs that formed. We're not saying that ethidium was the original midwife, but we've shown that the principle of a small molecule working as a midwife is sound. In our lab, we're now searching for the identity of a molecule that could have helped make the first genetic polymers, a sort of 'unselfish' molecule that was not part of the first genetic polymers, but was critical to their formation," said Hud.

The work was supported by the National Aeronautics and Space Administration and the National Science Foundation.

1-page questionnaire is effective screening tool for common psychiatric disorders

CHAPEL HILL – A one-page, 27-item questionnaire that is available free online is a valid and effective tool to help primary care doctors screen patients for four common psychiatric illnesses, a study led by University of North Carolina at Chapel Hill researchers concludes. Results of the My Mood Monitor (M-3) checklist study are published in the March/April 2010 issue of *Annals of Family Medicine*. The checklist was developed by M-3 Information of Bethesda, Md., and is available at <http://www.mymoodmonitor.com>.

"About one in 10 Americans who suffer from depression and anxiety-related mental health disorders never receives treatment because they don't understand what's wrong, and when they go to their family doctor these treatable illnesses are too often missed," said Bradley Gaynes, M.D., M.P.H, lead author of the study and an associate professor of psychiatry in the University of North Carolina at Chapel Hill School of Medicine.

"For these millions of people and their primary care providers, the M-3 screener is a tremendously helpful resource," Gaynes said.

The M-3 checklist is designed to screen for depression, bipolar disorder, anxiety disorders and post-traumatic stress disorder (PTSD). For most people who suffer from any of these conditions, Gaynes said, their initial diagnosis is made by a primary care provider, not by a psychiatrist. In addition, the majority of prescriptions for antidepressant medications are written by primary care physicians. For those reasons, a single tool that can screen for multiple disorders would be very helpful, Gaynes said.

To evaluate the M-3 checklist, Gaynes and study co-authors enrolled 647 adults age 18 or older who sought care at the UNC Family Medicine Center between July 2007 and February 2008. Each participant filled out a paper version of the checklist while waiting to see their doctor. Each participant's completed checklist was then given to their doctor, and the doctors used the checklist to discuss emotional health with their patients.

Researchers later interviewed each person who filled out the checklist, within 30 days of their doctor visit, and assigned final diagnoses after reviewing each interview with Gaynes. These diagnoses were then compared to the answers each participant gave on their checklists. The results showed that the M-3 was effective in screening for any mood or anxiety disorder 83 percent of the time and for a specific disorder in 76 percent of cases.

Gaynes said the research team is currently designing a second study to measure the effectiveness of the M-3 checklist when used by individuals to monitor their mental health status over time. The company has developed a mobile phone version of the checklist that will be released later.

In addition to Gaynes, authors of the study were Joanne De-Veagh-Geiss, LPA, and Hongbin Gu, Ph.D., from UNC's Department of Psychiatry; David R. Rubinow, M.D., UNC's chair of psychiatry, Sam Weir, M.D. of UNC's Department of Family Medicine; Cora MacPherson, Ph.D., of Social & Scientific Systems Inc. in Silver Spring, Md.; Herbert C. Schulberg, Ph.D., M.S.Hyg., of Weill Cornell Medical College; and Larry Culpepper, M.D., M.P.H., professor and chairman of family medicine at Boston University and chief of family medicine at Boston Medical Center.

Abused children more likely to suffer unexplained abdominal pain, nausea or vomiting

CHAPEL HILL – Children who have been abused psychologically, physically or sexually are more likely to suffer unexplained abdominal pain and nausea or vomiting than children who have not been abused, a study led by University of North Carolina at Chapel Hill researchers concludes.

"Therefore, when young patients complain about unexplained gastrointestinal symptoms, their doctors should ask questions to determine if they might have been abused," said Miranda van Tilburg, Ph.D., lead author of the study, an assistant professor of gastroenterology and hepatology in the UNC School of Medicine and a member of UNC's Center for Functional GI & Motility Disorders.

The study is published in the March/April 2010 issue of *Annals of Family Medicine*. In the study, van Tilburg and study co-authors analyzed data that was obtained as part of the Longitudinal Studies of Child Abuse and Neglect (LONGSCAN). Their analysis included 845 children ages 4 through 12 years. Every two years they collected information about the children's gastrointestinal symptoms from their parents and maltreatment allegations concerning these children from child protective services agencies. Then the children, at age 12, gave their own reports of GI symptoms, life-time maltreatment and psychological distress. A statistical method called logistic regression was used to analyze the data.

The results showed that among children in the study, sexual abuse preceded or coincided with abdominal pain in 91 percent of cases. In addition, in children who said they recalled ever being abused physically, psychologically or sexually, there was a statistically significant association between abuse and both abdominal pain and nausea/vomiting.

An additional analysis aimed at separating the effect of psychological distress alone from physical or sexual abuse showed that most effects dropped below the level of statistical significance, except for the relationship between physical abuse and nausea/vomiting. This is consistent with other results reported in the medical literature, van Tilburg said, but psychological distress was only partly responsible for weakening the relation between physical abuse and nausea. Other factors, such as permanent changes in the nervous system due to injury associated with physical abuse, must play a role as well, she said.

In addition to van Tilburg, UNC co-authors of the study are Desmond K. Runyan, M.D. Dr.P.H., Adam J. Zolotor, M.D., M.P.H., Denesh K. Chitkara, M.D. and William E. Whitehead, Ph.D.

Co-authors from outside UNC include J. Christopher Graham, Ph.D. (University of Washington), Howard Dubowitz, M.D., M.S. (University of Maryland), Alan J. Litrownik, Ph.D. (San Diego State University), Emalee Flaherty, M.D. (Northwestern University Feinberg School of Medicine).

Women who drink moderately appear to gain less weight than nondrinkers

Normal-weight women who drink a light to moderate amount of alcohol appear to gain less weight and have a lower risk of becoming overweight and obese than non-drinkers, according to a report in the March 8 issue of Archives of Internal Medicine, one of the JAMA/Archives journals.

More than half of American adults drink alcoholic beverages, according to background information in the article. Alcohol contains about 7 calories per gram (with approximately 28 grams per ounce) and alcohol drinking may possibly lead to weight gain through an imbalance of energy consumed and energy burned. However, research has not consistently provided evidence that consuming alcohol is a risk factor for obesity.

Lu Wang, M.D., Ph.D., of Brigham and Women's Hospital, Boston, and colleagues studied 19,220 U.S. women age 39 or older who had a body mass index (BMI) in the range classified as normal (18.5 to 25). On an initial questionnaire, participants reported how many alcoholic beverages they typically drank per day. A total of 7,346 (38.2 percent) reported drinking no alcohol; 6,312 (32.8 percent) drank less than 5 grams; 3,865 (20.1 percent) drank 5 to less than 15 grams; 1,129 (5.9 percent) drank 15 to less than 30 grams; and 568 (3 percent) drank 30 grams per day or more.

Over an average of 13 years of follow-up, women on average gained weight progressively. Women who did not drink alcohol at all gained the most weight, with weight gain decreasing as alcohol intake increased. A total of 7,942 (41.3 percent) women who initially had normal weight become overweight or obese (BMI of 25 or higher), including 732 (3.8 percent) who become obese (BMI of 30 or higher). Compared with women who did not drink at all, those who consumed some but less than 40 grams per day of alcohol were less likely to become overweight or obese. Women who drank 15 to less than 30 grams per day had the lowest risk, which was almost 30 percent lower than that of non-drinkers.

"An inverse association between alcohol intake and risk of becoming overweight or obese was noted for all four types of alcoholic beverages [red wine, white wine, beer and liquor], with the strongest association found for red wine and a weak yet significant association for white wine after multivariate adjustment," the authors write.

The authors caution that, given potential medical and psychosocial problems related to drinking alcohol, its beneficial and adverse effects for each individual must be considered before making any recommendation about its use. "Further investigations are warranted to elucidate the role of alcohol intake and alcohol metabolism in energy balance and to identify behavioral, physiological and genetic factors that may modify the alcohol effects," they conclude.

(Arch Intern Med. 2010;170[5]:453-461. Available pre-embargo to the media at www.jamamedia.org.)

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When a Scratch or a Nosebleed Turns Into a Flood

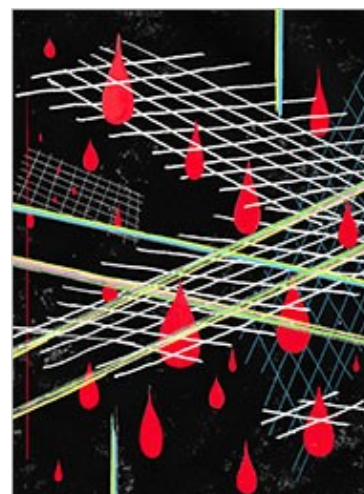
By PERRI KLASS, M.D.

My friend Dr. Eileen Costello still remembers her terror at the baby who was brought into her office bleeding.

The little girl "not only had unbelievable petechiae" - the tiny red dots caused by broken blood vessels bleeding into the skin - "she had a bloody nose, she had bleeding gums," Dr. Costello, a pediatrician in Boston, told me.

But what worried her most was that the baby might bang her head on the way to the emergency room, causing her to bleed uncontrollably inside her skull. "I was so nervous I went down to the basement and got a bike helmet," Dr. Costello said.

It turned out that the child had a disorder called I.T.P., for idiopathic thrombocytopenic purpura, which can develop after a routine viral illness. The immune system, revved up to fight the virus, somehow begins to attack the body's own platelets. Fortunately, the baby made a full recovery. The disorder usually resolves on its own, with drug treatments available for children whose platelet counts dip dangerously low.



Jon Han

When the occasional nosebleed becomes frequent and uncontrolled, or the routine bumps of an active toddler turn into constant bruising, it is frightening for parents and often challenging for doctors to diagnose. Successful hemostasis - the stopping of bleeding after a blood vessel is broken or torn - is an incredibly complex process.

Consider von Willebrand disease, an inherited disorder that - like the better-known hemophilia - is caused by a deficiency in one of the essential factors that govern the blood's ability to clot. (The two disorders are caused by different deficiencies.) Screening tests have suggested that as much as 1 percent of the population may have the abnormally low levels, or abnormal function, of von Willebrand factor that cause the disease, although many never have bleeding problems. Children with this condition often have severe nosebleeds that will not stop, and they can bleed dangerously after a routine tonsillectomy.

Von Willebrand disease is most commonly treated - if it needs to be treated at all - with a drug called desmopressin, which can be used when a child needs surgery, or at the beginning of a menstrual period.

Abnormally heavy menstrual flow, or menorrhagia, is another common problem for girls and women with von Willebrand disease - which, unlike hemophilia, is not a sex-linked trait.

Most types of hemophilia are inherited on the X chromosome and therefore show up only in males, who have no second, normally functioning X chromosome. Queen Victoria, herself unaffected, was a carrier - thus that famous pedigree by which royal children with hemophilia married into so many ruling families of Europe.

Von Willebrand disease, in contrast, is inherited on a nonsex chromosome, and it shows up in males and females. The National Hemophilia Foundation is running an awareness campaign aimed at women who may have von Willebrand disease without knowing it.

Hemophilia, too, can show up unannounced. Dr. Catherine Manno, a hematologist who is the head of pediatrics at New York University, points out that almost a third of cases occur in children without a known family history of it. "They usually present after the first birthday," she told me. "Even with no clotting factor, children with hemophilia can have completely normal births, and if they're not circumcised, they can have little to suggest they have a bleeding disorder."

It's when they become more active, as they learn to walk, that they begin to have the bumps and bruises that signal something is amiss. Hemophilia is treated with replacement therapy; the missing clotting factor is provided as a concentrate injected or infused into the blood.

Many parents, seeing increased bruising, think first of leukemia. Dr. James B. Bussel, an expert on I.T.P. who is a professor of pediatrics at Weill Cornell Medical School, told me that part of his job was to reassure those parents that leukemia can be ruled out if the red and white cell counts look normal and if the child does not have enlarged lymph nodes or an abnormal liver and spleen.

"If they present with bleeding and/or bruising and they get checked by the pediatrician, and the platelet count is very low, then if the other counts are normal and there's no major finding other than signs of bleeding on exam, then they almost certainly have I.T.P., especially if the bleeding developed recently," he said.

There's another concern that often comes to mind for doctors - or teachers, or neighbors - when a child has abnormal bruising. "The public has been educated to report this sort of thing," said Dr. Manno, of N.Y.U. It's important not to miss abuse, but it can be hard to endure that recurrent suspicion.

"If you're living with the burden of a chronic disease in your beloved child," she went on, "and someone approaches you and says, 'How did your kid get those bruises?' that's very offensive to people."

Some bruising is to be expected in active children. The most common sites are the outer side of the arm and the front of the leg; bruises that show up elsewhere are more worrisome, and bruises that show up where there has been no bang or bump are most worrisome of all. Pediatric hematologists describe parents who report that their children develop bruises where they're touched or picked up, and those children definitely need to be evaluated.

"In this day and age when doctors have to turn around four to six patients in an hour, trying to take a careful history is not easy to do sometimes," said Dr. Robert R. Montgomery, a pediatric hematologist and von Willebrand expert at the Blood Research Institute in Milwaukee.

And sometimes, he continued, "bruising will be dismissed - oh, all children have bruises - but it's important."

'Pay it forward' pays off

UC San Diego and Harvard deliver first experimental findings on spread of cooperation in a social network

For all those dismayed by scenes of looting in disaster-struck zones, whether Haiti or Chile or elsewhere, take heart: Good acts - acts of kindness, generosity and cooperation - spread just as easily as bad. And it takes only a handful of individuals to really make a difference.

In a study published in the March 8 early online edition of the Proceedings of the National Academy of Sciences, researchers from the University of California, San Diego and Harvard provide the first laboratory evidence that cooperative behavior is contagious and that it spreads from person to person to person. When people benefit from kindness they "pay it forward" by helping others who were not originally involved, and this creates a cascade of cooperation that influences dozens more in a social network.

The research was conducted by James Fowler, associate professor at UC San Diego in the Department of Political Science and Calit2's Center for Wireless and Population Health Systems, and Nicholas Christakis of Harvard, who is professor of sociology in the Faculty of Arts and Sciences and professor of medicine and medical sociology at Harvard Medical School. Fowler and Christakis are coauthors of the recently published book "Connected: The Surprising Power of Our Social Networks and How They Shape Our Lives."

In the current study, Fowler and Christakis show that when one person gives money to help others in a "public-goods game," where people have the opportunity to cooperate with each other, the recipients are more likely to give their own money away to other people in future games. This creates a domino effect in which one person's generosity spreads first to three people and then to the nine people that those three people interact with in the future, and then to still other individuals in subsequent waves of the experiment.

The effect persists, Fowler said: "You don't go back to being your 'old selfish self.'" As a result, the money a person gives in the first round of the experiment is ultimately tripled by others who are subsequently (directly or indirectly) influenced to give more. "The network functions like a matching grant," Christakis said.

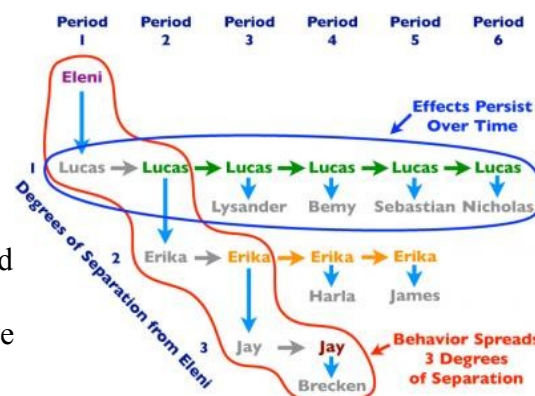
"Though the multiplier in the real world may be higher or lower than what we've found in the lab," Fowler said, "personally it's very exciting to learn that kindness spreads to people I don't know or have never met. We have direct experience of giving and seeing people's immediate reactions, but we don't typically see how our generosity cascades through the social network to affect the lives of dozens or maybe hundreds of other people."

The study participants were strangers to each other and never played twice with the same person, a study design that eliminates direct reciprocity and reputation management as possible causes.

In previous work demonstrating the contagious spread of behaviors, emotions and ideas – including obesity, happiness, smoking cessation and loneliness – Fowler and Christakis examined social networks re-created from the records of the Framingham Heart Study. But like all observational studies, those findings could also have partially reflected the fact that people were choosing to interact with people like themselves or that people were exposed to the same environment. The experimental method used here eliminates such factors.

The study is the first work to document experimentally Fowler and Christakis's earlier findings that social contagion travels in networks up to three degrees of separation, and the first to corroborate evidence from others' observational studies on the spread of cooperation.

This diagram illustrates how a single act of kindness can spread between individuals and across time. Cooperative behavior spreads three degrees of separation: if Eleni increases her contribution to the public good, it benefits Lucas (one degree of separation), who gives more when paired with Erika (two degrees of separation) in period 2, who gives more when paired with Jay (three degrees of separation) in period 3, who gives more when paired with Brecken in period 4. The effects also persist over time, so that Lucas gives more when paired with Erika (period 2) and also when paired with Lysander (period 3), Bemy (period 4), Sebastian (period 5), and Nicholas (period 6). The effect also persists at two degrees of separation, as Erika not only gives more when paired with Jay (period 3), but also when paired with Harla (period 4) and James (period 5). All the paths in this illustrative cascade are supported by results in the experiments, and it is important to note that if Eleni decreases her initial contribution then her uncooperative behavior can spread and persist as well. Courtesy James Fowler, UC San Diego



The contagious effect in the study was symmetric; uncooperative behavior also spread, but there was nothing to suggest that it spread any more or any less robustly than cooperative behavior, Fowler said.

From a scientific perspective, Fowler added, these findings suggest the fascinating possibility that the process of contagion may have contributed to the evolution of cooperation: Groups with altruists in them will be more altruistic as a whole and more likely to survive than selfish groups.

"Our work over the past few years, examining the function of human social networks and their genetic origins, has led us to conclude that there is a deep and fundamental connection between social networks and goodness," said Christakis. "The flow of good and desirable properties like ideas, love and kindness is required for human social networks to endure, and, in turn, networks are required for such properties to spread. Humans form social networks because the benefits of a connected life outweigh the costs."

The research was funded by the National Institute on Aging, the John Templeton Foundation, and a Pioneer Grant from the Robert Wood Johnson Foundation.

Deceptive model

Stem cells of humans and mice differ more strongly than suspected. New study calls research factors into question

They are considered to be the most important model organism for research into human biology: mice may look totally different, but they are in many ways similar to *Homo sapiens* on a fundamental level. For instance, an impressive 99 per cent of the mouse genes are matched by a corresponding sequence in the human genome. That is also why the law in this part of the world only permits scientists to conduct research on human embryo stem cells when they have "clarified in advance" their specific questions by using animal cells as far as possible. However, such tests are often pointless - and sometimes even misleading, as a recent study by scientists working with Hans Schöler at the Max Planck Institute for Molecular Biomedicine in Münster demonstrates. (Cell Stem Cell, March 5th, 2010)

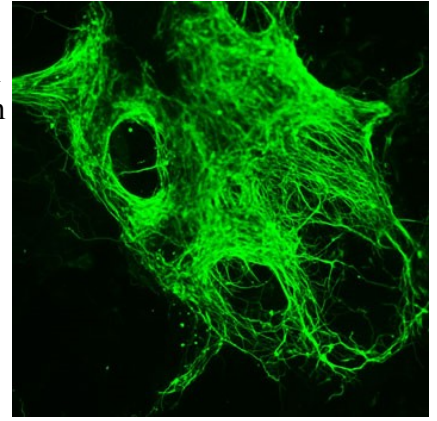


Fig.: Neural differentiation of mouse epiblast stem cells by inactivating the FGF signalling pathway. Molecular mechanisms to differentiate human and mouse stem cells may be similar but may also vary substantially on occasion.

For years scientists have puzzled over to what extent the findings of studies on the embryonic stem cells (ES cells) of mice are transferable to humans. It is certainly true that human and mouse ES cells are both pluripotent. That means they are capable of forming any of the body's cell types, numbering more than 200 in all. And both types of cells have an active Oct4 transcription factor, for example. This is the gene that is essential for maintaining pluripotency, and is what makes egg cells, as well as embryonic stem cells and early embryos, potentially immortal.

In other aspects, though, as scientists have known for some time now, human and mouse ES cells differ enormously. Certain signalling substances that can be used to turn mouse cells into liver, nerve or muscle cells, for instance, produce either no effect or totally different effects in human ES cells.

The reasons for this are still uncertain. However, in 2007 two research teams succeeded in isolating a promising new type of pluripotent cells from mice embryos (see Brons et al., Nature 448, 2007). Known as epiblast stem cells (EpiSC), these cells are also pluripotent. However, they stem from a later stage of embryonic development: unlike 'traditional' ES cells, which are harvested from a few-days-old embryo in the blastocyst stage, these are harvested from an embryo that has just lodged itself in the uterus and which is referred to as an epiblast.

The astonishing thing about it is that although epiblast stem cells are actually a step ahead in their development, they appear to be more similar to human ES cells than 'classic' mouse ES cells are. For example, both epiblast stem cells and human ES cells can, with the addition of a certain hormone, the FGF2 growth factor, be grown and held in a state in which they can turn into any tissue at all. "Epiblast stem cells from mice are therefore more-or-less equated with human ES cells in the general scientific discussion," says Boris Greber, the lead author of the study.

Differing effects of signal molecules

But Greber, a biochemist, wanted to know more. In their latest study, he and his fellow scientists therefore looked at how mouse epiblast and human embryonic stem cells react to different growth factors and inhibitors - and they found that the two types of cells do, in fact, differ on a crucial point. Whereas the FGF growth factor actively supports the self-renewal of human ES cells, this is not the case with mouse epiblast cells.

"Ultimately, what this means is that many preliminary tests on animal cells - particularly in medically relevant projects - may not only be useless, but the findings from this kind of early testing may even be misleading," explains Hans Schöler, who goes on to say that human ES cells will therefore continue to be absolutely essential for stem cell research in the future. "The recent successes in reprogramming mature human somatic cells sometimes make it look as though tests using human ES cells are nowadays redundant. But appearances are deceptive." Neither the technologies for reprogramming nor those for purposefully differentiating cells are as yet fully-developed.

Human stem cells remain indispensable

Only a fraction of the cells that the scientists treat with their formulas go on to display the right attributes. And only through elaborate, time-consuming tests can the successfully transformed cells be picked out from among the large numbers of cells that failed to be completely reprogrammed. "Our latest study demonstrates that animal model systems are inadequate for a great many tests of this kind," says Schöler. "Particularly when we're talking about developing safe and effective stem cell therapies, we will still need human ES cells as the

gold standard against which to compare everything else. In such cases, lengthy preliminary testing on animal cells risks wasting valuable time and resources." [JMK]

Original work: Boris Greber, Guangming Wu, Christof Bernemann, Jin Young Joo, Dong Wook Han, Kinarm Ko, Natalia Tapia, Davood Sabour, Jared Sternecker, Paul Tesar, Hans R. Schöler

Conserved and divergent roles of FGF signaling in mouse epiblast stem cells and human embryonic stem cells
Cell Stem Cell, 5 March 2010, doi:10.1016/j.stem.2010.01.003

Infection Defense May Spur Alzheimer's

By GINA KOLATA

For years, a prevailing theory has been that one of the chief villains in Alzheimer's disease has no real function other than as a waste product that the brain never properly disposed of. The material, a protein called beta amyloid, or A-beta, piles up into tough plaques that destroy signals between nerves. When that happens, people lose their memory, their personality changes and they stop recognizing friends and family.

But now researchers at Harvard suggest that the protein has a real and unexpected function — it may be part of the brain's normal defenses against invading bacteria and other microbes.

Other Alzheimer's researchers say the findings, reported in the current issue of the journal PLoS One, are intriguing, though it is not clear whether they will lead to new ways of preventing or treating the disease.

The new hypothesis got its start late one Friday evening in the summer of 2007 in a laboratory at Harvard Medical School. The lead researcher, Rudolph E. Tanzi, a neurology professor who is also director of the genetics and aging unit at Massachusetts General Hospital, said he had been looking at a list of genes that seemed to be associated with Alzheimer's disease.

To his surprise, many looked just like genes associated with the so-called innate immune system, a set of proteins the body uses to fight infections. The system is particularly important in the brain, because antibodies cannot get through the blood-brain barrier, the membrane that protects the brain. When the brain is infected, it relies on the innate immune system to protect it.

That evening, after the lab's usual end-of-the-week beer hour, Dr. Tanzi wandered into the office of a junior faculty member, Robert D. Moir, and mentioned what he had seen. As Dr. Tanzi recalled, Dr. Moir turned to him and said, "Yeah, well, look at this." He handed Dr. Tanzi a spreadsheet. It was a comparison of A-beta and a well-known protein of the innate immune system, LL-37. The likenesses were uncanny. Among other things, the two proteins had similar structures. And like A-beta, LL-37 tends to clump into hard little balls.

In rodents, the protein that corresponds to LL-37 protects against brain infections. People who make low levels of LL-37 are at increased risk of serious infections and have higher levels of atherosclerotic plaques, arterial growths that impede blood flow.

The scientists could hardly wait to see if A-beta, like LL-37, killed microbes. They mixed A-beta with microbes that LL-37 is known to kill — listeria, staphylococcus, pseudomonas. It killed 8 out of 12. "We did the assays exactly as they have been done for years," Dr. Tanzi said. "And A-beta was as potent or, in some cases, more potent than LL-37." Then the investigators exposed the yeast *Candida albicans*, a major cause of meningitis, to tissue from the hippocampal regions of brains from people who had died of Alzheimer's and from people of the same age who did not have dementia when they died.

Brain samples from Alzheimer's patients were 24 percent more active in killing the bacteria. But if the samples were first treated with an antibody that blocked A-beta, they were no better than brain tissue from nondemented people in killing the yeast. The innate immune system is also set in motion by traumatic brain injuries and strokes and by atherosclerosis that causes reduced blood flow to the brain, Dr. Tanzi noted.

And the system is spurred by inflammation. It is known that patients with Alzheimer's disease have inflamed brains, but it has not been clear whether A-beta accumulation was a cause or an effect of the inflammation. Perhaps, Dr. Tanzi said, A-beta levels rise as a result of the innate immune system's response to inflammation; it may be a way the brain responds to a perceived infection.

But does that mean Alzheimer's disease is caused by an overly exuberant brain response to an infection?

That's one possible reason, along with responses to injuries and inflammation and the effects of genes that cause A-beta levels to be higher than normal, Dr. Tanzi said. However, some researchers say that all the pieces of the A-beta innate immune systems hypothesis are not in place.

Dr. Norman Relkin, director of the memory disorders program at New York-Presbyterian/Weill Cornell hospital, said that although the idea was "unquestionably fascinating," the evidence for it was "a bit tenuous."

As for the link with infections, Dr. Steven T. DeKosky, an Alzheimer's researcher who is vice president and dean of the University of Virginia School of Medicine, noted that scientists have long looked for evidence linking infections to Alzheimer's and have come up mostly empty-handed.

But if Dr. Tanzi is correct about A-beta being part of the innate immune system, that would raise questions about the search for treatments to eliminate the protein from the brain.

"It means you don't want to hit A-beta with a sledgehammer," Dr. Tanzi said. "It says what we need is the equivalent of a statin for the brain so you can dial it down but not turn it off." (Dr. Tanzi is a co-founder of two companies, Prana Biotechnology and Neurogenetic Pharmaceutical, that are trying to dial down A-beta.)

Dr. Relkin said that even if A-beta were not part of the innate immune system, it might not be a good idea to remove it all, along with the hard balls of plaque it makes in the brain.

In the past, Dr. Relkin said, scientists assumed "that the pathology was the plaque." Now, he likens removing plaque to digging up bullets at the Gettysburg battlefield.

The more bullets in an area, the more intense the fighting was. But "digging up bullets will not change the outcome of the battle," he said. "Most of us don't believe that removing plaque from the brain is the end-all."

But other scientists not connected with the discovery said they were impressed by the new findings.

"It changes our thinking about Alzheimer's disease," said Dr. Eliezer Masliah, who heads the experimental neuropathology laboratory at the University of California, San Diego. "I don't think we ever thought about that possibility for A-beta."

Dr. Masliah is intrigued by the idea that aggregates of A-beta may be killing bacteria and brain cells by the same mechanism. He noted that Dr. Tanzi had a track record of coming up with unusual ideas about Alzheimer's disease that later turn out to be correct.

"I think he's onto something important," Dr. Masliah said.

Infectious virus hidden in chromosomes during latency can be passed from parents to children

Virologists surprised to discover that a common herpesvirus hidden in chromosomes of some people can be reactivated to infectious form

Tampa, FL - Human herpesvirus 6 (HHV-6) infects nearly 100 percent of humans in early childhood, and the infection then lasts for the rest of a person's life. Now, a team led by Peter Medveczky, MD, a professor in the Department of Molecular Medicine at the University of South Florida (USF), has discovered that in some individuals, HHV-6 causes such a permanent infection by inserting or "integrating" its DNA into human chromosomes. From this harbor, the viral DNA cannot be eliminated by the immune system. The paper describing this research was published online March 8 in Proceedings of the National Academy of Sciences.

The USF team also confirmed preliminary results by other investigators that, a long time ago, the virus inserted its DNA into the DNA of human sperm and egg cells. As a result, some people (about 1 percent of people in the U.S.) are born with the virus's DNA in every cell in their body. Indeed, HHV-6 is the first functional virus of any type reported to be passed through the human germ line.

The team presented clear evidence that the virus can insert its DNA specifically into telomeres – structures at the ends of each chromosome that play key roles in both aging and cancer. Finally, the team showed that the chromosomally integrated HHV-6 (CIHHV-6) genomes can be reactivated to an infectious form.

The findings are a surprise, since other human herpesviruses cause permanent infection by a different mechanism. The round up their DNA into a little circle that resides inside the nucleus of the cell: they do not insert their DNA into the chromosomes.

There are many unanswered questions that the USF team hopes to sort out. "We would like to know whether the location of the integration has an impact on pathology," Dr. Medveczky said. "We'd also like to know more about which drugs can provoke reactivation in patients that carry this virus in every cell... It would be important for these patients to avoid drugs that may reactivate the virus."

"This is an exciting and provocative series of observations. The questions raised by this work will keep herpes virologists busy for years," predicted HHV-6 expert Phil Pellett, PhD of Wayne State University.

HHV-6 was discovered in 1986 in the laboratory of Dr. Robert C. Gallo at the National Cancer Institute after Gallo asked his co-workers to look for a herpesvirus in AIDS lymphoma cases that might be triggering cancer. "In my mind these findings also should stimulate further studies on a possible role of HHV-6 in some cancers as suggested by others who have found a possible link to some lymphomas," Dr. Gallo commented. "However, clearly more work will be needed to advance any conclusion in this regard."

HHV-6 causes roseola, a generally benign rash and fever in infants. The virus can reactivate in individuals with suppressed immune systems, sometimes causing serious consequences such as encephalitis, hepatitis, myocarditis, and pneumonia.

Recent research has suggested that HHV-6 may also be associated with diseases in people with apparently healthy immune systems: encephalitis, mesial temporal lobe epilepsy, multiple sclerosis, myocarditis, and

idiopathic cardiomyopathy. While there is no proof that the virus plays a causal role in these diseases, the virus has been found more often in the diseased tissue than in healthy tissue.

Previous studies had used a visual technique called fluorescence in situ hybridization (FISH), which showed that the viral DNA was present at the same location (near the telomeres) of the same chromosome in both parent and child. This strongly suggested but did not prove that the virus was inherited through the germ line in these children. By determining the DNA sequence of the ends of the chromosome, the Medveczky team clearly demonstrated that the HHV-6 genome was integrated into telomere DNA. The team also showed that HHV-6 DNA, unlike other human herpesviruses, does not curl into a circle inside the nucleus.

The great majority of people, however, do not inherit HHV-6 DNA from their parents and do not have it in every cell of their body. Yet nearly everyone becomes permanently infected with the virus. So Medveczky and colleagues wondered if the virus might take up permanent residence in the body by integrating its DNA into the chromosomes of just some cells.

To examine this possibility, the investigators took cells that had never been exposed to HHV-6 and infected them with HHV-6 that had been engineered to make infected cells glow bright green. Sure enough, once the infection died down, the green cells contained HHV-6 DNA integrated into the ends of the chromosomes. When the investigators stimulated the cells with chemicals known to activate other herpesviruses, cells with integrated viral DNA began producing infectious virus. It will be important to learn whether a similar process occurs during the form of HHV-6 infection that occurs in most individuals.

For the approximately 1 percent of the population born with viral DNA in every cell in their body, several questions arise. Are such people more prone to diseases because they have a greater risk of viral reactivation? If so, which diseases? If a person is born with viral proteins present from birth, would that person's immune system be "fooled" into thinking that the virus was not foreign and need not be attacked? If so, is that a bad thing or a good thing for a person's health? Finally, the virus inserts itself into the telomeres and could theoretically disrupt the function of the telomeres. Since the telomeres are important in cellular aging and in cancer, could the insertion of viral DNA in the telomeres have any effect on a cell's tendency to age or to turn cancerous?

While unique among known human herpesviruses, the capacity of HHV-6 to integrate into human chromosomes is not unique in nature. A herpesvirus that infects chickens, called Marek's disease virus, appears to behave the same way. Interestingly, although the viruses are not otherwise closely related, the DNA sequence used by Marek's disease virus to integrate into chicken chromosomes is remarkably similar to the DNA sequence used for chromosomal integration by HHV-6.

Doctoral student Jesse Arbuckle and research associate Maria Medveczky, both of the USF Department of Molecular Medicine, were lead authors of the study. Other contributing authors were from Bioworld Consulting Laboratories, the HHV-6 Foundation, University of Minnesota, University of Brussels, Stanford University School of Medicine and Harvard Medical School.

The USF study was funded by the HHV-6 Foundation, a non-profit organization that supports virology research, as well as by a grant from the National Institutes of Health.

Researchers Show How Far South American Cities Moved In Quake

Columbus, Ohio – The massive magnitude 8.8 earthquake that struck the west coast of Chile last month moved the entire city of Concepcion at least 10 feet to the west, and shifted other parts of South America as far apart as the Falkland Islands and Fortaleza, Brazil.

These preliminary measurements, produced from data gathered by researchers from four universities and several agencies, including geophysicists on the ground in Chile, paint a much clearer picture of the power behind this temblor, believed to be the fifth-most-powerful since instruments have been available to measure seismic shifts.

Buenos Aires, the capital of Argentina and across the continent from the quake's epicenter, moved about 1 inch to the west. And Chile's capital, Santiago, moved about 11 inches to the west-southwest. The cities of Valparaiso and Mendoza, Argentina, northeast of Concepcion, also moved significantly.

The quake's epicenter was in a region of South America that's part of the so-called "ring of fire," an area of major seismic stresses which encircles the Pacific Ocean. All along this line, the tectonic plates on which the continents move press against each other at fault zones.

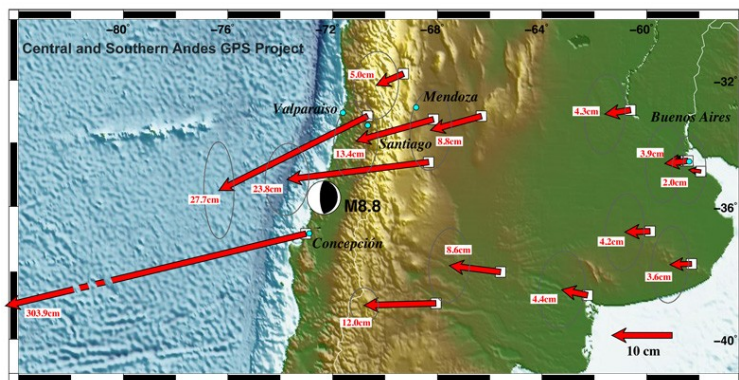
The February Chilean quake occurred where the Nazca tectonic plate was squeezed under, or "subducted," below the adjacent South American plate. Quakes routinely relieve pent-up geologic pressures in these convergence zones.

The research team deduced the cities' movement by comparing precise GPS (global positioning satellite) locations known prior to the major quake to those almost 10 days later. The US Geological Survey reported

that there have been dozens of aftershocks, many exceeding magnitude 6.0 or greater, since the initial event February 27.

Mike Bevis, professor of earth sciences at Ohio State University, has led a project since 1993 that has been measuring crustal motion and deformation in the Central and Southern Andes. The effort, called the Central and Southern Andes GPS Project, or CAP, hopes to perhaps triple its current network of 25 GPS stations spread across the region.

"By reoccupying the existing GPS stations, CAP can determine the displacements, or 'jumps', that occurred during the earthquake," Bevis said. "By building new stations, the project can monitor the postseismic deformations that are expected to occur for many years, giving us new insights into the physics of the earthquake process."



Preliminary Coseismic Displacement Field M 8.8 Maule Earthquake, Chile, Feb 27 2010

This is the preliminary solution obtained by Project CAP (Central and Southern Andes GPS Project) for the coseismic displacement field associated with the recent M 8.8 Maule earthquake in south-central Chile. Peak measured displacement is 3.04 m near the city of Concepcion, Chile. Significant displacements are evident as far east as Buenos Aires, Argentina (2-4 cm) and as far north as the Chilean border with Peru.

Ben Brooks, an associate researcher with the School of Ocean and Earth Science and Technology at the University of Hawaii and co-principal investigator on the project, said that the event, tragic as it was, offers a unique opportunity to better understand the seismic processes that control earthquakes.

"The Maule earthquake will arguably become one of the, if not the most important great earthquake yet studied. We now have modern, precise instruments to evaluate this event, and because the site abuts a continent, we will be able to obtain dense spatial sampling of the changes it caused.

"As such the event represents an unprecedented opportunity for the earth science community if certain observations are made with quickly and comprehensively," Brooks said.

Working with Bevis and Brooks on the project are Bob Smalley, the University of Memphis, who is leading field operations in Argentina; Dana Caccamise at Ohio State, who is lead engineer, and Eric Kendrick, also from Ohio State, who is with Bevis now in Chile making measurements in the field.

Along with Ohio State University and the University of Hawaii, scientists from the University of Memphis and the California Institute of Technology are participating in the project. Additionally the Instituto Geografica Militar, the Universidad de Concepcion and the Centro de Estudios Cientificos, all in Chile, also were partners.

In Argentina, the Instituto Geografica Militar, the Universidad Nacional de Cuyo in Mendoza and the Unversidad Nacional de Buenos Aires are collaborating in the work. UNAVCO, a consortium of more than 50 institutions and agencies involved in research in the geosciences, is providing equipment for the project.

The researchers have constructed a map showing the relative movement of locations after the Maule, Chile earthquake. Images showing that map are available at <http://researchnews.osu.edu/archive/chilequakemap.htm>.

Geraniums could help control devastating Japanese beetle

Geraniums may hold the key to controlling the devastating Japanese beetle, which feeds on nearly 300 plant species and costs the ornamental plant industry \$450 million in damage each year, according to scientists with the Agricultural Research Service (ARS).

The beetle, *Popillia japonica* Newman, can feast on a wide variety of plants, including ornamentals, soybean, maize, fruits and vegetables. But within 30 minutes of consuming geranium petals, the beetle rolls over on its back, its legs and antennae slowly twitch, and it remains paralyzed for several hours. The beetles typically recover within 24 hours when paralyzed under laboratory conditions, but they often succumb to death under field conditions after predators spot and devour the beetles while they are helpless.

ARS entomologist Chris Ranger at the agency's Application Technology Research Unit in Wooster, Ohio, is working on developing a way to use geraniums to control the beetles.

Ohio and neighboring Michigan are some of the largest producers of horticultural plants, most of them grown in greenhouses. Other research to benefit the horticultural industry includes that of Susan Stieve, curator of Ohio State University's Ornamental Plant Germplasm Center in Columbus, Ohio. Stieve is working with OSU collaborators and horticulturist Jonathan Frantz of the ARS Greenhouse Production Research Group in Toledo, Ohio, to see whether a specialized breed of begonias can tolerate colder temperatures.

The scientists are screening the begonias at two production temperatures: 5 degrees Fahrenheit colder than normal, and 10 degrees F colder than normal. Begonias are found naturally in a wide variety of climates and

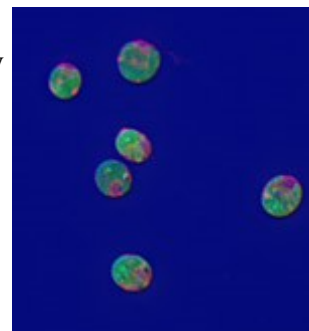
altitudes - ecological clues that can be used to identify promising germplasm. Being able to grow begonias at cooler temperatures could reduce greenhouse heating bills for ornamental growers in northern climates.

Study Shows Potential for Using Algae to Produce Human Therapeutic Proteins

By Kim McDonald

Pharmaceutical companies could substantially reduce the expense of costly treatments for cancer and other diseases produced from mammalian or bacterial cells by growing these human therapeutic proteins in algae—rapidly growing aquatic plant cells that have recently gained attention for their ability to produce biofuels.

That's the conclusion of a study, published online this week in *Plant Biotechnology Journal*, which sought to determine whether seven diverse human therapeutic proteins could be produced in *Chlamydomonas reinhardtii*, a green alga used widely in biology laboratories as a genetic model organism, much like the fruit fly *Drosophila* and the bacterium *E. coli*.



Chlamydomonas reinhardtii is used widely as a genetic model organism. Credit: Beth Rasala, UCSD

“What surprised us was that of the seven genes chosen, four expressed proteins at levels sufficient for commercial production,” said Stephen Mayfield, a professor of biology at the University of California, San Diego who headed the study, which involved scientists at The Scripps Research Institute, San Diego biofuel company Sapphire Energy and ProtElix, a protein engineering company in Hayward, CA.

The scientists reported in their paper that all of the algal-produced proteins in their study showed biological activity comparable to the same proteins produced by traditional commercial techniques. And because algae cells can be grown cheaply and quickly, doubling in number every 12 hours, they noted that algae could be superior to current biological systems for the production of many human therapeutic proteins.

“Currently, human therapeutic proteins are primarily produced from either bacteria or mammalian cell culture,” they said. “Complex mammalian proteins and monoclonal antibodies are primarily produced by the culture of transgenic mammalian cells, while simpler proteins are generally produced by *E. coli*.”

“Due to high capital and media costs, and the inherent complexity of mammalian cell culture, proteins produced by mammalian cell culture are very expensive,” they added. “Bacterial production is generally more economical in terms of media components, but bacteria are often inefficient at producing properly folded complex proteins, requiring a denaturation and renaturation step that adds significant costs to bacterial protein production.”

The scientists said the percentage of human proteins produced in their algal cultures that were properly folded in three dimensions was comparable to the fraction produced by mammalian cell cultures and much better than that produced by bacterial systems. And because algae generate their energy from sunlight and have relatively simple nutrient needs, they said the costs for using them at large scale to commercially produce human proteins should be much lower than for mammalian cell culture, which require expensive fermentation facilities.

To conduct their study, the scientists picked seven proteins that were either currently being used as standard treatments for diseases or are now undergoing human clinical trials. They include human interferon $\beta 1$, which is used to treat Multiple Sclerosis and costs patients from \$1,600 to \$2,000 for a one month supply; human erythropoietin or EPO, used to increase red blood production in patients undergoing chemotherapy; and human proinsulin, a hormone with a multi-billion dollar market used to treat Type 1 diabetes. Two other proteins were human vascular endothelial growth factor or VEGF, used to treat patients suffering from pulmonary emphysema, and high mobility group protein B1 (HMGB1), which activates immune cells and is being investigated for its potential to enhance other cancer therapies. The remaining two proteins were domains 10 and 14 of human fibronectin, which are being investigated for their ability to mimic certain kinds of antibodies.

Mayfield and his colleagues at The Scripps Research Institute demonstrated two years ago that they could produce a mammalian serum amyloid protein from algae and, last year, demonstrated success producing a human antibody. Both of these proteins had biological activities similar to the real proteins from mammalian cells. “That was the proof of concept,” said Mayfield. “It showed us that the system works—that we could produce complex mammalian proteins in algae. What we did in this next study was to say, ‘Let’s take seven diverse human therapeutic proteins and see if we can express them in algae and report the good and the bad.’”

The scientists found that in algae they were able to produce VEGF, HMGB1 and domain 14 of human fibronectin at levels above one percent of total soluble protein, levels sufficient for easy purification. Domain 10 of human fibronectin could also be produced from algae at these levels when fused to the protein M-SAA, which they had previously used to increase the accumulation of other proteins. Human proinsulin could be produced by algae, but only at lower levels, the study showed, while human interferon $\beta 1$ and EPO were not produced by algae.

“What our results show is that algae are a robust platform for the production of human therapeutic proteins,” said Mayfield. “While not every protein can be produced in algae, a good fraction can, just like in any other system. You can get expression of about 25 percent in bacteria and about 40 to 50 percent in mammalian cells, so we’re in the same ball park as these other systems.”

What makes algae particularly attractive compared to bacterial and mammalian systems, the scientists say, is its ability to produce proteins cheaply and at very large scale. With algae currently being produced at about \$3 per kilogram at commercial scale, the researchers estimate that making recombinant protein would cost about 60 cents per gram prior to purification.

“This is about the same cost estimates for the least expensive protein expression systems presently available, and considerably cheaper than mammalian cell culture,” they said in their paper. With expected improvements in the ability to express proteins in algae, “and the continued reduction in algal biomass cost associated with the large scale efforts to use algae for biofuel production, we anticipate at least a ten-fold reduction in the costs over the next few years, which should make algal protein production the least expensive platform available. This reduced cost of goods, coupled with an ability to rapidly scale production in inexpensive bioreactors, suggests that algae may become an economically superior platform for therapeutic protein production in the future.”

In a separate, but related effort, Mayfield and his colleagues are using various species of algae to investigate ways of generating renewable forms of transportation fuel from algae that could eventually be competitive with the cost of gasoline.

Other researchers involved in the therapeutic proteins study were Beth Rasala and Michal Jager of UCSD; Machiko Muto of TSRI; Mike Mendez, Philip Lee, Rosa Cardoso and Craig Behnke of Sapphire Energy; and Peter Kirk and Roberto Creo of ProtElix. Grants and other financial support from the National Institutes of Health, Sapphire Energy and the San Diego Foundation supported the study.

New method to grow arteries could lead to 'biological bypass' for heart disease

A new method of growing arteries could lead to a "biological bypass" - or a non-invasive way to treat coronary artery disease, Yale School of Medicine researchers report with their colleagues in the April issue of Journal of Clinical Investigation.

Coronary arteries can become blocked with plaque, leading to a decrease in the supply of blood and oxygen to the heart. Over time this blockage can lead to debilitating chest pain or heart attack. Severe blockages in multiple major vessels may require coronary artery bypass graft surgery, a major invasive surgery.

"Successfully growing new arteries could provide a biological option for patients facing bypass surgery," said lead author of the study Michael Simons, M.D., chief of the Section of Cardiology at Yale School of Medicine.

In the past, researchers used growth factors - proteins that stimulate the growth of cells - to grow new arteries, but this method was unsuccessful. Simons and his team studied mice and zebrafish to see if they could simulate arterial formation by switching on and off two signaling pathways - ERK1/2 and P13K.

"We found that there is a cross-talk between the two signaling pathways. One half of the signaling pathway inhibits the other. When we inhibit this mechanism, we are able to grow arteries," said Simons. "Instead of using growth factors, we stopped the inhibitor mechanism by using a drug that targets a particular enzyme called P13-kinase inhibitor."

"Because we've located this inhibitory pathway, it opens the possibility of developing a new class of medication to grow new arteries," Simons added. "The next step is to test this finding in a human clinical trial."

Other authors on the study included Bin Ren, Yong Den, Arpita Mukhopadhyay, Anthony A. Lanahan, Zhen W. Zhuang, Karen L. Moodie, Mary Jo Mulligan-Kehoe, Tatiana V. Byzova, and Randall T. Peterson
The Journal of Clinical Investigation Vol. 120, No. 4 (April 2010)

Did 'midwife molecule' assemble first life on Earth?

* 10:59 09 March 2010 by **Bob Holmes**

The primordial soup that gave birth to life on Earth may have had an extra, previously unrecognised ingredient: a "molecular midwife" that played a crucial role in allowing the first large biomolecules to assemble from their building blocks.

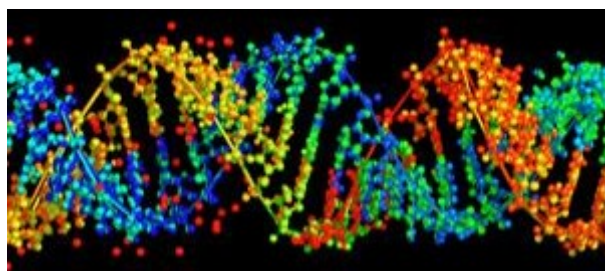
The earliest life forms are thought by many to have been based not on DNA but on the closely related molecule RNA, because long strands of RNA can act as rudimentary enzymes. This would have allowed a primitive metabolism to develop before life forms made proteins for this purpose.

RNA strands are formed from building blocks called nucleotides linked together head to tail in a long chain. This happens easily if the nucleotides can bind to another RNA strand that guides their assembly. However, the earliest RNA molecules to form, billions of years ago, would have had no pre-existing RNA to guide them.

Round in circles

Till now, attempts to mimic this first synthesis have always hit a fatal obstacle: instead of binding to the tail of a new nucleotide, the head of a growing chain latches onto its own tail instead. This tendency to form circles keeps RNA molecules from growing much longer than three to six nucleotides – far too short to function as enzymes.

"That is a big problem," says Nicholas Hud, a chemist at Georgia Institute of Technology in Atlanta. "How do we get a molecule long enough to do something interesting?"



Forming a double helix prevents the RNA from going round in circles (Image: Laguna Design/SPL)

The answer, Hud thinks, may be the presence of a "molecular midwife" – a molecule that nestles between adjacent nucleotides and encourages two growing RNA strands to bind together in a double helix. Since this double helix is much stiffer than a single RNA strand, it is less likely to bend around on itself and form a circle.

If the concentration of molecules in the solution later decreased – as, for example, if rain diluted a primordial puddle – the midwives would tend to slip back out of their slots in the RNA molecule. This would allow the two RNA strands to separate, leaving exactly the sort of long, single-stranded RNA molecule that might act as a catalyst in the RNA world.

Double helices

Sure enough, when Hud and his colleagues added ethidium – which is known to slip between a double helix – to a solution of nucleotides, they found that they joined up into long double helices instead of short circles.

The team studied DNA nucleotides, because the resulting chains are easier to work with, but the same should apply for RNA, they say.

Ethidium itself is a rather complicated molecule with several benzene-like or "aromatic" rings, and is unlikely to have been available to fill this role in the primordial soup. However, molecules found in ancient meteorites suggest that the prebiotic Earth was rich in compounds with a similar structure. Hud's next challenge is to show that some of these polycyclic aromatic molecules can indeed help RNA molecules assemble.

"Ethidium demonstrates the principle. Is there something among that mix that serves the same purpose?" says Gerald Joyce, a biochemist who studies the origin of life at Scripps Research Institute in La Jolla, California.

Journal reference: Proceedings of the National Academy of Sciences, DOI: 10.1073/pnas.0914172107

Study suggests need for broader use of individualized learning plans for physicians

Sacramento, Calif. - Physicians would be better prepared for the accelerating rate of scientific discovery - and more in step with the latest in patient-care - if they added an important tool to their medical bags: a plan for how to keep pace with emerging health-care advances. That is the finding of a national study published online today in the journal *Academic Pediatrics* which examines whether pediatric residents know how to develop plans to ensure they'll keep abreast of current medical practice.

"Medicine is not a static profession," said Su-Ting Li, assistant professor and associate residency director in the Department of Pediatrics at the UC Davis School of Medicine. "It's a profession where things change all the time. If you don't keep up, you're not going to be providing the best care for your patients."

The study, "Factors Associated with Successful Self-Directed Learning Using Individualized Learning Plans During Pediatric Residency," involved 46 - or 23 percent - of all pediatric residency programs in the United States and nearly 1,000 of the approximately 1,700 pediatric residents surveyed. Participants were dispersed throughout the country, in the north, south, east and west, at large and small hospitals, and university-affiliated and community institutions.

Residents are physicians who have finished medical school and are completing their training under the guidance of fully licensed physicians. There is widespread agreement that residents - and all doctors - must participate in lifelong learning activities. Many are required to document those efforts with self-directed "individualized learning plans," or ILPs.

For the study, the residents responded to computerized survey questions developed at UC Davis about their ability to continuously assess their level of skill and their use of ILPs. Ninety percent of respondents said they knew their strengths and 92 percent knew their weaknesses. But only 26 percent said they tracked their progress toward achieving their learning goals.

But tracking progress on achieving their learning goals was found to be one of the most important factors in attaining them. The finding suggests that among the many ways that training programs could support self-directed learning, "putting in place systems that make it easier for residents to track their progress toward achieving their goals would likely be the most effective and bring the greatest return on investment."

"The residents were confident in their ability to identify their strengths and areas for improvement. But they were less confident in their ability to write goals to improve their performance and develop plans and follow through with them. This tells us that this is something that faculty mentors can do to help our residents be better doctors," said Li, the study's lead author. For example, at UC Davis, pediatric residents are required to create individualized learning plans three times a year and have them reviewed with their faculty advisor.

The study findings are important and have implications for all physicians, not just pediatric residents, Li said.

Research has shown that once doctors complete their residencies, if they do not continue to keep up with current advances in medicine, they quickly have a "knowledge base that is lower in terms of current treatment regimens for disease than more recent graduates.

"There is all of this wonderful new technology and there are all of these research papers being published all the time, and you'd love to be able to read them all. But there is such a large proliferation of biomedical advances that you have to figure out how to prioritize more than ever before," Li said. "Then you need to figure out how to incorporate the information into your practice."

Other study authors include Daniel J. Tancredi of UC Davis, John Patrick T. Co of Massachusetts General Hospital/Brigham and Women's Hospital, Harvard Medical School and Daniel C. West of UC San Francisco. The study was funded by the Association of Pediatric Program Directors.

Nanotube cuff is 'solar cell' for exhaust pipes

* 12:54 09 March 2010 by Colin Barras

The hot gases passing through a vehicle's exhaust could be tapped to generate power, using "cuffs" made from a new carbon-nanotube-based material. The "thermocell" produces electricity at a similar cost per watt as commercial solar cells.

All around us there are opportunities to soak up wasted heat and convert it into electricity, says Ray Baughman, who works on thermocells with colleagues at the University of Texas at Dallas. Car exhaust pipes and power stations are just two forms of technology that waste a lot of heat and could be improved by building thermocells into their designs to recover lost energy.

However, to date the most effective thermocells have been based around expensive platinum electrodes, making them impractical. Baughman and colleagues have now shown that cheaper carbon nanotubes can be used instead, because the nanotubes pack a huge surface area into a tiny volume, and electrons transfer quickly between the electrolyte and nanotube electrodes. They have made thermocells three times as efficient as any before.

Energy flow

The basic design is simple. Each thermocell contains two electrodes, positioned at either end of a temperature gradient: for example, one right next to a hot pipe and the other closer to the surrounding cooler air.

In between is a chemical mix, in which the heat encourages chemical reactions that push electrons around an external circuit. Ions in the mix shed electrons at the hotter electrode and pick up electrons at the cooler one to complete the circuit.

One of the team's thermocell designs is intended to be wrapped around a hot pipe, inspired by the fact that heat leaks out from such structures in many situations, such as chemical factories and power plants. "You could harvest energy from the tailpipe of a car," adds Baughman.

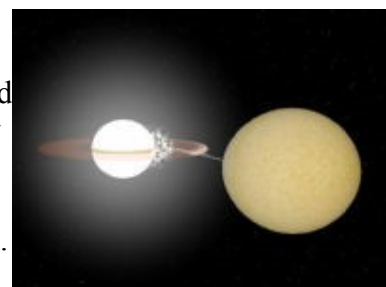
The "hot" electrode wrapped around the pipe is surrounded by a heat-resistant layer, which is itself encased in a 'cold' electrode. An aqueous solution can move through pores in the heat-resistant layer, allowing ions to circulate between the reactions at the two electrodes.

In tests, a prototype thermocell functioned well for 90 days. With an electrode temperature difference of 60 °C it produced energy for \$5.14 per watt based on materials costs for the prototype – comparable with that of mass-produced silicon solar cells. *Journal reference: Nano Letters, DOI: 10.1021/nl903267n*

Most extreme white dwarf binary system found with orbit of just 5 minutes

Graphic of HM Cancri An international team of astronomers, including Professor Tom Marsh and Dr Danny Steeghs from the University of Warwick, have shown that the two stars in the binary HM Cancri definitely revolve around each other in a mere 5.4 minutes. This makes HM Cancri the binary star with by far the shortest known orbital period. It is also the smallest known binary. The binary system is no larger than 8 times the diameter of the Earth which is the equivalent of no more than a quarter of the distance from the Earth to the Moon.

The binary system consists of two white dwarfs. These are the burnt-out cinders of stars such as our Sun, and contain a highly condensed form of helium, carbon and oxygen. The two white dwarfs in HM Cancri are so close together that mass is flowing from one star to the other. HM Cancri



was first noticed as an X-ray source in 1999 showing a 5.4 minutes periodicity but for a long time it has remained unclear whether this period also indicated the actual orbital period of the system. It was so short that astronomers were reluctant to accept the possibility without solid proof.

The team of astronomers, led by Dr Gijs Roelofs of the Harvard-Smithsonian Center of Astrophysics, and including Professor Tom Marsh and Dr Danny Steeghs at the University of Warwick in the UK, have now used the world's largest telescope, the Keck telescope on Hawaii, to prove that the 5.4 minute period is indeed the binary period of the system. This has been done by detecting the velocity variations in the spectral lines in the light of HM Cancri. These velocity variations are induced by the Doppler effect, caused by the orbital motion of the two stars revolving around each other. The Doppler effect causes the lines to periodically shift from blue to red and back.

The observations of HM Cancri were an ultimate challenge due to the extremely short period that needed to be resolved and the faintness of the binary system. At a distance of close to 16,000 light years from Earth, the binary shines at a brightness no more than one millionth of the faintest stars visible to the naked eye.

Professor Tom Marsh from the University of Warwick said; "This is an intriguing system in a number of ways: it has an extremely short period; mass flows from one star and crashes down onto the equator of the other in a region comparable in size to the English Midlands where it liberates more than the Sun's entire power in X-rays. It could also be a strong emitter of gravitational waves which may one day be detected from this type of star system."

Dr Danny Steeghs of the University of Warwick, said " A few years ago we proposed that HM Cancri was indeed an interacting binary consisting of two white dwarfs and that the 5.4 minute period was the orbital period. It is very gratifying to see this model confirmed by our observations, especially since earlier attempts had been thwarted by bad weather."

The article describing the observations of HM Cancri entitled Spectroscopic Evidence For a 5.4 Minute Orbital Period in HM Cancri will be published in the Astrophysical Journal Letters of March 10, 2010

"This type of observations is really at the limit of what is currently possible. Not only does one need the biggest telescopes in the world, but they also have to be equipped with the best instruments available", explains Professor Paul Groot of the Radboud University Nijmegen in the Netherlands.

"The binary HM Cancri is a real challenge for our understanding of stellar and binary evolution," adds Dr Gijs Nelemans of the Radboud University. "We know the system must have come from two normal stars that somehow spiralled together in two earlier episodes of mass transfer, but the physics of this process is very poorly known. The system is also a big opportunity for general relativity. It must be one of the most copious emitters of gravitational waves. These distortions of space-time we hope to detect directly with the future LISA satellite, and HM Cancri will be a cornerstone system for this mission."

Intentional variation increases result validity in mouse testing

West Lafayette, Ind. - For decades, the traditional practice in animal testing has been standardization, but a study involving Purdue University has shown that adding as few as two controlled environmental variables to preclinical mice tests can greatly reduce costly false positives, the number of animals needed for testing and the cost of pharmaceutical trials.

Joseph Garner, a Purdue assistant professor of animal sciences, said the finding challenges the assumption in drug discovery and related fields that animal experiments should eliminate all variables. He said that despite standardization efforts, two experiments in different labs could never truly be exactly the same because of uncontrollable variables such as the scent of the researchers or background noises.

"Human drug trials get around this problem by deliberately including variability in the experiment in a controlled manner so that the effect of a drug can be tested across a variable human population," Garner said.

Garner and his co-authors compared results from multiple mice experiments set up in a standardized manner against multiple experiments set up with controlled variables as if the mice were people.

"Overall, the differences between experiments are much, much greater in the standardized setups than in the ones where we deliberately varied the environment as if the experiment was a human drug trial," said Garner, whose results were published in the current issue of the journal Nature Methods. "In fact, the traditional standardized experiments generally disagreed with each other, while the experiments designed like a human drug trial generally agreed with each other."

The study is a follow-up of another published last year in Nature Methods in which Garner, Hanno Würbel, a co-author on the papers and professor at the University of Giessen in Germany, and Helene Richter, Würbel's graduate student, suggested that adding controlled variation to animal experiments would lead to more accurate results. Garner said the original study, which demonstrated the idea in principle, had met resistance because it was unclear what environmental features scientists should vary to improve study results.

"In theory, if you introduce enough variables, it shouldn't matter what they are because you create spread in the mice. But other scientists were reasonable to ask whether this would be a practical approach. So, in this experiment, we wanted to address this concern and see whether it was logistically feasible to add enough variation to make the approach work." Garner said. "We were surprised by how little variation we needed to add. In fact, we found that using as few as two variables, regardless of what we actually varied, was enough to virtually eliminate disagreement between laboratories. Given our previous results, this should reduce the incidence of false positives five to tenfold."

Reducing false positives could be worth billions of dollars in the pharmaceutical industry where the cost of human clinical trials is high. Garner said about 90 percent of drugs thought to be effective in mice fail in human trials. Reducing the number of drugs that won't be successful could eliminate hundreds of millions of dollars per drug in some cases and reduce the cost of research and development.

"The real cost of producing a drug is the cost of all the drugs that were tested and failed at the same time, and this cost is passed on to the consumer," Garner said. "Weeding out these failures in animal trials could transform the economics of drug development."

Garner analyzed data from a series of behavioral tests Würbel performed in Germany. The tests compared behaviors commonly used in drug and gene discovery between two strains of mice. The experiment was repeated in four different model laboratories, each of which differed according to variables such as background noise, the age of the mice, lighting levels and cage size. In each laboratory, standardized mice were treated identically - as they would be in a traditional experiment - while heterogenized mice were tested in four different conditions made by varying two environmental variables in a controlled manner, just like a human drug trial.

Mice from the same strain should have exhibited the same behavior in each laboratory, such as showing fear and curiosity. However, in 33 of the 36 behavioral characteristics, variation was lower in the heterogenized design than the standardized design, and, on average, the standardized group exhibited as much as five times the variation between laboratories as the heterogenized group.

"The reason why this happens is because when you keep everything standardized, the variation is very low within the lab, but the variation between labs is huge and unpredictable," Garner said. "You would have to do the same experiment in many standardized labs to really know the true result, or you could do it in one lab with a heterogenized design, like a human drug trial, to find the true result. This is a win-win because you need to use far few animals, and you get a much better understanding of whether, for instance, a drug really does have an effect that is replicable."

Garner said the next step in the research is to do the same experiments in different labs across Europe to eliminate the simulation of labs in the experiment. The German Research Foundation funded the study.

Grandfathered drug for high potassium has no proven benefit

Ion exchange resins probably wouldn't be approved today, review suggests

For more than half a century, products containing ion exchange resins have been used in patients with dangerously high levels of potassium. However, there is no convincing evidence that these products are actually effective, according to an article appearing in an upcoming issue of the Journal of the American Society Nephrology (JASN). "We suspect that if ion exchange resins were introduced today, they would not be approved," comments Richard H. Sterns, MD (Rochester General Hospital, University of Rochester School of Medicine and Dentistry, Rochester, NY).

High potassium levels (hyperkalemia) are a potentially life-threatening problem, commonly occurring in patients with kidney disease. Ion exchange resins, mixed with a cathartic called sorbitol, have long been used to treat hyperkalemia. Millions of doses of this product are prescribed every year in the United States—yet it has never been studied with controlled trials to prove it works. Explains Sterns, "these agents came into widespread use in 1958—four years before drug manufacturers were required to prove the effectiveness of their products before gaining FDA approval. Their approval was essentially 'grandfathered.'"

Last year, the FDA issued a warning against giving ion exchange resins with sorbitol, based on reported cases of potentially fatal bowel injury. Yet pre-mixed preparations of the resin with sorbitol are still marketed and widely used. Sterns asks, "If ion exchange resins were presented to the FDA today, with the data available, would the agency rule them safe and effective?"

The answer, according to Sterns, based on a review of the available data is "probably not." "We found no rigorous scientific evidence that ion exchange resins are effective in ridding the body of excess potassium," says Sterns. "In fact, we found some evidence showing that, on rare occasions, they might be harmful."

"We found no evidence that would meet modern standards for drug approval," Sterns and coauthors conclude. They call for further studies to weigh the harms versus benefits of these products. Meanwhile, they

believe that doctors should first try other alternatives to managing high potassium levels, "before turning to these largely unproven and potentially harmful therapies."

Study co-authors are Maria Rojas, Paul Bernstein, and Sreedevi Chennupati, all of Rochester General Hospital.

Disclosures: The authors reported no financial disclosures.

The article, entitled "Ion-Exchange Resins for the Treatment of Hyperkalemia: Are They Safe and Effective?" is available online at <http://jasn.asnjournals.org>, 2009, doi 10.1681/ASN.2010010079.

New study questions benefits of elective removal of ovaries during hysterectomy Evidence suggests procedure may do more harm than good

Philadelphia, PA, - Removal of the ovaries (bilateral oophorectomy) while performing a hysterectomy is common practice to prevent the subsequent development of ovarian cancer. This prophylactic procedure is performed in 55% of all U.S. women having a hysterectomy, or approximately 300,000 times each year. An article in the March/April issue of The Journal of Minimally Invasive Gynecology suggests that this procedure may do more harm than good.

William H. Parker, MD, John Wayne Cancer Institute at Saint John's Health Center, Santa Monica, CA, provides a comprehensive analysis of the medical literature relating to the benefit of oophorectomy at the time of hysterectomy. His investigation includes studies of post-hysterectomy cancer incidence, all cause mortality, cardiovascular disease, osteoporosis and hip fractures, coronary artery disease, and a number of other conditions. He concludes that, on balance, removal of the ovaries is not generally warranted for all women undergoing hysterectomy. In women not at high risk for development of ovarian or breast cancer, removing the ovaries at the time of hysterectomy should be approached with caution.

Dr. Parker states, "Presently, observational studies suggest that bilateral oophorectomy may do more harm than good. Given that 300 000 U.S. women a year undergo elective oophorectomy, the findings of increased long-term risks have important public health implications...Prudence suggests that a detailed informed consent process covering the risks and benefits of oophorectomy and ovarian conservation should be conducted with women faced with this important decision."

Premenopausal oophorectomy causes a rapid decline in circulating ovarian estrogens and androgens. Postmenopausal ovaries continue to produce significant amounts of the androgens testosterone and androstenedione, which are converted to estrogen. Estrogen deficiency has been associated with higher risks of coronary artery disease and hip fracture, and neurologic conditions. Although approximately 15,000 U.S. women die each year of ovarian cancer, 350,000 women die of coronary artery disease. Therefore reducing a woman's risk of ovarian cancer with oophorectomy may be outweighed by increased risks of coronary artery disease and neurologic conditions.

In an accompanying editorial, G. David Adamson, MD, FRCSC, FACOG, FACS, Director of Fertility Physicians of Northern California, Palo Alto and San Jose, CA, and past-president of both the American Society for Reproductive Medicine and the American Association of Gynecologic Laparoscopists, comments, "Dr. Parker has performed a valuable service to his fellow gynecologists and to women everywhere who have to make the difficult decision regarding ovarian conservation or removal at the time of hysterectomy. Oophorectomy is not necessarily the wrong decision for many women, but assessment of these data leads to the conclusion that more women are undergoing oophorectomy than should."

The article is "Bilateral Oophorectomy versus Ovarian Conservation: Effects on Long-term Women's Health" by William H. Parker, MD. The editorial is "Ovarian Conservation" by G. David Adamson, MD. Both appear in the Journal of Minimally Invasive Gynecology, Volume 17, Number 2 (March/April 2010) published by Elsevier.

Eyeless hydra sheds light on evolution of the eye

* 00:01 10 March 2010 by **Debora MacKenzie**

One of creationists' favourite claims is that an organ as intricate as the eye could never have simply evolved. Fresh evidence to the contrary has now arrived, courtesy of a creature related to jellyfish.

The tiny freshwater hydra has no eyes but it will contract into a ball when exposed to sudden bright light. David Plachetzki and colleagues at the University of California, Santa Barbara, have found that hydras "see" light using two proteins closely related to those in our own eyes.

"If you look at something as complex as an eye, you might be at a loss to explain how the whole structure evolved at once," says Plachetzki, now at the University of California, Davis. "But if you look at its components you can start to piece together how it happened." That's especially feasible now that genes from the earliest animals, such as the hydra, are being sequenced.

Rod and cone cells in the human retina contain proteins called opsins that change shape when light strikes them. This causes another type of protein, an ion channel, to generate an electrical signal along nerves connecting the eye to the brain – a process called phototransduction.

Hydras have the same types of opsins and ion channels as we do. Plachetzki's team found that they make them together in nerve cells. Moreover, they found that a drug that blocks those channels stopped hydras responding to light, showing they are used for phototransduction.

Seeing like us

"This is conclusive evidence that these animals, the Cnidaria, have light sensitivity based on this kind of opsin and transduction, just as we do," says Dan Nilsson of the University of Lund in Sweden, who has also investigated hydras' light reception.

Plachetzki's team then built a family tree of opsin gene sequences from 22 highly diverse creatures, and found that opsins in hydras and humans evolved from those in a common ancestor. Another line of descendants from the same ancestor gave rise to somewhat different opsins and ion channels in insect and mollusc eyes. This supports other indirect evidence, says Nilsson, that the hydras' light-sensing equipment was the original model, and the insects' came later.

The hydra is the most primitive animal with functioning opsins, so the team concludes that it represents "the very origin of animal phototransduction", which was incorporated into more complex eyes as they evolved.

Journal reference: Proceedings of the Royal Society B, DOI: 10.1098/rspb.2009.1797

Years of smoking associated with lower Parkinson's risk, not number of cigarettes per day

ST. PAUL, Minn. – Researchers have new insight into the relationship between Parkinson's disease and smoking. Several studies have shown that smokers have a lower risk of developing Parkinson's disease. A new study published in the March 10, 2010, online issue of *Neurology*®, the medical journal of the American Academy of Neurology, shows that smoking for a greater number of years may reduce the risk of the disease, but smoking a larger number of cigarettes per day may not reduce the risk.

"These results could guide the development of studies on various tobacco components with animal models to help understand the relationship between smoking and Parkinson's disease," said study author Honglei Chen, MD, PhD, of the National Institute of Environmental Health Sciences in Research Triangle Park, N.C.

"Research to reveal the underlying chemicals and mechanisms is warranted; such studies may lead to a better understanding of the causes of Parkinson's disease. However, given the many adverse consequences of smoking, no one would suggest smoking in order to prevent Parkinson's disease."

The study involved 305,468 AARP members age 50 to 71 who completed a survey on diet and lifestyle at the time and again about 10 years later. During that time, 1,662 of the people had developed Parkinson's disease, or about one-half of one percent.

Current smokers were 44 percent less likely to develop Parkinson's disease than people who had never smoked. People who had smoked in the past and quit were 22 percent less likely to develop Parkinson's than people who had never smoked.

People who smoked for 40 or more years were 46 percent less likely to develop Parkinson's disease than people who never smoked. Those who smoked for 30 to 39 years were 35 percent less likely to have the disease than nonsmokers. In contrast, those who smoked for one to nine years were only eight percent less likely to get the disease. The risk of developing Parkinson's disease did not change based on how many cigarettes a person smoked per day.

Chen noted that studies have shown that smoking is not associated with a slower progression of the disease once Parkinson's develops or a reduced risk of death, so he said there is no evidence to support the use of nicotine or other smoking-related chemicals in treating the disease.

The study was supported by the National Institutes of Health, the National Institute of Environmental Health Sciences and the National Cancer Institute.

UC Davis researchers demonstrate link between brain chemical, cognitive decline in schizophrenia

In one of the first such studies involving human patients with schizophrenia, researchers at UC Davis have provided evidence that deficits in a brain chemical may be responsible for some of the debilitating cognitive deficits - poor attention, memory and problem-solving abilities - that accompany the delusions and hallucinations that are the hallmarks of the disorder.

The study, published online today in the *Journal of Neuroscience*, suggests an important avenue of inquiry for improving cognitive function in the more than 2 million Americans who suffer from schizophrenia, according to Jong H. Yoon, an assistant professor of psychiatry and behavioral sciences at UC Davis Health System and the study's lead author.

"We still know very little about the neurobiology of schizophrenia, particularly at the level of specific circuits and molecules and how their impairments affect behavior and cognition in the disease," said Yoon, a

researcher at the UC Davis Imaging Research Center. "We need this level of specificity to guide targeted treatment development. This is one of the first studies to show that there is a strong association between cognitive deficits and a decrease in a particular neurotransmitter."

Schizophrenia is characterized by psychosis - abnormalities in the perception or expression of reality. Sufferers may experience visual or auditory hallucinations and have paranoia, delusions and disorganized speech and thinking. But they also experience profound cognitive difficulties that interfere with daily functioning.

Psychosis is treated with a variety of antipsychotic medications that dampen overactivity of the neurotransmitter dopamine, an acknowledged cause of psychotic behavior. But no medications are available to address cognitive deficits in schizophrenia because the source of the deficits has not been determined. Deficits in one brain chemical, the neurotransmitter gamma-aminobutyric acid, or GABA, have been implicated as playing a causal role in cognitive difficulties in people with schizophrenia in research involving animal models and post-mortem analyses of GABA concentrations in human schizophrenic brains.

"People think of schizophrenia as being related to psychosis. But patients' cognitive limitations can be even more debilitating for them," said Cameron Carter, professor of psychiatry and behavioral sciences, director of the Imaging Research Center and the study's senior author. "This study actually looked at brain chemistry in live patients in relation to cognitive performance to determine the underlying neurobiology of the cognitive deficits. Our ultimate goal is discovering ways to help patients lead more productive lives."

Yoon and his colleagues measured the levels of GABA in the visual cortexes of the brains of 13 study subjects with schizophrenia and 13 control subjects without the disorder. The measurements were conducted with high-field magnetic resonance spectroscopy, a technique that involves using a magnetic resonance imaging scanner to examine neurotransmitter activity. The schizophrenic patients were found to have a deficit in GABA of about 10 percent when compared with their non-schizophrenic counterparts.

The second half of the study involved demonstrating the significance of the neurochemical deficit on cognition and behavior. To do this the researchers measured the visual perception of the subjects for whom GABA levels were assessed by showing them a well-known illusion in which the presence of a high-contrast surrounding region inhibits the ability to perceive information in the center of the visual field.

The researchers showed that this surround-suppression illusion had less of an effect on patients with schizophrenia, resulting in a highly unusual situation in which they outperformed healthy subjects when baseline differences in generalized task performance were accounted for. The researchers then found that the lower levels of GABA in patients were responsible for this behavioral abnormality.

"The link between changes in patients' brain chemistry and the cognitive impairments they experience never has been shown before in this way," Carter said. "This work provides tremendous support for targeting the GABA system for treatment of cognitive decline in schizophrenia."

Other study authors include Richard Maddock, Michael Minzenberg, and J. Daniel Ragland of UC Davis, and Ariel Rokem and Michael Silver of the University of California, Berkeley, School of Optometry and Helen Wills Neuroscience Institute. The study was funded by grants from the National Alliance for Research on Schizophrenia and Depression (NARSAD) and a grant from the National Institute of Health's National Institute of Mental Health.

New methods needed to ID cardiac catheterization candidates

DURHAM, NC – It's time to re-think how patients are selected for cardiac catheterization, say doctors at Duke University Medical Center, after reporting in a new study that the invasive procedure found no significant coronary artery disease in nearly 60 percent of chest pain patients with no prior heart disease.

"Our data show that up to two thirds of the patients undergoing invasive cardiac catheterization are found not have significant obstructive disease," says Manesh Patel, MD, a cardiologist with the Duke Heart Center. He's the lead author of the study published in the March 11 issue of the New England Journal of Medicine.

"We're spending a lot of energy and money to evaluate chest pain which often leads to cardiac catheterization, which, we now know, often finds that patients don't have significant obstructive disease," Patel says. "Our research shows that our methods for identifying patients at risk for obstructive disease need significant improvement."

More than 10 million Americans experience chest pain each year and many undergo testing like cardiac catheterization to determine if blocked arteries are the culprit. It's standard care for people who experience heart attack or unstable chest pain. The invasive test is not cheap, nor is it without some risk. But it allows doctors to visualize the vessels and arteries leading to the heart.

The main goal of cardiac catheterization is to identify the presence, location, and severity of coronary atherosclerosis, Patel says. "This is done with the understanding that some patients with severe obstruction may benefit from angioplasty or bypass surgery to relieve symptoms and to reduce the risk of a heart attack or death."

The researchers identified two million people who underwent cardiac catheterization at 663 hospitals nationwide over a four-year-period. About a fifth of those patients had stable chest pain without a previous diagnosis of heart disease. Most of them had undergone a noninvasive test before catheterization, but only 38 percent of patients turned out to have significant obstructive disease.

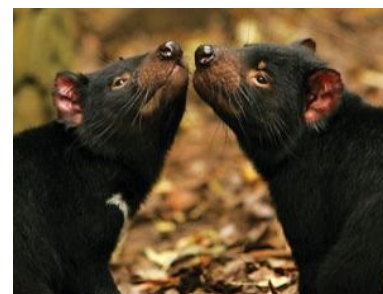
What is needed, Patel stresses, is a re-evaluation of the entire decision-making process of caring for patients with chest pain. That runs the gamut from how patients' histories are taken, how risk factors are assessed, to the role of diagnostic testing. Patel and other Duke researchers who co-authored the NEJM paper are working on several efforts to address these concerns. They include national standards on appropriate use of technology, and clinical trials to evaluate different non invasive imaging technologies.

The NEJM study was funded by the American College of Cardiology's National Cardiovascular Data Registries-Cath PCI. Co-authors include Eric Peterson, MD, David Dai, J. Matthew Brennan, MD, and Pamela S. Douglas, MD, of Duke University Medical Center, Rita F. Redberg, MD and Ralph G. Brindis, MD of University of California at San Francisco, and H. Vernon Anderson, MD of the University of Texas Health Science Center, Houston, TX.

The luck of the Tasmanian devils is in their genes

A carnivorous marsupial on the verge of being wiped out by a transmissible cancer could be saved - by the discovery of animals resistant to the disease.

Since 1996 Tasmanian devils have lost 90 per cent of some populations to the deadly and highly infectious devil facial tumour disease, which is spread by biting. But widespread pockets of Australia's island state, such as the north-west and Bronte Park, remain unscathed. Biologists were unsure if this was luck - perhaps the disease hadn't reached the areas yet - or resilience.



Resistant devil Image: AFP/Stringer

It turns out to be the latter. Kathy Belov's team at the University of Sydney has found that the immune system of infected and unharmed devils works differently.

Belov already knew that devils in eastern Tasmania are vulnerable because their immune system mistakes foreign cancer cells for "self" cells. Now her team has analysed the immune system's key controller genes for the first time and found that resistant devils have genes that equip them to attack the disease (*Proceedings of the Royal Society B*, DOI: 10.1098/rspb.2009.2362).

Experimental drug that mimics thyroid hormone safely lowers 'bad' cholesterol

Small study shows eprotirome decreases LDL cholesterol as much as doubling statin dose

People whose "bad" cholesterol and risk of future heart disease stay too high despite cholesterol-lowering statin therapy can safely lower it by adding a drug that mimics the action of thyroid hormone. In a report published in the Mar. 11, issue of the New England Journal of Medicine, Johns Hopkins and Swedish researchers say an experimental drug called eprotirome lowered cholesterol up to 32 percent in those already on statins, an effect equal to that expected from doubling the statin drug doses, without harmful side effects.

The researchers caution that the results don't suggest that eprotirome will or should replace statins, which are the current gold standard for treating high LDL cholesterol. However, the results of their small trial on 168 patients do suggest that eprotirome may eventually be a promising addition to statin therapy, a substitute for statins in people who can't tolerate their side effects, or a novel treatment for mixed dyslipidemia, a condition in which people have high levels of lipids other than cholesterol such as triglycerides or apolipoprotein B (apo B).

The researchers found that eprotirome lowered blood lipids that are little affected by statin therapy but known to increase the risk for cardiovascular disease, including triglycerides and lipoprotein A (Lp(a)).

"This drug represents a new class of medications that might offer hope to those at risk of future cardiovascular disease whose lipid profiles are not effectively altered with statin therapy, and perhaps for about a quarter of those who have tried statins but cannot tolerate their side effects," says study leader Paul W. Ladenson, M.D., professor of endocrinology and metabolism at the Johns Hopkins University School of Medicine. Ladenson is a consultant to Karo Bio, maker of eprotirome.

Researchers have long known that thyroid hormones, produced by the butterfly-shaped thyroid gland in the neck, act on numerous tissues in the body. One organ affected profoundly by thyroid hormones is the liver, which processes lipids, including cholesterol. Ladenson says previous research has shown that when people have abnormally high levels of thyroid hormones owing to a diseased thyroid gland, they tend to have low levels of bad, or LDL, cholesterol. However, high levels of a person's natural thyroid hormones also come with potentially dangerous side effects, including increased heart rate and irregular heart rhythms, loss of bone mass, and other troubling symptoms.

Seeking to seize upon thyroid hormones' benefits while avoiding these side effects, Ladenson and his colleagues tested eprotirome, a thyroid hormone mimetic developed by Swedish pharmaceutical company Karo

Bio, on 168 patients at 15 sites in Sweden and Norway. All of the patients had been treated with statins for at least three months prior to the study start, but still had an LDL cholesterol higher than recommended, 116 mg/deciliter, with a mean level of 141 mg/deciliter (an optimal LDL measurement is considered less than 100 mg/deciliter).

These volunteers started the study with a four-week lead-in on a diet developed by the U.S. National Institutes of Health to reduce cholesterol. Continuing this diet, for the next 12 weeks, the patients took a placebo or 25, 50, or 100 mg of eprotrirome in addition to whatever statin they had already been taking. The researchers then analyzed the patients' levels of LDL cholesterol, HDL (or "good") cholesterol, triglycerides, apo B, and Lp(a).

The researchers found that among the patients taking the 25, 50 or 100 mg doses of eprotrirome reduced their LDL cholesterol levels by 22 percent, 28 percent, and 32 percent respectively, compared to only 6.5 percent in those taking placebo. Remarkably, they also found similar dose-related reductions in triglycerides, apo B, and Lp(a).

They also found modest reductions in HDL cholesterol of approximately 3 percent. Low HDL has been associated with increased cardiovascular disease risk, since HDL levels reflect how much artery-blocking cholesterol is being ferried away from blood vessels and back to the liver. However, Ladenson says he and his colleagues believe this small decrease could reflect the livers' increased processing of cholesterol in general, which could actually lower cardiovascular disease risk.

When the researchers evaluated study subjects for the harmful side effects that can accompany increased thyroid hormone, they found no indications of increased heartbeat abnormalities, increased bone turnover, or other symptoms of thyroid hormone excess.

Ladenson adds that though previous studies have shown that high levels of Lp(a) are associated with an increased risk of cardiovascular disease, no drug existed to lower this lipid.

"Although we've long known a high Lp(a) is strongly associated with increased risk of future cardiovascular disease, we've had no idea if lowering Lp(a) actually diminishes cardiovascular disease risk," he says. "We can finally address this question with this drug."

'Underwear Bomber' Could Not Have Blown Up Plane

An experiment that detonated a bomb similar to the so-called "underwear bomber's" shows that the plane would have withstood the impact.

By Eric Bland Wed Mar 10, 2010 09:22 AM ET

THE GIST:

- * *A test explosion shows the "underwear bomber's" device would not have ruptured the airplane's fuselage.*
- * *Blown ear drums would have accounted for most of the injuries among the passengers.*
- * *Newer planes with composite materials are likely even safer in the event of an explosion.*

Even if the "Underwear Bomber" Umar Farouk Abdulmutallab had exploded his device on Christmas day, 2009, the Airbus A330 would have survived, according to an experiment conducted by a BBC documentary team.

And while the person sitting next to Abdulmutallab probably would have died, the worst injury most passengers would have suffered would have been ruptured eardrums.

"What we tried to do was simulate, as far as we could, what might have happened over Detroit," said explosives expert John Wyatt, who was part of the BBC experiment. "We used the same type of explosive and the same amount and put it in the same position as the bomber. The supports adjacent to the seat lost five or six rivets and the metal bowed out, but the structure didn't fail," said Captain J. Joseph, an aviation expert also featured in the BBC documentary, which is also airing on Discovery Channel this week. "The actual aircraft would have remained intact."

On Dec. 25, 2009 Abdulmutallab boarded Northwest Airlines Flight 253, flying from Amsterdam to Detroit. Sewn into Abdulmutallab's underwear was pentaerythritol tetranitrate, or PETN, a powerful explosive.

As the Airbus A330 was about to touch down in Detroit, Abdulmutallab allegedly removed a syringe and tried to ignite the PETN and blow up the aircraft. Instead of a powerful explosion, however, Abdulmutallab created a small fire, which was extinguished. The would-be bomber was subdued by other passengers and crew members on the flight.

[**WATCH VIDEO: On Christmas Day 2009, an alleged Al-Qaeda plot to blow up a plane was thwarted. But what if it had succeeded? Watch Thursday, March 11 at 10 PM E/P on the Discovery Channel.**](#)

Using a decommissioned Boeing 747, Joseph, Wyatt and the BBC team set about recreating the conditions of last year's attempted bombing. They placed about 80 grams of PETN's base material, pentaerythritol, near the 747's fuselage where Abdulmutallab was seated. Eighty grams of pentaerythritol contains about the same

explosive power as a hand grenade, but lacks the the hot, sharp metal fragments of an actual grenade that cause so much damage. The BBC set up cameras and Wyatt set off the explosives.

In the BBC documentary, entitled "How Safe Are Our Skies," the controlled detonation of the explosives lasted a scant 0.94 milliseconds, but the results were clear to cameras. Shock waves rippled through the exterior aluminum skin of the aircraft like fat water drops of water hitting the surface of a smooth pond.

The metal was permanently bowed out, and a handful of rivets were punched out, but no gaping holes appeared. The pressurized air inside the cabin would have slowly leaked out of the missing rivets, said Joseph, a non- life-threatening situation. The amount of explosives was "nowhere near enough" to bring down the plane, concluded Wyatt and Joseph.

The aircraft would have survived, but some of the passengers would not have. The alleged would-be bomber and the person seated next to him would both have likely died, said Wyatt.

The passengers sitting in front of and behind the terrorist would probably have been protected from serious bodily injury the the aircraft's metal seats. Most passengers on the plane would have suffered ruptured eardrums as the shock wave created by the bomb traveled through the plane's cabin.

The BBC also used a decommissioned Boeing 747 and not a newer Airbus A330 for the test. An actual test would be necessary to prove this, but Wyatt and Joseph think that the newer plane, which was made with lighter and stronger composite materials instead of aluminum, would have performed even better.

The newest commercial passenger jet, the Boeing 747 or Dreamliner, which has even more composite materials, would likely perform even better, said Wyatt, although he doesn't know for sure. The BBC test plane was at rest under normal atmospheric pressure, not pressurized. The difference in pressure was irrelevant, said Wyatt. "It's over so quickly that the difference in pressure wouldn't make a difference," said Wyatt. "By the time the shock wave got to the door the pressure would have normalized."

The Claim: A Glass of Wine With Dinner Aids Digestion

By ANAHAD O'CONNOR

THE FACTS Pairing the right wine with a meal can round out flavors and stimulate conversation. But can it really help digest the meal, as suggested by a host of authorities through the ages, even the Bible? ("Drink no longer water, but use a little wine for thy stomach's sake.")

Millenniums later, scientists are still working on that one. Some have found that alcoholic beverages speed the emptying of food from the stomach and stimulate gastric acid, while others maintain there is little effect. One study by German researchers, in the aptly named journal *Gut*, may explain the discrepancy: it found an effect from fermented drinks (wine, sherry and beer) but not from drinks that were fermented and distilled, like rum, cognac and whiskey.

"The alcoholic beverage constituents that stimulate gastric acid output and release of gastrin are most probably produced during the process of fermentation and removed during distillation," they concluded.

Other studies help explain why red wine and red meat pair so well. Protein softens the wine's tannins, and red wine also helps counteract potentially harmful substances — oxidized fats called malonaldehydes, or MDA - released when meat is digested.

A 2008 study found that a serving of dark meat from turkey elevated levels of the substance in subjects' blood. But when they combined it with a glass of cabernet sauvignon or shiraz, the increase in MDA was "completely prevented."

THE BOTTOM LINE In more ways than one, a glass of wine may aid digestion.

A huge step toward mass production of coveted form of carbon

Scientists have leaped over a major hurdle in efforts to begin commercial production of a form of carbon that could rival silicon in its potential for revolutionizing electronics devices ranging from supercomputers to cell phones. Called graphene, the material consists of a layer of graphite 50,000 times thinner than a human hair with unique electronic properties. Their study appears in *ACS' Nano Letters*, a monthly journal.

Victor Aristov and colleagues indicate that graphene has the potential to replace silicon in high-speed computer processors and other devices. Standing in the way, however, are today's cumbersome, expensive production methods, which result in poor-quality graphene and are not practical for industrial scale applications.

Aristov and colleagues report that they have developed "a very simple procedure for making graphene on the cheap." They describe growing high-quality graphene on the surface of commercially available silicon carbide wafers to produce material with excellent electronic properties. It "represents a huge step toward technological application of this material as the synthesis is compatible with industrial mass production," their report notes.

ARTICLE FOR IMMEDIATE RELEASE "Graphene Synthesis on Cubic SiC/Si Wafers. Perspectives for Mass Production of Graphene-Based Electronic Devices" <http://pubs.acs.org/stocken/presspac/presspac/full/10.1021/nl904115h>

Ancient Tribal Meeting Ground Found in Australia

The 40,000-year-old site may hold the world's southernmost traces of early human life.

content provided by Amy Coopes, AFP

THE GIST:

- * An archaeology survey conducted ahead of roadwork has found an ancient, Aboriginal meeting ground.***
- * Up to three million artifacts were believed to be buried in the area.***
- * Only around 470,000 of Australia's original inhabitants are still alive today.***

Australian archaeologists have uncovered what they believe to be the world's southernmost site of early human life, a 40,000-year-old tribal meeting ground, an Aboriginal leader said Wednesday.

The site appears to have been the last place of refuge for Aboriginal tribes from the cannon fire of Australia's first white settlers, said Michael Mansell of the Tasmanian Aboriginal Centre.

The find came during an archaeological survey ahead of roadwork near Tasmania's Derwent River and soil dating had established the age of the artifacts found there.

"When the archaeological report came out it showed that (life there) had gone back longer than any other recorded place anywhere else in Tasmania, dating back to 40,000 years," Mansell told AFP.

Up to three million artifacts, including stone tools, shellfish fragments and food scraps, were believed to be buried in the area, which appeared to have been a meeting ground for three local tribes.

They died out after white settlers arrived in the late 18th century. "They (settlers) hunted people here to this place and shot them just so they could get the land," said Mansell. "Many others were imprisoned until they died."

"In terms of culture and history this region now represents Tasmania's Valley of the Kings," he added, referring to the world heritage listed Egyptian tombs on the west bank of the Nile.

"When you get something like this that evokes memory of what your people did before we were born and evokes a memory about the legacy that they left us ... it makes the place irreplaceable."

The survey was finished last week and chief archaeologist Rob Paton said he had been surprised at the age of the items found. "We haven't even done a reading on the bottom sample yet, I was expecting 17,000 (years) for the base of the trench and about four or 5,000 (years) for the top," Paton told state radio.

Paton said luminescence readings -- measuring the age of the artefacts based on how much exposure they had received to sunlight -- had been "nice and statistically tight". "That suggests to me that they're probably correct, giving us a top reading of 28,000 (years old) and certainly seeming to go back another 10,000 (years) at least beyond that," he said. The readings indicated that "we do have the oldest, most southern site anywhere in the world", said Paton, making it "an important site for anyone and quite exciting for us".

"I think the thing to stress is no matter what the age of the site it's important anyway," he added.

Mansell said the tribes were famous for their defiant stand against the settlers, and so frustrated the authorities they ultimately issued an order that any Aborigine in the area be shot on sight.

He said the dig's findings were merely the "tip of the iceberg" and called for plans to build a bridge over the site to be scrapped. "The Tasmanian government must immediately declare it a protected site, not just for Aboriginal people but for peoples of the world," said Mansell.

Australia's original inhabitants, with cultures stretching back tens of thousands of years, are believed to have numbered around one million at the time of white settlement.

There are now just 470,000 out of a population of 21 million and Australia's most impoverished minority.

Panel questions 'VBAC bans,' advocates expanded delivery options for women

Parents' preferences and risk factors should be weighed when choosing whether to pursue a vaginal birth after cesarean (VBAC) or plan a repeat cesarean delivery

An independent panel convened this week by the National Institutes of Health confronted a troubling fact that pregnant women currently have limited access to clinicians and facilities able and willing to offer a trial of labor after previous cesarean delivery because of so-called VBAC bans. Many, even those at low risk for complications in a trial of labor, are not offered this option. The panel affirmed that a trial of labor is a reasonable option for many women with a prior cesarean delivery. They also urged that current VBAC guidelines be revisited, malpractice concerns be addressed, and additional research undertaken to better understand the medical and non-medical factors that influence decision making for women with previous cesarean deliveries.

"Declining VBAC rates and increasing cesarean delivery rates over the last 15 years would seem to indicate that planned repeat cesarean delivery is preferable to a trial of labor. But the currently available evidence suggests a very different picture: a trial of labor is worth considering and may be preferable for many women,"

said Dr. F. Gary Cunningham, panel chair, and chair of obstetrics and gynecology at the University of Texas Southwestern Medical Center at Dallas.

Rigorous research shows that a trial of labor is successful in nearly 75 percent of cases, and maternal mortality is actually lower for women who have a trial of labor, regardless of whether they end up delivering vaginally or by cesarean, though those women who have an unsuccessful trial of labor and undergo a repeat cesarean delivery experience higher morbidity than those who have a successful VBAC.

In light of their assessment of VBAC's relative safety, the panel urged professional societies to revisit existing VBAC guidelines, in particular, the recommendation for "immediate availability" of surgical and anesthesia personnel as prerequisites for offering a trial of labor; two recent surveys of hospital administrators found that 30 percent of hospitals had stopped offering trial of labor or providing VBAC services because they could not meet this standard, creating a serious barrier to that option.

The panel thus advocated for additional research to develop clear, evidence-based risk assessment tools to assist mothers and providers in the decision-making process from early pregnancy through delivery, accounting for individual risk factors, values, and preferences.

The panel also expressed concern that medico-legal considerations exacerbate other barriers to trial of labor for women with a previous cesarean delivery. They strongly recommended that policymakers and providers collaborate in the development and implementation of appropriate strategies to address malpractice concerns and mitigate this problem. "There's still a lot we don't know about which women will be successful in having a VBAC, but we believe it's essential that women's desires and preferences be respected throughout the decision making process," said Dr. Cunningham.

Safety is the chief concern for women and their providers in deciding whether to attempt a trial of labor or plan a repeat cesarean delivery. Each option carries important benefits and risks for both mother and baby. This poses a profound dilemma because benefits for the woman may come at the price of increased risks for the baby, and vice versa. For example, hysterectomy rates were comparable across both modes of delivery, but uterine rupture was higher in women who have a trial of labor. Conversely, women who had a VBAC had reduced abnormalities of placental growth and position in subsequent pregnancies. Unfortunately, the lack of high-quality evidence about many medical and non-medical factors prevents precise risk calculations that could inform the decision-making process.

Factors contributing to some women's desire to attempt a trial of labor include desire for their partner's involvement in the delivery, belief that labor and vaginal delivery can be deeply empowering, enhanced opportunity for maternal-infant bonding, greater ease in establishing breast feeding, and easier recovery. Conversely, scheduling convenience, the desire to avoid labor pain, fear of failed trial of labor, avoidance of possible emergency cesarean section, and desire for surgical sterilization at the time of delivery may all contribute to a preference for planned cesarean delivery.

Prior to 1980, VBACs were generally discouraged because of the widely held idea that once a woman had a cesarean delivery, any subsequent pregnancies would also have to be delivered by cesarean. After a 1980 consensus statement questioned routine repeat cesarean delivery, VBAC rates increased steadily until 1996 when rates began to decline again. This panel's deliberations took place in the context of this trend, in which the current overall cesarean delivery rate is 31 percent and the VBAC rate is less than 10 percent compared to 28 percent in 1996.

An updated version of the panel's draft consensus statement, which incorporates comments received during this morning's public session, will be posted later today at <http://consensus.nih.gov>.

Animal Suicide Sheds Light on Human Behavior

Suicide is not just a human behavior -- and studying it can help us understand human suicide.

By Larry O'Hanlon

THE GIST:

- * **Animals of all sorts kill themselves.**
- * **Animal suicides can teach us a lot about human suicides.**
- * **For centuries people either denied animal suicides or took them as evidence of human-like intentions.**

Whether it's a grieving dog, a depressed horse or even a whale mysteriously beaching itself, there is a long history of animals behaving suicidally, behavior that can help explain human suicide, says newly published research.

The idea that animals could actually be very good models for human suicide started to take root in the 20th century, said Edmund Ramsden, one of the authors of the study published in the latest issue of the journal *Endeavour*, along with Duncan Wilson of the University of Manchester.

"You begin to challenge the definition of suicide. The body and mind are so damaged by stress and so it leads to self destruction. It's not necessarily even a choice," Ramsden told Discovery News.

"It becomes reversed, in a sense," said Ramsden. Animal and human suicides are no longer seen as willful acts but as responses to conditions.

There are many stories of animal suicide dating back centuries. In 1845, for example, the Illustrated London News reported a "Singular Case of Suicide" involving a "fine, handsome and valuable black dog, of the Newfoundland species." The dog had for days been acting less lively than usual, but then was seen "to throw himself in the water and endeavor to sink by preserving perfect stillness of the legs and feet."

The dog was rescued and tied up. But as soon as he was released he entered the water again and tried to sink himself. This occurred several times until at last the dog appeared to tire and "by dint of keeping his head determinedly under water for a few minutes, succeeded at last in obtaining his object, for when taken out this time he was indeed dead."

Such anecdotes tend to reflect the values of the societies they are from, said Ramsden. In the 19th century, animal suicides were often seen as acts of abuse, madness, love or loyalty -- the same causes then given for human suicides. In earlier times, such qualities weren't assigned, but animals were still used to help define suicide. "For (St.) Augustine and (Thomas) Aquinas it goes against natural law and so goes against God's law," Ramsden told Discovery News. They called on the lack of suicide in Nature as proof that people should not kill themselves.

But Aquinas couldn't have been more wrong, says psychologist Thomas Joiner of Florida State University and author of the newly-published book "Myths of Suicide."

"It's incredible how actually pervasive it is in nature," said Joiner. Organisms of all sorts are known to self-destruct in one way or another, usually in order to protect their relatives -- and so to save their genes.

"If you take the statement: 'My death will be worth more than my life,' that plays out in all sorts of organisms," said Joiner. "That calculation is the same, whether it's written in the genes or English."

Pea aphids, for instance, when threatened by a lady bug can explode themselves, scattering and protecting their brethren and sometimes even killing the lady bug. They are literally tiny suicide bombers, Joiner told Discovery News.

The big difference is that in modern humans that calculation can go wrong. There are some acts of suicide that do save lives. But most of the millions or so human suicides each year worldwide benefit no one, Joiner explained. They are acts that perhaps used to serve a purpose in early human societies, he said, but have lost their function in the modern world.

What that suicidal Newfoundland was telling us, then, is not so much that animals and humans think alike, but that it is, as Joiner said "...a fatal consequence of biologically-based and extremely serious illness."

Huge meat-eater plant prefers poo

By Matt Walker Editor, Earth News

The largest meat-eating plant in the world is designed not to eat small animals, but small animal poo.

Botanists have discovered that the giant montane pitcher plant of Borneo has a pitcher the exact same size as a tree shrew's body. But it is not this big to swallow up mammals such as tree shrews or rats.

Instead, the pitcher uses tasty nectar to attract tree shrews, then ensures its pitcher is big enough to collect the feeding mammal's droppings. Details of the discovery are published in the journal *New Phytologist*.

Big reputation

Pitcher plants have elaborate structures which entice creatures such as ants or spiders into a precarious position, from which they fall into a fluid-filled trap, where they drown and are ingested. These arthropods are thought to provide the plant with vital nitrogen and phosphorus, which it cannot obtain any other way.



A large N. raja pitcher awaits its fill

Pitchers are the largest carnivorous plants, and the largest pitchers grow in Borneo. One, known as *Nepenthes rajah*, is believed to be the largest meat-eating plant in the world, growing pitchers that can hold two litres of water if filled to the brim. This plant's pitcher is so big that they are reputed to catch vertebrates.

"This species has always been famous for its ability to trap rodents, but I've been looking at the pitchers of this species on and off since 1987, and I've never seen a trapped rat inside," says Dr Charles Clarke, an expert on carnivorous plants based at Monash University's Sunway Campus in Selangor, Malaysia.

"This made me wonder: if it is large enough to trap rats, but it only traps them very rarely, it is likely that the pitchers are large because of some other reason?"

To find out, Dr Clarke and colleagues Ms Lijin Chin of Monash University and Dr Jonathan Moran of Royal Roads University in Victoria, British Columbia, Canada turned their attention to tree shrews, which inhabit the same forest as *N. rajah*.

They did so after noticing that tree shrews, which are a similar size to rodents but most closely related to primates, sometimes left faeces in the traps of large pitchers.

"All of a sudden we realised that there may be some relationship between big pitchers and tree shrews. So we decided to look at the pitcher geometry. What they found "totally blew us away", says Dr Clarke.

Precise dimensions

N. rajah pitchers have huge orifices, but they also grow large concave lids held at an angle of about 90 degrees away from the orifice. The inside of these lids are covered with glands that exude huge amounts of nectar.

Most importantly, the distance from the front of the pitcher's mouth to the glands corresponds exactly to the head to body length of mountain tree shrews.

The same is true for two other species of large meat-eating pitcher plant, *N. lowii* and *N. macrophylla* that are also visited by tree shrews.

However, the pattern does not hold for other pitcher species not associated with the small mammals. "In order for the tree shrews to reach the exudates, they must climb onto the pitchers and orient themselves in such a way that their backsides are located over the pitcher mouths," explains Dr Clarke. The tree shrews then appear to defecate as a way of marking their feeding territory.

That suggests these supposedly "meat-eating" plants have evolved a mutualistic relationship with tree shrews.

The tree shrews get nectar, a valuable food source, and in return, the plants get to catch and absorb the tree shrew's faeces which likely supplies the majority of nitrogen required by the plant.

These particular species of pitcher also live in the highlands where insects and other arthropods are more scarce.

Such creatures would normally provide the nitrogen needed by the pitcher, forcing it to evolve its huge size to attract tree shrews instead.

Radical rethink

"150 years after the discovery of *N. rajah*, we finally have an explanation for why the largest carnivorous plant in the world produces such big pitchers," says Dr Clarke.

Dr Clarke says it is the "neatest" discovery he has made in more than 20 years of studying *Nepenthes* meat-eating plants. The findings should radically alter how we look at these plants," he says.

He believes there is much we still have to learn about the true habits of carnivorous plants.

They suspect another highland species, *N. ehippiata*, likely feeds on faeces too, as may a huge meat-eating plant called *N. attenboroughii* which was only discovered last year.

In the lowlands of Borneo, bats roost in the pitchers of yet more *Nepenthes* species, suggesting these plants may too feed off the faeces of other small mammals.

These researchers really can read your mind

New evidence suggests that researchers can tell which memory of a past event a person is recalling from the pattern of their brain activity alone.

The results, reported online on March 11th in *Current Biology*, a Cell Press publication, follow an earlier discovery by the same University College London team that they could tell where a person was standing within a virtual reality room in precisely the same way (http://www.eurekalert.org/pub_releases/2009-03/cp-cts030509.php). The researchers say the new results move this line of research along because our episodic memories—those recollections of the everyday events that make up the autobiography of our lives—are expected to be more complex, and thus more difficult to crack, than your basic spatial memory would be.

"We've been able to look at brain activity for a specific episodic memory—to look at actual memory traces," said senior author of the study Eleanor Maguire. "We found that our memories are definitely represented in the hippocampus. Now that we've seen where they are, we have an opportunity to understand how memories are stored and how they may change through time."

In order to pull this off, Maguire and her colleagues Martin Chadwick, Demis Hassabis, and Nikolaus Weiskopf showed ten people each of three very short films before brain scanning. Each movie featured a different actress and a fairly similar everyday scenario. For instance, Maguire explained, in one of the films a



woman rifles through her purse to find an envelope that she then drops in a mailbox. In a second film, another actress finishes her cup of coffee and drops the empty cup in a trash can.

The researchers scanned the participants' brains using functional magnetic resonance imaging (fMRI) while the participants were asked to recall each of the films. The researchers then ran the imaging data through a computer algorithm designed to identify patterns in the brain activity associated with memories for each of the films. Finally, they showed that those patterns could be identified in independent fMRI data to accurately predict which film a given person was thinking about when he or she was scanned.

The results imply that the neuronal traces of episodic memories are stable, and thus predictable, even over many re-activations, the researchers report. Although the patterns in individual brains do vary from one another, they also showed remarkable similarities in the parts of the hippocampus that were active, Maguire added.

"Now that we have shown it is possible to directly access information about individual episodic memories in the human hippocampus in vivo and noninvasively, this offers new opportunities to examine important properties of episodic memory, to explore possible functional topographies, and to examine neural computations within hippocampal subfields," the researchers conclude.

The researchers include Martin J. Chadwick, Demis Hassabis, Nikolaus Weiskopf, and Eleanor A. Maguire, of University College London, London, UK.

Water oxidation advance boosts potential for solar fuel

Emory University chemists have developed the most potent homogeneous catalyst known for water oxidation, considered a crucial component for generating clean hydrogen fuel using only water and sunlight. The breakthrough, published March 11 in the journal *Science*, was made in collaboration with the Paris Institute of Molecular Chemistry.

The fastest, carbon-free molecular water oxidation catalyst (WOC) to date "has really upped the standard from the other known homogeneous WOCs," said Emory inorganic chemist Craig Hill, whose lab led the effort. "It's like a home run compared to a base hit."

In order to be viable, a WOC needs selectivity, stability and speed. Homogeneity is also a desired trait, since it boosts efficiency and makes the WOC easier to study and optimize. The new WOC has all of these qualities, and it is based on the cheap and abundant element cobalt, adding to its potential to help solar energy go mainstream. Benjamin Yin, an undergraduate student in Hill's lab, is the lead author on the *Science* paper. Emory chemists who are co-authors include Hill, Yurii Gueletii, Jamal Musaev, Zhen Luo and Ken Hardcastle. The U.S. Department of Energy funded the work.

The WOC research is a component of the Emory Bio-inspired Renewable Energy Center, which aims to mimic natural processes such as photosynthesis to generate clean fuel. The next step involves incorporating the WOC into a solar-driven, water-splitting system.

The long-term goal is to use sunlight to split water into oxygen and hydrogen. Hydrogen becomes the fuel. Its combustion produces the by-product of water – which flows back into a clean, green, renewable cycle.

Three main technical challenges are involved: developing a light collector, a catalyst to oxidize water to oxygen and a catalyst to reduce water to hydrogen. All three components need improvement, but a viable WOC may be the most difficult scientific challenge. "We are aiming for a WOC that is free of organic structure, because organic components will combine with oxygen and self-destruct," Hill says. "You'll wind up with a lot of gunk."

Enzymes are nature's catalysts. The enzyme in the oxygen-evolving center of green plants "is about the least stable catalyst in nature, and one of the shortest lived, because it's doing one of the hardest jobs," Hill says.

"We've duplicated this complex natural process by taking some of the essential features from photosynthesis and using them in a synthetic, carbon-free, homogeneous system. The result is a water oxidation catalyst that is far more stable than the one found in nature."

For decades, scientists have been trying to imitate Mother Nature and create a WOC for artificial photosynthesis. Nearly all of the more than 40 homogeneous WOCs developed by labs have had significant limitations, such as containing organic components that burn up quickly during the water oxidation process.

Two years ago, Hill's lab and collaborators developed the first prototype of a stable, homogenous, carbon-free WOC, which also worked faster than others known at the time. The prototype, however, was based on ruthenium, a relatively rare and expensive element.



Emory University chemists have developed the most potent homogeneous catalyst known for water oxidation, considered a crucial component for generating clean hydrogen fuel using only water and sunlight.
Benjamin Yin, Emory University

Building on that work, the researchers began experimenting with the cheaper and more abundant element cobalt. The cobalt-based WOC has proved even faster than the ruthenium version for light-driven water oxidation.

Communication often fumbled during patient hand-offs in hospital ***Restrictions on physician work hours may lead to more miscommunication***

As shifts change in a hospital, outgoing physicians must "hand off" important information to their replacements in a brief meeting. But a new study of this hand-off process finds that the most important information is not fully conveyed in a majority of cases, even as physicians rate their communication as successful.

The research, published by University of Chicago researchers in the March issue of *Pediatrics*, highlights the importance of educating doctors about successful communication skills during hand-offs. The results also emphasize the risk inherent in increased hand-offs necessitated by restrictions on medical resident work hours, even as further work limits are being discussed.

"When resident hours are shortened, you have more hand-offs," said Vineet Arora, MD, assistant professor of medicine at the University of Chicago Medical Center. "You could have concerns about either a tired physician who knows the patient or a well-rested physician that may not know the patient. The tradeoff is between fatigue and familiarity."

Conducted through a unique collaboration between physicians and psychologists at the University of Chicago, the study observed hand-off communication between pediatric interns - first-year residents - at Comer Children's Hospital at the University of Chicago. Interns at the end of an overnight shift would spend a total of 10-15 minutes sharing information about hospitalized patients with the resident relieving them in a designated hand-off room.

Both the outgoing and incoming interns were then asked by researchers about what they thought was the most important information conveyed during the hand-off about each patient. Surprisingly, what the outgoing intern identified as the most important information was not successfully communicated to the incoming intern 60 percent of the time. The rationale for certain medical decisions – such as why a patient is on a particular drug or why the primary care physician should be contacted – was also not understood by the receiving intern in a majority of cases.

But despite these miscommunications, interns on both sides of the hand-off consistently rated the quality of their communication as very high. Boaz Keysar, PhD, a professor of psychology at the University of Chicago and co-author of the paper, said that this disconnect between perceived and actual success of communication is common in other settings.

"You would imagine the kind of miscommunication we discover elsewhere actually might be reduced when the stakes are high in a clinical setting, because it matters so much," Keysar said. "But the opposite is true, which I think is counter-intuitive and important to know."

The results were even more striking given the optimal hand-off conditions for interns at Comer Children's Hospital. In each hand-off, a conversation takes place in a designated room under supervision by more experienced physicians. In previous research, Arora found that many hospitals and programs have much less organized hand-off procedures – if they occur at all.

In illustrating the communication breakdowns that plague even best-case hand-off conditions, Arora and Keysar hope to inform medical centers and schools of the need for better education about hand-offs. The study found that "anticipatory guidance" – offering to-do items or if-then advice – was a more effective way of communicating information between interns than passing on knowledge items in bulk. Currently, Arora and colleagues are working on a simulation exercise for fourth-year medical students to train more effective hand-off communication skills.

Such training, they hope, will be more effective than relying upon computer programs and electronic medical records to facilitate hand-off communication. A verbal exchange of information remains important so that young doctors can make quick, informed decisions about patients, Arora said.

"IT solutions cannot substitute for a successful communication act," Arora said. "We aren't at the point where computers are going to do that for us. Technology solutions can help so that you have the information that you need when you need it, but to look at that information and be able to make a judgment about what to do, that is what the hand-off conversation is for."

But while researchers look for the best way to improve those conversations, Arora and Keysar hope that medical policymakers are aware of the risks inherent in the current hand-off model. As the Accreditation Council for General Medical Education ponders further restrictions upon the number of hours residents and interns can work, the consequences of those reduced hours must be acknowledged, they said.

"We tend to be very myopic in the way we think about this problem," Keysar said. "Reducing hours is good, but there's a cost that is not obvious at all, and this study really spells that cost out. It's very difficult for us to gauge how well we are understood, and this should be taken into account in the trade-off between number of work hours and fatigue."

The article, "Interns Overestimate the Effectiveness of Their Hand-off Communication," appears in the March 2010 issue of Pediatrics. Vivian Chang, MD, now at the University of California, Los Angeles, Shiri Lev-Ari, MA, of the University of Chicago Department of Psychology and Michael D'Arcy, BA, now at the University of California, Berkeley are also listed as authors.

Obesity and alcohol act together to increase the risk of liver disease

Research: Body mass index and risk of liver cirrhosis in middle aged women in UK: prospective study; Research: Effect of body mass index and alcohol consumption on liver disease: analysis of data from two prospective cohort studies

Two studies published on bmj.com today show that obesity and alcohol act together to increase the risk of liver disease in both men and women. Together, these findings have important clinical and public health implications.

Rates of liver disease and obesity are increasing in the UK. While alcohol is a major cause of liver cirrhosis, recent evidence suggests that excess body weight may also play a role.

In the first study, researchers from the University of Oxford examined the link between body mass index (BMI) and liver cirrhosis in 1.2 million middle-aged UK women as part of the Million Women Study.

Each woman was tracked for an average of 6.2 years, and risks were adjusted for factors such as age, alcohol consumption, smoking, socioeconomic status and physical activity.

Compared to women of a healthy weight, women who were overweight or obese had an increased relative risk of liver cirrhosis. Although this relative risk did not differ significantly by alcohol consumption, the absolute risk did. For example, among women who reported drinking an average of about a third to half a drink a day, 0.8 in 1000 will be admitted to hospital with or will die from liver cirrhosis over five years if they are of healthy weight compared with 1 in 1000 women who are obese.

However, among women who reported drinking an average of two and a half drinks a day, 2.7 in 1000 will be admitted to hospital with or will die from liver cirrhosis over five years if they are of healthy weight compared with 5 in 1000 women who are obese.

In the second study, researchers from the Universities of Glasgow and Bristol investigated the joint effects of BMI and alcohol consumption on liver disease in more than 9,000 men in Scotland. Participants were tracked for an average of 29 years.

Both factors were related to liver disease and, more importantly, the combination of high BMI and alcohol consumption was greater than the additive effect of the two separate factors.

For example, obese men who reported drinking 15 or more units per week had the greatest risk of liver disease: almost 19 times higher than underweight or normal weight non-drinkers. The authors suggest that lower, BMI specific "safe" limits of alcohol consumption may need to be defined for people who are overweight. Preventive efforts are also needed to limit the affordability and availability of alcohol and to increase physical activity, they say.

Both studies conclude that, from a public health perspective, strategies to jointly reduce both excessive alcohol consumption and excessive body weight should lead to a reduction in the incidence of liver disease.

In an accompanying editorial, Professor Christopher Byrne at the University of Southampton and Dr Sarah Wild from the University of Edinburgh say that future research must focus on better diagnosis and treatment of non-alcoholic fatty liver disease (a build-up of fat in the liver caused by obesity, high alcohol intake and diabetes, which can lead to cirrhosis).

In the meantime, the old adage of "prevention is better than cure" remains pertinent, they write. "Reducing alcohol consumption and obesity are, at present, our only weapons against non-viral liver disease. The progression of non-alcoholic fatty liver disease to end stage liver disease can now be added to the list of the undesirable consequences of modern lifestyles."

An end to lice: The effectiveness of a new oral treatment has been demonstrated

French medical researchers from the AP-HP (Henri Mondor Hospital and Avicenne Hospital) and Inserm (Unit 738 "Models and methods for therapeutic evaluation of chronic illnesses" and CIC 202, at Tours) have recently demonstrated the effectiveness of a new molecule in the fight against lice. Faced with the emergence of increasing resistance to conventional treatments by these parasites, this new medication represents a real therapeutic alternative which is effective in 95% of cases.

This work has been published in the March 11th edition of The New England Journal of Medicine.

Lice are parasites which infest more than 100 million people worldwide each year. Children between the ages of 3 and 11 years are particularly vulnerable because of their social behaviour (games etc.) which is favourable to the propagation of parasites.

Although conventional anti-lice lotions are effective in a many cases, an ever increasing resistance to these treatments has been observed. Like many parasites, lice have evolved their own strategy for survival in difficult conditions. Through evolution of their genetic inheritance, they have become insensitive to the usual insecticides (malathion and pyrethrin) contained in the lotions. In the case of pyrethrin, mutations in the amino acids involved in the development of the sodium channels, acting at the central nervous system level of the lice, have been identified and are responsible for this resistance.

The appearance of new forms of resistance seems to be constantly increasing and lice epidemics are becoming ever more difficult to treat and eradicate. Hence the necessity to find new therapeutic alternatives.

A multi-centre international study

Researchers from AP-HP and Inserm have therefore performed a clinical trial to compare the effectiveness of a new oral treatment (oral Ivermectin administered at 400 µg per kilogram) with that of a conventional anti-lice treatment (0.5% malathion lotion). The trial was conducted by applying one or other of the products twice, at an interval of seven days, to 812 contaminated individuals from 376 families.

Ivermectin is a compound from the avermectin family which acts by blocking neurotransmissions in the brains of invertebrates.

The results obtained by the researchers are convincing: 95% of the 398 individuals who received Ivermectin were free from lice 15 days after the start of treatment, as compared to 85% of the 414 individuals treated with malathion. Ivermectin is already available on the market. It is prescribed, in particular, for treatment of scabies.

For Olivier Chosidow, coordinator of the study, no doubt remains, "When conventional treatments against lice do not work, taking Ivermectin twice, with a seven-day interval, offers excellent results and represents a real alternative to conventional anti-lice lotions."

Source: Oral Ivermectin versus Malathion Lotion for Difficult-to-Treat Head Lice

Olivier Chosidow, M.D., Ph.D., Bruno Giraudeau, Ph.D., Jeremy Cottrell, M.S., Arezki Izri, M.D., Robert Hofmann, M.D., Ph.D., Stephen G. Mann, M.D., and Ian Burgess, Ph.D.

English Sets High Hurdles to Learning ABCs

Given the inherent complexity of English, reading to young children is critical to developing their language skills.

By Cristen Conger

THE GIST:

- * **English is a difficult language to learn because of its inconsistent letter-sound relationship.**
- * **Parents should try to read to their children for at least 20 minutes three times a week.**
- * **Computer reading programs can supplement at-home learning.**

At-home reading instruction benefits any young child, but it makes a bigger difference to those learning in English, according to a recent study in Learning and Instruction.

Since letters in the English alphabet can sound different from word to word, it's a harder language to master than Greek or Finnish, for instance, which have more consistent letter sounds, or phonemes.

For that reason, English-speaking parents should promote literacy development through actively teaching children letter names and sounds -- not just reading stories aloud.

It's not only purchasing the book and perhaps reading to the child, and the child having a passive role in this interaction," said George Georgiou, an educational psychologist at the University of Alberta who contributed to the study. "It should be very active. You should be asking questions to your child: Would you change the title of the book? What do you think about the character names? What about the events of the story?"

These kinds of challenges, however, don't just affect children studying English. Children learned to read Chinese also have to grapple with an inconsistent letter-to-phoneme relationship and, consequently, start learning to read earlier.

"The paradigm of Chinese, we know, is that because of the extreme difficult nature of the language, the kids go to school earlier," Georgiou said. "They start teaching them these simple characters early on."

For English-speaking children, extra instruction at home can jump-start reading skills.

"If you can afford to spend 20 minutes with your child, that would be extremely helpful," Georgiou told Discovery News. "I don't think there's a single parent who can't devote reading 20 minutes to their children, and it doesn't even have to happen every single day; it could be three times a week."

Time-strapped parents can also turn to educational computer reading programs to supplement at-home learning.

"We've found that (computer reading programs) help increase all aspects of literacy and concepts of print for very young children if they're using software that's interactive and not just something they're sitting there listening to," said Linda Robinson, assistant director of Center of Best Practices for Early Childhood at Western Illinois University.

But Robinson also noted that while beneficial, technology can't fully replace the interface value of an adult and child reading together, a theory underscored by Georgiou's study.

"I think it's more the physical presence of the parents and the natural interaction with them that makes the difference," Georgiou said. *Cristen Conger is a writer for HowStuffWorks.com.*

Mother's flu during pregnancy may increase baby's risk of schizophrenia

The study, published online by the journal Biological Psychiatry, is the first study done with monkeys that examines the effects of flu during pregnancy.

CHAPEL HILL – Rhesus monkey babies born to mothers who had the flu while pregnant had smaller brains and showed other brain changes similar to those observed in human patients with schizophrenia, a study at the University of Wisconsin-Madison in collaboration with the University of North Carolina at Chapel Hill has found.

The study, published online by the journal Biological Psychiatry, is the first study done with monkeys that examines the effects of flu during pregnancy. Results from this study support findings from rodent studies suggesting this type of infection may increase the risk of schizophrenia in the offspring, said lead author Sarah J. Short, Ph.D. Short worked on the study while earning her doctorate at Wisconsin and now is a post-doctoral fellow at UNC working with John H. Gilmore, M.D., professor of psychiatry in the UNC School of Medicine.

"This was a relatively mild flu infection, but it had a significant effect on the brains of the babies," Short said. "While these results aren't directly applicable to humans, I do think they reinforce the idea, as recommended by the Centers for Disease Control and Prevention, that pregnant women should get flu shots, before they get sick."

In the study, 12 rhesus macaques were infected with a mild influenza A virus 1 month before their baby's due date, early in the third trimester of pregnancy. For comparison, the study also included 7 pregnant monkeys who did not have the flu. When the babies were 1 year old, magnetic resonance imaging (MRI) scans were taken of their brains. Researchers also assessed the babies' behavioral development at that time.

The babies born to flu-infected mothers showed no evidence of direct viral exposure. Their birth weight, gestation length and neuromotor, behavioral and endocrine responses were all normal.

However, the MRI scans revealed significant reductions in overall brain size in the flu-exposed babies. In addition, the scans found significant reductions of "gray matter" (the portion of brain tissue that is dark in color) especially in areas of the brain called the cingulate and parietal lobe, and significant reductions of "white matter" (brain tissue that is lighter in color) in the parietal lobe.

The cingulate is located in the middle of the brain, but spans a broad distance from front to back and relays information from both halves of the brain. This structure is important for numerous cognitive function related to emotions, learning, memory, and executive control of these processes to aid in decision-making and anticipation of rewards. In addition this structure also plays a role in regulating autonomic processes, such as blood pressure and respiratory control. The parietal lobe comprises a large section on both sides of the brain between the frontal lobes and the occipital lobes, in the back of the brain. This part of the brain integrates information from all the senses and is especially important for combining visual and spatial information.

"The brain changes that we found in the monkey babies are similar to what we typically see in MRI scans of humans with schizophrenia," said Gilmore. "This suggests that human babies whose mothers had the flu while pregnant may have a greater risk of developing schizophrenia later in life than babies whose mothers did not have the flu. Normally that risk affects about 1 of every 100 births. Studies in humans suggest that for flu-exposed babies, the risk is 2 or 3 per 100 births."

Most of the work of the study was done at the Harlow Center for Biological Psychology, which is part of Wisconsin's Department of Psychology. The center's director, Christopher Coe, Ph.D., is senior author of the study. Gilmore, a schizophrenia researcher who has led several studies that used MRI scans of newborn human brains, led the analysis of MRI data in the pregnancy and influenza study.

Complete genomics finds its first diseases

Ewen Callaway, reporter

Whole-genome sequencing is touted as the tech that will finally unmask our genetic "dark matter" - as-yet unknown disease-drivers that are missed by current gene scans. It hasn't done that yet, but for the first time two separate groups of researchers have used it to uncover mutations underlying rare diseases. The breakthrough shows both the promise and challenges facing the field of personal genomics.

Right now, most personal genomics is based on gene scans that identify single-letter mutations in the genetic code known as SNPs, which can indicate that someone is at higher risk of various disorders. But complete genome sequences might tell us a lot more. This week's breakthroughs give us a taste of what that might be like.

One team identified a previously unknown mutation that almost certainly causes a neuromuscular disorder by sequencing the genome of one of its members, James Lupski, who has Charcot-Marie-Tooth syndrome. Mutations in more than two dozen genes have previously been linked to the diseases but Lupski, a medical geneticist at Baylor College of Medicine in Houston, Texas, is negative for all of them.

Whole-genome sequencing revealed that Lupski has two mutations in both copies of a gene called SH3TC2. The gene has previously been linked to neurological disease, but these specific mutations have not. "Lupski's three sick siblings also had both of these mutations, whereas his four healthy siblings and parents (who do not have the disease) carried only one mutated gene," ScienceNOW reports.

Meanwhile another team, led by Leroy Hood - a pioneer of DNA sequencing - and David Galas, both at the Institute for Systems Biology in Seattle, sequenced the complete genomes of a family of four to figure out which genes are responsible for a craniofacial condition called Miller syndrome and another rare disease called primary ciliary dyskinesia.

Unlike Lupski's team, they didn't home in on a single gene for each condition, but they did narrow it down to four candidate genes. "The basic problem here is that we're still extremely bad at differentiating between mutations causing serious disease and perfectly benign polymorphisms," notes the blog Genetic Future.

Nonetheless, researchers are confident that as whole-genome sequencing gets cheaper, it will deliver further on its promise of uncovering new, disease-causing mutations - at least in rare conditions caused by single genes, such as the ones identified in these studies.

A bigger challenge will be to identify the exact genetics underlying diseases caused by large numbers of mutations, such as cancer and mental illnesses such as schizophrenia, which have mostly evaded studies based on scanning for single-letter differences peppered across the genome.

Why female moths are big and beautiful

In most animal species, males and females show obvious differences in body size. But how can this be, given that both sexes share the same genes governing their growth? University of Arizona entomologists studied this conundrum in moths and found clues that had been overlooked by previous efforts to explain this mystery of nature.

Take a look around in the animal world and you will find that, in most organisms, individuals of one sex are larger than the other of the species.

Even though evolutionary biologists have long recognized this discrepancy, called sexual dimorphism, they have struggled for decades to solve a major paradox: How can males and females of one species be of different sizes, given that they share the same genetic blueprints dictating their development and growth?

Researchers from the University of Arizona have discovered that the key to unraveling this mystery lies in the early developmental stages during which the sexes begin to grow apart and that females can respond to selection on size almost twice as fast as can males. Their findings are published online before print in Proceedings of the Royal Society of London, Series B.

"In mammals, the males tend to be larger because there is an advantage in being bigger and stronger when it comes to fighting over who gets the female," explained Craig Stillwell, lead author of the study and a UA Center for Insect Science postdoctoral fellow in the lab of Goggy Davidowitz, an assistant professor of entomology at the UA. "In most arthropods, on the other hand, we find the opposite: the females are bigger than the males. Think of spiders, for example. In some species, the female can be hundreds of times larger than the male. "The question we asked was, 'how do females and males come to be different in size?'"

Many biologists have tried to solve this puzzle over time, but when Stillwell and Davidowitz looked at the literature, they realized something was missing in the picture.

"Since there is no difference - at least that we know of - between the male and female genes controlling growth, nobody could figure out why we see what we see in nature: differently sized males and females," said Stillwell.

Scientists have known that growth rates do not differ between female and male caterpillars and thus cannot account for the observed size difference. Rather, the sexual dimorphism observed in the adult animals more likely has to do with differences in the time the two sexes spent as growing larvae. Even in light of that, nearly all research has focused on the adult animals.

"We are the first ones to look at the larvae with this question in mind," Stillwell said.

Stillwell and Davidowitz chose the giant hawk moth (*Manduca sexta*), a species native to Arizona, as a model organism, mostly because this insect species is well-studied, easily bred in the lab and large enough to allow for ease of handling and measuring.

The researchers followed more than 1,200 caterpillars from the time they hatched, all the way through four molts and until they pupated. They weighed and measured the animals at different times during development and fed the data into a complex statistical model they developed.

For most of their lives as caterpillars, females and males do not appear much different.

"The final larval stage is when it all happens," Stillwell said. "There is a point in the caterpillar's life when an inner clock and environmental cues tell the animal it's time to become an adult. Hormonal changes make them stop feeding and wander around looking for a place to pupate. Within a few hours they develop into a pupa, from which the adult moth will emerge a few weeks later."

Stillwell and Davidowitz discovered that female caterpillars initiate this fundamental change a bit later than the males. By the time the female caterpillars pupate, they are larger, making for larger moths when they emerge.

So where is the advantage in being larger if you're a female insect?

"Biologists think selection favors large females because they can produce more offspring," Stillwell said.

"Another exciting result of this study is that we found a lot more variation in the physiological makeup of the female caterpillars compared to male individuals. Therefore, over generations, the females are able to respond to selective pressures nudging them toward large body size much faster than the males."

Reference: R. Craig Stillwell and Goggy Davidowitz, A developmental perspective on the evolution of sexual size dimorphism of a moth. Proceedings of the Royal Society of London, Series B, published online before print on March 10, 2010.

HDTV reveals brainy octopus has no personality

* 12:32 12 March 2010 by Shanta Barley

Octopuses make for discerning TV viewers: it seems they prefer high-definition to traditional cathode ray images (CRT). What's more, the first study using video to trick octopuses, finds that they may be the Jekyll and Hydes of the oceans: aggressive one day, shrinking violets the next.

"People have been trying for over a decade to get proper behavioural responses from octopuses and other cephalopods using videos," says Roger Hanlon, an octopus researcher at the Marine Resources Center, Woods Hole, Massachusetts, who was not involved in the study. "But this is the first time anyone has managed it."

Gloomy octopuses (*Octopus tetricus*) reacted to films shown on liquid crystal high definition television (HDTV) as if they were seeing the real thing, according to a new study by Renata Pronk at Macquarie University in Sydney, Australia, and colleagues. "They lunge forwards to attack crabs and back off from other octopuses, much as they do in the wild," says Hanlon.

Surprisingly, an octopus that was bold, aggressive and exploratory on one day was just as likely to be shy, submissive and stationary the next. "This suggests that the gloomy octopus does not have personality," writes Pronk in the new study.

No personality

By "personality", researchers mean consistency in behaviour. You might expect an individual to respond to crabs, other octopuses, jars, for example, by being consistently bold, shy or aggressive.

In contrast, the octopuses in Pronk's study were more moody than gloomy. The team captured 31 gloomy octopuses in Sydney harbour and showed them a set of 3-minute videos displayed on a screen at the front of their tank. The videos were filmed at 50 frames per second and featured a crab (their prey), another gloomy octopus, a jar and a water-filled aquarium.

Previous attempts to get octopuses to respond to videos failed, probably because they used CRT, which displays footage at a rate of 24 frames per second – too slowly for their sophisticated eyes. "The images that they see on CRT screens are incomplete and probably incoherent," says Hanlon.

To Pronk's surprise, the octopuses behaved as if animals in the film were real. They lunged forwards at crabs using jet propulsion, often striking the front of the aquarium. But when they saw films of other octopuses, which they avoid in the wild, they cowered behind a terracotta pot placed in the aquarium.

Octopuses that reacted to one film aggressively tended to respond to all films on a particularly day in the same way. But over longer periods of time, any trace of "personality" or consistency evaporated. They might react aggressively one day, but much less so on another day. "It's a bit of a surprise," says Hanlon. Other cephalopods, such as the dumpling squid, display consistent personalities for most of their lives.

Huge brains

This lack of consistent behaviour may be related to octopuses's huge brain size, relative to other cephalopods. Big brains may "afford octopuses considerable behavioural flexibility that allows them to change their behaviour adaptively over time," write the researchers.

Lack of personality may not necessarily be a bad thing. They live in dynamic environments (shallow coastal waters and reefs) and "these conditions may select for behavioural flexibility as individuals could then optimise their behaviour in a variety of typical environmental conditions". For example, behaving shyly may be an octopus's best response when it is threatened by a predator, but behaving boldly may be the best behaviour when foraging.

Hormones may drive short-term changes in the octopuses' behaviour from day to day, the authors also speculate.

The new video technology used in the experiment could help to settle several long-standing debates, says Hanlon. "For example, scientists have debated since 1992 whether or not an octopus can learn behaviours simply by watching each other," he says. "This technology will open many doors."

Journal reference: The Journal of Experimental Biology, DOI: 10.1242/jeb.040675

Proposed mission would return sample from asteroid 'time capsule'

Meet asteroid 1999 RQ36, a chunk of rock and dust about 1,900 feet in diameter that could tell us how the solar system was born, and perhaps, shed light on how life began. It also might hit us someday.

"This asteroid is a time capsule from before the birth of our solar system," said Bill Cutlip of NASA's Goddard Space Flight Center in Greenbelt, Md., one of the leaders of Goddard's effort to propose a mission called OSIRIS-REx that will return a sample from RQ36.

If selected, Goddard will provide overall mission management for OSIRIS-REx, working with the Principal Investigator, Dr. Michael Drake, Director of the Lunar and Planetary Laboratory at the University of Arizona, who will lead the OSIRIS-REx team. Lockheed Martin Space Systems will build the spacecraft.

"You can't underestimate the value of a pristine sample," Cutlip added. Meteorites, pieces of asteroids that break away and plunge to Earth, are "toasted on their way through Earth's atmosphere," Cutlip explained. "Once they land, they then soak up the microbes and chemicals from the environment around them."

"With a pristine sample — especially one from an asteroid type not available in NASA's meteorite collections — scientists will learn more about the time before the birth of our solar system, the initial stages of planet formation, and the source of organic compounds available for the origin of life," said Dr. Joseph Nuth of NASA Goddard, OSIRIS-REx Project Scientist.

Asteroids are leftovers from the cloud of gas and dust – the solar nebula -- that collapsed to form our sun and the planets about 4.5 billion years ago. As such, they contain the original material from the solar nebula, which can tell us about the conditions of our solar system's birth.

In some asteroids, this material got altered by heat and chemical reactions, either because they collided with other asteroids, or because they grew so large that their interiors became molten. That's what makes RQ36 special. It's small and appears to have been altered very little, preserving the snapshot of our solar system's infancy. It's also rich in carbon, an element used in many of the organic molecules necessary for life. Organic molecules have been found in meteorite and comet samples, indicating that some of life's ingredients can be created in space. Scientists want to see if they are also present in RQ36.

Sample return, however, isn't the only objective for the mission. This asteroid crosses Earth orbit, and the International Astronomical Union's Minor Planet Center has officially classified RQ36 as a "potentially hazardous asteroid," with a slight chance – one in 1,800 – of an impact in the year 2170.

"We'll orbit RQ36 for about a year to analyze its surface and select a sample site. This will give us experience with operating spacecraft in the vicinity of an asteroid, experience that will be useful if we ever have to send a mission to deflect one," said Nuth.

Piloting a spaceship near an asteroid is not easy. Most are lumpy and rotate more rapidly than planets, which makes for challenging landings. These small objects have feeble gravity, so other forces can significantly influence the spacecraft's position.

"Gravity on this asteroid is so weak, if you were on the surface, held your arm out straight and dropped a rock, it would take about half an hour for it to hit the ground. Pressure from the sun's radiation and the solar wind on the spacecraft and the solar panels is about 20 percent of the gravitational attraction from RQ36. It will be more like docking than landing," adds Nuth.

The mission will also help to better track the orbits of asteroids that might hit Earth by accurately measuring the "Yarkovsky effect" for the first time. The Yarkovsky effect is a small push on an asteroid that happens when the asteroid absorbs sunlight and emits heat. The small push adds up over time, and it is uneven due to an asteroid's various surface materials, wobble, and rotation. There's no sure way to predict an Earth-approaching asteroid's orbit unless you can factor in how the Yarkovsky effect will change that orbit, according to the team. "It's like trying to make a complex, banking shot in a game of pool with someone shaking the table and kicking the legs," said Nuth.

"OSIRIS-REx" spells out what the mission will do. "O" stands for the scientific theme, origins, as in the origin of life. "SI" is for spectral interpretation, or taking images of the RQ36 at wavelengths that will reveal its composition. "RI," or resource identification, is surveying the asteroid for such useful resources as water and metals. "S" stands for security, learning how to predict the detailed motion of Earth-approaching asteroids. REx stands for "Regolith Explorer". Regolith is a layer of broken-up rock and dust, formed by meteorite impacts, which covers the surface of many asteroids and moons in our solar system.

If approved, the mission will be significantly more capable than the original OSIRIS proposal. "OSIRIS was a basic sample return mission," says Nuth. "OSIRIS-REx adds more instruments to give us a complete map of the surface composition and 3-D shape, or topography, of the asteroid. It will allow us to put our sample in the proper geologic context, so we'll have a much better idea of what we're really sampling," says Nuth.

Additional instruments include a mass spectrometer, which separates and identifies atoms and molecules based on their weight and electric charge. The mass spectrometer will be built at NASA Goddard.

Two infrared spectrometers will also be added. Infrared light is invisible to the human eye, but we perceive it as heat, and it can be measured by special instruments. These spectrometers will separate the infrared light into its component "colors," or wavelengths, like a prism separates white light into a rainbow. Each element and molecule on the asteroid will emit or absorb a unique combination of infrared wavelengths, creating a specific signal in the spectrometer that will be used to identify it. Goddard will provide one of the spectrometers, the Visible to Near-Infrared spectrometer, and Arizona State University will provide the other, called the OSIRIS Thermal Emission Spectrometer.

The mission will also feature a more precise and accurate LIDAR (Light Detection And Ranging) instrument. This instrument will bounce laser pulses off the surface of the asteroid to measure its topography. The OSIRIS Laser Altimeter will be provided by MacDonald, Dettwiler and Associates Ltd., Richmond, British Columbia, Canada, and funded by the Canadian Space Agency.

Once the asteroid has been completely analyzed from orbit, the science team will pick the location to take a sample. OSIRIS-REx will be gradually brought closer to the site, and an arm with a sampling mechanism at the end will be extended to touch the surface and collect the sample. The sample will be stored in a capsule and returned to Earth, slowing its final descent through the lower atmosphere with a parachute like the successful Stardust capsule that returned samples of comet Wild 2 on January 15, 2006.

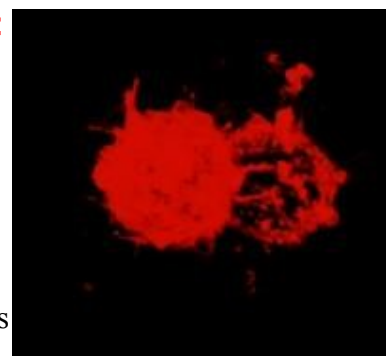
"Like the Moon rocks from the Apollo missions, samples of RQ36 will keep on giving. They'll be analyzed for decades after mission is complete, using new techniques we can't even imagine now, to test new theories of how we came to be," said Nuth.

OSIRIS-REx was one of three proposals selected by NASA on December 29, 2009 for more study under its New Frontiers program. NASA Goddard received \$3.3 million for a 12-month study to develop the concept in more detail, called the "Phase A Concept Study Effort". After the detailed mission concept studies are completed and reviewed, NASA will select one of the three to be built. The selected mission must be ready for launch no later than December 30, 2018 and must not exceed \$650 million, excluding the cost of the launch vehicle. In addition to the two instruments mentioned above, Goddard will also provide overall mission management, systems engineering, and safety and mission assurance.

'Microtentacles' on tumor cells appear to play role in how breast cancer spreads

University of Maryland research may provide potential target for new therapies to limit metastasis of primary cancers

Researchers at the University of Maryland Marlene and Stewart Greenebaum Cancer Center have discovered that "microtentacles," or extensions of the plasma membrane of breast cancer cells, appear to play a key role in how cancers spread to distant locations in the body. Targeting these microtentacles might prove to be a new way to prevent or slow the growth of these secondary cancers, the scientists say.



[The video shows two breast tumor cells attaching to each other. The red color shows the surface of both tumor cells, while the green color shows how the microtentacles from one cell encircle the neighboring cell.](#) University of Maryland

Greenebaum Cancer Center

They report in an article to be published online March 15, 2010, in the journal *Oncogene* that a protein called "tau" promotes the formation of these microtentacles on breast tumor cells which break away from primary cancers and circulate in the bloodstream. While twisted remnants of tau protein have been seen in the brain tissue of patients with Alzheimer's disease, this is the first report that tau could play a role in tumor metastasis

by changing the shape of cancer cells. These tau-induced microtentacles can help the cells reattach to the walls of small blood vessels to create new pockets of cancer.

"Our study demonstrates that tau promotes the creation of microtentacles in breast tumor cells. These microtentacles increase the ability of circulating breast tumor cells to reattach in the small capillaries of the lung, where they can survive until they can seed new cancers," says the senior author, Stuart S. Martin, Ph.D., a researcher at the University of Maryland Greenebaum Cancer Center and associate professor of physiology at the University of Maryland School of Medicine. Michael A. Matrone, Ph.D., is the study's lead author.

Healthy cells are programmed to die – a process called apoptosis – after they break off of epithelial layers that cover internal organs in the body. They also can be crushed if they are forced through small capillaries. However, cancer cells are able to survive for weeks, months and even years in the body. Once they are trapped in small blood vessels, the cells can squeeze through microscopic gaps in the vessels' lining and spread to organs such as the brain, lung and liver.

"We hope that through our research, we will be able to identify drugs that will target the growth of these microtentacles and help to stop the spread of the original cancer. Drugs that reduce tau expression may hold potential to inhibit tumor metastasis," Dr. Martin says. He notes that metastatic cancers are the leading cause of death in people with cancer, but methods used to treat primary tumors have limited success in treating metastatic cancer. In breast cancer, metastases can develop years after primary tumors are first discovered.

Tau is present in a subset of chemotherapy-resistant breast cancers and is also associated with poor prognosis, but Dr. Martin adds, "While tau expression has been studied in breast cancers for contributing to chemotherapy resistance, the protein's role in tumor cells circulating in the bloodstream hasn't been investigated. And that's the focus of our research."

In this recent study, the University of Maryland researchers analyzed breast tumor cells from 102 patients and found that 52 percent had tau in their metastatic tumors and 26 percent (27 patients) showed a significant increase in tau as their cancer progressed. Twenty-two of these patients even had tau in metastatic tumors despite having none in their primary tumors.

Dr. Martin says more studies are needed to determine if tau is a clear predictor of metastasis. Given the complex nature of tumors, there most likely are other factors involved in causing cancers to spread, he says.

"Metastasis is a very major concern for people diagnosed with cancer, and the discovery of these microtentacles and the role that tau plays in their formation is a very exciting development that holds great promise for developing new drugs," says E. Albert Reece, M.D., Ph.D., M.B.A., acting president of the University of Maryland, Baltimore, and dean of the University of Maryland School of Medicine.

The University of Maryland, Baltimore, has filed patents on the microtentacle discoveries of Dr. Martin's lab group and is looking to partner with biopharmaceutical companies on new drug development. The researchers identified these cell extensions while they were studying the effects of two drugs that prevent cell division, or mitosis. Most chemotherapy drugs target cell division, aiming to slow or stop tumor growth.

Dr. Martin says his team found that a popular chemotherapy drug, taxol, actually causes cancer cell microtentacles to grow longer and allows tumor cells to reattach faster, which may have important treatment implications for breast cancer patients. Their studies are continuing.

"We think more research is needed into how chemotherapies that slow down cell division affect metastasis. The timing of giving these drugs can be particularly important. If you treat people with taxol before surgery to shrink the primary tumor, levels of circulating tumor cells go up 1,000 to 10,000 fold, potentially increasing metastasis," he adds.

The study being published in Oncogene was funded by grants from the National Cancer Institute, the USA Medical Research and Materiel Command, and the Flight Attendants Medical Research Institute.

Chinese medicine societies reject tiger bones ahead of CITES conference

Doha, Qatar – WWF and TRAFFIC welcome a World Federation of Chinese Medicine Societies (WFCMS) statement urging its members not to use tiger bone or any other parts from endangered wildlife.

The statement was made at a symposium Friday in Beijing and notes that some of the claimed medicinal benefits of tiger bone have no basis. The use of tiger bones was removed from the traditional Chinese medicine (TCM) pharmacopeia in 1993, when China first introduced a domestic ban on tiger trade.

"Tiger conservation has become a political issue in the world. Therefore, it's necessary for the traditional Chinese medicine industry to support the conservation of endangered species, including tigers," said Huang Jianyin, deputy secretary of WFCMS.

Illegal trade in Asian big cat products is a key issue at the Convention on International Trade in Endangered Species of Wild Fauna and Flora (CITES) Conference of Parties meeting at Doha, Qatar. China is among the 175 countries that are signatories to this international treaty governing wildlife trade.

"CITES governments should be encouraged by this statement and use the opportunity they have at this meeting to pass measures, that if properly enforced, can help put an end to tiger trade," said Dr. Colman O'Criodain, Wildlife trade analyst, WWF International.

The statement also calls on all WFCMS' members to promote tiger conservation and encourages them to abide by all relevant international and national regulations on wildlife trade. "The Societies' public declaration is a clear signal that the traditional Chinese medicinal community is now backing efforts to secure a future for wild tigers," said Professor Xu Hongfa, head of TRAFFIC's programme in China.

As an international traditional Chinese academic organization, the WFCMS stated that it had a duty to research the conservation of endangered species, including tigers.

"We will ask our members not to use endangered wildlife in traditional Chinese medicine, and reduce the misunderstanding and bias of the international community," said the WFCMS' Huang Jianyin. "The traditional Chinese medicine industry should look for substitutes and research on economical and effective substitutes for tiger products, which will improve the international image and status of traditional Chinese medicine and promote TCM in the world."

The WFCMS is an international academic organization based in Beijing, with 195 member organizations spanning 57 nations where traditional Chinese medicine is used. It aims to promote the development of traditional Chinese medicine, which is a primary form of healthcare delivery in China, and widely regarded as an important part of China's rich cultural heritage.

WWF and TRAFFIC are calling for a permanent ban on all trade in tiger parts and products, and for a curtailment of commercial captive breeding operations. Wild tigers are especially in the spotlight as 2010 marks the celebration of the Year of the Tiger in the Chinese lunar calendar. This year is seen as a unique opportunity to galvanize international action to save this iconic species.

Your Friday Dose of Weird: Two new Cambrian critters

Posted on: March 12, 2010 11:22 AM, by **Brian Switek** ResearchBlogging.org

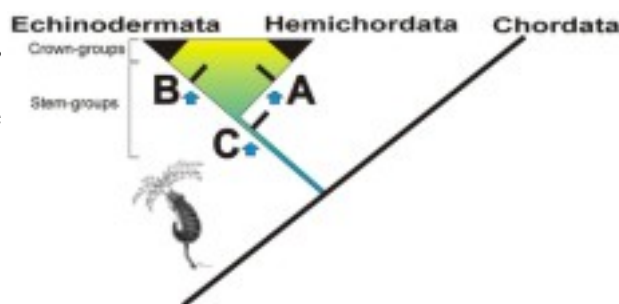
When it comes to aliens, Hollywood really does not have much imagination. Most extraterrestrials that have appeared on the big screen look very much like us, or are at least some kind of four-to-six-limbed vertebrate, and this says more about our own vanity than anything else. It would be far more interesting, I think, to take the weird and wonderful organisms of the Cambrian as inspiration for alien life forms, and two new critters have just been added to the odd Cambrian menagerie.

What was three centimeters long, had bilateral symmetry, and grew tentacles out of its head? According to paleontologists Jean-Bernard Caron, Simon Conway Morris, Degan Shu, it was *Herpetogaster collinsi*, the latest fossil to be named from the famous 505 million year old Burgess Shale of Canada. As described in PLoS One, this small invertebrate may have attached itself to sponges by way of a structure called a stolon, and there it waited for tiny prey to drift into its tentacles. The fact that so many have been found in close association suggests that they often lived in close proximity, so perhaps sponges were the hot hangout for this strange suspension feeder.



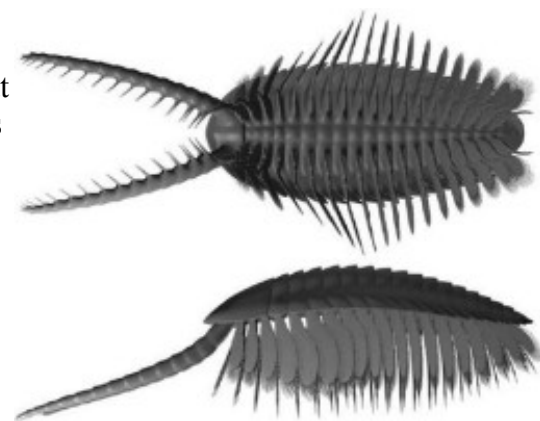
A restoration of Herpetogaster collinsi by Marianne Collins. From Caron et al, 2010.

But just what kind of animal was *Herpetogaster*? It shows some resemblance to both an enigmatic Cambrian animal from China's Chengjiang fauna named *Phlogites* and members of another group called eldoniids, but this is not especially helpful since these previously-known forms have been just as tricky to interpret. According to Caron, Conway Morris, and Shu *Herpetogaster* and its relatives could be closely related to echinoderms (sea stars, sandollars, and the like), hemichordates (worm-like organisms such as acorn worms), or then then again may be close to the common ancestor of both groups. At present it is difficult to test these competing hypotheses, but regardless of where *Herpetogaster* ultimately falls in the evolutionary tree it was certainly a fantastic creature.



Hypothetical positions of Herpetogaster collinsi and its relatives to other organisms. From Caron et al, 2010.

The other newly-announced Cambrian creature, described by Martin Stein in the *Zoological Journal of the Linnean Society*, is quite different from the small suspension feeders scrutinized by Caron and colleagues. Found in the Early Cambrian (~540-510 million years ago) rocks of North Greenland, *Kiisortoqia soperi* was an arthropod with a simple head shield, a segmented body, and two long appendages sticking out in front of it. As bizarre as it was, however, *Kiisortoqia* had affinities to both "true" arthropods and a group of marine predators called anomalocaridids, all of which had modified versions of the same grasping appendages. As yet the exact feeding habits of *Kiisortoqia* are unclear, but if it was anything like its relatives it probably snatched prey out of the water with its appendages. The spikes along the structures would have helped to impale prey, and as they coiled around the food item it would have been brought back to the mouth of *Kiisortoqia*.



Two computer-generated restorations of Kiisortoqia soperi (above- a view of its underside; below-a view from the side). From Stein, 2010.

Caron, J., Conway Morris, S., & Shu, D. (2010). *Tentaculate Fossils from the Cambrian of Canada (British Columbia) and China (Yunnan) Interpreted as Primitive Deuterostomes* PLoS ONE, 5 (3) DOI: 10.1371/journal.pone.0009586

STEIN, M. (2010). *A new arthropod from the Early Cambrian of North Greenland, with a 'great appendage'-like antennula* *Zoological Journal of the Linnean Society*, 158 (3), 477-500 DOI: 10.1111/j.1096-3642.2009.00562.x

Star Predicted to Blast Through the Solar System

By Ian O'Neill Sat Mar 13, 2010 02:40 AM ET

In 1.5 million years time, the solar system could be in for a rough ride. An orange dwarf star named Gliese 710 is powering in our direction and an astronomer has calculated an 86 percent chance of the interstellar interloper smashing through the Oort Cloud, located in the outermost reaches of our solar system. This could have the devastating effect of scattering the icy Oort Cloud objects (or OCOs), causing them to plunge toward the sun and the inner planets, potentially bombarding Earth with comets. Vadim Bobylev of the Pulkovo Astronomical Observatory in St Petersburg has published revised calculations of local star positions and velocities to arrive at this prediction.



Image: The orange dwarf approaches. Could this be the scene as Gliese 710 crashes through our solar system? (ESO)

In 1997, the European Space Agency's Hipparcos spacecraft analyzed data from 100,000 stars, compiling what is known as the Hipparcos Catalogue. 156 of these local stars are of particular interest to astronomers as the sun was thought to be a lot closer to them in the past and there is a high possibility they will make a close approach again.

In a paper submitted to the arXiv preprint service, Bobylev has combined the catalogue data with new star databases and discovered nine new stars that will buzz past the sun in the future or have done so in the past.

But one star has raised a red flag. Gliese 710 is out there and it wants to "play chicken" with our sun. Unfortunately, neither star will be able to steer out of the way at last minute.

Judging by its trajectory, there's an 86 percent chance the star will punch through the Oort Cloud (thought to be located about 50,000 AU -- or nearly a light-year -- from the sun). This may sound like a flesh wound, a near miss in cosmological distances, but any gravitational interaction with the huge chunks of cometary nuclei in the outermost extent of the solar system is bad news.

It is hypothesized that close encounters of the stellar kind have kicked OCOs out of the Oort Cloud in the past, creating some of the long period comets we see today, such as comet Hale Bopp. It is also thought that such encounters could periodically cause mass extinction events on Earth through comet impacts.

Although the star -- currently located 63 light years from Earth and approximately half the mass of our sun -- has been known to be heading for us for some time, this is the first time such a high probability for a close encounter has been calculated.

But could Gliese 710 penetrate even deeper into the solar system? Possibly, although those odds are more cheery. The chances of the star reaching as deep as the Kuiper Belt (near the orbit of Pluto) is around 1 in 1000.

This might not be an imminent threat, and it's debatable whether any human descendants will be watching the cosmic flyby, it's nice to know when the next risk of comet bombardment may occur. Although I doubt we'd be able to do much about it anyway.