

Lice genomes: Pieces of a new puzzle

Parents and school nurses take note. Lice are a familiar nuisance around the world and vectors of serious diseases, such as epidemic typhus, in developing regions. New research indicates that lice may actually be quite unique in the animal world. In a study published online in *Genome Research* (www.genome.org), scientists have analyzed the mitochondrial genome of the human body louse and discovered that it is fragmented into many pieces – a remarkable finding in animals that will surely spark discussion about how it evolved and what advantages it might confer.

The lice that plague humans (head lice, body lice, and pubic lice) fall into the category of "sucking lice," feeding on the blood of the host. Scientists have recently sequenced the genome of one of these sucking lice, the body louse (*Pediculus humanus*). With the louse genetic code mapped, researchers will be able to develop new strategies for treatment and prevention of infestation. Importantly, these sequencing efforts also included the *P. humanus* mitochondrial genome (mtDNA), and detailed analysis has revealed how genetically extreme these creatures are.

In this study, scientists from the University of Queensland and the J. Craig Venter Institute found that in stark contrast to the single circular mitochondrial chromosome typical of most animals, the human body louse has evolved a set of 18 "minichromosomes." While multiple mitochondrial minichromosomes have been previously described in plants and protists, this is the first report of an animal adopting a highly fragmented mtDNA structure.



A female human body louse (Pediculus humanus corporis) on human skin after blood feeding. Photo courtesy of Richard Webb (Centre for Microscopy and Microanalysis, University of Queensland) and Renfu Shao (Parasitology Section, School of Chemistry and Molecular Biosciences, University of Queensland).

The group also looked at mtDNA structure in other sucking lice, including human head and pubic lice, as well as sucking lice that infest other primates, and found that the mtDNA of these lice is also fragmented. Interestingly, they report that "chewing lice," closely related lice that feed on the hair or feathers of other animals, do not have fragmented mtDNA chromosomes, suggesting that multiple minichromosomes may have coevolved with blood feeding.

Dr. David Rand of Brown University, a mitochondrial DNA evolution expert, said this exciting discovery raises new questions in the field. "Why is it restricted to this lineage? Why don't we see transitional stages of this organization in related lice?" Rand also asked whether fragmented minichromosomes has implications for gene regulation. "Does this organization provide an advantage for more control over individual gene expression in mitochondrial genomes?"

Rand noted that this work and the intriguing questions raised will motivate researchers to take advantage of new technologies to investigate the mtDNA structure of other animals. "As new sequencing tools allow researchers to move away from single-gene studies to whole genome analyses of mtDNA, we may see that the sucking lice story is more common than we expected."

Scientists from the University of Queensland (Brisbane, Australia) and the J. Craig Venter Institute (Rockville, MD) contributed to this study.

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Aussie meat ants may be invasive cane toad's Achilles' heel

Ecologists in Australia have discovered that cane toads are far more susceptible to being killed and eaten by meat ants than native frogs. Their research – published in the British Ecological Society's journal *Functional Ecology* – reveals a chink in the cane toad's armour that could help control the spread of this alien invasive species in tropical Australia.

Professor Rick Shine and his colleagues Georgia Ward-Fear, Matt Greenlees and Greg Brown from the University of Sydney's Team Bufo (from the Latin name for the toxic toad) compared habitat use and activity patterns in meat ants, metamorph cane toads and seven native Australian frog species. They found that, unlike the native frogs, cane toads are poorly equipped to escape the meat ants.

According to Shine: "The spread of cane toads through tropical Australia has created major ecological problems. The ideal way to control toad numbers would be to find a predator that kills and eats toads but leaves native frogs alone. However, bringing in a predator from overseas might have catastrophic consequences, like those that occurred when cane toads themselves were brought in. So we've explored an alternative approach –

to see if we could use a native predator. Meat ants are abundant around tropical waterbodies, and we often see them eating small toads, so we suspected that there might be some kind of mismatch between the invader and its newly invaded range, for example something about the toads' behaviour that makes them vulnerable to a predator that poses little danger to native frogs."

Through a series of laboratory experiments, Team Bufo looked at when the ants, frogs and toads were most active, where they chose to live, and how good the frogs and toads were at escaping attacking meat ants. They found cane toads opt to live in open microhabitats and are active during the day, patterns that match those of meat ants. By contrast, native frogs are nocturnal and are safely ensconced in vegetation or other shelters during the day, when meat ants are on the hunt.

Cane toads are also less well equipped to escape attacking meat ants, Team Bufo found. Using a specially-built runway, they tested the frogs' and toads' sprint speed and endurance. They found that compared with the quick and nimble native frogs, cane toads' hops are shorter and slower due to their shorter shin bones. Native frogs were also more vigilant for meat ants than cane toads, they discovered.

The results are interesting not only because they reveal the cane toad's Achilles' heel – a weakness that could be exploited to help control the spread of the toxic toad – but because the same "evolutionary trap" could be used to snare invasive species elsewhere.

"The end result of this mismatch between traits of metamorph cane toads, which evolved in the Americas, and the ecological interaction between metamorph toads and meat ants in tropical Australia, is an 'evolutionary trap'. That is, characteristics that increased toad survival where they evolved in the Americas are now a disadvantage, because the toads are facing different challenges in Australia – challenges they have not evolved to deal with. Such evolutionary traps should be especially common for invasive species, because so many aspects of their environment differ from those in which the traits of that species evolved," says Shine.

Georgia Ward-Fear et al (2009). Maladaptive traits in invasive species: in Australia, cane toads are more vulnerable to predatory ants than are native frogs, Functional Ecology, doi: 10.1111/j.1365-2435.2009.01556.x, is published online on 31 March 2009.

Handwashing more important than isolation in controlling MRSA superbug infection

Regular handwashing by hospital staff and visitors did more to prevent the spread of the MRSA superbug than isolating infected patients.

At the Society for General Microbiology meeting in Harrogate today (Tuesday 31 March), Dr Peter Wilson from University College Hospital, London, reported on a year-long study in two hospital intensive care units. In the middle six months of the year patients with MRSA were not moved to single rooms or nursed in separate MRSA bays. The rates of cross infection with MRSA were compared to the periods when patients were moved. Patients were tested for MRSA weekly and hand hygiene by staff and visitors audited and encouraged. There was no evidence of increased transmission of infection when patients were not moved.

Moving seriously-ill patients when they are identified as having MRSA can be hazardous and it involves ward staff in extra hygiene measures.

MRSA are *Staphylococcus aureus* bacteria that are resistant to the methicillin class of antibiotics. Many people carry these bacteria and it is generally not harmful if they are healthy. MRSA can cause serious illness in patients with weak or damaged immune systems and the elderly and it is widespread in hospitals. Treatment options are limited and it is vitally important to develop strategies to stop the spread of MRSA in healthcare environments.

"If a patient carrying MRSA is critically ill, moving them to a single room is less of a priority than clinical care," said Dr Wilson. "If the criteria are strictly applied, compliance with hand hygiene practices on intensive care units is less than on a general ward because of the very high number of contacts per hour. Another study is needed in a general ward where a high level of compliance with hand hygiene is easier to achieve."

Colon cancer and the microbes in your gut

A typical Western diet, rich in meat and fats and low in complex carbohydrates, is a recipe for colon cancer, Professor Stephen O'Keefe from the University of Pittsburgh, USA, told the Society for General Microbiology meeting at Harrogate today (Tuesday 31 March). He described an expanding body of evidence to show that the composition of the diet directly influences the diversity of the microbes in the gut, providing the link between diet, colonic disease and colon cancer.

People eating a healthy diet containing high levels of complex carbohydrate had significant populations of micro-organisms in their gut called Firmicutes. These bacteria use the undigested residues of starch and proteins in the colon to manufacture short-chain fatty acids and vitamins such as folate and biotin that maintain colonic health. One of these fatty acids, butyrate, not only provides most of the energy to maintain a healthy gut

wall, but it also regulates cell growth and differentiation. Both experimental and human studies support its role in reducing colon cancer risk.

However, gut microbes may also make toxic products from food residues. Diets high in meat will produce sulphur - this decreases the activity of 'good' bacteria that use methane and increases the production of hydrogen sulphide and other possible carcinogens by sulphur-reducing bacteria.

"Colon cancer is the second leading cause of cancer-related deaths in adults in Westernized communities." said Professor O'Keefe, "Our results suggest that a diet that maintains the health of the colon wall is also one that maintains general body health and reduces heart disease".

"A diet rich in fibre and resistant starch encourages the growth of good bacteria and increases production of short chain fatty acids which lessen the risk of cancer, while a high meat and fat diet reduces the numbers of these good bacteria." Professor O'Keefe went on. "Our investigations to date have focused on a small number of bacterial species and have therefore revealed but the tip of the iceberg, our colons harbour over 800 bacterial species and 7,000 different strains. The characterization of their properties and metabolism can be expected to provide the key to colonic health and disease".

Study shows that allergic reactions to Plavix can be treated with steroids and antihistamines

Discontinuation of the popular drug plavix due to allergy can be fatal for stent patients

PHILADELPHIA – A clinical study of cardiac patients who suffered an allergic reaction to the widely-prescribed drug clopidogrel, also known by the pharmaceutical name Plavix, found that treatment with a combination of steroids and antihistamines can alleviate the allergic reaction symptoms thereby allowing patients to remain on the drug, say doctors from Thomas Jefferson University Hospital. The study followed 24 patients, who developed Plavix allergies after undergoing coronary stent procedures. Eighty-eight percent (21 of 24) were able to stay on Plavix uninterrupted after being treated with the antihistamines and a short course of steroids. Primary Investigator Michael P. Savage, M.D., director, Cardiac Catheterization Laboratory at Thomas Jefferson University Hospital and Kimberly L. Campbell, M.D., cardiology fellow and lead author, presented their findings at the American College of Cardiology's Annual Scientific Session on March 30 2009.

"This is a very important study for many cardiac patients but especially those with stents," said Savage. "Every patient who receives a stent must take Plavix to help prevent stent thrombosis which is clotting of the stent. This obviously poses major problems if the patient suffers an allergic reaction to the medication. To discontinue taking the drug can lead to a heart attack which may be fatal. Those with a drug eluting stent are required to be on the drug for at least one year. Our patients with drug eluting stents actually averaged 17 months on Plavix versus the minimum of one year. That's a very long time to not be on a medication that may save your life."

Plavix is one of the most prescribed drugs world-wide. Data from 2007 shows Plavix is the fourth most sold drug in the United States with almost four billion dollars in sales, according to IMS Health, a leading pharmaceutical industry monitoring company. It is estimated that about six percent of those taking the drug showed some signs of an allergic reaction.

John R. Cohn, M.D., chief of Adult Allergy at Thomas Jefferson University and Hospitals and a key contributor to the study noted, "Previously, when patients had an allergic reaction to Plavix we would give an alternative drug but they can have their own side effects. Rather than giving the secondary drug we concentrated on suppressing the patient's allergic symptoms they were having to Plavix by administering low doses of steroids and antihistamines while continuing the drug. What we found was that most of our patients became tolerant to Plavix, essentially becoming 'desensitized' to the drug enabling them to continue treatment. Once this occurred we were able to discontinue the steroids and even the antihistamines."

Previous anecdotal studies showed some evidence that patients could be desensitized to Plavix, but this is the first systematic study to demonstrate allergy to the drug could be managed without stopping the drug after a reaction was found.

"The saying goes 'necessity is the mother of invention' and that's exactly what we have here," said Campbell. "Plavix is a necessity in treating many cardiac patients, especially those with stents. Patients with allergic reactions have few alternatives and stopping Plavix can result in life-threatening complications. We needed to find a way to keep Plavix-allergic cardiac patients on this drug to help ensure positive cardiovascular outcomes and in this small group we did. Hopefully, in the future, we can expand the study and investigate ways to apply this in treating allergic reactions to other life-saving drugs."

Optimal Running Speed Associated With Evolution Of Early Human Hunting Strategies

ScienceDaily - Runners, listen up: If your body is telling you that your pace feels a little too fast or a little too slow, it may be right.

A new study, published online March 18 in the *Journal of Human Evolution*, shows that the efficiency of human running varies with speed and that each individual has an optimal pace at which he or she can cover the greatest distance with the least effort.

The result debunks the long-standing view that running has the same metabolic cost per unit of time no matter the speed - in other words, that the energy needed to run a given distance is the same whether sprinting or jogging. Though sprinting feels more demanding in the short term, the longer time and continued exertion required to cover a set distance at a slower pace were thought to balance out the difference in metabolic cost, says Karen Steudel, a zoology professor at the University of Wisconsin-Madison.

However, Steudel and Cara Wall-Scheffler of Seattle Pacific University have now shown that the energetic demands of running change at different speeds. "What that means is that there is an optimal speed that will get you there the cheapest," metabolically speaking, Steudel says.

Peak efficiency was determined by measuring runners' metabolic rates at a range of speeds enforced by a motorized treadmill. Metabolic energy costs increased at both fast and slow speeds and revealed an intermediate pace of maximal efficiency.

The most efficient running speed determined in the study varied between individuals but averaged about 8.3 miles per hour for males and 6.5 miles per hour for females in a group of nine experienced amateur runners. Much of the gender difference may be due to variations in body size and leg length, which have been shown to affect running mechanics, Steudel says. In general, the larger and taller runners had faster optimum speeds.

Interestingly, the slowest speeds - around 4.5 miles per hour, or about a 13-minute mile - were the least metabolically efficient, which Steudel attributes to the gait transition between walking and running. For example, she points out, both a very fast walk and a very slow run can feel physically awkward.

While holding great interest for athletes and trainers, the mechanics of running may also hold clues to the evolution of the modern human body form: tall and long-limbed with broad chests and defined waists.

Modern humans are very efficient walkers and fairly good runners, Steudel says, and efficient locomotion probably provided our ancestors with an advantage for hunting and gathering food. Distant ancestral forms, the australopithecines, had shorter, boxier frames with stubbier legs.

"They wouldn't have had noticeable waists - their torso looked more like the torso of an ape, except they were walking on two legs," Steudel says. "With the genus *Homo*, you start getting taller individuals, larger individuals, and they started developing a more linear body form" with distinct waists that pivot easily, allowing longer and more efficient strides.

Human walking is also known to have an optimally efficient speed, so the new findings may help researchers determine the relative importance of the different gaits in driving human evolution, Steudel says. "This is a piece in the question of whether walking or running was more important in the evolution of the body form of the genus *Homo*."

Journal reference: 1. Karen L., Steudel-Numbers; Cara M., Wall-Scheffler. *Optimal running speed and the evolution of hominin hunting strategies. Journal of Human Evolution, 2009; DOI: 10.1016/j.jhevol.2008.11.002*

Study of cat diet leads to key nervous system repair discovery

MADISON - Scientists studying a mysterious neurological affliction in cats have discovered a surprising ability of the central nervous system to repair itself and restore function.

In a study published today (March 30, 2009) in the *Proceedings of the National Academy of Sciences*, a team of researchers from the University of Wisconsin-Madison reports that the restoration in cats of myelin - a fatty insulator of nerve fibers that degrades in a host of human central nervous system disorders, the most common of which is multiple sclerosis - can lead to functional recovery.

"The fundamental point of the study is that it proves unequivocally that extensive remyelination can lead to recovery from a severe neurological disorder," says Ian Duncan, the UW-Madison neuroscientist who led the research. "It indicates the profound ability of the central nervous system to repair itself."

The finding is important because it underscores the validity of strategies to reestablish myelin as a therapy for treating a range of severe neurological diseases associated with the loss or damage of myelin, but where the nerves themselves remain intact.

Myelin is a fatty substance that forms a sheath for nerve fibers, known as axons, and facilitates the conduction of nerve signals. Its loss through disease causes impairment of sensation, movement, cognition and other functions, depending on which nerves are affected.

The new study arose from a mysterious affliction of pregnant cats. A company testing the effects on growth and development in cats using diets that had been irradiated reported that some cats developed severe neurological dysfunction, including movement disorders, vision loss and paralysis. Taken off the diet, the cats recovered slowly, but eventually all lost functions were restored.

"After being on the diet for three to four months, the pregnant cats started to develop progressive neurological disease," says Duncan, a professor of medical sciences at the UW-Madison School of Veterinary Medicine and an authority on demyelinating diseases. "Cats put back on a normal diet recovered. It's a very puzzling demyelinating disease."

The afflicted cats were shown to have severe and widely distributed demyelination of the central nervous system, according to Duncan. And while the neurological symptoms exhibited by the cats are similar to those experienced by humans with demyelination disorders, the malady does not seem to be like any of the known myelin-related diseases of humans.

In cats removed from the diet, recovery was slow, but all of the previously demyelinated axons became remyelinated. The restored myelin sheaths, however, were not as thick as healthy myelin, Duncan notes.

"It's not normal, but from a physiological standpoint, the thin myelin membrane restores function," he says. "It's doing what it is supposed to do."

Knowing that the central nervous system retains the ability to forge new myelin sheaths anywhere the nerves themselves are preserved provides strong support for the idea that if myelin can be restored in diseases such as multiple sclerosis, it may be possible for patients to regain lost or impaired functions: "The key thing is that it absolutely confirms the notion that remyelinating strategies are clinically important," Duncan says.

The exact cause of the neurological affliction in the cats on the experimental diet is unknown, says Duncan, who was not involved in the original study of diet.

"We think it is extremely unlikely that [irradiated food] could become a human health problem," Duncan explains. "We think it is species specific. It's important to note these cats were fed a diet of irradiated food for a period of time."

In addition to Duncan, authors of the new PNAS study include Alexandra Brower of the Wisconsin Veterinary Diagnostic Laboratory; Yoichi Kondo and Ronald Schultz of the UW-Madison School of Veterinary Medicine; and Joseph Curlee, Jr. of Harlan Laboratories in Madison.

New theory on largest known mass extinction in the history of the earth

Did volatile halogenated gases from giant salt lakes at the end of the Permian Age lead to a mass extinction of species?
LEIPZIG/HEIDELBERG. The largest mass extinction in the history of the earth could have been triggered off by giant salt lakes, whose emissions of halogenated gases changed the atmospheric composition so dramatically that vegetation was irretrievably damaged. At least that is what an international team of scientists have reported in the most recent edition of the "Proceedings of the Russian Academy of Sciences". At the Permian/Triassic boundary, 250 million years ago about 90 percent of the animal and plant species ashore became extinct. Previously it was thought that volcanic eruptions, the impacts of asteroids, or methane hydrate were instigating causes. The new theory is based on a comparison with today's biochemical and atmospheric chemical processes. "Our calculations show that airborne pollutants from giant salt lakes like the Zechstein Sea must have had catastrophic effects at that time", states co-author Dr. Ludwig Weißflog from the Helmholtz-Center for Environmental Research (UFZ). Forecasts predict an increase in the surface areas of deserts and salt lakes due to climate change. That is why the researchers expect that the effects of these halogenated gases will equally increase.

The team of researchers from Russia, Austria, South Africa and Germany investigated whether a process that has been taking place since primordial times on earth could have led to global mass extinctions, particularly at the end of the Permian. The starting point for this theory was their discovery in the south of Russia and South Africa that microbial processes in present-day salt lakes naturally produce and emit highly volatile halocarbons such as chloroform, trichloroethene, and tetrachloroethene. They transcribed these findings to the Zechstein Sea, which about 250 million years ago in the Permian Age, was situated about where present day Central Europe is. The Zechstein Sea with a total surface area of around 600.000 km² was almost as large as France is today. The hyper saline flat sea at that time was exposed to a predominantly dry continental desert climate and intensive solar radiation - like today's salt seas. "Consequently, we assume that the climatic, geo-chemical and microbial conditions in the area of the Zechstein Sea were comparable with those of the present day salt seas that we investigated," Weißflog said.

In their current publication the authors explain the similarities between the complex processes of the CO₂-cycle in the Permian Age as well as between global warming from that time and at present. Based on comparable calculations from halogenated gas emissions in the atmosphere from present-day salt seas in the

south of Russia, the scientists calculated that from the Zechstein Sea alone an annual VHC emissions rate of at least 1.3 million tonnes of trichloroethene, 1.3 million tonnes of tetrachloroethene, 1.1 million tonnes of chloroform as well as 0.050 million tonnes of methyl chloroform can be assumed. By comparison, the annual global industrial emissions of trichloroethene and tetrachloroethene amount to only about 20 percent of that respectively, and only about 5 percent of the chloroform from the emissions calculated for the Zechstein Sea by the scientists. Incidentally, the industrial production of methyl chloroform, which depletes the ozone layer, has been banned since 1987 by regulation of the Montreal Protocol.

"Using steppe plant species we were able to prove that halogenated gases contribute to speeding up desertification: The combination of stress induced by dryness and the simultaneous chemical stressor 'halogenated hydrocarbons' disproportionately damages and destabilize the plants and speeds up the process of erosion," Dr. Karsten Kotte from the University of Heidelberg explained.

Based on both of these findings the researchers were able to form their new hypothesis: At the end of the Permian Age the emissions of halogenated gases from the Zechstein Sea and other salt seas were responsible in a complex chain of events for the world's largest mass extinction in the history of the earth, in which about 90 percent of the animal and plant species of that time became extinct.

According to the forecast from the International Panel on Climate Change (IPCC), increasing temperatures and aridity due to climate change will also speed up desertification, increasing with it the number and surface area of salt seas, salt lagoons and salt marshlands. Moreover, this will then lead to an increase in naturally formed halogenated gases. The phytotoxic effects of these substances become intensified in conjunction with other atmospheric pollutants and at the same time increasing dryness and exponentiate the eco-toxicological consequences of climate change.

The new theory could be like a jigsaw piece that contributes to solving the puzzle of the largest mass extinction in the history of the earth. "The question as to whether the halogenated gases from the giant salt lakes alone were responsible for it or whether it was a combination of various factors with volcanic eruptions, the impact of asteroids, or methane hydrate equally playing their role still remains unanswered," Ludwig Weißflog said. What is fact however is that the effects of salt seas were previously underestimated. In their publication the researchers working with Dr. Ludwig Weißflog from the UFZ and Dr. Karsten Kotte from the University of Heidelberg want to prove that recent salt lakes and salt deserts of south-east Europe, Middle Asia, Australia, Africa, America can not only influence the regional but also the global climate. The new findings on the effects of these halogenated gases are important for revising climate models, which form the basis for climate forecasts.

'Polypill' brings benefit of five drugs for the hassle of one

* 17:55 30 March 2009 by Linda Geddes

A "polypill" containing three blood-pressure-lowering drugs, as well as a statin and aspirin, could slash the risk of heart attack and stroke in healthy people. That's the implication of a study of 2053 people – the first time a pill containing so many drugs has been tested in a large group of adults.

The idea of a polypill is to try and treat multiple components of cardiovascular disease all at once, reducing the number of separate medications people have to take, and therefore increasing compliance.

Salim Yusuf at McMaster University in Hamilton, Canada, and his colleagues tested the five-drug polypill – called Polycap – in healthy individuals with one cardiovascular risk factor, such as being overweight, having smoked in the past five years, or having type-2 diabetes.

"This is equivalent to your average Joe or Jane walking down the street," says Christopher Cannon at Brigham and Women's Hospital in Boston, Massachusetts, who was not involved in the study.

'Reduce heart burden'

The pill reduced systolic (peak) blood pressure by 7.4 millimetres of mercury and diastolic (minimum) blood pressure by 5.6 mm Hg over three months – similar to when all three blood pressure drugs were given individually.

It also reduced heart rate and blood clotting to a similar degree as aspirin or the beta-blocker atenolol achieve when given individually, and cut cholesterol – although not as much as when a statin was given on its own.

This may be because the formulation of the pill interfered with its absorption. Importantly, the side-effects of the polypill were similar to when the drugs were given individually.

The next step is to test the polypill in a larger group, over a longer period of time to see if it cuts heart attacks and stroke.

"This study takes a first and crucial step forward and raises hope that, in conjunction with other global efforts to improve diet and exercise, the polypill could one day substantially reduce the burden of cardiovascular disease in the world," says Cannon. *Journal reference: The Lancet (DOI: 10.1016/S0140-6736(09)60611-5)*

Oxycodone effective against shingles pain

The painkiller oxycodone is effective at treating the acute pain of shingles, an illness that often causes severe pain which can become long-lasting and sometimes even permanent.

The study, published in the April issue of the journal *Pain*, is one of the first to carefully evaluate different methods to relieve pain during a course of shingles, which many patients say causes the worst pain they have ever experienced. Effective pain treatment is crucial. Not only can the pain of shingles disrupt people's quality of life, but it is also possible that the less effectively the pain is treated, the more likely it will become a long-term problem that can change a person's life forever.

Shingles is caused by reactivation of the varicella zoster virus, the same bug that causes chicken pox, and only people who have had chicken pox are vulnerable to shingles. About 20 to 30 percent of people will get shingles at some point in their lives; the odds climb to 50 percent for people who live to the age of 85.

For most patients, the first symptom of the infection is pain, quickly followed by a rash where the pain first appeared. The rash appears most often on one side of the chest or face, oftentimes causing dozens of small pimple-sized lesions. Some patients also get flu-like symptoms like a headache and lethargy. The illness usually lasts about three or four weeks.

Pain is the hallmark and typically the most troubling symptom. Nearly all patients hurt to some degree, some severely. It's a mix of pain that results from damage to nerves – known as neuropathic pain – as well as inflammatory pain in the skin and surrounding tissues.

"Oftentimes patients are told that the rash will heal in two or three weeks anyway, and the pain will go away, so they're not given something for the pain unless it's excruciating," said Robert Dworkin, Ph.D., the University of Rochester Medical Center pain expert who led the study. "But moderate pain can stop people from working, or enjoying their hobbies, and it can also make some people depressed or anxious. So there's good reason to treat all pain from the infection."

Doctors have a variety of choices to treat shingles pain. Medications like ibuprofen or acetaminophen are often used. More severe cases might call for use of Tylenol with codeine or oxycodone. But there haven't been placebo-controlled studies done to prove that any of these drugs actually work to treat shingles pain, said Dworkin, who is professor of Anesthesiology, Neurology, Oncology, and Psychiatry, and director of the Anesthesiology Clinical Research Center.

So Dworkin and colleagues studied 87 shingles patients in Rochester, N.Y., and Houston, Texas. The team studied the effectiveness of oxycodone and gabapentin, which both effectively treat pain associated with nerve damage.

The participants were divided into three groups and received oxycodone, gabapentin, or placebo. Patients, whose average age was 66, had moderate to severe pain. All patients also received an antiviral medication, which is standard treatment for patients with the infection.

The team found that oxycodone was quite effective. Patients taking the medication, which is sold as Oxycontin but is also available in other formulations, were more than twice as likely to experience a meaningful reduction in their pain – at least a 30-percent decrease – compared to their counterparts taking a placebo. Though the medication was effective, nearly one-third of the participants on oxycodone withdrew from the study, mainly because of problems with constipation.

The team was surprised that gabapentin did not appear useful to treat pain. Dworkin said it's possible that a higher dose would be necessary to adequately treat shingles pain. But the medication must be increased over the course of three weeks or more, which is often too long to have much of an effect on a fast-moving infection like shingles that can run its course in a few weeks.

The team chose to study oxycodone and gabapentin because they are often effective for treating patients in whom the severe pain of shingles persists for months or even years. In that condition, known as postherpetic neuralgia, the virus damages nerves during the shingles infection, and the pain then persists long after the shingles rash heals. The result can be terrible shooting pain, burning pain, the sensation of electric shocks in the body, or skin that is extremely sensitive to light touch.

"For some patients, even the light touch of a Q tip on their skin is excruciating," said Dworkin.

The shingles patients most likely to develop postherpetic neuralgia are those who are older, who have a more extensive rash, or who have severe pain during the initial illness. That's a big reason why initial pain treatment may be so crucial, Dworkin said.

Doctors estimate that overall, about 1 out of 4 or 5 patients with shingles who are treated quickly with antiviral medications will develop postherpetic neuralgia. For older patients not treated with antivirals, the odds of getting postherpetic neuralgia jump to 40 to 50 percent.

It was Dworkin who, in 2007, headed a group that published the first international consensus guidelines for treating shingles. The guidelines call for definite use of antiviral medications in all patients older than 50 years of age, and in younger patients under certain conditions, as well as consideration of a broad group of medications ranging from over-the-counter drugs like ibuprofen to Tylenol with codeine or oxycodone.

In 2007 he also led an international group of scientists who came out with the first international treatment guidelines for neuropathic pain. He is the founder of the International Conference on the Mechanisms and Treatment of Neuropathic Pain, which meets annually.

Funding from the National Institute of Neurological Disorders and Stroke provided the impetus for the study, which was funded directly by Novartis and Pfizer. Endo, Novartis, Pfizer, and Purdue Pharma provided medications and placebo for the study. In the past year, Dworkin has consulted with or spoken on behalf of Endo and Pfizer as well as several other companies and organizations that fund pain research or produce medications designed to alleviate pain.

In addition to Dworkin, other authors include, from Rochester, Richard Barbano, Karl Kiebertz and Cornelia Kamp of Neurology; Robert Betts of Medicine; Janet Pennella-Vaughan of Anesthesiology; and Michael McDermott and Carrie Irvine of the Department of Biostatistics and Computational Biology.

Other authors include Stephen Tyring of University of Texas Health Science Center; Gary Bennett of McGill University; Erhan Berber of Novartis Pharmaceuticals; John Gnann of the University of Alabama at Birmingham; Mitchell Max of the University of Pittsburgh; and Kenneth Schmader of Duke University.

Subsurface ice on Mars exposed by recent impacts

* 19:22 30 March 2009 by **Kelly Beatty, The Woodlands, SkyandTelescope.com**

Impacts are the most ubiquitous geologic features in our solar system. Roughly 1600 named craters (and countless lesser pits) scar the Moon's ancient surfaces. On Earth, where wind and water continually wear down the land, the census of confirmed impact craters stands at just 176.

Mars, a mixed bag of ancient and modern terrains, lies somewhere in between. Over the years spacecraft have glimpsed ever-finer features in the Martian landscape. These days, the HiRISE camera aboard NASA's Mars Reconnaissance Orbiter (MRO) can pick out objects only 0.3 metres in size; the High Resolution Stereo Camera on the European Space Agency's Mars Express is no slouch either, with a ground resolution of 2 metres.

So HiRISE researchers were elated, but not particularly surprised, to discover some small, freshly gouged craters in images taken in 2008. Seen at five sites over a latitude range of 43° to 56° north, the excavations are typically 3 to 6 metres across and a third to two-thirds of a metre deep. One cluster must have appeared sometime between June and August, and a somewhat larger pit showed up between January and September.

What did astound the team were splashes of white seen in and around a handful of these craterlets. Could it be water ice? Colleagues operating the spacecraft's CRISM instrument soon confirmed, for the one case large enough to yield a spectrum, that it was! Apparently fist-sized impactors had punched into a layer of ice hidden by a topping of dust about a third of a metre deep.



Formed sometime between January and September 2008, this fresh crater has dredged up barely buried water ice and splashed it onto the Martian surface. The HiRISE camera aboard NASA's Mars Reconnaissance Orbiter recorded this colour close-up image on 1 November 2008. The scene is about 30 metres across. Image: NASA/JPL/University of Arizona

Disappearing act

In the months that followed, these snowy splashes gradually faded from view. Water ice isn't stable at the craters' latitudes, so most likely it gradually sublimated, or vaporised, into the atmosphere, leaving behind a veneer of any dust that had been mixed with it.

The disappearing act might also be due in part to a coating of dust blown in from the atmosphere. Either way, notes HiRISE investigator Shane Byrne of the University of Arizona, the icy deposits had to be at least a couple of inches (several centimetres) thick, and they couldn't have been unearthed from more than a foot or two (0.3-0.6 m) down.

Byrne announced these findings on Friday at the Lunar and Planetary Science Conference in The Woodlands, Texas. He points out that prior surveys, particularly one done by the neutron spectrometer aboard NASA's Mars Odyssey orbiter, show that vast reservoirs of ice lay barely buried across most of the planet's polar and mid-latitude regions.

So close

But scientists are only now realising just how near the surface the ice lies – and how easily it can be reached. When NASA's Phoenix lander dropped onto a northern polar plain last May, its braking engine blew off a few inches of loose dirt and revealed slabs of nearly pure ice.

The irony in all this is that the Viking 2 lander, which arrived in September 1976, sits just 800 km southeast of the ice-splashed craterlet shown above, and scientists now realise that a layer of water ice almost certainly lies not far beneath its footpads.

"It's probably just tens of centimetres down," says HiRISE team leader Alfred McEwen. Had Viking's sampling scoop been able to dig a little deeper, he adds, "we might have sampled ice on Mars 30 years ago."

Courtesy of Sky and Telescope magazine

Time of conception linked to birth defects in United States

INDIANAPOLIS – A study published in the April 2009 issue of the medical journal *Acta Pædiatrica* is the first to report that birth defect rates in the United States were highest for women conceiving in the spring and summer. The researchers also found that this period of increase risk correlated with increased levels of pesticides in surface water across the United States.

Studying all 30.1 million births which occurred in the U.S. between 1996 and 2002, the researchers found a strong association between the increased number of birth defects in children of women whose last menstrual period occurred in April, May, June or July and elevated levels of nitrates, atrazine and other pesticides in surface water during the same months. While many of these chemicals, including the herbicide atrazine which is banned in European countries but permitted in the U.S., are suspected to be harmful to the developing embryo, this is the first study to link their increased seasonal concentration in surface water with the peak in birth defects in infants conceived in the same months.

The correlation between the month of last menstrual period and higher rates of birth defects was statistically significant for half of the 22 categories of birth defects reported in a Centers for Disease Control database from 1996 to 2002 including spina bifida, cleft lip, clubfoot and Down's syndrome.

"Elevated concentrations of pesticides and other agrochemicals in surface water during April through July coincided with significantly higher risk of birth defects in live births conceived by women whose last menstrual period began in the same months. While our study didn't prove a cause and effect link, the fact that birth defects and pesticides in surface water peak during the same four months makes us suspect that the two are related," said Paul Winchester, M.D., Indiana University School of Medicine professor of clinical pediatrics, the first author of the study.

"Birth defects, which affect about 3 out of 100 newborns in the U.S., are one of the leading causes of infant death. What we are most excited about is that if our suspicions are right and pesticides are contributing to birth defect risk, we can reverse or modify the factors that are causing these lifelong and often very serious medical problems," said Dr. Winchester, a Riley Hospital for Children neonatologist.

Birth defects are known to be associated with risk factors such as alcohol, smoking, diabetes or advanced age. However, the researchers found that even mothers who didn't report these risk factors had higher overall birth defect rates for babies conceived from April to July.

The study relies on findings by U.S. Geological Survey, the U.S. Environmental Protection Agency and other agencies on the seasonal variations in nitrates, atrazine and other pesticides in the surface water.

"These observations by Dr. Winchester are extremely important, as they raise the question for the first time regarding the potential adverse effect of these commonly used chemicals on pregnancy outcome – the health and well-being of our children," said James Lemons, M.D., Hugh McK. Landon Professor of Pediatrics at the IU School of Medicine. Dr. Lemons is director of the section of neonatal-perinatal medicine at Riley Hospital. *Co-authors of this study, which was funded by the Division of Neonatology of the Department of Pediatrics of the IU School of Medicine, were Jordan Huskins, B.A., a fourth year I.U. School of Medicine student, and Jun Ying, Ph.D. of the University of Cincinnati.*

Researchers discover link between schizophrenia and diabetes

Jennifer Hilliard - 2009 March 30

AUGUSTA, Ga. – People with schizophrenia are at increased risk for type 2 diabetes, Medical College of Georgia researchers have found.

In a study of 50 people newly-diagnosed with schizophrenia or a related psychotic disorder with no other known risk factors, 16 percent had either diabetes or an abnormal rate of glucose metabolism, says Dr. Brian Kirkpatrick, vice chair of the MCG Department of Psychiatry and Health Behavior. In a similar size control group of people without schizophrenia, none had signs of or had developed the disease.

People with diabetes cannot produce or properly use insulin, a hormone that converts glucose, starches and other food into energy.

“These findings point toward there being some shared environmental factors or genetic factors between the development of schizophrenia and diabetes,” he says.

Dr. Kirkpatrick presented his findings at the International Congress on Schizophrenia Research in San Diego March 28-April 1.

Researchers have long suspected that schizophrenia led to an increased risk of diabetes, Dr. Kirkpatrick says.

To find out whether there was a link, he and colleagues at the University of Barcelona in Spain and the University of Maryland administered a two-hour oral glucose test to patients who had not yet been placed on anti-psychotic medication. Catching them before prescriptive treatment was important because researchers already knew that some of the most effective schizophrenia drugs also cause rapid weight gain – a risk factor for type 2 diabetes. “We know the medicine causes problems but we wanted to know whether the disease also causes them,” he says.

Schizophrenia symptoms include memory and attention problems, hallucinations, disorganized thinking and behavior and delusions. Psychotic symptoms typically start in late adolescence and early adulthood. But researchers believe that developmental abnormalities they don’t yet know about also increase diabetes risk.

One recent study – based on data from the Clinical Antipsychotic Trials of Intervention Effectiveness Schizophrenia Trial – showed the prevalence rate of metabolic syndrome, a group of risk factors that include abdominal obesity, high lipid and cholesterol blood levels and insulin resistance, is more than 50 percent in women and about 37 percent in men with schizophrenia.

“Many people focus on the brain function part of the disease, but patients also have other medical problems that can’t be attributed to other factors,” Dr. Kirkpatrick says. “Bad things that happen in utero and at birth, such as prenatal famine and low birth weight, have both been shown to increase the risk of diabetes and schizophrenia. Problems in early development can leave a lasting impact.”

Establishing the link between the diseases may help scientists further understand the genetics of schizophrenia, he says.

“And that may eventually enable some sort of intervention strategy.”

A little java makes it easier to jive, researcher says

CHAMPAIGN, Ill. - Stopping to smell the coffee – and enjoy a cup of it – before your morning workout might do more than just get your juices flowing. It might keep you going for reasons you haven't even considered.

As a former competitive cyclist, University of Illinois kinesiology and community health professor Robert Motl routinely met his teammates at a coffee shop to fuel up on caffeine prior to hitting the pavement on long-distance training rides.

"The notion was that caffeine was helping us train harder ... to push ourselves a little harder," he said.

The cyclists didn't know why it helped, they just knew it was effective.

"I think intuitively a lot of people are taking caffeine before a workout and they don't realize the actual benefit they're experiencing. That is, they're experiencing less pain during the workout," Motl said.

He said it's becoming increasingly common for athletes – before competing – to consume a variety of substances that include caffeine, motivated by "the notion that it will help you metabolize fat more readily."

"That research isn't actually very compelling," Motl said. "What's going on in my mind is ... people are doing it for that reason, but they actually take that substance that has caffeine and they can push themselves harder. It doesn't hurt as much."

The U. of I. professor has been investigating the relationship between caffeine and physical activity since taking a slight detour during his doctoral-student days, when his work initially was focused on exploring possible links between caffeine intake, spinal reflexes and physical activity.

Seven years later, with several studies considering the relationship between physical activity and caffeine behind him, Motl has a much better understanding of why that cuppa Joe he used to consume before distance training and competing enhanced his cycling ability.

Early in his research, he became aware that "caffeine works on the adenosine neuromodulatory system in the brain and spinal cord, and this system is heavily involved in nociception and pain processing." Since Motl knew caffeine blocks adenosine from working, he speculated that it could reduce pain.

A number of studies by the U. of I. professor support that conclusion, including investigations considering such variables as exercise intensity, dose of caffeine, anxiety sensitivity and gender.

Motl's latest published study on the effects of caffeine on pain during exercise appears in the April edition of the International Journal of Sport Nutrition and Exercise Metabolism.

"This study looks at the effects of caffeine on muscle pain during high-intensity exercise as a function of habitual caffeine use," he said. "No one has examined that before."

"What we saw is something we didn't expect: caffeine-naïve individuals and habitual users have the same amount of reduction in pain during exercise after caffeine (consumption)."

The study's 25 participants were fit, college-aged males divided into two distinct groups: subjects whose everyday caffeine consumption was extremely low to non-existent, and those with an average caffeine intake of about 400 milligrams a day, the equivalent of three to four cups of coffee.

After completing an initial exercise test in the lab on an ergometer, or stationary cycle, for determination of maximal oxygen consumption or aerobic power, subjects returned for two monitored high-intensity, 30-minute exercise sessions.

An hour prior to each session, cyclists – who had been instructed not to consume caffeine during the prior 24-hour period – were given a pill. On one occasion, it contained a dose of caffeine measuring 5 milligrams per kilogram of body weight (equivalent to two to three cups of coffee); the other time, they received a placebo.

During both exercise periods, subjects' perceptions of quadriceps muscle pain was recorded at regular intervals, along with data on oxygen consumption, heart rate and work rate.

"What's interesting," Motl said, "is that when we found that caffeine tolerance doesn't matter, we were perplexed at first. Then we looked at reviews of the literature relative to caffeine and tolerance effects across a variety of other stimuli. Sometimes you see them, sometimes you don't. That is, sometimes regular caffeine use is associated with a smaller response, whereas, other times, it's not."

No one's been able to figure out the reason for the inconsistency, Motl said.

"Clearly, if you regularly consume caffeine, you have to have more to have that bigger, mental-energy effect. But the tolerance effect is not ubiquitous across all stimuli. Even brain metabolism doesn't show this tolerance-type effect. That is, with individuals who are habitual users versus non-habitual users, if you give them caffeine and do brain imaging, the activation is identical. It's really interesting why some processes show tolerance and others don't."

Regarding the outcome of the current research, he said, "it may just be that pain during exercise doesn't show tolerance effects to caffeine."

Motl said one of the next logical steps for his research team would be to conduct studies with rodents in order to better understand the biological mechanism for caffeine in reducing pain.

"If we can get at the biological mechanism, we can begin to understand why there may or may not be this kind of tolerance."

Motl said another research direction might be to determine caffeine's effect on sport performance.

"We've shown that caffeine reduces pain reliably, consistently during cycling, across different intensities, across different people, different characteristics. But does that reduction in pain translate into an improvement in sport performance?"

Meanwhile, the current research could prove encouraging for a range of people, including the average person who wants to become more physically active to realize the health benefits.

"One of the things that may be a practical application, is if you go to the gym and you exercise and it hurts, you may be prone to stop doing that because pain is an aversive stimulus that tells you to withdraw. So if we could give people a little caffeine and reduce the amount of pain they're experiencing, maybe that would help them stick with that exercise."

"Maybe then they'll push a little harder as well ... maybe get even better adaptations to the exercise."

Co-authors of the newly published study are U. of I. professor of kinesiology and community health Steven P. Broglio; former U. of I. graduate students Rachael C. Gliottoni and John R. Meyers; and Sigurbjorn A. Arngrimsson, Center for Sport and Health Sciences, Iceland University of Education.

Early humans may have cared for disabled young

* 14:03 31 March 2009 by **Ewen Callaway**

A recently unearthed ancient human skull shows signs of a disorder that might have caused mental retardation. This offers the earliest evidence that ancestors of Homo sapiens did not abandon young with severe birth defects.

The 500,000-year-old skeleton belonged to a five to 12-year-old child who suffered from craniosynostosis. The rare congenital condition occurs when two of the flat bones that make up the skull fuse together along their margins (sutures) too early during fetal development, hindering brain growth.

Spanish researchers discovered the first pieces of the skull near Atapuerca, Spain, in 2001, but they only recently pieced enough of it together to make a conclusive diagnosis.

"We were sure we had evidence of a real pathology," says Ana Gracia, a palaeoanthropologist at Complutense University in Madrid, who led the new study. "It's obvious – you only have to look at the cranium."

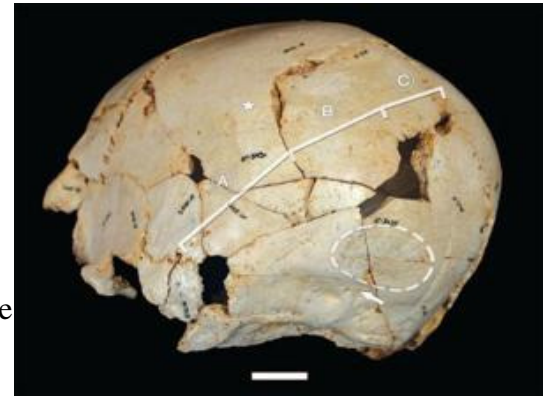
Different appearance

The child suffered from a form of craniosynostosis that occurs in about 1 in every 200,000 children.

He or she was a member of the species *Homo heidelbergensis*, – early humans that lived in Europe up to 800,000 years ago and may have given rise to Neanderthals.

The discovery marks the earliest example of a human skeleton with signs of a physical deformity that that might have made the individual dependent on others for survival.

Most animals, including primates, sacrifice or abandon young born with crippling deformities, Gracia says. It's impossible to know whether the child suffered from any cognitive problems, but he or she would undoubtedly have looked different from family and friends, she says.



The part of the skull showing prematurely fused sutures: (A) The first segment is completely fused. (B) The second segment is fused, but still noticeable. (C) The lambdoid portion of the suture is completely open (Image: National Academy of Sciences, PNAS)

'Not clear-cut'

"The obvious conclusion is that [this child] was being helped by other members of the social group," says Erik Trinkaus, a paleoanthropologist at Washington University in Saint Louis, Missouri.

However, Matthew Speltz, a psychologist at the University of Washington in Seattle, says the link between craniosynostosis and cognitive problems is not so clear-cut. Speltz is leading an ongoing study to track the development of children born with various forms of the condition.

His team has found that children with craniosynostosis are more likely than other kids to have cognitive and motor problems. But the condition is by no means a guarantee of severe learning difficulties. "There might be a slight increased risk of mental retardation," he says.

Journal reference: Proceedings of the National Academy of Science (DOI: 10.1073/pnas.0900965106)

Rigorous Visual Training Teaches the Brain to See Again After Stroke

By doing a set of vigorous visual exercises on a computer every day for several months, patients who had gone partially blind as a result of suffering a stroke were able to regain some vision, according to scientists who published their results in the April 1 issue of the *Journal of Neuroscience*.

Such rigorous visual retraining is not common for people who suffer blindness after a stroke. That's in contrast to other consequences of stroke, such as speech or movement difficulties, where rehabilitation is common and successful.

"We were very surprised when we saw the results from our first patients," said Krystel Huxlin, Ph.D., the neuroscientist and associate professor who led the study of seven patients at the University of Rochester Eye Institute. "This is a type of brain damage that clinicians and scientists have long believed you simply can't recover from. It's devastating, and patients are usually sent home to somehow deal with it the best they can."

The results are a cause for hope for patients with vision damage from stroke or other causes, said Huxlin. The work also shows a remarkable capacity for "plasticity" in damaged, adult brains. It shows that the brain can change a great deal in older adults and that some brain regions are capable of covering for other areas that have been damaged.

Huxlin studied seven people who had suffered a stroke that damaged an area of the brain known as the primary visual cortex or V1, which serves as the gateway to the rest of the brain for all the visual information that comes through our eyes. V1 passes visual information along to dozens of other brain areas, which process and make sense of the information, ultimately allowing us to see.

Patients with damage to the primary visual cortex have severely impaired vision – they typically have a difficult or impossible time reading, driving, or getting out to do ordinary chores like grocery shopping. Patients may walk into walls, oftentimes cannot navigate stores without bumping into goods or other people, and they may be completely unaware of cars on the road coming toward them from the left or right.

Depending on where in the brain the stroke occurred, most patients will be blind in one-quarter to one-half of their normal field of view. Everything right or left of center, depending on the side of the stroke, might be gray or dark, for instance.

Building on blindsight

Despite the stroke, the patients' eyes are taking in visual information. It's just that the damaged brain cannot make sense of it to create vision.

Huxlin's team sought to build on this "blindsight" – visual information, of which the patient is unaware, that still reaches the brain. A few past studies have shown promise for the idea of building on blindsight to improve a person's vision.

"The question is whether we can we recruit other, healthy regions of the brain to benefit the person's vision. Can we train those brain regions so hard and stimulate the brain to such a degree that this visual information is brought to consciousness, so the person is aware of what they're seeing?" said Huxlin.

Huxlin began the study with seven people, four women and three men, ranging from their 30s to their 80s, who had had a stroke anywhere from eight to 40 months before the experiment began. All had suffered substantial damage to the primary visual cortex. The funding to support the work came from Research to Prevent Blindness, the Pfeiffer Foundation, the Schmitt Foundation, and the National Eye Institute.

The team focused on motion perception, since it's an aspect of vision critical for most everyday tasks. The team's aim was to see if the brain's middle temporal region, which was healthy in the participants, could be stimulated so extensively that it could take on some of the tasks normally handled by the visual cortex.

The five participants who performed the training and completed the experiment had significantly improved vision. They were able to see in ways they weren't able to before the experiment began. A few found the experiment life-changing – a couple of participants are driving again, for instance, or have gained the confidence to go shopping and exercise frequently.

Following the dancing dots that can't be "seen"

To do the experiment, participants fix their gaze on a small black square in the middle of a computer screen; scientists use a sensitive eye tracker to make sure patients keep staring at the square.
test screen from eye re-training

Every few seconds, a group of about 100 small dots appears within a circle on the screen, somewhere in the person's damaged visual field – in other words, when the patients stare at the square, they don't initially see the dots. The dots twinkle into existence, appear to move as a group either to the left or the right, then disappear after about one-half second. Then the patient has to choose whether the dots are moving left or right. A chime indicates whether he or she chose correctly, providing feedback that lets the brain know whether it made the right choice and speeding up learning.

But how do patients choose if they can't consciously see the dots?

"The patients can't see the dots, but they're aware that there is something happening that they can't quite see. They might say, 'I know that there's something there, but I can't make any sense of it,'" said Huxlin, who is also a faculty member in the departments of Ophthalmology, Neurobiology and Anatomy, Brain and Cognitive Sciences, and in the Center for Visual Science.

But the brain is able to make some sense of it all, even though the patient is unaware that he or she is seeing anything. When forced to make a choice, patients typically start out with a success rate of around 50 percent by guessing. Over a period of days, weeks or months, that number goes to 80 or 90 percent, as the brain learns to "see" a new area, and the visual information moves from blindsight to consciousness. Patients eventually become aware of the dots and their movement.

As patients improve, researchers move the dots further and further into what was the patient's blind area, as a way to challenge the brain, to coax it to see a new area.

"Basically, it's exercising the visual part of the brain every day," said Huxlin. "It's very hard work, very grueling. By forcing patients to choose, you're helping the brain re-develop."

The patients in the study did about 300 tests at a time, which translated roughly to sitting in front of a computer for 15 to 30 minutes once or twice a day, every day, for nine to 18 months. It's an exhausting task, especially for someone whose brain is working extra-hard to accomplish it.

Working with Huxlin on the work were Tim Martin, Ph.D., post-doctoral research associate; Kristin Kelly, formerly a technical associate and now a medical student; former graduate student Meghan Riley; neuro-ophthalmologist Deborah Friedman, M.D.; neurologist W. Scott Burgin, M.D.; and Mary Hayhoe, Ph.D., formerly of the Department of Brain and Cognitive Sciences at the University of Rochester, and now at the University of Texas at Austin. The University of Rochester has filed a patent on the technology.

How infection may spark leukaemia

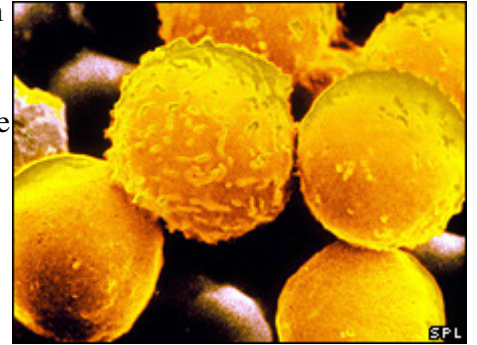
Scientists have shown how common infections might trigger childhood leukaemia.

They have identified a molecule, TGF, produced by the body in response to infection that stimulates development of the disease. It triggers multiplication of pre-cancerous stem cells at the expense of healthy counterparts. The Institute of Cancer Research study appears in the Journal of Clinical Investigation.

Leukaemia occurs when large numbers of white blood cells take over the bone marrow, leaving the body unable to produce enough normal blood cells.

The researchers had already identified a genetic mutation - a fusion of two genes - occurring in the womb that creates pre-leukaemic cells.

These cells then grow in the bone marrow, effectively acting as a silent time bomb that can stay in the body for up to 15 years.



Common infections may trigger cancer cell growth

Evidence suggests the mutation may be present in as many as one in 100 newborn babies, but only about one in 100 of these children then go on to develop leukaemia. This suggests that the cells will only complete the transformation to fully-fledged cancer cells if they are exposed to an independent trigger.

The latest study suggests production of TGF in response to an infection could be that trigger.

Because the molecule hugely increases the rate at which the pre-leukaemic cells multiply, this significantly raises the chance that some will become even further damaged in a way that results in the child developing leukaemia.

Preventative measures

Researcher Professor Mel Greaves said: "Identifying this step means we can determine how an unusual immune response to infection may trigger the development of the full leukaemia and eventually perhaps develop preventative measures such as a vaccine."

Dr Shabih Syed, scientific director at the charity Leukaemia Research, said: "Before this study, there had been only circumstantial evidence to implicate infections in the progression from a child carrying pre-leukaemic cells to actually having leukaemia.

"There was no evidence of the mechanism by which this might happen. "While infection is clearly only one factor in triggering progression, this study greatly increases the strength of evidence for its role in the commonest form of childhood leukaemia."

Genes may time loss of virginity

* 14:36 31 March 2009 by Ewen Callaway

Sexual precociousness is in our genes, new research suggests. A unique study of twins separated at birth finds a genetic link to the age at which a person first engages in sexual intercourse.

"It's not like there's a gene for having a sex at a certain date," says Nancy Segal, a psychologist at California State University in Fullerton who led the new study. Instead, heritable behavioural traits such as impulsivity could help determine when people first have sex, she says.

As genetic determinism goes, the new findings are modest. Segal's team found that genes explain a third of the differences in participants' age at first intercourse – which was, on average, a little over 19 years old. By comparison, roughly 80% of variations in height across a population can be explained by genes alone.

However, determining the extent to which sexual precociousness is inherited is trickier than making a similar calculation for height. A common family environment – whether it promotes or hinders early sex – could cause scientists to overestimate the effect of genes.

Social effect

By studying 48 pairs of twins raised apart, as well as 23 individual twins, Segal's team sidesteps this confounding factor. "This gives us a pure estimate about how much genes affect behaviour," she says.

On the other hand, conservative social mores might delay a teen's first sexual experience, causing scientists to low-ball the effect of genes. Indeed, Segal's team noticed a less pronounced genetic effect among twins born before 1948, compared with those who came of age in the 1960s or later.

Other factors may also make the effects of genes harder to discern. For example, Segal's team also found that female participants who felt unhappy and unfulfilled in their home life were more likely to have sex at a younger age.

Essential function

As for the specific genes involved, another team previously found that a version of a gene encoding a receptor for the neurotransmitter dopamine is associated with age at first intercourse. Others have linked the same version of the gene – called DRD4 – to impulsive, risk-taking behaviour.

This might be one explanation for early sexual activity, says Joseph Rodgers, a psychologist at the University of Oklahoma in Norman. Yet unlike other risky behaviours, such as drug use or reckless driving, sex serves an essential biological function.

"For most of our evolutionary past, sexual behaviour hasn't been risk taking, it's about reproduction and success of the species," Rodgers says.

Journal reference: Personality and Individual Differences (DOI: 10.1016/j.paid.2009.02.010)

Multi-colored uniforms improve perceptions of hospital nurses among children and parents

Putting hospital nurses in brightly coloured, unconventional uniforms makes children more comfortable and parents more confident, according to a study in the April issue of the Journal of Clinical Nursing.

Researchers from the University of Florence, Italy, surveyed a total of 112 children before and after nurses on two paediatric wards at Meyer Children's Hospital started wearing colourful new uniforms. The children, who had an average age of 10, were split into two groups of 56 and one parent was interviewed for each child taking part.

Five different uniforms were chosen by a local charity, from 4,500 designs drawn by pre-school and school age children who had been admitted to paediatric wards all over Italy. They were then manufactured by a commercial company and donated to the hospital.

Before the new uniforms were introduced to the wards, the nurses wore conventional single-coloured trousers and tops.

Key findings included:

* The researchers asked the children to give them one word that described the nurse. 96% used positive words about the nurses after the new uniforms were introduced, compared with 82% before.

* The parents also gave the nurses higher scores on a one to five scale. Adequacy in the role rose from 4.0 to 4.7, not frightening for their child rose from 4.4 to 4.7, reassuring for the parent rose from 4.0 to 4.5 and fun doubled from 2.3 to 4.6.

* Although the children's perception of the nurses improved, their perceptions of the hospital itself only showed slight improvements in the more fun and less frightening categories.

* 76% of the children preferred the new uniforms, 13% preferred the traditional attire and 4% would have preferred to see them in ordinary clothes.

The 112 children who took part in the study ranged from six to 16 and the before and after groups of 56 were matched as closely as possible. There were 35 boys and 21 girls in each group, the average age was just over 10 and 32 children were from a medical ward and 24 from a surgical ward. They had been in hospital for an average of three to four days when they took part in the study.

"Our study showed that parents and children alike preferred to see the paediatric nurses in brightly coloured, non-conventional uniforms" says lead author Filippo Festini, Professor of Nursing Science at the University of Florence.

"The children told us they felt more positive about the nurses who were caring for them and a particularly significant result was that the parents did not see the new uniforms as less professional. In fact, it increased their positive perceptions of the nurses.

"Although the new uniforms did not significantly improve the children's view on the hospital itself, they made the children feel more comfortable about the nurses who were caring for them and that is a very important factor on a paediatric ward."

Notes to editors Use of non-conventional nurses' attire in a paediatric hospital: a quasi-experimental study. Festini et al. Journal of Clinical Nursing. 18, 1018-1026 (April 2009).

Basics

The Biggest of Puzzles Brought Down to Size

By NATALIE ANGIER

Ah, yes, \$500 billion in bailout money here, a trillion in troubled asset purchases there. We taxpayers are getting so insouciant about the extraordinary figures being bandied about by the captains of finance these days, you'd think we were still the designated banker in one of those endless games of Monopoly we're sorry we suggested to our cousin Dan but he won't let us quit. Fine, fine, you smug little top hat with all four railroads. A trillion, a quintillion. You want that in pinks, greens, yellows or blues?

Grim though the economic spur may be, some scientists see a slim silver lining in the sudden newswiness of laughably large numbers. As long as the public is chatting openly about quantities normally expressed in scientific notation, they say, why not talk about what those numbers really mean? In fact, they shamelessly promote the benefits of quantitative and scientific reasoning generally. As they see it, anyone, no matter how post-scholastic or math allergic, can learn basic quantitative reasoning skills, and everyone would benefit from the effort - be less likely to fall for vitamin hucksters, for example, or panic when their plane hits a bumpy patch.

One excellent way to start honing such skills is with a few so-called Fermi problems, named for Enrico Fermi, the physicist who delighted in tossing out the little mental teasers to his colleagues whenever they needed a break from building the atomic bomb.

Here is how it works. You take a monster of a ponder like, What is the total volume of human blood in the world? or, If you put all the miles that Americans drive every year end to end, how far into space could you travel? and you try to estimate what the answer might be. You resist your impulse to run away or imprecate. Instead, you look for a wedge into the problem, and then you calmly, systematically, break it down into edible bits. Importantly, you are not looking for an exact figure but rather a ballpark approximation, something that would be within an order of magnitude, or a factor of 10, of the correct answer. If you got the answer 900, for example, and the real answer is 200, you're good; if you got 9,000, or 20, you go back and try to find where you went astray.

"It's really just critical thinking, breaking down seemingly complicated problems into simpler problems," said John A. Adam, a professor of mathematics at Old Dominion University in Norfolk, Va. "Once you get over the hurdle and realize that, good grief, any question can be answered to this level of precision, to the nearest power of 10, it's quite exciting, and you start looking for things to apply it to."

Dr. Adam and his colleague Lawrence Weinstein, a professor of physics, offer a wide and often amusing assortment of Fermi flexes in a book that just caught my eye, "Guesstimation: Solving the World's Problems on the Back of a Cocktail Napkin" (Princeton University Press, 2008). (Try some questions from the book in this estimation quiz.)

So let's say you want to make a quickie estimate of the world's human blood supply, but you don't know how much blood an individual human holds. The authors suggest thinking about what happens when you donate blood. You're asked to give a pint of blood, which suggests this is a pretty safe quantity to lose. Let's put it at 10 percent of the body's total blood volume, bringing us up to 10 pints, or five quarts, per person. Multiply five quarts by six billion humans, and you get 30 billion quarts, or 7.5 billion gallons of blood. And just to give you a gut feel for that figure, the authors estimate what would happen if you poured all those gallons over Central Park: the square-mile incarnadine pool would be 50 feet deep.

On to the less macabre consideration of the great American road trip, vertically repurposed. How many miles does our autophilic nation compile each year? When I recently had the tires changed on my five-year-old car, the mechanic saw that my odometer read 30,000 miles and guffawed politely. Most people drive twice as much as you do, he said. O.K., 12,000 miles annually per car. And how many cars are we talking - one for every two people? That comes to 150 million cars, times 12,000 miles, bringing us to roughly, um, two trillion miles. We are embarking on a serious space junket here, way beyond our favorite plutoid Pluto, at some three billion miles from Earth. A dozen years at this rate, and we'll make it to the nearest star.

Dr. Weinstein points out that it's not all idle doodles. You can sully your napkin with plenty of topical estimates, too. Among his favorite examples is to consider how much cropland we would need if we decided to fuel our cars entirely with ethanol from corn. There's one piece of knowledge you need here, he acknowledged: that there are 30,000 calories in a gallon of gasoline. From there, you cruise. A car needs a gallon or two a day. You eat 2,000 to 3,000 calories a day. "Your car uses 10 to 20 times as much energy a day as you do," he said. "If we're going to fuel our cars with ethanol, we'll need 20 times more farmland, so it could be this is a bad idea."

Dr. Weinstein also thinks it's a bad idea to cede all personal agency to the Internet, and to argue that, why bother guesstimating when you can look it up on Google? "I hate to tell you this, but not everything on the Web can be believed," he said. "You need a bull sensor." Moreover, he said, the habit of sizing up the world can have an oddly grounding effect. "It gets people out of a crisis mode of thinking," he said.

To further enhance one's quantitative prowess, Dr. Adam suggests translating amorphous figures into familiar terms. A million seconds, for example, is about 10 days, while a billion seconds amounts to some 32 years. And a trillion seconds ago, in circa 30,000 B.C., the last of the Neanderthals were betting the rent on a Powerball lottery, without bothering to consider the odds.

Bad mix of bacterial remnants and genetics leads to arthritis

New research published in the Journal of Leukocyte Biology shows that the NOD2 gene is activated by muramyl dipeptide

Here's another reason to hate leftovers. A research study appearing in the April 2009 issue of the Journal of Leukocyte Biology (<http://www.jleukbio.org>) sheds light on one cause of arthritis: bacteria. In the study, scientists from the United States and The Netherlands show that a specific gene called NOD2 triggers arthritis or makes it worse when leftover remnants of bacteria cell walls, called muramyl dipeptide or MDP, are present. This discovery offers an important first step toward new treatments to prevent or lessen the symptoms of inflammatory arthritis.

"Despite recent advances in the treatment of arthritis, none target its cause," said Michael Davey, Associate Chief of Staff for Research at the Portland Oregon Veteran's Affairs Medical Center and one of the researchers involved in the study. "Our work with MDP and NOD2 is a step toward understanding the root cause of arthritis which one day may allow certain forms of arthritis to be prevented altogether."

Davey and colleagues made this discovery through experiments using two groups of mice, one group was normal and the other had been genetically modified so that their NOD2 gene was deactivated (commonly referred to as "knocked out"). Then they administered MDP to the joints of mice in each group, and unlike the normal group of mice, the mice with the deactivated NOD2 gene did not experience signs of arthritis. This may also be an important advance in the understanding and treatment of Blau Syndrome, a rare genetic disease characterized by granulomatous arthritis (arthritis caused by bacteria), uveitis (inflammation in the middle layer of the eye), skin rash and cranial neuropathy (a disorder affecting nerves that control sight, eye movement, hearing, and taste).

"Now that we know that bacterial products can activate this NOD2 pathway and that this signal contributes to arthritis," said John Wherry, Ph.D., Deputy Editor of the Journal of Leukocyte Biology, "the next step is to find treatments that either rid the body of this inflammatory signal or mask it. Either way, the net effect would be the same: people would be spared from a very crippling disease. "

According to the U.S Centers for Disease Control and Prevention more than 40 million American say that they have been told by a doctor that they have arthritis or another rheumatic condition. Arthritis is the most common cause of disability in the United States and limits activities of nearly 19 million people.

The Journal of Leukocyte Biology (<http://www.jleukbio.org>) publishes peer-reviewed manuscripts on original investigations focusing on the cellular and molecular biology of leukocytes and on the origins, the developmental biology, biochemistry and functions of granulocytes, lymphocytes, mononuclear phagocytes and other cells involved in host defense and inflammation. *The Journal of Leukocyte Biology* is published by the Society for Leukocyte Biology.

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<http://www.jleukbio.org/cgi/content/abstract/85/4/711>

Observatory

Near-Complete Fossil Offers Insight on Early Fish

By HENRY FOUNTAIN

In trying to make evolutionary sense of the bony fish (and, by extension, land vertebrates) scientists have been hampered by a lack of completeness. Most of the earliest fossils of bony fish, dating to the Silurian period more than 416 million years ago, are fragmentary - a jawbone here, a tooth there.

A new find from limestone deposits in southern China is helping to clarify the situation. In a paper in *Nature*, Min Zhu and colleagues at the Institute of Vertebrate Paleontology and Paleoanthropology of the Chinese Academy of Sciences describe a well-preserved and practically complete fish fossil that is 418 million years old.

The fish, which they call *Guiyu oneiros*, is about a foot long. Only the tail fin is lacking from the fossil, which even shows skin scales. The fish has a jaw, which makes it the oldest near-complete jawed vertebrate ever found. The fish is lobe-finned, meaning its fins are fleshier than ray-finned fish, and counts among its few living relatives the coelacanth.



An illustration of a bony fish, a fossil of which was found in southern China. The finding suggests a date for the split between lobe- and ray-finned fish. Brian Choo/Victoria Museum

The finding also establishes a minimum date for the evolutionary divergence between lobe- and ray-finned fish. Since this lobe-finned one existed 418 million years ago, the split must have occurred sometime before.

More Than Skin Deep

By C. CLAIBORNE RAY

Q. My mother used to tell me that the white stuff sticking to orange segments was good for me. Is it?

A. The underside of the peel, called the albedo, contains carbohydrates and vitamin C but is especially rich in a soluble fiber called pectin, said Dr. Renee M. Goodrich, associate professor of food science and human nutrition at the University of Florida. "We are beginning to see links between consumption of such fiber and cholesterol lowering," she said.

The layer also has a variety of interesting molecules that are under study for possible health benefits, said Dr. Sheldon S. Hendler, co-editor of *The Physicians' Desk Reference for Nutritional Supplements*.

One group of chemicals, called polymethoxylated flavones, includes nobiletin, tangeretin and sinesetin. They make up an orange's defense system against fungi, pests and predators, Dr. Hendler said, and may also have activities that counter high cholesterol, prevent cancer, fight fungus and reduce inflammation.

Preliminary studies are under way.



Victoria Roberts

Other chemicals of interest include the essential oil terpinoids citral and d-limonene and four flavonoid antioxidants, called hesperidin, neohesperiden, naringin and rutin. "D-limonene is under study as a possible cancer chemopreventive," Dr. Hendler said.

D-glucarate, also found in the layer, is under study as a possible anticancer agent, particularly for hormone-sensitive tumors like breast and prostate cancer, he said.

Dr. Goodrich acknowledged that the layer is bitter and that "you might have to eat quite a lot of the stuff to get clinical effects."

Blood test for brain injuries gains momentum

Rochester scientists study new tool for screening, clinical trials

A blood test that can help predict the seriousness of a head injury and detect the status of the blood-brain barrier is a step closer to reality, according to two recently published studies involving University of Rochester Medical Center researchers.

News stories about tragic head injuries – from the death of actress Natasha Richardson to brain-injured Iraq war soldiers and young athletes – certainly underscore the need for a simpler, faster, accurate screening tool, said brain injury expert Jeffrey Bazarian, M.D., M.P.H., associate professor of Emergency Medicine, Neurology and Neurosurgery at URM, and a co-author on both studies.

The S-100B blood test recently cleared a significant hurdle when a panel of national experts, including Bazarian, agreed for the first time that it could be a useful tool for patients with a mild injury, allowing them to safely avoid a CT scan.

Previous studies have shown the S-100B serum protein biomarker to increase rapidly after an injury. If measured within four hours of the injury, the S-100B test accurately predicts which head injury patients will have a traumatic abnormality such as hemorrhage or skull fracture on a head CT scan. It takes about 20 minutes to get results and could spare many patients unnecessary radiation exposure.

Physicians at six Emergency Departments in upstate New York, including the ED at Strong Memorial Hospital in Rochester, this year will continue to study the accuracy of the test among 1,500 patients. Scientists plan to use the data to apply for U.S. Food and Drug Administration approval.

"The S-100B blood test is an important part of the tool set we need to improve our treatment of patients with brain injuries," Bazarian said. "It's not the ultimate diagnostic test, but it may make things easier for patients, and it will help doctors sort through difficult clinical decisions."

The test is used routinely in 16 European countries as a screening device. If a person falls and gets a head injury in Munich, Germany, during Oktoberfest, for example, a neurosurgeon is on duty within 500 meters of the beer tent, ready to administer the blood test, Bazarian said.

But in the United States, the current, accepted standard screening tool for head injuries is still the CT scan, which shows bleeding in the brain but does not detect more subtle injury to the brain's neurons, which can result in lasting neurological defects. In fact, 95 percent of CT scans look normal for patients with a relatively mild but potentially life-altering injury, Bazarian said.

There are more than 1 million emergency visits annually for traumatic brain injury (TBI) in the U.S. The majority of these visits are for mild injuries, primarily the result of falls and motor vehicle crashes. The

challenge for doctors is to identify which of these patients has an acute, traumatic intracranial injury, something that is not always evident, and which patients can be observed and sent home.

Widespread use of the blood test could result in a 30 percent reduction of CT scans, according to the report by the national panel of brain experts, which published updated clinical guidelines in the December 2008 *Annals of Emergency Medicine*, and the April 2009 *Journal of Emergency Nursing*.

Bazarian and colleague Brian J. Blyth, M.D., assistant professor of Emergency Medicine at URMC, additionally found that the S-100B test can relay critical information about how the blood-brain barrier (BBB) is functioning after a head injury. Blyth was the first author on this study, reported electronically March 3, 2009, in the *Journal of Neurotrauma*.

In the context of head injuries, the BBB acts like a gate between the brain tissue and peripheral circulation. The gate often opens after injury, but not always. Knowing the status of the BBB helps doctors to decide if medications given to repair damage will actually reach the brain. The time between injury and irreversible brain swelling is short – and many drug studies have failed to find a therapy that leverages this time frame and works as designed.

Before the S-100B blood test, the best way to know if the BBB was open was to perform an invasive procedure called a ventriculostomy. (Doctors insert a catheter through the skull and into the brain, withdraw fluid, and compare the concentration of albumin protein in the cerebrospinal fluid to the concentration in the blood.)

In a pilot study of 20 patients, however, Blyth found that serum S-100B concentrations could accurately predict the function of the blood-brain barrier 12 hours after injury, eliminating the need for the invasive procedure.

The study compared levels of S-100B proteins to the CSF-serum albumin quotient (Qa), the gold standard measurement signaling a brain injury. Researchers compared nine people with a known severe head injury, to 11 people who suffered from non-traumatic headaches.

Blyth and Bazarian believe the research may impact future drug studies. "The disability and death rates from brain injuries have not improved much in the past 20 years," Blyth said. "Many clinical trials for new medications have failed, probably because it was difficult to know if the blood-brain barrier was open and the drugs were reaching its target. Our study shows that any diagnostic test for brain injury should incorporate a way to measure the status of the blood-brain barrier into its design."

The National Institutes of Health and the American Geriatrics Society: Jahnigen Career Development Scholars Award funded the research.

Co-authors from the URMC include: Arash Farhavar M.D., Ph.D., a resident in Neurosurgery; Christopher Gee, M.D., a fellow in Emergency Medicine; Hua He, Ph.D., assistant professor, Department of Biostatistics and Computational Biology; and Akshata Nayak, laboratory technician.

3-D printing hits rock-bottom prices with homemade ceramics mix

This story is, literally, stone age meets digital age: University of Washington researchers are combining the ancient art of ceramics and the new technology of 3-D printing. Along the way, they are making 3-D printing dramatically cheaper.

About five years ago, Mark Ganter, a UW mechanical engineering professor and longtime practitioner of 3-D printing, became frustrated with the high cost of commercial materials and began experimenting with his own formulas. He and his students gradually developed a home-brew approach, replacing a proprietary mix with artists' ceramic powder blended with sugar and maltodextrin, a nutritional supplement. The results are printed in a recent issue of *Ceramics Monthly*. Co-authors are Duane Storti, UW associate professor of mechanical engineering, and Ben Utela, a former UW doctoral student.



These pots were inspired by Southwest Native American pottery and created using potter's clay. They emerged from a high-tech 3-D printer before being fired in the usual way. The fine horizontal lines are an artifact of the printing process. University of Washington

"Normally these supplies cost \$30 to \$50 a pound. Our materials cost less than a dollar a pound," said Ganter. He said he wants to distribute the free recipes in order to democratize 3-D printing and expand the range of printable objects. Recipes are available on the magazine's Web site at <http://tinyurl.com/d5lcpa>.

Glitzy three-dimensional printers have become common in the industrial world, churning out fast 3-D prototypes of everything from airplane parts to running shoes. But the machines also are becoming popular among artists, hobbyists and educational institutions.

For the past 15 years Ganter has taught an engineering course introducing students to rapid prototyping that draws students from engineering, art and architecture.

"When powders are \$30 a pound, I can't let students try something new or experimental," Ganter said. "But when it's \$1 a pound, I don't care. I encourage them to try new things."

The lab can go through \$4,000 of materials per quarter, he said. In the 15 years of the lab's operation, bills for materials dwarf the roughly \$20,000 initial costs for a printer.

Lab fees were already at the maximum, Ganter said, so instead the group went looking for a different approach – cheaper materials.

"If we're in trouble financially, imagine what's it like at a high school or a technical school?"

Three-dimensional printers are based on inkjet technology and look like photocopying machines that spit out solid objects. The inkjets are filled with an adhesive, or binder, that prints onto thin layers of powder. Any surface with binder will be included in the finished object. Users generally create their designs on a computer and send the completed design file to the printer. The object gets built up layer by layer, each about the thickness of a piece of paper, over 10 to 60 minutes. Users then dust or blow away the excess powder to reveal the prototype.

The UW group has initially published results and formulas using three different types of ceramic powders, which are sold at local pottery or clay stores by the 50-pound bag. Most other supplies are purchased at local restaurant supply stores. "Clay is dirt cheap," commented Ganter. Using anything but company product may violate the printers' warranties.

"We can fix our own printers, so we're not worried," Ganter said. "And most of our materials are so close to what's being used that the risk of damaging the machine is small. In the worst-case scenario, if we can't fix the machine ourselves, we would have to pay for a repair."



After printing, loose powder falls away from the printed ceramic objects. These cups were created using the UW recipe, which costs about 3 percent as much as commercial 3-D printing powders. University of Washington

Ganter describes his lab, strewn with fanciful objects, as a toy shop. The UW's Solheim Rapid Manufacturing Laboratory houses two do-it-yourself kits (Fab@Home systems) assembled by undergraduate students, a homemade 3-D printer designed by a team of students, and several state-of-the-art commercial machines used in teaching and research.

The low-cost ceramics experiment began about four years ago when the group had a National Science Foundation grant to print custom dental implants. Utela began experimenting with different materials and processes, and eventually published papers describing how to figure out if one could 3-D print in a given material, and suggesting many of the required parameters.

The ceramic printing follows from Utela's work. Three-dimensional printing was already possible for engineering-grade ceramics that have high firing temperatures. This is one of the first 3-D printers to use artist-grade ceramics, which fire at lower temperatures.

Creating the actual formulas was a process of experimentation and sometimes trial and error. Graduate student Ian Blanch spent six months perfecting the procedures and formula for a single powder-and-binder combination, Ganter said. Much progress has been made since then, and the team continues to experiment with new materials, including rice flour.

Now that the ceramics formulas are working, it should make the technology more accessible to anyone who are used to working with traditional art ceramics, he said.

"I'm printing in the exact materials they use. So they can even use all the same glazes and glazing techniques," Ganter said. Artists and museum curators are already investigating possible collaborations, he said.

The More Oral Bacteria, the Higher the Risk of Heart Attack, UB study shows.

BUFFALO, N.Y. -- Several studies have suggested there is a connection between organisms that cause gum disease, known scientifically as periodontal disease, and the development of heart disease, but few studies have tested this theory.

A study conducted at the University at Buffalo, where the gum disease/heart disease connection was uncovered, now has shown that two oral pathogens in the mouth were associated with an increased risk of having a heart attack, but that the total number of germs, regardless of type, was more important to heart health.

Results of the study will be presented during a poster session at the International Association of Dental Research (IADR) General Session being held in Miami, Fla., from April 1-4.

Oelisoa M. Andriankaja, D.D.S., Ph.D., conducted the study in UB's Department of Oral Biology in the School of Dental Medicine, as a postdoctoral researcher. She currently is an adjunct professor at the University of Puerto Rico's School of Dental Medicine.

"The message here," said Andriankaja, "is that even though some specific periodontal pathogens have been found to be associated with an increased risk of coronary heart disease, the total bacterial pathogenic burden is more important than the type of bacteria.

"In other words, the total number of 'bugs' is more important than one single organism," she said.

The study involved 386 men and women between the ages of 35 and 69 who had suffered a heart attack and 840 people free of heart trouble who served as controls. Samples of dental plaque, where germs adhere, were collected from 12 sites in the gums of all participants.

The samples were analyzed for the presence of the six common types of periodontal bacteria, as well as the total number of bacteria.

The patients harbored more of each type of bacteria than the controls, the analysis showed. However, only two species, known as *Tannerella Forsynthesis* and *Preventella Intermedia*, had a statistically significant association with an increased risk of heart attack.

An increase in the number of different periodontal bacteria also increased the odds of having a heart attack, results showed.

Prospective studies -- those that measure oral bacteria in participants who have had no heart problems when they enter the study, and again when a heart attack occurs in a participant -- are needed to better assess this potential association, noted Andriankaja.

Additional researchers on the study from UB were Karen L. Falkner, Ph.D., Robert J. Genco, D.D.S., Ph.D., Sreenivasa Sarikonda, a doctoral candidate, Joan Dorn, Ph.D., and Kathleen Hovey, M.S.

Tania Mendoza, D.D.S., from the University of North Carolina at Chapel Hill, and Maurizio Trevisan, M.D., M.S., former dean of the UB School of Public Health and Health Professions, now vice chancellor and chief executive officer of the University of Nevada Health Sciences System, also contributed to the study.

The study was funded by the National Institute of Dental and Craniofacial Research (NIDCR).

Aircraft could be brought down by DIY 'E-bombs'

* 01 April 2009 **by Paul Marks**

ELECTROMAGNETIC pulse weapons capable of frying the electronics in civil airliners can be built using information and components available on the net, warn counterterrorism analysts.

All it would take to bring a plane down would be a single but highly energetic microwave radio pulse blasted from a device inside a plane, or on the ground and trained at an aircraft coming in to land.

Yael Shahaar, director of the International Institute for Counter-Terrorism in Herzliya, Israel, and her colleagues have analysed electromagnetic weapons in development or used by military forces worldwide, and have discovered that there is low-cost equipment available online that can act in similar ways. "These will become more of a threat as the electromagnetic weapons technology matures," she says.

For instance, the US and Russian military have developed electromagnetic pulse (EMP) warheads that create a radio-frequency shockwave. The radio pulse creates an electric field of many hundreds of thousands of volts per metre, which induces currents that burn out nearby electrical systems, such as microchips and car electronics.

Speculation persists that such "e-bombs" have been used in the Persian Gulf, and in Kosovo and Afghanistan - but this remains unconfirmed. But much of what the military is doing can be duplicated by others, Shahaar says. "Once it is known that aircraft are vulnerable to particular types of disruption, it isn't too much of a leap to build a device that can produce that sort of disruption. And much of this could be built from off-the-shelf components or dual-use technologies."

For example, government labs use high-energy EMP devices to test what would happen to critical electronic systems if a nuclear weapon detonated, generating a vast electromagnetic pulse, says Robert Iannini, founder of Information Unlimited in Amherst, New Hampshire, which sells EMP test systems.

EMPs can be created in a number of ways. A machine called a Marx generator can quickly dump an extremely high charge stored in a bank of capacitors into an antenna, which then releases a highly energetic radio pulse. Devices like this are often used to test power lines for their resistance to lightning strikes. An alternative, known as a flux compression device, uses a small explosive to push an armature through a current-carrying coil that is generating a magnetic field. This compresses the magnetic field, again producing a devastating EMP.

Iannini says his company only sells such devices to legitimate buyers. "The only people that buy these things are qualified researchers at labs like Sandia. They never find their way into the labs of pseudo or amateur

scientists," he says. "If we get any unknown overseas purchaser we immediately alert the office of export enforcement at the US Department of Commerce."

But Shahar told delegates at the annual Directed Energy Weapons conference in London last month that security at some labs can be lax, while basic EMP generators can be built from descriptions available online, using components found in devices such as digital cameras. "These are technologically unchallenging to build and most of the information necessary is available," she says.

The increasing use of carbon-fibre reinforced composite in aircraft fuselages is also making them more vulnerable, she says, because composites provide poor shielding against electromagnetic radiation compared with metal. "What is needed is extensive shielding of electronic components and the vast amount of cables running down the length of the aircraft," she says.

Jerome Bruel, an electrical systems expert at the European Aviation Safety Agency in Cologne, Germany, agrees that newer all-composite planes like the Airbus A350 will probably need some means of protecting their cabling from all radio energy sources, including TV transmitters. "They may need a metal mesh surrounding them to absorb interference," he says.

Douglas Beason, a director at the Los Alamos National Laboratory in New Mexico, says it may be straightforward to build a do-it-yourself EMP weapon, but more difficult to make one that can be stowed in an aircraft. "A lot of work would need to go into dramatically decreasing the weight, shrinking the power supply and antenna," he says.

Nevertheless, governments are taking the threat seriously. A spokesperson at the UK Department of Transport said the government is well aware of this security issue and has close links with agencies "able to provide a balanced picture in regards to EMP weapons, and their potential to compromise civilian aircraft".

Drug commonly used for alcoholism, drug addiction, curbs urges of compulsive stealers
MINNEAPOLIS / ST. PAUL – It appears that a drug commonly used to treat alcohol and drug addiction has a similar effect on the compulsive behavior of kleptomaniacs – it curbs their urge to steal, according to new research at the University of Minnesota.

The Medical School's Department of Psychiatry conducted an eight-week, double-blind study of 25 men and women ages 17-75, who spent an average of at least one hour a week stealing. Those who took the drug Naltrexone (mean dose of 117mg/day) reported significantly greater decline in stealing behavior compared to those taking placebo. The research is published in the April 1 issue of the Journal of Biological Psychiatry.

"It gets rid of that rush and desire," said Jon Grant, M.D., J.D., M.P.H., a University of Minnesota associate professor of psychiatry and principal investigator of the study. "The difference in their behavior was significant, and these people were really troubled by their behavior."

A recent, large epidemiological study of about 43,000 adults found that more than 11 percent of the general population admitted to having shoplifted in their lifetime. It is unclear, however, how many people who steal suffer from kleptomania.

While the drug is not a cure for kleptomania, Grant said it offers hope to those who are suffering from the addiction. He also said the drug would most likely work best in combination with individual therapy.

"These are people who steal even though they can easily afford not to," Grant said.

Naltrexone is approved by the FDA for use in alcohol and opiate dependence, but it also has been studied and proved successful in helping gambling addicts. Naltrexone is sold under the brand names Revia and Depade. An extended-release formulation is sold under the name Vivitrol.

The research was supported by a Career Development Award from the National Institute of Mental Health and the University of Minnesota Academic Health Center.

Our complex brains thrive on the edge of chaos

CHAOTIC thinking is rarely a recipe for success, but evidence is emerging that operating at the edge of chaos may drive our brain's astonishing capabilities.

Neuroscientists have long suspected that the network of neurons in our brains might be connected in such a way that they achieve a state of "self-organised criticality" (SOC), in which they are neither ordered nor random, but somewhere in between. In such a state, even a minor change can prompt a large reaction: for example, forest fires, earthquakes and avalanches tend to propagate under SOC.

In 2003, neuroscientists showed that the propagation of electrical signals in a slice of brain tissue from a rat followed patterns expected for a state of SOC (The Journal of Neuroscience, vol 23, p 11167). To see whether this was also true in people, Ed Bullmore of the University of Cambridge and his colleagues mapped electrical brain activity in 19 volunteers.

One mark of SOC is that signals should show similar patterns at all frequencies - a property known as scale invariance. Sure enough, when Bullmore's team measured the length of time that two electrical signals from

random locations in the brain were "in phase", it was the same at all signal frequencies (PLoS Computational Biology, DOI: 10.1371/journal.pcbi.1000314).

Computer models have shown that when neural networks are in a state of SOC, they maximise information processing and storage. "It might be advantageous for the brain," Bullmore says.

New Studies Examine Elimination of Hepatitis B and C

Two new studies in the April issue of *Hepatology* explore the ways that hepatitis B virus (HBV) and hepatitis C virus (HCV) can be cleared from patients' bodies. *Hepatology* is a journal published by John Wiley & Sons on behalf of the American Association for the Study of Liver Diseases (AASLD). The articles are also available online at Wiley Interscience (www.interscience.wiley.com).

Both HBV and HCV are global health problems. They can lead to cirrhosis and liver cancer and they cause millions of deaths each year. Treatments to contain or cure these infections have been difficult to find. Researchers continue to explore potential therapies and the immune system response to the diseases.

The first new study sheds light on the immunological response to coinfection with HBV and HCV. Researchers led by Evangelista Sagnelli of Naples, Italy, report that for patients with chronic HCV, HBV superinfection can lead to clearance of the HCV.

They compared 29 HCV patients to 29 people, matched by age, gender and risk factors, who did not have HCV. All of the patients developed acute HBV during the same time period. The patients with HCV were more likely to have a severe course of illness, and one died of liver failure. However, nearly a quarter (six out of 24) emerged HCV-free.

"Extensive acute hepatocellular necrosis, although life-threatening, may lead to a clearance of chronic HCV infection," the authors report. Still, the severity of acute HBV in HCV patients raises "the concern that this clinical event could become an emerging health care problem in countries with a wide spread of both HBV and HCV infection," they write. "Further efforts should be made to extend the use of HBV vaccination in patients with chronic HCV infection" they also suggest.

The second study, headed by Maurizia Brunetto of Pisa, Italy, recommends interferon-based therapies as a first-line approach for patients with chronic HBV, because these have the best chance of clearing hepatitis B virus surface antigen (HBsAg). The reduction of HBsAg serum levels leading to HBsAg clearance is the hallmark of a newly achieved immune control of the infection by mean of a significant reduction of virus infected hepatocytes.

The researchers retrospectively investigated the relationship between treatment regimens and changing levels of HbsAg in 386 patients in a multinational study.

"Significantly more patients treated with peginterferon alfa-2a (21 percent) or peginterferon alfa-2a plus lamivudine (17 percent) achieved HBsAg levels under 100 IU/mL at the end of treatment compared with lamivudine (1 percent)," they report.

"HBsAg clearance represents the best possible and closest to cure outcome of antiviral therapy in patients with chronic hepatitis B, but is realistic almost exclusively among patients receiving interferon-based regimens, which are recommended as a first-line therapeutic approach," they conclude. Interferon therapy switches the chronic active hepatitis B patient in the non-active HBV carrier who lose serum HBsAg during the years after the end of therapy. If the case occurs before the development of liver cirrhosis it endows the patient with the same life expectancy of the non-HBV infected subject.

Article: "HBV Superinfection in HCV Chronic Carriers, A Disease That Is Frequently Severe But Associated With the Eradication of HCV." Sagnelli, Evangelista; Coppola, Nicola; Pisaturo, Marianonietta; Masiello, Addolorata; Tonziello, Gilda; Sagnelli, Caterina; Messina, Vincenzo; Filippini, Pietro. *Hepatology*; April 2009.

Article: "Hepatitis B Virus Surface Antigen Levels - A Guide to Sustained Response to Peginterferon Alfa-2a in HBeAg-negative Chronic Hepatitis B." Brunetto, Maurizia; Moriconi, Francesco; Bonino, Ferruccio; Lau, George; Farci, Patrizia; Yurdaydin, Cihan; Piratvisuth, Teerha; Luo, Kangxian; Yuming, Wang; Hadziyannis, Stephanos; Wolf, Eva; McCloud, Philip; Batria, Richard; Marcellin, Patrick. *Hepatology*; April 2009.

Health Benefits, Consequences of Folic Acid Dependent on Circumstances

Boston, MA and Washington, D.C. - For the past several decades, evidence has shown that greater dietary intake of the B-vitamin, folate, offers protection against the development of certain common cancers and reduces neural tube defects in newborns, opening new avenues for public health interventions that have a great impact on health. However, folate's central role as an essential factor in DNA synthesis also means that abundant availability of the vitamin can enhance the development of pre-cancerous and cancerous tumors. Further, the intake of folic acid that results from consuming foods that are voluntarily fortified (e.g.: ready-to-eat cereals) in combination with the additional intake received from mandatory fortification of flour means that supplementary intake of folic acid is unnecessary for many segments of the population, and may even present a risk. Nevertheless, the

issue is a complicated one since women of child-bearing age seem to benefit from supplemental folic acid in regard to its protection against birth defects. In the April issue of the journal *Nutrition Reviews*, two new articles by Omar Dary, Ph.D., and Joel B. Mason, M.D., assess the conditions under which folic acid can be beneficial and harmful and contribute to guidelines for the healthful intake of folic acid as a complement to dietary folate.

The consequences of inadequate folate intake remain prevalent in many countries, even in industrial countries where specific interventions of folic acid have not been implemented. Moreover, there continues to be some concern - which, to date, lacks compelling scientific evidence - that the synthetic form of the vitamin, folic acid, might have adverse effects that do not exist with natural sources of folate.

Under most circumstances, adequate intake of folate appears to assume the role of a protective agent against cancer, most notably colorectal cancer. However, in select circumstances in which an individual who harbors a pre-cancerous or cancerous tumor consumes too much folic acid, the additional amounts of folate may instead facilitate the promotion of cancer. In countries in which the fortification of flour with folic acid is working well, additional supplementation in the form of vitamin pills can lead to excessive intakes of the vitamin, which can then have undesirable adverse effects.

Thus, folate appears to assume different guises depending on the circumstances. The level of intake of this micronutrient that is safe for one person may be potentially harmful to another.

"These effects of folate on the risk of developing cancer have created a global dilemma in the efforts to institute nationwide folic acid fortification programs around the world," Mason notes.

Most individuals in the U.S. population are now folate-replete, so one consideration would be to reduce the doses of the vitamin that are present in most over-the-counter supplements. Many people receive sufficient amounts of folate through their diet.

Now that the supply of folic acid in the diet is much larger than it was prior to mandatory fortification, food policies may need to be adjusted to the current knowledge and the new circumstances.

"The design of cogent public health policies that effectively optimize health for many while presenting no or minimal risk to others, must often occur in the absence of complete information," Mason concludes. "However, we are nevertheless obliged to deliberate with as much of an in-depth understanding as the existing science allows."

Einstein scientists propose new theory of autism

Symptoms of the disorder may be reversible: Fever may hold clues

BRONX, NY - Scientists at Albert Einstein College of Medicine of Yeshiva University have proposed a sweeping new theory of autism that suggests that the brains of people with autism are structurally normal but dysregulated, meaning symptoms of the disorder might be reversible.

The central tenet of the theory, published in the March issue of *Brain Research Reviews*, is that autism is a developmental disorder caused by impaired regulation of the locus coeruleus, a bundle of neurons in the brain stem that processes sensory signals from all areas of the body.

The new theory stems from decades of anecdotal observations that some autistic children seem to improve when they have a fever, only to regress when the fever ebbs. A 2007 study in the journal *Pediatrics* took a more rigorous look at fever and autism, observing autistic children during and after fever episodes and comparing their behavior with autistic children who didn't have fevers. This study documented that autistic children experience behavior changes during fever.

"On a positive note, we are talking about a brain region that is not irrevocably altered. It gives us hope that, with novel therapies, we will eventually be able to help people with autism," says theory co-author Mark F. Mehler, M.D., chairman of neurology and director of the Institute for Brain Disorders and Neural Regeneration at Einstein.

Autism is a complex developmental disability that affects a person's ability to communicate and interact with others. It usually appears during the first three years of life. Autism is called a "spectrum disorder" since it affects individuals differently and to varying degrees. It is estimated that one in every 150 American children has some degree of autism.

Einstein researchers contend that scientific evidence directly points to the locus coeruleus–noradrenergic (LC-NA) system as being involved in autism. "The LC-NA system is the only brain system involved both in producing fever and controlling behavior," says co-author Dominick P. Purpura, M.D., dean emeritus and distinguished professor of neuroscience at Einstein.

The locus coeruleus has widespread connections to brain regions that process sensory information. It secretes most of the brain's noradrenaline, a neurotransmitter that plays a key role in arousal mechanisms, such

as the "fight or flight" response. It is also involved in a variety of complex behaviors, such as attentional focusing (the ability to concentrate attention on environmental cues relevant to the task in hand, or to switch attention from one task to another). Poor attentional focusing is a defining characteristic of autism.

"What is unique about the locus coeruleus is that it activates almost all higher-order brain centers that are involved in complex cognitive tasks," says Dr. Mehler.

Drs. Purpura and Mehler hypothesize that in autism, the LC-NA system is dysregulated by the interplay of environment, genetic, and epigenetic factors (chemical substances both within as well as outside the genome that regulate the expression of genes). They believe that stress plays a central role in dysregulation of the LC-NA system, especially in the latter stages of prenatal development when the fetal brain is particularly vulnerable.

As evidence, the researchers point to a 2008 study, published in the *Journal of Autism and Developmental Disorders*, that found a higher incidence of autism among children whose mothers had been exposed to hurricanes and tropical storms during pregnancy. Maternal exposure to severe storms at mid-gestation resulted in the highest prevalence of autism.

Drs. Purpura and Mehler believe that, in autistic children, fever stimulates the LC-NA system, temporarily restoring its normal regulatory function. "This could not happen if autism was caused by a lesion or some structural abnormality of the brain," says Dr. Purpura.

"This gives us hope that we will eventually be able to do something for people with autism," he adds.

The researchers do not advocate fever therapy (fever induced by artificial means), which would be an overly broad, and perhaps even dangerous, remedy. Instead, they say, the future of autism treatment probably lies in drugs that selectively target certain types of noradrenergic brain receptors or, more likely, in epigenetic therapies targeting genes of the LC-NA system.

"If the locus coeruleus is impaired in autism, it is probably because tens or hundreds, maybe even thousands, of genes are dysregulated in subtle and complex ways," says Dr. Mehler. "The only way you can reverse this process is with epigenetic therapies, which, we are beginning to learn, have the ability to coordinate very large integrated gene networks."

"The message here is one of hope but also one of caution," Dr. Mehler adds. "You can't take a complex neuropsychiatric disease that has escaped our understanding for 50 years and in one fell swoop have a therapy that is going to reverse it - that's folly. On the other hand, we now have clues to the neurobiology, the genetics, and the epigenetics of autism. To move forward, we need to invest more money in basic science to look at the genome and the epigenome in a more focused way."

The paper by Drs. Mehler and Purpura, "Autism, fever, epigenetics and the locus coeruleus," was published in the March issue of Brain Research Reviews.

New evidence explains poor infant immune response to certain vaccines, says MU researcher

COLUMBIA, Mo. - For years, researchers and physicians have known that infants' immune systems do not respond well to certain vaccines, thus the need for additional boosters as children develop. Now, in a new study from the University of Missouri, one researcher has found an explanation for that poor response. In the study, the MU scientist found evidence that the immune systems of newborns might require some time after birth to mature to a point where the benefits of vaccines can be fully realized.

Habib Zaghouani, a professor of molecular microbiology and immunology and child health at the MU School of Medicine, recently found that a slowly maturing component of the immune system might explain why newborns contract infections easily. In his work, Zaghouani studied newborn mice and how their immune systems reacted when they were repeatedly exposed to an antigen that simulates a virus.

Zaghouani found that while the antigen would prompt a response of the immune system, it was not the expected response. In the adult immune system, two major types of cells, known as T-helper 1 (Th-1) and T-helper 2 (Th-2) cells, are instrumental in the development of an effective immune response. Typically, Th-1 cells respond when dangerous microbes enter the body. The Th-1 cells then work to help destroy the foreign microbes. When an antigen from a vaccine enters a body with a mature immune system, Th-1 cells respond and, after destroying the invader, the Th-1 cells "remember" how to fight the antigen for future battles. Th-2 cells typically develop when the body is exposed to allergens. The responses of Th-2 cells are usually strong and manifest in the form of allergic reactions.

When Zaghouani gave the newborn mice an antigen shortly after birth, he noticed the presence of both Th-1 and Th-2 cells. However, when he gave the antigen a second time, he noticed an abundance of Th-2 cells that responded to the antigen instead of Th-1 cells. Zaghouani was surprised to notice that the Th-2 cells worked to destroy the small contingent of Th-1 cells that had responded to the antigen given at birth.

"Perhaps we should test vaccines at a very early age in animals to establish a regimen with the most effectiveness," Zaghouani said.

When a baby first gets an infection, the immature immune system responds with both types of T cells. Unfortunately, Th-1 cells have an unusual receptor that binds to a specific hormone, which is deadly to the Th-1 cells. Ironically, this particular hormone is produced by the Th-2 cells. This results in an overabundance of Th-2 cells during the first few days of life.

"We found that after six days, the immune systems in the mice matured enough to stop the death of the Th-1 cells," Zaghouani said. "After those initial days, the immune system is producing Th-1 cells with diminished hormonal receptors, thus surviving the effect of the compound that the Th-2 cells make."

Zaghouani's publication, "Delayed maturation of an IL-12-producing dendritic cell subset explains the early Th2 bias in neonatal immunity," was published in The Journal of Experimental Medicine.

NOTE: To hear an interview with Zaghouani about this study, please visit:

http://jem.rupress.org/biobytes/biobytes_Sept_22_2008_gen.shtml and click on the "listen now" link near the bottom of the page.

Ali Shilatifard and Colleagues Aim to Clarify the Definition of "Epigenetics"

Kansas City, Mo. – Ali Shilatifard, Ph.D., Investigator, has joined with a team of colleagues to propose an operational definition of "Epigenetics" - a rapidly growing research field that investigates heritable alterations in gene expression caused by mechanisms other than changes in DNA sequence.

Dr. Shilatifard's publication appeared today in *Genes and Development* and resulted from a meeting on December 7-10, 2008 that he co-organized at Cold Spring Harbor Laboratory in New York to discuss aspects of epigenetic control in genomic function and to develop a consensus definition of "epigenetics" for consideration by the broader research community.

The definition is intended to address confusion within the scientific community about the distinction between the mechanisms of epigenetic memory during early development versus those of dynamic chromatin regulation involved in differential expression of genes throughout adult life. The mechanisms underlying epigenetic memory are of great importance to human development and disease, but they are poorly understood.

The proposed definition reads: "an epigenetic trait is a stably inherited phenotype resulting from changes in a chromosome without alterations in the DNA sequence." Shilatifard and colleagues have also proposed three categories of signals that operate in the establishment of a stably heritable epigenetic state. The first is a signal from the environment, the second is a responding signal in the cell that specifies the affected chromosomal location, and the third is a sustaining signal that perpetuates the chromatin change in subsequent generations.

"The field of 'epigenetics' has been an exciting one and has grown swiftly over the past several years, extending well beyond an initial discovery phase and identification of fundamental non-genetic and chromatin-based regulatory mechanisms," said Dr. Shilatifard. "This collective effort to define and discuss 'epigenetics' is an attempt to add focus and clarity to this exciting and growing area of research."

Dr. Shilatifard joined the Stowers Institute in 2007 from the Saint Louis University School of Medicine. Learn more about his work at www.stowers.org/labs/ShilatifardLab.asp.

Take This Medicine: The Story of the Sign 'Rx'

How a special sign came to mean a doctor's prescription.

Now, the VOA Special English program, WORDS AND THEIR STORIES. ([Audio Here](#))

Every week at this time, the Voice of America tells about popular words and expressions used in the United States. Some of these words and expressions are old. Some are new. Together, they form the living speech of the American people.

Our story today is very old. It goes back about five-thousand years. It is about a sign that is used to represent some words.

We see this sign on drug stores and whenever we visit a doctor to get an order for medicine. It also appears on bottles of pills and other medicines.

The sign is formed by a line across the right foot of the letter "R." It represents the word "prescription." It has come to mean "take this medicine."

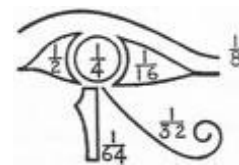
The sign has its beginnings five thousand years ago in Egypt. At that time, people prayed to Horus, the god of the Sun. It was said that when Horus was a child, he was attacked by Seth, the demon of evil.



The evil Seth put out the eye of the young Horus. The mother of Horus called for help. Her cry was answered by Thoth, the god of learning and magic. Thoth, with his wisdom and special powers, healed the eye of Horus. And the child was able to see again.

The ancient Egyptians used a drawing of the eye of Horus as a magic sign to protect themselves from disease, suffering and evil. They cut this sign in the stones they used for buildings. And it was painted on the papyrus rolls used for writing about medicine and doctors.

For thousands of years, the eye of Horus remained as a sign of the god's help to the suffering and sick. Long after the fall of the ancient Egyptian civilization, doctors and alchemists in Europe continued the custom of showing a sign of the gods' help and protection. But over the years, the sign changed from the eye of Horus to the sign for Jupiter, the chief god of the Romans. Jupiter's sign looked much like the printed number "four." That sign changed, also. Today, it is the easily-recognized capital "R" with a line across its foot. The sign no longer offers heavenly assistance to the sick. It now means "take this medicine."



This VOA Special English program WORDS AND THEIR STORIES was written by Frank Beardsley. The narrator was Maurice Joyce. I'm Warren Sheer.

Fake company gets approval for risky trial

YOU would hope that a fake company, proposing to test a risky medical procedure, would be turned down flat. But that's not what happened in an elaborate "sting" operation set up to probe the US system for protecting volunteers in clinical research.

Trials of new drugs or medical devices can only begin if approved by an Institutional Review Board (IRB). Often these are attached to the hospitals or universities where the research will take place. But the task is increasingly being performed for profit by commercial IRBs, prompting fears that some may be rubber-stamping risky trials without proper scrutiny.

Now it appears these fears may be justified. At a congressional hearing on 26 March, the Government Accountability Office revealed the results of an investigation commissioned by the US House of Representatives Committee on Energy and Commerce. To test the responses of commercial IRBs, the GAO created a proposal from a fictitious company called Device Med-Systems that wanted to test the ability of a gel, poured into the abdomen, to reduce the growth of scar tissue after surgery. The protocol for the trial matched multiple examples described as posing "significant risk" by the Food and Drug Administration.

The GAO submitted the fake proposal to three commercial IRBs, two of which rejected it. But Coast IRB of Colorado Springs approved the proposed trial by a unanimous vote, describing it as "probably very safe". The Committee on Energy and Commerce also found that Coast approved all 356 proposals it received in the past five years, and earned \$9.3 million for its services in 2008 alone.

Committee chairman Henry Waxman has vowed to "push for reforms that will protect the health and safety of the American people".

Autism linked with stress hormone levels

Some of the symptoms of the autistic condition Asperger Syndrome, such as a need for routine and resistance to change, could be linked to levels of the stress hormone cortisol, suggests new research led by the University of Bath.

Normally, people have a surge of this hormone shortly after waking, with levels gradually decreasing throughout the day. It is thought this surge makes the brain alert, preparing the body for the day and helping the person to be aware of changes happening around them.

However, a study led by Dr Mark Brosnan and Dr Julie Turner-Cobb from the Department of Psychology at the University of Bath, and Dr David Jessop from the University of Bristol, has found that children with Asperger Syndrome (AS) do not experience this surge.

The researchers believe these findings may help to explain why individuals with this condition have difficulties with minor changes to their routine or changes in their environment.

The study has been published in the peer-reviewed journal Psychoneuroendocrinology.

Dr Brosnan explained: "Cortisol is one of a family of stress hormones that acts like a 'red alert' that is triggered by stressful situations allowing a person to react quickly to changes around them.

"In most people, there is a two-fold increase in levels of this hormone within 30 minutes of waking up, with levels gradually declining during the day as part of the internal body clock.

"Our study found that the children with AS didn't have this peak although levels of the hormone still decreased during the day as normal. "Although these are early days, we think this difference in stress hormone levels could be really significant in explaining why children with AS are less able to react and cope with unexpected change."

Dr Julie Turner-Cobb, Senior Lecturer in Psychology at Bath and co-author on the study, said: "These findings are important as they give us a clearer understanding about how some of the symptoms we see in AS are linked to how an individual adapts to change at a chemical level."

Dr David Jessop analysed samples from the children for levels of hormone at the Henry Wellcome Laboratories for Integrative Neuroscience and Endocrinology at the University of Bristol.

He added: "This study suggests that children with AS may not adjust normally to the challenge of a new environment on waking. "This may affect the way they subsequently engage with the world around them."

The researchers hope that by understanding the symptoms of AS as a stress response rather than a behavioural problem it could help carers and teachers develop strategies for avoiding situations that might cause distress in children with the condition.

The next step in the research will be to look at whether children with other types of autism also lack a peak of cortisol after waking.

Parents' sexuality influences adoption choices

Study looks at heterosexual, lesbian and gay male couples preferences when choosing gender of child

A couple's sexual orientation determines whether or not they prefer to adopt a boy or a girl. Gay men are more likely to have a gender preference for their adopted child whereas heterosexual men are the least likely. What's more, couples in heterosexual relationships are more likely to prefer girls than people in same-gender relationships, according to Dr. Abbie Goldberg from Clark University in the US. These couples also have very different reasons for their preferences, depending on their sexuality. These findings (1), from the first study to compare the child gender preferences of prospective adoptive parents according to their sexuality, are published online in Springer's journal *Sex Roles*.

Unlike biological parents, adoptive parents can choose the gender of their child. Heterosexual, lesbian and gay male couples approach adoption with very different experiences and expectations as those of expectant biological parents. Dr. Goldberg looked at whether the unique contexts of adoption and sexual orientation have distinct implications for men's and women's child gender preferences.

She explored adoptive parents' child gender preferences in a geographically diverse American sample of 93 heterosexual, 61 lesbian and 48 gay male couples waiting to adopt their first child. The participants were recruited through adoption agencies in the US as well as national gay and lesbian organizations. They were interviewed between 2005 and 2008.

Dr. Goldberg found that many couples, irrespective of sexuality, had no preference for the gender of their adopted child. They were simply grateful to finally have a child and gender was insignificant in the context of their larger goal of becoming parents.

Among those who expressed a preference, gay men were the most likely to have a preference and heterosexual men were the least likely. Couples in heterosexual relationships were less likely to prefer boys than couples in same-gender relationships.

The study participants provided a range of reasons for their preferences for girls. The most common reason among heterosexual women was their inexplicable desire for a daughter, whereas heterosexual men most frequently listed a combination of their inexplicable desire to have a girl, their ideas about father-daughter relationships and their perceived characteristics of girls. Men felt girls would be easier to bring up, and more interesting and complex than boys, and less physically challenging than boys. Lesbians tended to focus on their perceived inability to socialize a child of the opposite gender, and gay men most frequently cited concerns about boys being more likely to encounter harassment than girls.

The most common reason for preferring boys among heterosexual women was an inexplicable desire for a son, whereas heterosexual men's preference for a son reflected patriarchal norms, including keeping the family name going and gender identity considerations i.e. their own masculine interests. When explaining their preference for a boy, lesbians most frequently mentioned their own atypical gender identities, including the fact that their own interests tended to be more masculine and tomboyish, whereas gay men most often highlighted that they felt more confident about their ability to raise and socialize boys.

Dr Goldberg concludes: "This study represents the first investigation known to date that explores the child gender preferences of both heterosexual and sexual minority preadoptive parents. The data suggest that both the adoption context and the sexual orientation context may have implications for how men and women think about the gender of their future children."

Reference 1. Goldberg AE (2009). *Heterosexual, lesbian, and gay preadoptive parents' preferences about child gender*. *Sex Roles*; DOI 10.1007/s11199-009-9598-4

Bird can 'read' human gaze

We all know that people sometimes change their behavior when someone is looking their way. Now, a new study reported online on April 2nd in *Current Biology*, a Cell Press publication, shows that jackdaws—birds related to crows and ravens with eyes that appear similar to human eyes—can do the same.

"Jackdaws seem to recognize the eye's role in visual perception, or at the very least they are extremely sensitive to the way that human eyes are oriented," said Auguste von Bayern, formerly of the University of Cambridge and now at the University of Oxford.

When presented with a preferred food, hand-raised jackdaws took significantly longer to retrieve the reward when a person was directing his eyes towards the food than when he was looking away, according to the research team led by Nathan Emery of the University of Cambridge and Queen Mary University of London. The birds hesitated only when the person in question was unfamiliar and thus potentially threatening.

In addition, the birds were able to interpret human communicative gestures, such as gaze alternation and pointing, to help them find hidden food, they found. The birds were unsuccessful in using static cues, including eye gaze or head orientation, in that context.

Unlike most birds, jackdaws' eyes have a dark pupil surrounded by a silvery white iris. The researchers said they believe jackdaws are probably sensitive to human eyes because, as in humans, eyes are an important means of communication for them. The hand-raised birds examined in the study may be even better than wild jackdaws at attending to human gaze and responding to the gestures of the people who have raised them.

The findings are particularly notable given that most other species investigated so far, including our closest relatives the chimpanzee and "man's best friend," the dog, are not particularly sensitive to eye orientation and eye gaze, von Bayern said. Rather, she continued, chimps and dogs seem to rely on other cues such as head or body orientation in determining the looking direction of others and do not appear to appreciate the eyes as the visual organs. The results suggest that birds may deserve more respect for their mental abilities.

"We may have underestimated the psychological realms of birds," von Bayern said. "Jackdaws, amongst many other birds, form pair bonds for life and need to closely coordinate and collaborate with their partner, which requires an efficient way of communicating and sensitivity to their partner's perspective."

The researchers include Auguste M.P. von Bayern, of University of Cambridge, Madingley, UK; and Nathan J. Emery, of University of Cambridge, Madingley, UK, and Queen Mary University of London, UK.

MIT: Novel needle could cut medical complications Device borrows from oil industry to keep jabs on target

Written by Elizabeth Thomson, MIT News Office

CAMBRIDGE, Mass.--Each year, hundreds of thousands of people suffer medical complications from hypodermic needles that penetrate too far under their skin. A new device developed by MIT engineers and colleagues aims to prevent this from happening by keeping needles on target.

The device, which is purely mechanical, is based on concepts borrowed from the oil industry. It involves a hollow S-shaped needle containing a filament that acts as a guide wire. When a physician pushes the device against a tissue, she is actually applying force only to the filament, not the needle itself, thanks to a special clutch.

When the filament, which moves through the tip of the needle, encounters resistance from a firm tissue, it begins to buckle within the S-shaped tube. Due to the combined buckling and interactions with the walls of the tube, the filament locks into place "and the needle and wire advance as a single unit," said Jeffrey Karp, an affiliate faculty member of the Harvard-MIT Division of Health Sciences and Technology (HST) and co-corresponding author of a recent paper on the work in the *Proceedings of the National Academy of Sciences*.

The needle and wire proceed through the firm tissue. But once they reach the target cavity (for example, a blood vessel) there is no more resistance on the wire, and it quickly advances forward while the needle remains stationary. Because the needle is no longer moving, it cannot proceed past the cavity into the wrong tissue.

Karp believes that the device could reach clinics within three to five years pending further pre-clinical and clinical testing.

First author Erik K. Bassett, now at Massachusetts General Hospital (MGH), developed the device for his MIT master's thesis. He did so under Alexander Slocum, the Neil and Jane Pappalardo Professor of Mechanical Engineering, with guidance from Karp and Omid Farokhzad of HST, Harvard Medical School (HMS) and Brigham and Women's Hospital (Karp is also affiliated with the latter two). Additional authors are also from HMS and MGH.

The work was funded by the Deshpande Center for Technological Innovation at MIT and the Center for Integration of Medicine and Innovative Technology (CIMIT).

Titan's squashed shape hints at soggy interior

* 19:21 02 April 2009 by David Shiga

Saturn's moon Titan is surprisingly non-spherical, suggesting it may hide vast reserves of liquid methane beneath its surface, according to a new study.

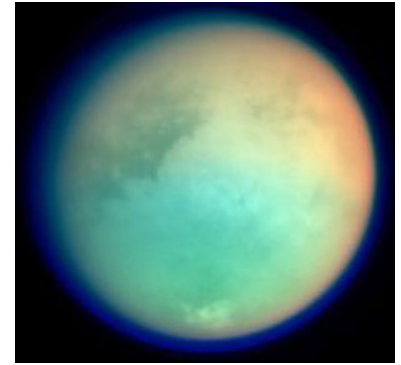
Titan is 5150 kilometres across, making it larger than Mercury and only slightly smaller than the largest moon in the solar system, Jupiter's Ganymede.

By bouncing radar signals off the moon's smog-enshrouded surface, the Cassini spacecraft has now measured Titan's shape precisely for the first time.

"What we have are the first actual measurements showing that Titan's not an exact sphere – this distorted egg-shaped thing best fits the observed shape," study leader Howard Zebker of Stanford University told New Scientist.

Compared to a perfect sphere, Titan is squashed at its poles, with the ground at the poles about 700 metres lower than at the equator. Titan, which always shows the same face to Saturn, is also stretched out a little in the planet's direction, so the elevation around the equator itself varies by about 400 metres.

Titan may look like a sphere, but radar studies by the Cassini probe show it is slightly squashed (Image: NASA/JPL/Space Science Institute)



Migrating moon

Titan is more squashed than expected, which may be a sign that the moon was once closer to Saturn. In a closer, faster orbit, Titan also would have spun faster, assuming it had one face locked on Saturn back then as it does today. An orbit 23% closer than the one Titan occupies today would account for the extra squashing at the poles and bulging at the equator. But Zebker's team is not sure what would have caused the moon to move outward over time.

The lower elevation at the poles fits nicely with one proposed explanation for why Titan's lakes of hydrocarbons – made of liquid ethane and possibly also liquid methane – are found only in the polar regions.

If Titan has vast stores of hydrocarbons beneath its surface, the lakes could simply be places where the ground lies low enough to expose some of this liquid. This is similar to the way digging a well shaft on Earth will expose groundwater.

Methane mystery

In this scenario, it makes sense that the lakes appear preferentially at the lower-lying poles, says Stephen Clifford of the Lunar and Planetary Institute in Houston, Texas, who was not involved in the study.

"There's this potential for [liquid] to peek above the top of the solid body at the poles," he told New Scientist.. But he says it is not possible to rule out other possible explanations yet, for example that weather conditions over the poles produce more hydrocarbon rainstorms than elsewhere.

If Titan does conceal large reservoirs of methane and ethane beneath its icy surface, it could also explain why methane is so abundant in Titan's atmosphere. Chemical reactions should have converted the atmospheric methane into ethane long ago, unless it was replenished from a source much greater than what the lakes alone could supply. *Journal reference: Science Express (DOI: 10.1126/science.1168905)*

Amalgam fillings are safe, but skeptics still claim controversy, researcher says

Paula Hinely

AUGUSTA, Ga. – Dental amalgam has been proven safe and effective for years, yet unfounded controversy still surrounds it, a Medical College of Georgia researcher says.

Dentists have used amalgam, an alloy of mercury with at least one other metal, in fillings for over 200 years. Amalgam fillings don't contain enough mercury to cause potential health problems associated with larger doses, says Dr. Rod Mackert, professor of dental materials in the MCG School of Dentistry Department of Oral Rehabilitation.

"The dose makes the poison," he says, quoting 16th century Swiss physician Paracelsus. A person would need between 265 and 310 amalgam fillings before even slight symptoms of mercury toxicity could be felt. A person with seven fillings, which is average, absorbs only about one microgram of mercury daily. About six micrograms are absorbed daily from food, water and air, according to the Environmental Protection Agency.

To create a dental filling, liquid mercury dissolves and reacts with a powder of silver, tin and copper, forming a compound that contains no free mercury. "Anti-amalgam activists say mercury is soaked into metal powder, like water into a sponge, and can come back out of the fillings, but that's not at all true," Dr. Mackert says. In fact, the evaporation rate of mercury from amalgam is a million times lower than from pure mercury.

Anti-amalgam activists also say dental mercury pollutes the environment. However, dental mercury accounts for less than a quarter of a percent of mercury re-entering the environment.

Dr. Mackert presented an overview of amalgam, its controversy and its alternatives today at the 87th General Session of the International Association for Dental Research in Miami.

The amalgam controversy began in the 1970s. Awareness that dental fillings contained mercury was heightened and people were concerned by a couple of mercury-related health scares. In Japan, the release of methyl mercury into industrial wastewater caused a mercury buildup in shellfish and fish, leading to severe mercury poisoning and Minamata disease. Also, a grain covered in mercury fungicide was baked into bread and consumed in Iraq, killing hundreds. "Mercury poisoning was on people's minds and in the press," he says.

Urban legends abounded, including erroneous reports linking vapors from amalgam fillings to kidney damage and degenerative diseases such as Alzheimer's disease, multiple sclerosis and Parkinson's disease. The only documented health effects of amalgam fillings are rare allergic reactions, Dr. Mackert says, but the controversy led many people to have their fillings removed in the misguided hope of curing neurological diseases.

That controversy continues today. "It's mystifying that people persist in saying there is cause for concern with amalgam fillings when there's no evidence that they cause adverse health effects," Dr. Mackert says.

He also disputes claims that ulterior motives have influenced the American Dental Association position attesting to the safety and effectiveness of amalgam fillings. Anti-amalgam activists link the position to patent interests, but the association had only two amalgam patents, now expired, and neither was licensed, according to the U.S. Patent and Trademark Office. Most of the association's 78 patents are for white filling materials, including composite resin, an alternative to amalgam.

But composite fillings have their own problems. They cost more than amalgam and often are not covered by insurance. Numerous studies have shown that amalgam significantly outlasts composite, while composite causes more secondary cavities and may contribute to plaque formation, Dr. Mackert says.

"The bottom line is people don't need to be concerned with adverse health effects from any type of fillings – amalgam or composites," Dr. Mackert says. Since beginning his studies of amalgam in the early 1980s, his position has never changed. In fact, he has amalgam fillings himself.

Hobbit brain small, but organized for complex intelligence

Evolution may have endowed a controversial species with small but humanlike brains equipped to support advanced thinking

By Bruce Bower

CHICAGO — In the strange and contentious world of fossil hobbits, a chimp-sized brain may boast humanlike powers. An analysis of the inner surface of an 18,000-year-old skull assigned to *Homo floresiensis*, a species also known as hobbits, indicates that this tiny individual possessed a brain blessed with souped-up intellectual capacities needed for activities such as making stone tools, says anthropologist Dean Falk of Florida State University in Tallahassee.

Even as *H. floresiensis* evolved a relatively diminutive brain, the species underwent substantial neural reorganization that allowed its members to think much like people do, Falk contended on April 2 in a presentation at the American Association of Physical Anthropologists annual meeting. She also reported the findings in a paper published online February 28 in the *Journal of Human Evolution*.

Falk compared a cast of the cranium's inner surface, or endocast, obtained from the partial hobbit skeleton LB1 to endocasts from both modern humans and from other fossil skulls in the human evolutionary family, called hominids for short. These casts bring into relief impressions made by various anatomical landmarks on the brain's surface. "LB1 reveals that significant cortical reorganization was sustained in ape-sized brains of at least one hominid species," Falk said.

Evidence has shown that some hominid species experienced marked increases in brain size over time, but that neural reorganization took center stage for others, including hobbits, she proposes. Currently, no one knows whether a large-bodied or small-bodied species gave rise to hobbits, whose fossils have been found on the Indonesian island of Flores.

Although small in size, LB1's endocast displays a humanlike shape, Falk asserted. An endocast from *Australopithecus africanus*, a roughly 3-million-year-old South African hominid species, looks similar to that of LB1, Falk asserted.

Yet unlike the earlier *A. africanus*, LB1 possessed a set of brain features that other researchers have implicated in complex forms of thinking by people today, she said. These features ran from the back to the front

of the brain. Traits such as expanded frontal lobes and enlarged regions devoted to integrating information from disparate areas would have supported creative and innovative thinking, in Falk's view.

No signs of disease or abnormal development appear on LB1's brain surface, she noted. Some researchers argue that the specimen came from a modern human who had some type of growth disorder.

In another meeting presentation, anthropologist William Jungers of Stony Brook Health Sciences Center in New York presented evidence that LB1 did not suffer from cretinism, a growth disorder attributed to it last year by one group of researchers who doubt the fossils represent a separate species. Low levels of thyroid production cause an array of skeletal abnormalities in cretinism, as well as dwarfism.

CT scans of LB1 show no signs of dental, skull or limb conditions associated with cretinism, Jungers said. People with cretinism generally have much larger brains than that of LB1, he added.

Hobbit-fueled controversy remains strong, though. In another meeting presentation, anthropologist Robert Eckhardt of Pennsylvania State University in University Park reported that the height range within a foraging group of people now living on the hobbits' Indonesian island overlaps with height estimates for LB1. Eckhardt and his colleagues argue that, given this similarity to people today, LB1 can't be assigned to a new species.

Oldest Stone Blades Uncovered

By Ann Gibbons ScienceNOW Daily News

CHICAGO, ILLINOIS- Paleoanthropologists working in Africa have discovered stone blades more than a half-million years old. That pushes the date of the earliest known blades back a remarkable 150,000 years and raises a question: What human ancestor made them?

Not long ago, researchers thought that blades were so hard to make that they had to be the handiwork of modern humans, who had evolved the mental wherewithal to systematically strike a cobble in the right way to produce blades and not just crude stone flakes. First, they were thought to be a hallmark of the late Stone Age, which began 40,000 years ago. Later, blades were thought to have emerged in the Middle Stone Age, which began about 200,000 years ago when modern humans arose in Africa and invented a new industry of more sophisticated stone tools. But this view has been challenged in recent years as researchers discovered blades that dated to 380,000 years in the Middle East and to almost 300,000 years ago in Europe, where Neandertals may have made them (ScienceNOW, 1 December 2008).



Cutting-edge technology. A stone core (lower left) and three of the recently found blades. Cara Roure Johnson and Sally McBrearty/University of Connecticut

Now it appears that more than 500,000 years ago, human ancestors living in the Baringo Basin of Kenya collected lava stone cobbles from a riverbed and hammered them in just the right way to produce stone blades. Paleoanthropologists Cara Roure Johnson and Sally McBrearty of the University of Connecticut, Storrs, recently discovered the blades at five sites in the region, including two that date to between 509,000 and 543,000 years ago. "This is the oldest known occurrence of blades," Johnson reported Wednesday here at the annual meeting of the Paleoanthropology Society.

Johnson and McBrearty found the stone blades in a basalt outcrop known as the Kapthurin Formation, including four cores from which the blades were struck. "These assemblages would have been made by a different species of human," Johnson said. "Who were they?" The blades come from the same part of the formation where researchers have found two lower jaws that have been variously described as belonging to *Homo heidelbergensis* or *H. rhodesiensis*, human ancestors in Europe and Africa that predate the origin of our species, *H. sapiens*.

Regardless of the identity of the toolmakers, other researchers say that the discovery of blades this early suggests that these toolmakers were capable of more sophisticated behavior than previously thought, perhaps as a result of the last dramatic expansion of brain size in the human lineage about 600,000 years ago. "It's reflective of a major shift in human cognition," says Alison Brooks, a paleoanthropologist at George Washington University in Washington, D.C.

To convince most researchers that such a dramatic breakthrough really took place so early in human evolution, however, anthropologists will have to find more blades this ancient, says paleoanthropologist Rick Potts of the Smithsonian Institution in Washington, D.C. Stay tuned: The search is already under way for more African blade runners.

Heart Muscle Renewed Over Lifetime, Study Finds

By NICHOLAS WADE

In a finding that may open new approaches to treating heart disease, Swedish scientists have succeeded in measuring a highly controversial property of the human heart: the rate at which its muscle cells are renewed during a person's lifetime.

The finding upturns what has long been conventional wisdom: that the heart cannot produce new muscle cells and so people die with the same heart they were born with.

About 1 percent of the heart muscle cells are replaced every year at age 25, and that rate gradually falls to less than half a percent per year by age 75, concluded a team of researchers led by Dr. Jonas Frisen of the Karolinska Institute in Stockholm. The upshot is that about half of the heart's muscle cells are exchanged in the course of a normal lifetime, the Swedish group calculates. Its results are to be published Friday in the journal *Science*.

"I think this will be one of the most important papers in cardiovascular medicine in years," said Dr. Charles Murry, a heart researcher at the University of Washington in Seattle. "It helps settle a longstanding controversy about whether the human heart has any ability to regenerate itself."

If the heart can generate new muscle cells, researchers can hope to develop drugs that might accelerate the process, since the heart fails to replace cells that are killed in a heart attack.

The dogma that the heart cannot generate new muscle cells has been challenged since 1987 by a somewhat lonely skeptic, Dr. Piero Anversa, now of the Harvard Medical School. Dr. Anversa maintains that heart muscle cells are renewed so fast that a person dying at age 80 has replaced the heart four times over. Many other researchers have doubted this assertion.

Cell turnover rates can easily be measured in animals by making their cells radioactive and seeing how fast they are replaced. Such an experiment, called pulse-labeling, could not ethically be done in people. But Dr. Frisen realized several years ago that nuclear weapons tested in the atmosphere until 1963 had in fact labeled the cells of the entire world's population.

The nuclear blasts generated a radioactive form of carbon known as carbon-14. The amount of carbon-14 in the atmosphere has gradually diminished since 1963, when above-ground tests were banned, as it has been incorporated into plants and animals or diffused into the oceans.

In the body, carbon-14 in the diet gets into the DNA of new cells and stays unchanged for the life of the cell. Because the level of carbon-14 in the atmosphere falls each year, the amount of carbon-14 in the DNA can serve to indicate the cell's birth date, Dr. Frisen found.

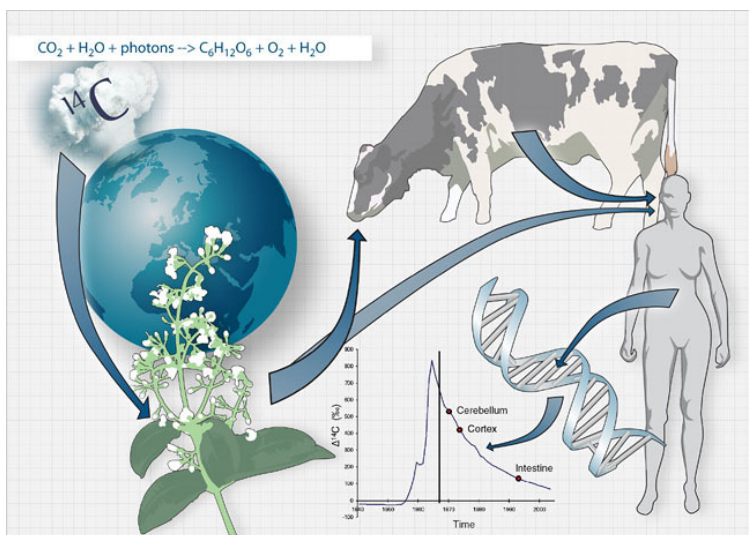
Four years ago he used his new method to assess the turnover rate of various tissues in the body, concluding that the average age of the cells in an adult's body might be as young as 7 to 10 years. But there is a wide range of ages — from the rapidly turning over cells of the blood and gut to the mostly permanent cells of the brain.

Dr. Frisen has successfully applied his method to the heart muscle cells, but had to navigate a series of technical obstacles created by the special behavior of the cells. Many have two nuclei, instead of the usual one, and within these double nuclei the DNA may be duplicated again. "I was really impressed at the level of rigor they put into this analysis," Dr. Murry said, calling it a "scientific tour de force."

The finding that heart muscle cells do regenerate, though at a considerably slower rate than Dr. Anversa predicted, is a "reasonable conclusion to a hotly contested issue," Dr. Murry said. "Anversa went out on a limb, and I think he was partly right."

Tests of nuclear weapons in the atmosphere, which lasted until 1963, generated a radioactive form of carbon, carbon-14. The carbon-14 in carbon dioxide is breathed in by plants, turned into glucose (see equation) and enters the human diet. In the body, the carbon-14 is incorporated into new DNA, and once a new cell is made, its DNA does not change.

The level of carbon-14 in the atmosphere has dropped each year since 1963 (see graph), so the exact amount in a cell marks the year the cell was born. From a cell's birth date, researchers can calculate how quickly different tissues such as the intestine, brain and heart are renewed.



Dr. Loren Field, a heart expert at the Indiana University School of Medicine, said he had found that heart muscle cells regenerated in mice at the same rate that Dr. Frisen had found in people. Despite the controversy created by Dr. Anversa's claims, there has long been agreement that there is a low but detectable rate of cell renewal in the heart, Dr. Field said. The goal now, in his view, is "to try to tickle the system to enhance it."

Dr. Anversa, for his part, said he was "ecstatic" at Dr. Frisen's confirmation of his view that the heart could generate new muscle cells, but suggested that the new measurements might have underestimated the rate at which new cells are formed. Since heart muscle cells contract 70 times a minute, they seem likely to need renewing more often than Dr. Frisen's measurements suggest, he said. "Now let's discuss the magnitude of the process, and that will let us think about how we can apply this concept to heart failure," Dr. Anversa said.

Dr. Frisen said he did not agree that the rate of regeneration had been underestimated. He said it would now be worth trying to understand how the regeneration of heart muscle cells was regulated.

A zebrafish, for instance, can regenerate large regions of its heart after injury, and possibly a similar response could be induced in people. It could also be that the heart does generate many new muscle cells after a heart attack but that the cells fail to establish themselves. Drugs that kept any such new cells alive could be helpful, Dr. Frisen said.

The first cocktail arose in Mesopotamia 5,000 years ago

A sort of grog was probably drunk by Etrurians, a population that knew vine before than Greek arrived in Italy

A particular archaic blend of wine, beer, apple juice and honey. This is the composition of a sort of Grog, as Patrick McGregor says, an archaic drink that has been recently market in USA and named "Midas Touch".

McGovern, professor at the Pennsylvania University, Philadelphia, studied the evolution of viticulture in the East and West, finding some earthenware along the Tigris river showing traces of tartaric acid (an element which is characteristic of the grape fermentation), honey, apple juice and brew barley (a sort of beer ante litteram).

It is noteworthy that probably this grog was drunk also by Etrurians, as it can be infer by analyzing some pottery from South Tuscany. As a matter of fact, it is assumed that the domestication of vine in Etruria was previous than the diffusion on Greek wine in the South coastlines.

According to Osvaldo Failla, researcher at the Milan University, it is possible that the wild vine domestication took place in circumscribed areas, and not only after the introduction of external vines. This was probably possible thank to the care that men took to their environment, improving in this way the genetic variability and plant breeding.

In the context of the Vinum research project, it was analyzed the genetic characteristics of various wild vine found at different archaeological places in Maremma (Tuscany) with some vines present in non anthropized places. These studies demonstrated that, where the men were in contact with wild vines, the local genetic variability grew. It was also possible to genetically distinguish the populations of wild vines deriving from anthropized zones in respect to non-anthropized areas. *by T N*

Gutsy germs succumb to baby broccoli

A small, pilot study in 50 people in Japan suggests that eating two and a half ounces of broccoli sprouts daily for two months may confer some protection against a rampant stomach bug that causes gastritis, ulcers and even stomach cancer.

Citing their new "demonstration of principle" study, a Johns Hopkins researcher and an international team of scientists caution that eating sprouts containing sulforaphane did not cure infection by the bacterium *Helicobacter pylori* (*H. pylori*). They do not suggest that eating this or any amount of broccoli sprouts will protect anyone from stomach cancer or cure GI diseases.

However, the study does show that eating a daily dose of broccoli sprouts reduced by more than 40 percent the level of HpSA, a highly specific measure of the presence of components of *H. pylori* shed into the stool of infected people. There was no HpSA level change in control subjects who ate alfalfa sprouts. The HpSA levels returned to pretreatment levels eight weeks after people stopped eating the broccoli sprouts, suggesting that although they reduce *H. pylori* colonization, they do not eradicate it.

"The highlight of the study is that we identified a food that, if eaten regularly, might potentially have an effect on the cause of a lot of gastric problems and perhaps even ultimately help prevent stomach cancer," says Jed W. Fahey, M.S., Sc.D., an author of the paper who is a nutritional biochemist in the Lewis B. and Dorothy Cullman Cancer Chemoprotection Center at the Johns Hopkins University School of Medicine.

The discovery that sulforaphane is a potent antibiotic against *H. pylori* was reported in 2002 by Fahey and colleagues at Johns Hopkins. "Broccoli sprouts have a much higher concentration of sulforaphane than mature heads," Fahey explains, adding that further investigation is needed to affirm the results of this clinical trial and move the research forward. The study, published April 6 in *Cancer Prevention Research*, builds on earlier test-tube and mouse studies at Johns Hopkins and elsewhere about the potential value of sulforaphane, a naturally occurring biochemical found in relative abundance in fresh broccoli sprouts.

(<http://www.hopkinsmedicine.org/press/2002/may/020528.htm>) Sulforaphane appears to trigger cells in the body, including in the gastrointestinal tract, to produce enzymes that protect against oxygen radicals, DNA-damaging chemicals, and inflammation.

In the new report, the team also shows that when *H. pylori*-infected mice sipped broccoli-sprout smoothies for eight weeks, there was up to a fourfold increase in the activity of two of these key enzymes that protect cells against oxidative damage. In addition, the number of *Helicobacter* bacteria in the mice's stomachs decreased by almost a hundredfold; it did not change in infected control animals that drank plain water. The researchers also noted a greater than 50 percent reduction in inflammation of the primary target of this bacterium – the body of the stomach – in treated mice but not in controls.

In a related experiment, the team fed the same dose of broccoli sprouts for the same amount of time to *H. pylori*-infected mice that had been genetically engineered to lack the Nrf2 gene that activates protective enzymes. "These knock-out mice didn't respond," Fahey says, which confirms previous findings for a role of Nrf2 in protection against *H. pylori*-induced inflammation and gastritis.

Classified a carcinogen by the World Health Organization, *H. pylori* is a gastrointestinal tract germ that manages to thrive in the lining of the stomach despite the strength of natural acids there that rival that of car batteries. Afflicting several billion people – roughly half of the world's population – this corkscrew-shaped bacterium has long been associated with stomach ulcers, which now are frequently cured by antibiotics. Research strongly suggests that the bacteria also are linked to high rates of stomach cancer in some countries, that strains resistant to standard antibiotics are prevalent, and that multiple courses of standard antibiotics do not always eliminate the infection.

Working in Japan where there is high incidence of chronic *H. pylori*-infection, the research team gave 25 *H. pylori*-infected subjects two and a half ounces (70 grams) per day of broccoli sprouts for two months. Another 25 infected people consumed an equivalent amount of alfalfa sprouts which, although rich in phytochemicals, don't contain sulforaphane.

The researchers assessed the severity of *Helicobacter* infection at the start of the study, after four and eight weeks of treatment, and again eight weeks after intervention was stopped. They used breath tests to assess colonization by *H. pylori* bacteria and blood tests to judge the severity of inflammation in the stomach lining; in addition, they looked for antigens in stool samples to help determine the extent of the infections.

"We know that a dose of a couple ounces a day of broccoli sprouts is enough to elevate the body's protective enzymes," Fahey says. "That is the mechanism by which we think a lot of the chemoprotective effects are occurring.

"What we don't know is whether it's going to prevent people from getting stomach cancer. But the fact that the levels of infection and inflammation were reduced suggests the likelihood of getting gastritis and ulcers and cancer is probably reduced."

In disclosure of a potential conflict of interest, Fahey is a cofounder of, but holds no equity in, a company that is licensed by The Johns Hopkins University to produce broccoli sprouts. A portion of the proceeds is used to help support cancer research, but no such funds were provided to support this study.

"It's exciting that a chronic bacterial infection that poses great hazards to hundreds of millions of people globally can be ameliorated by a specific dietary strategy," says Paul Talalay, M.D., John Jacob Abel Distinguished Service Professor of Pharmacology and Experimental Therapeutics and director of the Lewis B. and Dorothy Cullman Cancer Chemoprotection Center at Johns Hopkins' Institute for Basic Biomedical Sciences.

Talay directs the lab where, in 1992, his team discovered the health-promoting properties of sulforaphane. A longtime proponent of cancer prevention and chemoprotection, Talalay eats fresh broccoli sprouts regularly, as does Fahey.

"I like them," Fahey says. "I eat them all the time, but not every day. Variety is the spice of life: I eat blueberries on the other days."

In addition to Fahey, the authors of the paper are Akinori Yanaka, Atsushi Fukumoto, Mari Nakayama and Souta Inoue, Tokyo University of Science, Japan; Masayuki Yamamoto, Songhua Zhang, Masafumi Tauchi, Hideo Suzuki and Ichinosuke Hyodo, University of Tsukuba, Japan.

Bacterium eats electricity, farts biogas

* 17:45 05 April 2009 by **Michael Marshall**

Bacteria that can convert electricity into methane could help solve one of the biggest problems with renewable energy – its unreliability compared to the steady output of polluting fossil-fuel power stations.

Wind power is capricious, while solar cell output drops off at night or on cloudy days. That fluctuating output poses big problems for electricity grids that rely on steady levels throughout the day. Proposals to deal with the ups and downs of green power supply have included better batteries or redesigning the electricity grid.

An intriguing new idea involves "feeding" surplus power to bacteria instead, which combine it with carbon dioxide to create methane. That could then be stored and burned when needed. The method is sustainable too, as the carbon is taken from the atmosphere, not released from long-term storage in oil or coal.

Energy food

The new method relies on a bacterium discovered by Bruce Logan's team at Pennsylvania State University in University Park. When living on the cathode of an electrolytic cell, the organism can take in electrons and use their energy to convert carbon dioxide into methane.

Logan's team discovered this behaviour in a mixed culture of bacteria, dominated by *Methanobacterium palustre* – the first to be observed directly manufacturing methane in this way. The behaviour had been previously suspected but not confirmed.

Tom Curtis at the Institute for Research on Environment and Sustainability at Newcastle University, UK, says that the use of bacteria, rather than conventional catalysts, is a plus. "There are no noble metals involved, so it should be very cheap," he says.

Of the energy put into the system as electricity, 80% was eventually recovered when the methane was burned – a fairly high efficiency. "You don't get all the energy back, but that's a problem with any form of energy storage," says Curtis.

'Simple and scalable'

If the CO₂ used to make the methane was captured from the flue pipes of power stations or even – using more complex methods – from the open air, the methane would become a carbon-neutral fuel.

Logan is optimistic about the method's potential: "Commercial applications could be just a few years down the road," he says.

Curtis is also impressed. "If you have a windmill, say, you need a relatively simple way to store the energy. What I like about this method is it's simple, it's replicable and it's scalable."

Several similar techniques use bacteria to produce hydrogen fuel rather than methane. But the hydrogen economy is not here yet, Logan points out. "These methods are great, but hydrogen doesn't fit into our existing infrastructure. Methane does." *Journal reference: Environmental Science & Technology (DOI: 10.1021/es803531g)*

